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略号一覧表

略号又は略称	名称及び内容
ALT	alanine aminotransferase（アラニンアミノトランスフェラーゼ）
AST	aspartate aminotransferase（アスパラギン酸アミノトランスフェラーゼ）
CrCL	creatinine clearance（クレアチニン・クリアランス）
CRF	case report form（症例報告書）
DPd	daratumumab-pomalidomide-dexamethasone（本剤-ポマリドミド-デキサメタゾン）
DRd	daratumumab-lenalidomide-dexamethasone（本剤-レナリドミド-デキサメタゾン）
DVd	daratumumab-bortezomib-dexamethasone（本剤-ボルテゾミブ-デキサメタゾン）
ECOG	Eastern Cooperative Oncology Group
EU	European Union（欧州連合）
G-CSF	granulocyte-colony stimulating factor（顆粒球コロニー刺激因子）
IMiD	immunomodulatory drug（免疫調節薬）
IRR	infusion related reaction
ITT	intent-to-treat
LDH	lactic acid dehydrogenase（乳酸脱水素酵素）
MedDRA	Medical Dictionary for Regulatory Activities（医薬品規制用語集）
MM	multiple myeloma（多発性骨髄腫）
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
Pd	pomalidomide-dexamethasone（ポマリドミド-デキサメタゾン）
PI	proteasome inhibitor（プロテアソーム阻害剤）
PT	preferred term（基本語）
QT	QT interval（心電図 QT 間隔）
QTcF	QT interval corrected by Fridericia formula（Fridericia 法で補正した QT 間隔）
Rd	lenalidomide-dexamethasone（レナリドミド-デキサメタゾン）
SOC	system organ class（器官別大分類）
TEAE	treatment-emergent adverse event（治験薬投与後に発現した有害事象）
Vd	bortezomib-dexamethasone（ボルテゾミブ-デキサメタゾン）
vs	versus

2.7.4 臨床的安全性

2.7.4.1 医薬品への曝露

2.7.4.1.1 総括的安全性評価計画及び安全性試験の記述

2.7.4.1.1.1 安全性評価に用いた臨床試験

ダラツムマブ（以下本剤）の再発又は難治性の多発性骨髄腫（MM）患者に対する安全性評価に用いた臨床試験を表 2.7.4-1 に示す。

再発又は難治性の MM 患者に対する本剤と既存の抗悪性腫瘍剤との併用療法の安全性は，国内及び海外で実施した臨床試験 5 試験［海外第 III 相試験（54767414MMY3004 試験，以下 MMY3004 試験），日本を含む国際共同第 III 相試験（54767414MMY3003 試験，以下 MMY3003 試験），海外第 I/II 相試験（GEN503 試験），海外第 Ib 相試験（54767414MMY1001 試験，以下 MMY1001 試験）及び国内第 Ib 相試験（54767414MMY1005 試験，以下 MMY1005 試験）］の結果を用いて評価した。本剤とボルテゾミブ及びデキサメタゾンとの併用（DVd）療法については MMY3004 試験の中間解析結果（クリニカルカットオフ日：2016 年 1 月 11 日），本剤とレナリドミド及びデキサメタゾンとの併用（DRd）療法については MMY3003 試験（クリニカルカットオフ日：2016 年 3 月 7 日）及び GEN503 試験（クリニカルカットオフ日：2015 年 10 月 2 日）の併合解析結果，本剤とポマリドミド及びデキサメタゾンとの併用（DPd）療法については MMY1001 試験の中間解析結果（クリニカルカットオフ日：[redacted] 年 [redacted] 月 [redacted] 日）に基づき評価した。日本人の安全性評価に際しては，DRd 療法については MMY3003 試験の日本人集団の結果，DVd 療法については MMY1005 試験の解析結果（クリニカルカットオフ日：2016 年 6 月 3 日）を用いた。なお，日本人被験者での例数が限られることから，有害事象の発現割合等において全体集団との大きな隔たりが認められた場合に内因性民族的要因を検討する目的で，MMY3003 試験（DRd 療法）の東アジア人集団（日本，韓国及び台湾で組み入れられた被験者）の結果も提示した。

本剤の単剤療法の安全性は，国内及び海外で実施した臨床試験 3 試験［2015 年 1 月 9 日をクリニカルカットオフ日とした海外第 II 相試験（54767414MMY2002 試験，以下 MMY2002 試験）及び海外第 I/II 相試験（GEN501 試験），並びに 2015 年 2 月 6 日をクリニカルカットオフ日とした国内第 I 相試験（54767414MMY1002 試験，以下 MMY1002 試験）］の結果を用いて評価した。評価に際しては当該 3 試験の併合解析を実施し，その結果を中心に日本人を対象とした MMY1002 試験の最終解析の結果も含めて評価した。

表 2.7.4-1 安全性評価に用いた臨床試験概要

試験番号（資料区分）／実施地域／実施時期	試験デザイン／対象患者	治験薬／用法用量／投与期間	主な解析対象集団
併用療法試験			
MMY3004 （評価資料） 海外 2014 年 9 月 24 日～クリニカルカットオフ日：2016 年 1 月 11 日（中間解析），2016 年 6 月 30 日（安全性評価）	DVd 療法と Vd 療法を比較する第 III 相，ランダム化，非盲検，実薬対照，多施設共同試験 1 レジメン以上の前治療歴を有する再発又は難治性の MM 患者	1 サイクル：サイクル 1～8 は 21 日間，サイクル 9 以降は 28 日間 本剤 16 mg/kg をサイクル 1～3 は Day 1，8 及び 15（1 週間隔），サイクル 4～8 は Day 1（3 週間隔），サイクル 9 以降は Day 1（4 週間隔）に持続静脈内投与 ボルテゾミブ 1.3 mg/m^2 を最大 8 サイクルまで Day 1，4，8 及び 11 に皮下投与 デキサメタゾン 20 mg を最大 8 サイクルまで Day 1，2，4，5，8，9，11 及び 12 に静脈内投与又は経口投与（>75 歳，過少体重，コントロール不良の糖尿病又はステロイド治療に耐性がない被験者は 20 mg/週でも可） 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［安全性解析対象集団］ 全体：480 例 DVd 群：243 例 Vd 群：237 例
MMY3003 （評価資料） 国際共同 2014 年 6 月 16 日～クリニカルカットオフ日：2016 年 3 月 7 日（中間解析），2016 年 6 月 30 日（安全性評価）	DRd 療法と Rd 療法を比較する第 III 相，ランダム化，非盲検，実薬対照，多施設共同，並行群間試験 1 レジメン以上の前治療歴を有する再発又は難治性の MM 患者	1 サイクル：28 日間 本剤 16 mg/kg をサイクル 1 及び 2 は Day 1，8，15 及び 22（1 週間隔），サイクル 3～6 は Day 1 及び 15（2 週間隔），サイクル 7 以降は Day 1（4 週間隔）に持続静脈内投与 レナリドミド 25 mg（CrCL：>60 mL/min）又は 10 mg（CrCL：30～60 mL/min）を各サイクルの Day 1～21 に連日経口投与 デキサメタゾン 40 mg/週を静脈内投与又は経口投与（>75 歳又は過少体重の被験者は 20 mg/週でも可） 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［安全性解析対象集団］ 全体：564 例 （日本人 35 例） DRd 群：283 例 （日本人 20 例） Rd 群：281 例 （日本人 15 例）
GEN503 （参考資料） 海外 2012 年 6 月 12 日～クリニカルカットオフ日：2015 年 10 月 2 日（主解析），2016 年 6 月 30 日（安全性評価）	DRd 療法の安全性プロファイルを確立する第 I/II 相，非盲検，多施設共同試験 第 I 相部分：2～4 レジメンの治療歴を有する再発又は難治性の MM 患者 第 II 相部分：1 レジメン以上の前治療歴を有する MM 患者	1 サイクル：28 日間 本剤をサイクル 1 及び 2 は Day 1，8，15 及び 22（1 週間隔），サイクル 3～6 は Day 1 及び 15（2 週間隔），サイクル 7 以降は Day 1（4 週間隔）に持続静脈内投与 <u>本剤の用量</u> 第 I 相部分（用量漸増）：2，4，8 又は 16 mg/kg 第 II 相部分：16 mg/kg レナリドミド 25 mg を各サイクルの Day 1～21 に連日経口投与 デキサメタゾン 40 mg/週を静脈内投与又は経口投与（>75 歳又は過少体重の被験者は 20 mg/週でも可） 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［安全性解析対象集団］ 全体（DRd 群）：35 例 第 I 相部分 16 mg/kg：3 例 [a] 第 II 相部分：32 例

表 2.7.4-1 安全性評価に用いた臨床試験概要（続き）

試験番号（資料区分）／実施地域／実施時期	試験デザイン／対象患者	治験薬／用法用量／投与期間	主な解析対象集団
併用療法試験（続き）			
MMY1001 （参考資料） 海外 2014 年 3 月 10 日～クリニカルカットオフ日：[redacted] 年 [redacted] 月 [redacted] 日（中間解析），2016 年 6 月 30 日（安全性評価）	本剤と他の治療レジメンとの併用療法の安全性，忍容性及び投与レジメンを評価する第 Ib 相，非盲検，多施設共同試験 ［DPd 群］ 2 レジメン以上の前治療歴を有する再発又は難治性の MM であり，かつレナリドミド及びボルテゾミブの投与を 2 サイクル以上受けた患者	1 サイクル：28 日間 ［DPd 群］ 本剤 16 mg/kg をサイクル 1 及び 2 は Day 1，8，15 及び 22（1 週間隔），サイクル 3～6 は Day 1 及び 15（2 週間隔），サイクル 7 以降は Day 1（4 週間隔）に持続静脈内投与 ポマリドミド 4 mg を各サイクルの Day 1～21 に連日経口投与 デキサメタゾン 40 mg/週を静脈内投与又は経口投与（>75 歳の被験者は 20 mg/週） 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［安全性解析対象集団］ DPd 群 ：103 例 [b]
MMY1005 （評価資料） 国内 2015 年 8 月 5 日～クリニカルカットオフ日：2016 年 6 月 3 日	DVd 療法の忍容性及び安全性を評価する第 Ib 相，非盲検，多施設共同試験 再発又は難治性の日本人 MM 患者	1 サイクル：サイクル 1～8 は 21 日間，サイクル 9 以降は 28 日間 本剤 16 mg/kg をサイクル 1～3 は Day 1，8 及び 15（1 週間隔），サイクル 4～8 は Day 1（3 週間隔），サイクル 9 以降は Day 1（4 週間隔）に持続静脈内投与 ボルテゾミブ 1.3 mg/m^2 を最大 8 サイクルまで Day 1，4，8 及び 11 に皮下投与 デキサメタゾン 20 mg を最大 8 サイクルまで Day 1，2，4，5，8，9，11 及び 12 に静脈内投与又は経口投与（サイクル 1～3 では Day 15 にも投与。また，>75 歳，過少体重，コントロール不良の糖尿病又はステロイド治療に耐性がない被験者は 20 mg/週でも可） 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［安全性解析対象集団］ 全体（DVd 群） ：8 例
単剤療法試験			
MMY2002 （評価資料） 海外 2013 年 9 月 30 日～クリニカルカットオフ日：2015 年 1 月 9 日（主解析），2015 年 6 月 30 日（安全性評価：1 回目），2015 年 12 月 31 日（安全性評価：2 回目），[redacted] 年 [redacted] 月 [redacted] 日（安全性評価：3 回目）	本剤の有効性及び安全性を検討する第 II 相，非盲検，多施設共同試験 PI 及び IMiD を含む 3 レジメン以上の前治療歴を有する，又は PI 及び IMiD の両剤に対して治療抵抗性を示す MM 患者	Part 1：第 I/II 相 [c] 試験用製剤 A 群：本剤 16 mg/kg を 1 週間隔で 8 週間，2 週間隔で 16 週間，それ以降は 4 週間隔で持続静脈内投与 B 群：本剤 8 mg/kg を 4 週間隔で持続静脈内投与 Part 2：第 III 相試験用製剤 本剤 16 mg/kg を 1 週間隔で 8 週間，2 週間隔で 16 週間，それ以降は 4 週間隔で持続静脈内投与 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［全投与解析対象集団］ 全体：124 例 Part 1：59 例 16 mg/kg：41 例 8 mg/kg ：18 例 Part 2：65 例 16 mg/kg：65 例

表 2.7.4-1 安全性評価に用いた臨床試験概要（続き）

試験番号（資料区分）／実施地域／実施時期	試験デザイン／対象患者	治験薬／用法用量／投与期間	主な解析対象集団
単剤療法試験（続き）			
GEN501 （評価資料） 海外 2008 年 3 月 26 日～クリニカルカットオフ日：2015 年 1 月 9 日（主解析），2015 年 6 月 30 日（安全性評価：1 回目），2015 年 12 月 31 日（安全性評価：2 回目），[redacted] 年 [redacted] 月 [redacted] 日（安全性評価：3 回目）	本剤の安全性プロファイルを検討する第 I/II 相，非盲検，多施設共同試験 PI，IMiD，化学療法又は自家造血幹細胞移植を含む 2 レジメン以上の前治療歴を有する再発又は難治性の MM 患者	Part 1（用量漸増期）：第 I/II 相 [c] 試験用製剤 本剤 0.005～24 mg/kg を 8 週間持続静脈内投与（初回投与後 3 週間ウォッシュアウトし，続いて 1 週間隔で 6 週間投与） Part 2（用量維持期） スケジュール A-C：第 I/II 相 [c] 試験用製剤 本剤 8 mg/kg を 1 週間隔で 8 週間，2 週間隔で 16 週間，それ以降は 4 週間隔で持続静脈内投与 スケジュール D-E（D：第 I/II 相 [c] 試験用製剤，E：第 III 相試験用製剤） 本剤 16 mg/kg を初回投与後 3 週間ウォッシュアウトし，続いて 1 週間隔で 7 週間，2 週間隔で 14 週間，それ以降は 4 週間隔で持続静脈内投与 疾患進行又は許容できない毒性の発現まで継続	［全投与解析対象集団］ 全体：104 例 Part 1：32 例 ≤4 mg/kg：23 例 8 mg/kg ：3 例 16 mg/kg：3 例 24 mg/kg：3 例 Part 2：72 例 8 mg/kg ：30 例 16 mg/kg：42 例
MMY1002 （評価資料） 国内 2014 年 4 月 28 日～クリニカルカットオフ日：2015 年 2 月 6 日（安全性評価：1 回目），2015 年 6 月 30 日（安全性評価：2 回目），2015 年 9 月 25 日（最終解析）	本剤の忍容性及び安全性を評価する第 I 相，非盲検，多施設共同，用量漸増試験 2 レジメン以上の前治療歴を有する再発又は難治性の日本人 MM 患者	本剤 8 又は 16 mg/kg：第 III 相試験用製剤 第 1 期 投与頻度の高いレジメンで Week 9 まで［初回投与（Week 0）後 3 週間ウォッシュアウトし，続いて 1 週間隔で 6 週間持続静脈内投与］ 第 2 期 第 1 期に比べ投与頻度の低いレジメンで Week 10 から投与終了まで（28 日間を 1 サイクルとし，サイクル 1～4 は 2 週間隔，サイクル 5 以降は 4 週間隔で持続静脈内投与） 疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまで継続	［全投与解析対象集団］ 全体：9 例 8 mg/kg ：4 例 16 mg/kg：5 例

CrCL：クレアチニン・クリアランス，DPd：本剤-ポマリドミド-デキサメタゾン，DRd：本剤-レナリドミド-デキサメタゾン，DVd：本剤-ボルテゾミブ-デキサメタゾン，IMiD：免疫調節薬，MM：多発性骨髄腫，Pd：ポマリドミド-デキサメタゾン，PI：プロテアソーム阻害剤，Rd：レナリドミド-デキサメタゾン，Vd：ボルテゾミブ-デキサメタゾン

[a] 2.7.4 項には第 I 相部分に組み入れられた被験者のうち本剤 16 mg/kg を投与された被験者のデータを含めた。

[b] 2.7.4 項には DPd 群のみ含めた。

[c] 併合解析結果の表及び本文では「第 II 相試験用製剤」と記載した。

(1) 併用療法試験

1) 海外第 III 相試験（MMY3004 試験）

【CTD 5.3.5.1.2-1】

MMY3004 試験は，1 レジメン以上の前治療歴を有する再発又は難治性の MM 患者を対象に，DVd 療法とボルテゾミブ及びデキサメタゾンの併用療法（Vd 療法）を比較する第 III 相，ランダム化，非盲検，実薬対照，多施設共同試験である。被験者を DVd 群又は Vd 群のいずれかにランダムに割り付けた。21 日間を 1 サイクルとし，すべての被験者に Vd 療法（ボルテゾミブ 1.3 mg/m^2 を各サイクルの Day 1，4，8 及び 11 に皮下投与，デキサメタゾン 20 mg を各サイクルの Day 1，2，4，5，8，9，11 及び 12 に静脈内投与又は経口投与）を 8 サイクル実施した。Vd 群にランダム化された被験者は，8 サイクルの投与終了後は後観察期に移行した。DVd 群にランダム化された被験者には，Vd 療法に加えて本剤 16 mg/kg をサイクル 1～3 は 1 週間隔，サイクル 4～8 は 3 週間隔，サイクル 9 以降は 28 日間を 1 サイクルとして本剤のみを 4 週間隔で持続静脈内投与した。いずれの群も投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は死亡，追跡不能，同意撤回又は試験終了までとした。

2) 国際共同第 III 相試験（MMY3003 試験）

【CTD 5.3.5.1.1-1】

MMY3003 試験は，1 レジメン以上の前治療歴を有する再発又は難治性の MM 患者を対象に，DRd 療法とレナリドミド及びデキサメタゾンの併用療法（Rd 療法）を比較する第 III 相，ランダム化，非盲検，実薬対照，多施設共同，並行群間試験である。被験者を DRd 群又は Rd 群のいずれかにランダムに割り付けた。28 日間を 1 サイクルとし，すべての被験者に Rd 療法（レナリドミド 25 mg を各サイクルの Day 1～21 に連日経口投与，デキサメタゾン 40 mg/週を静脈内投与又は経口投与）を実施した。DRd 群にランダム化された被験者には，Rd 療法に加えて本剤 16 mg/kg をサイクル 1 及び 2 は 1 週間隔，サイクル 3～6 は 2 週間隔，サイクル 7 以降は 4 週間隔で持続静脈内投与した。いずれの群も投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は死亡，追跡不能，同意撤回又は試験終了までとした。

3) 海外第 I/II 相試験（GEN503 試験）

【CTD 5.3.5.4.1-1】

GEN503 試験は，再発又は難治性の MM 患者を対象に，DRd 療法の安全性プロファイルを確立する第 I/II 相，非盲検，多施設共同試験である。28 日間を 1 サイクルとし，すべての被験者に Rd 療法（レナリドミド 25 mg を各サイクルの Day 1～21 に連日経口投与，デキサメタゾン 40 mg/週を静脈内投与又は経口投与）の実施に加えて，本剤をサイクル 1 及び 2 は 1 週間隔，サイクル 3～6 は 2 週間隔，サイクル 7 以降は 4 週間隔で持続静脈内投与した。本剤の用量に関して，第 I 相（用量漸増）部分では本剤の用量を 2，4，8 又は 16 mg/kg で検討した結果，第 II 相部分の推奨用量を 16 mg/kg とした。第 II 相部分では 1 レジメン以上の前治療歴を有する MM 患者を対象に本剤 16 mg/kg を持続静脈内投与した。2.7.4 項では，本剤 16 mg/kg を投与された 35 例の

被験者（第 I 相部分の 3 例及び第 II 相部分の 32 例）の安全性の結果を MMY3003 試験との併合解析に含めた。投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は死亡，追跡不能，同意撤回又は試験終了までとした。

4) 海外第 Ib 相試験（MMY1001 試験）

【CTD 5.3.5.4.2-1】

MMY1001 試験は，MM 患者を対象に，本剤と他の治療レジメンとの併用療法の安全性，忍容性及び投与レジメンを評価する第 Ib 相，非盲検，多施設共同試験である。2.7.4 項では，2 レジメン以上の前治療歴を有する再発又は難治性の MM であり，かつレナリドミド及びボルテゾミブの投与を 2 サイクル以上受けた患者を対象とした DPd 群の結果を示した。28 日間を 1 サイクルとし，DPd 群の被験者には Pd 療法（ポマリドミド 4 mg を各サイクルの Day 1～21 に連日経口投与，デキサメタゾン 40 mg/週を静脈内投与又は経口投与）の実施に加えて本剤 16 mg/kg をサイクル 1 及び 2 は 1 週間隔，サイクル 3～6 は 2 週間隔，サイクル 7 以降は 4 週間隔で持続静脈内投与した。投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は死亡，追跡不能，同意撤回又は試験終了までとした。

5) 国内第 Ib 相試験（MMY1005 試験）

【CTD 5.3.5.2.4-1】

MMY1005 試験は，再発又は難治性の日本人 MM 患者を対象に，DVd 療法の忍容性及び安全性を検討する第 Ib 相，非盲検，多施設共同試験である。21 日間を 1 サイクルとし，被験者に Vd 療法（ボルテゾミブ 1.3 mg/m^2 を各サイクルの Day 1，4，8 及び 11 に皮下投与，デキサメタゾン 20 mg を各サイクルの Day 1，2，4，5，8，9，11 及び 12 に静脈内投与又は経口投与）の 8 サイクル実施に加えて，本剤 16 mg/kg をサイクル 1～3 は 1 週間隔，サイクル 4～8 は 3 週間隔，サイクル 9 以降は 28 日間を 1 サイクルとして本剤のみを 4 週間隔で持続静脈内投与した。投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は治験薬の最終投与後 8 週，死亡，追跡不能，同意撤回又は試験終了までとした。

(2) 単剤療法試験

1) 海外第 II 相試験（MMY2002 試験）

【CTD 5.3.5.2.1-1】【CTD 5.3.5.2.1-2】【CTD 5.3.5.2.1-3】

MMY2002 試験は，プロテアソーム阻害剤（PI）及び免疫調節薬（IMiD）を含む 3 レジメン以上の前治療歴を有する，又は PI 及び IMiD の両剤に対して治療抵抗性を示す MM 患者を対象に，本剤の有効性及び安全性を検討する第 II 相，非盲検，多施設共同試験である。Part 1 では，本剤 8 mg/kg を 4 週間隔で持続静脈内投与する群，又は本剤 16 mg/kg を 1 週間隔で 8 週間，2 週間隔で 16 週間，それ以降は 4 週間隔で持続静脈内投与する群のいずれかにランダムに割り付けた。Part 2 では，本剤 16 mg/kg を 1 週間隔で 8 週間，2 週間隔で 16 週間，それ以降は 4 週間隔で持続静脈内投与した。投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は死亡，追跡不能，同意撤回又は試験終了までとした。

2) 海外第 I/II 相試験（GEN501 試験）

【CTD 5.3.5.2.2-1】【CTD 5.3.5.2.2-2】【CTD 5.3.5.2.2-3】

GEN501 試験は，PI，IMiD，化学療法又は自家造血幹細胞移植を含む 2 レジメン以上の前治療歴を有する再発又は難治性の MM 患者を対象に，本剤の安全性プロファイルを検討する第 I/II 相，非盲検，多施設共同試験である。Part 1（用量漸増期）では，被験者に本剤を 0.005～24 mg/kg の用量範囲で 8 週間持続静脈内投与（初回投与後に 3 週間ウォッシュアウトし，続いて 1 週間隔で 6 週間投与）した。Part 2（用量維持期）では，疾患進行又は許容できない毒性の発現まで，最長 96 週間，本剤を 8 mg/kg（1 週間隔で 8 週間，2 週間隔で 16 週間，それ以降は 4 週間隔で投与）又は 16 mg/kg（初回投与後 3 週間ウォッシュアウトし，続いて 1 週間隔で 7 週間，2 週間隔で 14 週間，それ以降は 4 週間隔で投与）の用量で被験者に持続静脈内投与した。後観察期は追跡不能，同意撤回又は試験終了までとした。

3) 国内第 I 相試験（MMY1002 試験）

【CTD 5.3.5.2.3-1】

MMY1002 試験は，2 レジメン以上の前治療歴を有する再発又は難治性の日本人 MM 患者を対象に，本剤の忍容性及び安全性を評価する第 I 相，非盲検，多施設共同，用量漸増試験である。本剤を 8 又は 16 mg/kg の用量で被験者に持続静脈内投与することとした。第 1 期は投与頻度の高いレジメンで Week 0 から Week 9 までの期間とし，本剤を初回投与後 3 週間ウォッシュアウトし，続いて 1 週間隔で 6 週間投与した（計 7 回投与）。第 2 期は第 1 期に比べ投与頻度の低いレジメンで Week 10 から投与終了までとし，28 日間を 1 サイクルとし，サイクル 1～4 は 2 週間隔，サイクル 5 以降は 4 週間隔で投与した。投与期間は疾患進行，許容できない毒性の発現，又は治験薬投与中止基準に合致するまでとし，後観察期は治験薬の最終投与後 8 週，死亡，追跡不能，同意撤回又は試験終了までとした。

2.7.4.1.1.2 安全性の評価・解析方法

本剤 16 mg/kg の併用療法の安全性は，各試験のクリニカルカットオフ時点の結果を投与レジメン別に評価した。DVd 療法については MMY3004 試験，DPd 療法については MMY1001 試験の結果を評価した。DRd 療法については，MMY3003 試験及び GEN503 試験の結果を併合したデータを用いて評価した。

本剤の単剤療法の安全性は MMY2002 試験，GEN501 試験及び MMY1002 試験の各クリニカルカットオフ時点で得られた結果を併合し，用量別に解析した安全性データを用いた。なお，主に併合データの 16 mg/kg 群の被験者に認められた安全性プロファイルを評価することとした。

併用療法及び単剤療法の解析に用いた安全性の評価項目は，曝露状況，併用治療，有害事象，死亡，臨床検査値，バイタルサインであった。連続データは記述統計量（平均値，中央値，標準偏差，最小値及び最大値）を用いて要約し，カテゴリカルデータは例数とともに被験者割合を百分率で示した。曝露状況は本剤の投与期間，総投与量，総投与回数及び相対用量強度を算出した。併用薬は治療クラス別，薬剤別及び時期別にそれぞれ集計した。併用薬の分類は World Health

Organazation Collaborating Centre for Drug Statistics Methodology の Anatomical Therapeutic Chemical 分類に従った。

また，併用療法では 2016 年 6 月 30 日をクリニカルカットオフ日，単剤療法では 2015 年 6 月 30 日をクリニカルカットオフ日とした安全性更新情報をそれぞれ記載した。更に，GEN501 試験 Part 2 及び MMY2002 試験の 16 mg/kg 群に関して，2015 年 12 月 31 日及び [redacted] 年 [redacted] 月 [redacted] 日をクリニカルカットオフ日とした安全性更新情報をそれぞれ記載した。

(1) 安全性解析対象集団

1) 併用療法試験

併用療法試験では，解析対象集団は安全性解析対象集団（治験薬の投与を 1 回以上受けたすべての被験者）とした。MMY3004 試験，MMY3003 試験，GEN503 試験及び MMY1001 試験に組み入れられた被験者で，今回の安全性解析の対象となった 1,182 例のうち，664 例は本剤併用群，518 例が本剤非併用群であった。MMY3003 試験と GEN503 試験の一部は対象集団及び治験薬の用法・用量が同様であったことから，MMY3003 試験の DRd 群と GEN503 試験で DRd 療法（本剤 16 mg/kg）を受けた被験者の結果を併合した。投与レジメン別の被験者数の内訳は，Vd 群 237 例（MMY3004 試験），DVd 群 243 例（MMY3004 試験），Rd 群 281 例（MMY3003 試験），DRd 群 318 例（MMY3003 試験が 283 例，GEN503 試験が 35 例）及び DPd 群 103 例（MMY1001 試験）であった。また，注目すべき有害事象の一部の解析及び部分集団解析では，本剤併用群全体（DVd 群，DRd 群及び DPd 群）の 664 例のデータを併合した。

更に，日本人の安全性プロファイルを検討するため，DVd 療法については国内試験（MMY1005 試験の 8 例），DRd 療法については MMY3003 試験の日本人部分集団の結果をそれぞれ記載した。MMY3003 試験の日本人被験者の投与レジメン別の被験者数の内訳は Rd 群 15 例及び DRd 群 20 例であった。なお，MMY3003 試験の解析のうち，被験者の治験薬投与状況，人口統計学的特性，併用薬，死亡例及び主な死因の概要に関しては，解析対象集団を ITT 集団とした（Rd 群 15 例及び DRd 群 21 例）。

また，DRd 療法については，MMY3003 試験の東アジア人部分集団（日本，韓国及び台湾で組み入れられた被験者）の結果も記載した。東アジア人被験者の投与レジメン別の被験者数の内訳は Rd 群 44 例及び DRd 群 51 例であった。なお，MMY3003 試験の解析のうち，被験者の治験薬投与状況，人口統計学的特性，併用薬，死亡例及び主な死因の概要に関しては，解析対象集団を ITT 集団とした（Rd 群 44 例及び DRd 群 52 例）。

2) 単剤療法試験

単剤療法試験では，解析対象集団は全投与解析対象集団（本剤の投与を 1 回以上受けたすべての被験者）とした。MMY2002 試験，GEN501 試験及び MMY1002 試験の 237 例のデータを併合し，被験者が実際に投与を受けた用量に従い ≤4，8，16 及び 24 mg/kg の用量別に解析し，更に併合データの対象集団全体の結果も集計した。

また，単剤療法試験での安全性に関して，併合データの対象集団全体（MMY2002 試験，GEN501 試験及び MMY1002 試験を併合した 237 例）と比較するため国内試験（MMY1002 試験

の 9 例）の結果も各項に記載した。国内試験の評価では，併合解析時点（2015 年 2 月 6 日クリニカルカットオフ日）以降のデータも含めた MMY1002 試験の最終解析結果（2015 年 9 月 25 日データカットオフ）を記載した。

(2) 部分集団解析

1) 併用療法試験

MMY3004 試験，MMY3003 試験，GEN503 試験及び MMY1001 試験の本剤併用群（DVd 群，DRd 群及び DPd 群）で認められた有害事象を以下の部分集団別に解析した。

- 年齢（18～<65 歳，65～<75 歳，≥75 歳）
- 性別（男性，女性）
- 人種（白人，その他）
- ベースラインの腎機能［クレアチニン・クリアランス（CrCL）：正常（≥90 mL/min），軽度の障害（60～<90 mL/min），中等度の障害（30～<60 mL/min），高度の障害（<30 mL/min）］
- ベースラインの肝機能［正常，異常（軽度，中等度及び高度の障害）］
- 地域［欧州連合（EU）西部並びに米国及びカナダ，その他の地域］

2) 単剤療法試験

単剤療法試験の 16 mg/kg 群で認められた有害事象を以下の部分集団別に解析した。

- 年齢（18～<65 歳，65～<75 歳，≥75 歳）
- 性別（男性，女性）
- 人種（白人，その他）
- ベースラインの腎機能障害（CrCL：≥60 mL/min，30～<60 mL/min，<30 mL/min）
- ベースラインの肝機能（正常，軽度の障害，中等度の障害，高度の障害）
- 製剤別［第 I/II 相試験用製剤（以下，第 II 相試験用製剤），第 III 相試験用製剤］
- 地域（EU，北米及び日本）

(3) 有害事象

有害事象の集計対象は治験薬投与後に発現した有害事象（TEAE）とした。有害事象の重症度は National Cancer Institute Common Terminology Criteria for Adverse Events（NCI CTCAE）ver.4.03 に基づき Grade 分類した。有害事象と治験薬の因果関係は関連なし（not related），多分なし（doubtful），可能性小（possible），可能性大（probable）又はほぼ確実（very likely）の 5 段階

で評価され，関連なし（not related），多分なし（doubtful）と判断された事象を「関連性なし」，それ以外を「関連性あり」とした。

併合解析及び各試験の有害事象名は，医薬品規制用語集（MedDRA）を用いてコード化し，器官別大分類（SOC）別及び基本語（PT）別に集計した。有害事象は発現例数を集計し，発現割合を算出した。有害事象の項目は Grade 3 又は 4 の有害事象，治験薬と関連性がある有害事象及び重篤な有害事象とした。本剤単剤療法試験の併合解析の有害事象は，MedDRA ver. 17.0（[redacted]年[redacted]月[redacted]日をクリニカルカットオフとした安全性更新情報の解析では ver. 18.0），MMY1002 試験の最終解析及び併用療法試験の有害事象は MedDRA ver. 18.0 を用いてコード化し，それぞれ同バージョンの MedDRA/J を用いて和訳した。

また，その他の重要な有害事象として，併用療法試験では投与調節に至った有害事象及び治験薬の投与中止に至った有害事象を評価した。投与調節は本剤とその他の治験薬別に集計した。本剤の投与調節では，持続静脈内投与に関する処置が投与延期又は休薬に至った有害事象を集計した。その他の治験薬の投与調節では，各試験で使用された治験薬に応じて，投与延期，休薬，投与スケジュールの変更，減量又は再増量の処置を実施した有害事象を投与調節に至った有害事象として集計した。なお，すべての治験薬を休薬した場合は投与サイクルの遅延に至った有害事象とした。治験薬の投与中止に至った有害事象は，症例報告書（CRF）の「治験薬投与中止」ページの主な中止理由に入力された有害事象を集計した。また，CRF の「有害事象」ページで本剤の投与処置が中止と入力された有害事象を本剤の投与が中止となった有害事象として集計し，更に本剤のみ投与中止（その他の治験薬は継続）となった有害事象も集計した。

単剤療法試験ではその他の重要な有害事象として，本剤の投与延期に至った有害事象，本剤の投与中断に至った有害事象及び本剤の投与中止に至った有害事象を評価した。本剤の投与延期では，本剤の投与に関する処置が延期，サイクル内の投与延期又はサイクル開始の延期に至った有害事象，本剤の投与中断では，持続静脈内投与に関する処置が中断，投与の一時中断又は投与の中断に至った有害事象を集計した。本剤の投与中止に至った有害事象は，CRF の「治験薬投与中止」ページの主な中止理由に入力された有害事象を集計した。

(4) 死亡

併用療法試験では，治験期間中及び治験薬の最終投与後 30 日間，及び治験薬の初回投与から 60 日間に認められた死亡を要約し，死亡例一覧を作成した。また，死亡に至った有害事象を集計した。単剤療法試験では，治験期間中及び本剤の最終投与後 30 日目までの期間に認められた死亡を要約し，死亡例一覧を作成した。また，死亡に至った有害事象を集計した。

(5) 器官別又は症候群別有害事象

Infusion related reaction（IRR），好中球減少症，感染症及び寄生虫症，血小板減少症及び出血関連事象，溶血，間接クームス試験への干渉及び輸血への影響，心イベント，肝胆道系障害及び二次性悪性腫瘍を特に注目すべき有害事象とし，それぞれ評価した。特に注目すべき有害事象として評価した項目を表 2.7.4-2 に示す。これらの有害事象は，これまでに実施された in vitro 試験，動物を用いた毒性試験及び臨床試験結果に基づき選択した。また，特に注目すべき有害事象として評価した各項目に該当する事象の定義を示した一覧を表 2.7.4-付録-1 に示す。

表 2.7.4-2 特に注目すべき有害事象として評価した項目

特に注目すべき有害事象として評価した項目	併用療法試験					単剤療法試験	
	全体			日本人及び東アジア人		全体	国内試験
				国内試験	日本人集団及び東アジア人集団		
	MMY3004 試験	MMY3003 試験及び GEN503 試験併合	MMY1001 試験	MMY1005 試験	MMY3003 試験	MMY2002 試験，GEN501 試験及び MMY1002 試験併合	MMY1002 試験
	Vd 療法 vs DVd 療法	Rd 療法 vs DRd 療法	DPd 療法	DVd 療法	Rd 療法 vs DRd 療法		
IRR	X	X	X	X	X	X	X
好中球減少症	X	X	X	X	X	X	X
感染症及び寄生虫症	X	X	X	X	X	X	X
血小板減少症及び出血関連事象	X[a]	X[a]	X[a]	X	X[a]	X	X
溶血	X	X	X	X	X	X	X
間接クームス試験への干渉及び輸血への影響	X[b]	X[b]	X[b]	X[b]	X[b]	X	X
心イベント	X	X	X	X	X	X	X
肝胆道系障害	X	X	X	X	X	X	X
二次性悪性腫瘍	X	X	X	X	X	X	X

[a] 主解析のクリニカルカットオフ時点のデータ解析後に出血関連事象の集計対象となる事象が追加されたため，2016 年 6 月 30 日クリニカルカットオフ時点の安全性更新情報の出血関連事象のデータも併せて評価した。
[b] 本剤初回投与前のみ間接クームス試験を実施し，投与後の評価は実施しなかったため，輸血の判断への影響のみを評価した。

Infusion related reaction（IRR）

IRR の定義は，併用療法試験（MMY3004 試験，MMY3003 試験，GEN503 試験，MMY1001 試験及び MMY1005 試験）では治験担当医師が IRR と判断した事象とし，単剤療法試験では以下の事象とした。

・ MMY2002 試験及び MMY1002 試験：治験担当医師が IRR と判断した事象

・ GEN501 試験：本剤の投与から 48 時間以内に発現した事象（レトロスペクティブな検証）

遅発性の IRR とは，投与開始から 24 時間以降に発現した IRR とした。

併用療法試験及び単剤療法試験に関して，IRR を SOC 別，PT 別，重症度別（全 Grade，Grade 3 又は 4）及び発現時期別（初回，2 回目，3 回目以降の投与時）に集計した。併用療法試験（MMY1005 試験を除く）では，本剤併用群の併合データも併せて集計した。併用療法では本剤持続静脈内投与中の投与調節（投与中断，投与中止又は減速）及び本剤の投与中止に至った IRR，単剤療法では本剤持続静脈内投与中の投与中断及び本剤の投与中止に至った IRR をそれぞれ評価した。また，前投薬及び後投薬をそれぞれ要約した。更に，単剤療法では，製剤別（第 II 相試験用製剤，第 III 相試験用製剤）の IRR も要約した。

好中球減少症

好中球減少症はレナリドミド投与で認められる最も発現割合の高い既知の副作用の一つである[1)]。そのため，有害事象として報告された好中球減少症及び発熱性好中球減少症について評価した。

感染症及び寄生虫症

基礎疾患により低γグロブリン血症及び免疫抑制が引き起こされるため，MM 患者は感染症のリスクが高くなる[2)]。そのため，SOC が感染症及び寄生虫症に分類される有害事象を評価した。また，初回発現までの期間別（≤6 カ月，>6 カ月）又はサイクル回数別に集計した。

また，日和見感染に分類される有害事象を集計した（表 2.7.4-付録-1）。中でも特に注目すべき事象として帯状疱疹を評価した。

血小板減少症及び出血関連事象

CD38 は血小板表面に低レベルで発現している。血小板減少症はチンパンジーを用いた非臨床試験において認められており，臨床的にも本剤の投与において留意すべき有害事象の一つである。一方，血小板減少症は，悪性形質細胞の骨髄浸潤が原因でも起こり，MM 患者の多くに認められる。そのため，本剤の臨床試験で認められた血小板減少症が，本剤の投与による直接的影響か，又は基礎疾患によるものかを評価するのが望ましい。また，血小板数低値はボルテゾミブの投与を受けた患者に共通して認められる検査値異常であり[3)]，易出血性と関連することから，血小板減少症及び出血関連事象（表 2.7.4-付録-1）について評価した。

溶血

CD38 はヒト赤血球表面に低レベルで発現している。非臨床試験結果では，ヒト赤血球の存在下でダラツムマブ（遺伝子組換え）による補体介在性の溶血は認められなかった。しかし，理論的には，daratumumab がヒト赤血球に結合し，補体を介して溶血に関与する可能性があるため，有害事象として報告された溶血を評価した。

間接クームス試験への干渉及び輸血への影響

Daratumumab は赤血球表面上の CD38 と結合するため，間接クームス試験が陽性となり，赤血球の不規則抗体の検出に干渉する。非臨床試験結果では，daratumumab は間接クームス試験に干渉することが示されており，本剤の投与を受けた被験者の不規則抗体の評価が困難になる可能性がある。併用療法試験では，本剤の初回投与前に間接クームス試験を実施することが規定されていたが，本剤投与後の間接クームス試験の評価は規定されていなかった。単剤療法の GEN501 試験 Part 1 及び MMY1002 試験では，直接又は間接クームス試験を本剤の投与前及び投与後に実施した。更に，単剤 3 試験併合で本剤投与期間中の輸血及び赤血球輸血の実施に関連した有害事象を集計した。

心イベント

有害事象として報告された心房細動を評価した。また，QT 延長に関連する有害事象を集計した（表 2.7.4-付録-1）。

肝胆道系障害

SOC が肝胆道系障害に分類される有害事象を評価した。

二次性悪性腫瘍

二次性悪性腫瘍の発現割合は低いものの，MM 患者への治療では重要な考慮すべき事象である。複数のレトロスペクティブ及びプロスペクティブな検証結果から，MM 患者へのレナリドミド及びアルキル化剤の曝露が二次性悪性腫瘍のリスク因子である可能性が示唆されており，二次性悪性腫瘍は 12 カ月以上の潜伏期を経て 1～13%の割合で発現することが知られている[4)]。MM の治療においては，アルキル化剤への曝露後に骨髄異形成症候群及び急性骨髄性白血病が発生することが知られていたが，レナリドミドへの曝露においても同様であり，更には，大腸癌，乳癌及び前立腺癌等の固形腫瘍の発現も報告されている[4)]。そのため，併用療法及び単剤療法で報告された有害事象から MedDRA 標準検索式（SMQ）に基づく修正 MedDRA 検索式を用いて二次性悪性腫瘍を特定して集計した（表 2.7.4-付録-1）。

(6) 臨床検査値

臨床検査値（選択した血液学的検査値及び血液生化学検査値）の重症度を NCI CTCAE ver.4.03 に基づき Grade 化し，各検査項目のベースラインからの変化を評価した。臨床的に重要であると治験担当医師が判断した臨床検査結果を有害事象とした。

以下の臨床検査項目（MMY1002 試験では*印のついた項目）について要約した。

血液学的検査*：白血球数，ヘモグロビン，血小板数，リンパ球数，好中球数

血液生化学検査：アルブミン，アルカリフォスファターゼ，アラニンアミノトランスフェラーゼ（ALT）*，アスパラギン酸アミノトランスフェラーゼ（AST）*，ビリルビン*，補正カルシウム*，クレアチニン*，血糖（MMY1005 試験を除く），カリウム，ナトリウム，尿酸*，リン酸，マグネシウム（MMY1005 試験を除く），クレアチンホスホキナーゼ（MMY1005 試験を除く）

（単剤 3 試験併合のみ：ハプトグロビン，コレステロール，トリグリセリド，尿蛋白）

臨床検査値は，記述統計量（平均値，中央値，標準偏差，最小値及び最大値），ベースラインからの変化量，臨床検査値のベースラインの Grade から最悪 Grade への推移，経時的な推移図を用いて評価した。

(7) バイタルサイン

併用療法試験及び単剤療法試験の各試験でベースライン以降に認められたバイタルサインの変動を評価した。

(8) 腫瘍崩壊症候群

有害事象として報告された腫瘍崩壊症候群を評価した。

2.7.4.1.2 全般的な曝露状況

2.7.4.1.2.1 投与レジメン別集計

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の被験者の治験薬投与状況を表 2.7.4-3 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

クリニカルカットオフ時点で投与を中止した被験者の割合は，Vd 群が 43.9%，DVd 群が 30.5%であった。中止理由は両群とも疾患進行が最も多く，Vd 群が 25.3%，DVd 群が 19.3%であった。次いで有害事象が両群とも多く，Vd 群が 9.7%，DVd 群が 7.8%であった。8 サイクルの投与（投与期間 5.6 カ月）を完了した被験者の割合は，Vd 群が 57.4%，DVd 群が 79.8%であった。

クリニカルカットオフ時点で，Vd 群では 47.7%の被験者が 8 サイクルの投与を終了して後観察期に移行し，8.4%の被験者が投与継続中であった。8 サイクル投与後も本剤の単剤投与を継続する DVd 群では，69.5%の被験者が投与継続中であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

クリニカルカットオフ時点で投与を中止した被験者の割合は，Rd 群が 47.0%，DRd 群が 24.2%であった。中止理由は両群とも疾患進行が最も多く，Rd 群が 34.2%，DRd 群が 14.5%であった。次いで有害事象が両群とも多く，Rd 群が 8.2%，DRd 群が 6.9%であった。Rd 群では 53.0%，DRd 群では 75.8%の被験者が投与継続中であった。

MMY1001 試験（DPd 療法）

クリニカルカットオフ時点で投与を中止した被験者の割合は 57.3%であった。中止理由は疾患進行が 33.0%と最も多く，次いで有害事象が 13.6%であった。42.7%の被験者が投与継続中であった。

表 2.7.4-3 被験者の治験薬投与状況［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Subjects who had treatment ongoing	20 (8.4%)	169 (69.5%)	149 (53.0%)	241 (75.8%)	44 (42.7%)
Subjects who discontinued treatment	104 (43.9%)	74 (30.5%)	132 (47.0%)	77 (24.2%)	59 (57.3%)
Reason for discontinuation					
Progressive disease	60 (25.3%)	47 (19.3%)	96 (34.2%)	46 (14.5%)	34 (33.0%)
Adverse event	23 (9.7%)	19 (7.8%)	23 (8.2%)	22 (6.9%)	14 (13.6%)
Physician decision	0	0	2 (0.7%)	5 (1.6%)	4 (3.9%)
Death	4 (1.7%)	4 (1.6%)	1 (0.4%)	2 (0.6%)	2 (1.9%)
Non-compliance with study drug[a]	8 (3.4%)	3 (1.2%)	5 (1.8%)	1 (0.3%)	0
Withdrawal by subject	9 (3.8%)	1 (0.4%)	5 (1.8%)	1 (0.3%)	4 (3.9%)
Other	0	0	0	0	1 (1.0%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Percentages are calculated with the number of subjects in each group as denominator.
[a]Based on reason 'Subject refused to further study treatment' on 'End of Treatment' CRF page.
Note: MMY3004: Vd arm treated for 8 cycles and DVd arm treated until PD per protocol. Subjects in Vd arm who were treated for 8 cycles are not considered as treatment discontinuation.

[TSIDS01.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSIDS01.SAS] 01JUN2016, 10:47

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の被験者の治験薬投与状況を表 2.7.4-付録-2 に示す。

治験薬投与を受けた被験者（8 例）では，クリニカルカットオフ時点で 12.5%（1 例）が有害事象により投与を中止し，87.5%（7 例）の被験者が投与継続中であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の被験者の治験薬投与状況を表 2.7.4-付録-3 に示す。

日本人集団（ITT 集団：Rd 群 15 例，DRd 群 21 例）では，クリニカルカットオフ時点で投与を中止した被験者の割合は，Rd 群が 46.7%，DRd 群が 30.0%であった。中止理由は両群とも疾患進行が最も多く，Rd 群が 46.7%，DRd 群が 10.0%であった。有害事象による中止は DRd 群のみ 10.0%に認められた。

東アジア人集団（ITT 集団：Rd 群 44 例，DRd 群 52 例）では，クリニカルカットオフ時点で投与を中止した被験者の割合は，Rd 群が 50.0%，DRd 群が 31.4%であった。中止理由は両群とも疾患進行が最も多く，Rd 群が 47.7%，DRd 群が 19.6%であった。次いで有害事象が両群とも多く，Rd 群が 2.3%，DRd 群が 5.9%であった。

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の被験者の治験薬投与状況を表 2.7.4-4 に示す。

16 mg/kg 群では，クリニカルカットオフ時点で投与を中止した被験者の割合は 78.8%であった。中止理由は疾患進行（69.2%）が最も多く，次いで有害事象（3.8%）であった。21.2%の被験者（MMY2002 試験：16 例，GEN501 試験 Part 2：14 例，MMY1002 試験：3 例）が投与継続中であった。

表 2.7.4-4 被験者の治験薬投与状況

［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Discontinued from treatment	14 (60.9%)	49 (89.1%)	123 (78.8%)	1 (33.3%)	187 (78.9%)
Progressive disease	10 (43.5%)	49 (89.1%)	108 (69.2%)	0	167 (70.5%)
Adverse event	4 (17.4%)	0	6 (3.8%)	1 (33.3%)	11 (4.6%)
Physician decision	0	0	4 (2.6%)	0	4 (1.7%)
Withdrawal of consent	0	0	3 (1.9%)	0	3 (1.3%)
Non-compliance with study drug	0	0	1 (0.6%)	0	1 (0.4%)
Protocol violation	0	0	1 (0.6%)	0	1 (0.4%)
Death	0	0	0	0	0

Percentages are calculated with the number of subjects in each group as denominator.
Modified from: Appendix TSIDS01

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の被験者の治験薬投与状況を表 2.7.4-付録-5 に示す。

MMY1002 試験の最終解析時点（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，全例が投与を中止した。中止理由は疾患進行［8 mg/kg 群 100%（4 例），16 mg/kg 群 60.0%（3 例）］が最も多かった。

2.7.4.1.2.2 曝露及び投与期間

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の曝露状況及び投与期間を表 2.7.4-5 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

MMY3004 試験は Vd 群，DVd 群ともに 8 サイクル（投与期間 5.6 カ月）まで治験薬の投与を受け，その後 Vd 群は後観察期に移行し，DVd 群は本剤のみの投与を 4 週間隔で継続した。

投与期間の中央値は Vd 群が 5.224 カ月（範囲：0.16～8.02 カ月），DVd 群が 6.472 カ月（範囲：0.03～14.78 カ月）であった。DVd 群では本剤の総投与回数の中央値は 16.0 回（範囲：1～24 回），総投与量の中央値は 249.09 mg/kg，相対用量強度の中央値は 99.16%であった。

ボルテゾミブの相対用量強度の中央値は Vd 群が 93.48%，DVd 群が 86.54%であった。デキサメタゾンの相対用量強度の中央値は，Vd 群が 100.00%，DVd 群が 98.18%であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

投与期間の中央値は Rd 群が 12.287 カ月（範囲：0.23～20.14 カ月），DRd 群が 13.306 カ月（範囲：0.03～24.54 カ月）であった。DRd 群では本剤の総投与回数の中央値は 24.0 回（範囲：1～36 回），総投与量の中央値は 384.00 mg/kg，相対用量強度の中央値は 99.42%であった。

レナリドミドの相対用量強度の中央値は，Rd 群が 95.77%，DRd 群が 90.87%であった。デキサメタゾンの相対用量強度の中央値は，両群とも 100.00%であった。

MMY1001 試験（DPd 療法）

DPd 群の投与期間の中央値は 6.012 カ月（範囲：0.03～16.89 カ月）であった。本剤の総投与回数の中央値は 14.0 回（範囲：1～28 回），総投与量の中央値は 223.11 mg/kg，相対用量強度の中央値は 96.82%であった。ポマリドミドの相対用量強度の中央値は 77.50%，デキサメタゾンでは 90.00%であった。

表 2.7.4-5 曝露状況及び投与期間［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Duration of treatment (month)					
N	237	243	281	318	103
Mean (SD)	4.192 (1.6909)	6.711 (3.0154)	10.591 (4.9213)	12.505 (4.4630)	6.324 (4.5097)
Median	5.224	6.472	12.287	13.306	6.012
Range	(0.16; 8.02)	(0.03; 14.78)	(0.23; 20.14)	(0.03; 24.54)	(0.03; 16.89)
< 1 month	15 (6.3%)	16 (6.6%)	13 (4.6%)	8 (2.5%)	15 (14.6%)
>=1 - < 3 months	42 (17.7%)	14 (5.8%)	13 (4.6%)	12 (3.8%)	16 (15.5%)
>=3 - < 6 months	171 (72.2%)	72 (29.6%)	39 (13.9%)	16 (5.0%)	20 (19.4%)
>=6 - < 9 months	9 (3.8%)	82 (33.7%)	29 (10.3%)	20 (6.3%)	17 (16.5%)
>=9 - < 12 months	0	49 (20.2%)	39 (13.9%)	42 (13.2%)	21 (20.4%)
>=12 months	0	10 (4.1%)	148 (52.7%)	220 (69.2%)	14 (13.6%)
Total daratumumab dose received (mg/kg)					
N	0	243	0	318	103
Mean (SD)	-	235.82 (78.613)	-	358.70 (98.326)	223.90 (120.704)
Median	-	249.09	-	384.00	223.11
Range	-	(0.4; 386.5)	-	(0.8; 554.6)	(0.2; 448.0)
Total number of daratumumab infusions					
N	0	243	0	318	103
Mean (SD)	-	14.8 (4.88)	-	22.6 (6.20)	14.0 (7.56)
Median	-	16.0	-	24.0	14.0
Range	-	(1; 24)	-	(1; 36)	(1; 28)
Daratumumab relative dose intensity (%)					
N	0	243	0	318	103
Mean (SD)	-	93.36 (14.340)	-	95.66 (11.681)	90.12 (17.474)
Median	-	99.16	-	99.42	96.82
Range	-	(0.8; 105.3)	-	(1.2; 104.9)	(1.3; 104.8)
Bortezomib/Lenalidomide/Pomalidomide relative dose intensity (%)					
N	237	242	280	317	97
Mean (SD)	87.11 (15.237)	81.75 (19.128)	85.90 (18.417)	79.25 (22.483)	74.69 (21.614)
Median	93.48	86.54	95.77	90.87	77.50
Range	(32.7; 112.2)	(25.2; 103.6)	(16.8; 100.0)	(13.2; 100.0)	(5.7; 100.0)
Dexamethasone relative dose intensity (%)[a]					
N	237	243	281	283	103
Mean (SD)	91.00 (15.833)	87.35 (18.848)	99.38 (4.253)	99.00 (4.290)	84.60 (17.891)
Median	100.00	98.18	100.00	100.00	90.00
Range	(20.6; 104.7)	(20.3; 103.1)	(50.0; 104.2)	(63.9; 111.3)	(14.3; 106.3)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Note: MMY3004: Vd arm treated for 8 cycles and DVd arm treated until PD per protocol.
[a] GEN503 was excluded as relative dose intensity is hard to calculate due to the complexity on the planned dexamethasone dose.

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日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の投与期間を表 2.7.4-付録-6，投与量の要約を表 2.7.4-付録-7，相対用量強度を表 2.7.4-付録-8 に示す。

治験薬投与を受けた被験者（8 例）では，投与期間の中央値は 5.34 カ月（範囲：4.3～8.9 カ月）であった。本剤の総投与回数の中央値は 13.0 回（範囲：12～17 回），総投与量の中央値は 214.64 mg/kg，相対用量強度の中央値は 97.12%であった。ボルテゾミブの相対用量強度の中央値は 72.19%，デキサメタゾンでは 48.16%であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の投与期間を表 2.7.4-付録-9，投与量の要約を表 2.7.4-付録-10，相対用量強度を表 2.7.4-付録-11 に示す。

日本人集団の投与期間の中央値は Rd 群が 8.77 カ月（範囲：2.5～11.1 カ月），DRd 群が 9.89 カ月（範囲：2.6～12.6 カ月）であった。DRd 群では本剤の総投与回数の中央値は 20.0 回（範囲：10～24 回），総投与量の中央値は 323.69 mg/kg，相対用量強度の中央値は 98.44%であった。レナリドミドの相対用量強度の中央値は，Rd 群が 95.71%，DRd 群が 61.37%であった。デキサメタゾンの相対用量強度の中央値は，Rd 群が 100.00%，DRd 群が 99.74%であった。

東アジア人集団の投与期間の中央値は Rd 群が 9.68 カ月（範囲：0.2～17.3 カ月），DRd 群が 11.27 カ月（範囲：1.5～19.1 カ月）であった。DRd 群では本剤の総投与回数の中央値は 21.0 回（範囲：7～30 回），総投与量の中央値は 340.30 mg/kg，相対用量強度の中央値は 99.53%であった。レナリドミドの相対用量強度の中央値は，Rd 群が 94.35%，DRd 群が 69.88%であった。デキサメタゾンの相対用量強度の中央値は，両群とも 100.00%であった。

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の曝露状況及び投与期間を表 2.7.4-6 に示す。

16 mg/kg 群の投与期間の中央値は 3.253 カ月（範囲：0.03～14.19 カ月）であった。本剤の総投与回数の中央値は 11.0 回（範囲：1～26 回），総投与量の中央値は 176.72 mg/kg であった。92.9%の被験者は相対用量強度が 95%以上であった。

表 2.7.4-6 曝露状況及び投与期間

［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Duration of treatment (month)					
N	23	55	156	3	237
Mean (SD)	1.276 (0.6870)	3.692 (3.5641)	4.469 (3.4808)	1.676 (0.6085)	3.943 (3.4450)
Median	1.446	2.628	3.253	1.906	2.628
Range	(0.07; 1.94)	(0.03; 14.78)	(0.03; 14.19)	(0.99; 2.14)	(0.03; 14.78)
< 1 month	7 (30.4%)	14 (25.5%)	22 (14.1%)	1 (33.3%)	44 (18.6%)
>=1 - < 3 months	16 (69.6%)	21 (38.2%)	53 (34.0%)	2 (66.7%)	92 (38.8%)
>=3 - < 6 months	0	9 (16.4%)	29 (18.6%)	0	38 (16.0%)
>=6 - < 9 months	0	6 (10.9%)	35 (22.4%)	0	41 (17.3%)
>=9 - < 12 months	0	1 (1.8%)	10 (6.4%)	0	11 (4.6%)
>=12 months	0	4 (7.3%)	7 (4.5%)	0	11 (4.6%)
Total dose received (mg/kg)					
N	23	55	156	3	237
Mean (SD)	6.50 (8.407)	74.98 (54.936)	192.96 (99.623)	144.27 (55.404)	146.87 (108.493)
Median	4.20	70.12	176.72	170.40	136.19
Range	(0.0; 30.4)	(7.7; 222.5)	(1.9; 416.8)	(80.6; 181.8)	(0.0; 416.8)
Total number of Daratumumab infusions					
N	23	55	156	3	237
Mean (SD)	4.6 (2.41)	8.9 (6.07)	12.2 (6.27)	5.7 (2.31)	10.6 (6.41)
Median	5.0	9.0	11.0	7.0	10.0
Range	(1; 7)	(1; 26)	(1; 26)	(3; 7)	(1; 26)
Relative dose intensity (%)					
N	23	55	156	3	237
>= 95%	21 (91.3%)	53 (96.4%)	145 (92.9%)	3 (100.0%)	222 (93.7%)
< 95%	2 (8.7%)	2 (3.6%)	11 (7.1%)	0	15 (6.3%)

Percentages are calculated with the number of subjects in each group as denominator.

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MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の投与期間を表 2.7.4-付録-12，曝露状況を 表 2.7.4-付録-13 に示す。

MMY1002 試験（9 例）では，投与期間の中央値は 5.55 カ月（範囲：0～10.6 カ月）であった。本剤の総投与回数の中央値は 15.0 回（範囲：1～20 回），総投与量の中央値は 122.68 mg/kg であった。88.9%（8 例）の被験者は相対用量強度が 95%以上であった。

2.7.4.1.3 治験対象集団の人口統計学的特性及びその他の特性

2.7.4.1.3.1 人口統計学的特性及びその他のベースライン特性

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の人口統計学的特性及びベースラインの疾患特性を表 2.7.4-7 に示す。

対象集団全体の人口統計学的特性は，各投与群でおおむね同様であった。年齢の中央値は 63.0～65.0 歳であり，性別では男性（54.3～60.7%），人種では白人（65.5～88.2%）の被験者が多かった。また，Eastern Cooperative Oncology Group（ECOG）の performance status スコアが 0 又

は 1 の被験者の割合は 88.3～96.2%であった。腎機能（CrCL 値）が正常（≥90 mL/min），軽度の障害（60～<90 mL/min）又は中等度の障害（30～<60 mL/min）の被験者の割合は 95.3～99.6%であった。肝機能が正常の被験者の割合は 81.6～91.3%，軽度の障害は 8.4～17.5%であった。

表 2.7.4-7 人口統計学的特性及びベースラインの疾患特性［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Age, years					
N	237	243	281	318	103
Category, n (%)					
< 65	116 (48.9%)	129 (53.1%)	138 (49.1%)	155 (48.7%)	52 (50.5%)
>= 65	121 (51.1%)	114 (46.9%)	143 (50.9%)	163 (51.3%)	51 (49.5%)
Mean (SD)	64.1 (9.85)	62.6 (9.57)	64.5 (8.76)	64.0 (9.06)	63.0 (10.43)
Median	65.0	63.0	65.0	65.0	64.0
Range	(33; 85)	(30; 84)	(42; 87)	(34; 89)	(35; 86)
Sex, n (%)					
N	237	243	281	318	103
Male	142 (59.9%)	132 (54.3%)	163 (58.0%)	193 (60.7%)	57 (55.3%)
Female	95 (40.1%)	111 (45.7%)	118 (42.0%)	125 (39.3%)	46 (44.7%)
Race, n (%)					
N	237	243	281	318	103
White	209 (88.2%)	209 (86.0%)	184 (65.5%)	239 (75.2%)	79 (76.7%)
Other	28 (11.8%)	34 (14.0%)	97 (34.5%)	79 (24.8%)	24 (23.3%)
Weight (kg)					
N	235	243	2	315	103
Mean (SD)	77.17 (16.256)	78.19 (17.010)	64.00 (5.657)	74.65 (16.432)	80.78 (20.058)
Median	76.00	77.00	64.00	74.00	78.50
Range	(37.5; 131.6)	(45.0; 134.8)	(60.0; 68.0)	(37.0; 132.0)	(41.2; 137.8)
Height (cm)					
N	237	243	277	314	103
Mean (SD)	166.66 (9.821)	166.84 (10.010)	166.01 (10.559)	166.42 (10.505)	168.63 (10.100)
Median	167.00	167.00	166.00	166.05	167.60
Range	(139.0; 192.0)	(141.0; 194.0)	(137.0; 201.0)	(132.4; 195.0)	(149.0; 190.5)
Baseline ECOG score, n (%)					
N	237	242	281	318	103
0	110 (46.4%)	103 (42.6%)	150 (53.4%)	159 (50.0%)	28 (27.2%)
1	109 (46.0%)	126 (52.1%)	116 (41.3%)	147 (46.2%)	63 (61.2%)
2	18 (7.6%)	13 (5.4%)	15 (5.3%)	12 (3.8%)	12 (11.7%)
>2	0	0	0	0	0
Geographic region					
N	237	243	281	318	103
West EU+US+CAN region	102 (43.0%)	88 (36.2%)	165 (58.7%)	207 (65.1%)	103 (100.0%)
Asia/Pacific region	28 (11.8%)	31 (12.8%)	53 (18.9%)	60 (18.9%)	0
Other region	107 (45.1%)	124 (51.0%)	63 (22.4%)	51 (16.0%)	0
Baseline renal impairment(creatinine clearance)					
N	233	243	281	314	103
Normal (CrCl >= 90 mL/min)	89 (38.2%)	90 (37.0%)	88 (31.3%)	114 (36.3%)	36 (35.0%)
Mild (CrCl 60 to < 90 mL/min)	74 (31.8%)	96 (39.5%)	128 (45.6%)	117 (37.3%)	36 (35.0%)
Moderate (CrCl 30 to < 60 mL/min)	59 (25.3%)	49 (20.2%)	64 (22.8%)	80 (25.5%)	30 (29.1%)
Severe (CrCl < 30 mL/min)	11 (4.7%)	8 (3.3%)	1 (0.4%)	3 (1.0%)	1 (1.0%)

表 2.7.4-7 人口統計学的特性及びベースラインの疾患特性［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Baseline hepatic function					
N	235	242	273	311	103
Normal	210 (89.4%)	202 (83.5%)	242 (88.6%)	284 (91.3%)	84 (81.6%)
Mildly impaired	22 (9.4%)	38 (15.7%)	31 (11.4%)	26 (8.4%)	18 (17.5%)
Moderately impaired	3 (1.3%)	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
Severely impaired	0	1 (0.4%)	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: Hepatic function is classified into 4 levels per NCI Organ Dysfunction criteria: Normal: total bilirubin ≤ ULN and AST ≤ ULN; Mildly Impaired: (total bilirubin ≤ ULN and AST > ULN) or (ULN < total bilirubin ≤ 1.5×ULN); Moderately Impaired: 1.5×ULN < total bilirubin ≤ 3×ULN; and Severely Impaired: total bilirubin > 3×ULN.
West EU+US+CAN includes Belgium, Denmark, Greece, Netherlands, France, Great Britain, Sweden, Italy, Spain, USA, and Canada. Asia/Pacific region includes Australia, Japan, South Korea, and Taiwan. Other region includes Israel, Turkey, Poland, Brazil, Czech Republic, Hungary, Mexico, Russia, and Ukraine.

[TSIDEM01.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSIDEM01.SAS] 01JUN2016, 10:47

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の人口統計学的特性を表 2.7.4-付録-14，ベースラインの疾患特性を表 2.7.4-付録-15 に示す。

治験薬投与を受けた被験者（8 例）では，年齢の中央値は 74.5 歳（範囲：54～82 歳）であった。性別では男性（75.0%，6 例）の被験者が多かった。また，ECOG の performance status スコアは 0 が 75.0%（6 例），1 が 25.0%（2 例）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の人口統計学的特性を表 2.7.4-付録-16，ベースラインの疾患特性を表 2.7.4-付録-17 に示す。

日本人集団（ITT 集団：Rd 群 15 例，DRd 群 21 例）の年齢の中央値は Rd 群が 67.0 歳（範囲：50～81 歳），DRd 群が 68.0 歳（範囲：45～80 歳）であった。男性の被験者の割合は Rd 群が 60.0%，DRd 群が 52.4%であった。また，ECOG の performance status スコアが 0 又は 1 の被験者の割合は Rd 群が 93.3%，DRd 群が 100%であった。

東アジア人集団（ITT 集団：Rd 群 44 例，DRd 群 52 例）の年齢の中央値は Rd 群が 65.0 歳（範囲：44～85 歳），DRd 群が 64.0 歳（範囲：34～80 歳）であった。男性の被験者の割合は Rd 群が 61.4%，DRd 群が 50.0%であった。また，ECOG の performance status スコアが 0 又は 1 の被験者の割合は Rd 群が 97.7%，DRd 群が 96.2%であった。

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の人口統計学的特性及びベースラインの疾患特性を表 2.7.4-8 に示す。

16 mg/kg 群の年齢の中央値は 63.0 歳（範囲：31～84 歳）であった。性別では男性（53.8%），人種では白人（76.3%）の被験者が多かった。また，ECOG の performance status スコアは 0 が 29.5%，1 が 64.1%，2 が 6.4%であった。腎機能（CrCL 値）が≥90 mL/min，60～<90 mL/min 又は 30～<60 mL/min の被験者の割合は 96.8%であった。肝機能が正常の被験者の割合は 86.5%，軽度の障害は 13.5%であった。

表 2.7.4-8 人口統計学的特性及びベースラインの疾患特性

［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Age (years)					
N	23	55	156	3	237
Category, n (%)					
18 - <65	13 (56.5%)	32 (58.2%)	86 (55.1%)	2 (66.7%)	133 (56.1%)
65 - <75	9 (39.1%)	20 (36.4%)	54 (34.6%)	1 (33.3%)	84 (35.4%)
>=75	1 (4.3%)	3 (5.5%)	16 (10.3%)	0	20 (8.4%)
Mean (SD)	62.0 (8.65)	61.2 (9.20)	62.9 (9.50)	59.0 (9.54)	62.4 (9.33)
Median	64.0	62.0	63.0	58.0	63.0
Range	(42; 76)	(38; 76)	(31; 84)	(50; 69)	(31; 84)
Sex, n (%)					
N	23	55	156	3	237
Male	14 (60.9%)	38 (69.1%)	84 (53.8%)	3 (100.0%)	139 (58.6%)
Female	9 (39.1%)	17 (30.9%)	72 (46.2%)	0	98 (41.4%)
Race, n (%)					
N	23	55	156	3	237
White	23 (100.0%)	35 (63.6%)	119 (76.3%)	3 (100.0%)	180 (75.9%)
Black or African American	0	1 (1.8%)	16 (10.3%)	0	17 (7.2%)
Asian	0	4 (7.3%)	9 (5.8%)	0	13 (5.5%)
Other	0	0	2 (1.3%)	0	2 (0.8%)
Unknown	0	0	1 (0.6%)	0	1 (0.4%)
Not reported[a]	0	15 (27.3%)	9 (5.8%)	0	24 (10.1%)
Height (cm)					
N	23	55	154	3	235
Mean (SD)	171.74 (6.503)	171.99 (11.957)	168.02 (10.407)	179.00 (4.359)	169.45 (10.606)
Median	172.00	173.00	168.00	177.00	170.00
Range	(153.0; 182.0)	(137.4; 198.0)	(139.0; 196.0)	(176.0; 184.0)	(137.4; 198.0)
Weight (kg)					
N	23	55	156	3	237
Mean (SD)	81.35 (13.547)	79.42 (19.689)	75.90 (19.473)	77.33 (12.055)	77.26 (18.975)
Median	80.00	79.40	75.50	76.00	77.10
Range	(60.0; 117.0)	(46.2; 160.2)	(38.4; 141.8)	(66.0; 90.0)	(38.4; 160.2)
Baseline ECOG score, n (%)					
N	23	55	156	3	237
0	8 (34.8%)	18 (32.7%)	46 (29.5%)	2 (66.7%)	74 (31.2%)
1	14 (60.9%)	34 (61.8%)	100 (64.1%)	1 (33.3%)	149 (62.9%)
2	1 (4.3%)	3 (5.5%)	10 (6.4%)	0	14 (5.9%)
Geographic region, n (%)					
N	23	55	156	3	237
European Union	23 (100.0%)	30 (54.5%)	40 (25.6%)	3 (100.0%)	96 (40.5%)
Japan	0	4 (7.3%)	5 (3.2%)	0	9 (3.8%)
North America	0	21 (38.2%)	111 (71.2%)	0	132 (55.7%)
Baseline renal impairment, n (%)					
N	23	55	156	3	237
Stage 1	9 (39.1%)	16 (29.1%)	44 (28.2%)	2 (66.7%)	71 (30.0%)
Stage 2	12 (52.2%)	23 (41.8%)	51 (32.7%)	0	86 (36.3%)
Stage 3	2 (8.7%)	14 (25.5%)	56 (35.9%)	1 (33.3%)	73 (30.8%)
Stage 4	0	2 (3.6%)	4 (2.6%)	0	6 (2.5%)
Stage 5	0	0	1 (0.6%)	0	1 (0.4%)
Baseline hepatic function, n (%)					
N	23	55	155	3	236
Normal	15 (65.2%)	45 (81.8%)	134 (86.5%)	3 (100.0%)	197 (83.5%)
Mild	8 (34.8%)	10 (18.2%)	21 (13.5%)	0	39 (16.5%)

[a] Includes 22 subjects from the Netherlands (Study GEN501) where race is considered personal data restricted by law; therefore, not reported.

Note: Renal impairment is classified into 5 stages by creatinine clearance: Stage 1: ≥90 ml/min; Stage 2: 60 – <90 ml/min; Stage 3: 30 – <60 ml/min; Stage 4: 15 – <30 ml/min; and Stage 5: < 15 ml/min.

Hepatic function is classified into 4 levels per NCI Organ Dysfunction criteria: Normal: total bilirubin ≤ ULN and AST ≤ ULN; Mildly Impaired: (total bilirubin ≤ ULN and AST > ULN) or (ULN < total bilirubin ≤ 1.5×ULN); Moderately Impaired: 1.5×ULN < total bilirubin ≤ 3×ULN; and Severely Impaired: total bilirubin > 3×ULN.

Modified from Appendix TSIDEM01

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の人口統計学的特性を表 2.7.4-付録-19，ベースラインの疾患特性を表 2.7.4-付録-20 に示す。

MMY1002 試験（9 例）では，年齢の中央値は 65.0 歳（範囲：47～73 歳）であり，男性が 44.4%（4 例）であった。また，ECOG の performance status スコアは 0 が 77.8%（7 例），1 が 22.2%（2 例）であった。

2.7.4.1.3.2 併用治療

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の併用薬を表 2.7.4-付録-21 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

Vd 群及び DVd 群で使用割合が高かった併用薬（いずれかの群で 40%以上）は，全身用抗菌薬（Vd 群 72.2%，DVd 群 74.5%，以下同順），全身用抗ウイルス薬（63.7%，63.4%），胃酸関連疾患用薬（46.4%，52.7%）及び鎮痛薬（40.1%，54.7%）であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Rd 群及び DRd 群で使用割合が高かった併用薬（いずれかの群で 40%以上）は，全身用抗菌薬（Rd 群 81.5%，DRd 群 83.0%，以下同順），鎮痛薬（80.4%，80.8%），胃酸関連疾患用薬（47.3%，51.9%），全身用抗ウイルス薬（41.3%，49.7%），免疫賦活薬（28.5%，48.7%）及び全身用抗ヒスタミン剤（22.4%，42.5%）であった。

MMY1001 試験（DPd 療法）

DPd 群で使用割合が高かった併用薬（40%以上）は，鎮痛薬（79.6%），全身用抗菌薬（73.8%），免疫賦活薬（57.3%），胃酸関連疾患用薬（45.6%）及び全身用抗ヒスタミン剤（43.7%）であった。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の併用薬を表 2.7.4-付録-22 に示す。

治験薬投与を受けた被験者（8 例）で使用割合が高かった併用薬（70%以上）は，胃酸関連疾患用薬（100.0%，8 例），鎮痛薬及び全身用抗ウイルス薬（各 87.5%，7 例），全身用抗菌薬（75.0%，6 例）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の併用薬を表 2.7.4-付録-23 に示す。

日本人集団（ITT 集団：Rd 群 15 例，DRd 群 21 例）で使用割合が高かった併用薬（いずれかの群で 70%以上）は，鎮痛薬（Rd 群 100.0%，DRd 群 95.2%，以下同順），胃酸関連疾患用薬（100.0%，85.7%），全身用抗菌薬（86.7%，85.7%），便秘薬（73.3%，57.1%）及び全身用抗ウイルス薬（60.0%，71.4%）であった。

東アジア人集団（ITT 集団：Rd 群 44 例，DRd 群 52 例）で使用割合が高かった併用薬（いずれかの群で 70%以上）は，鎮痛薬（Rd 群 100.0%，DRd 群 96.2%，以下同順），胃酸関連疾患用薬（90.9%，86.5%）及び全身用抗菌薬（81.8%，78.8%）であった。

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の併用薬を表 2.7.4-付録-24 に示す。

16 mg/kg 群で使用割合が高かった併用薬（40%以上）は，鎮痛薬（87.2%），全身用抗菌薬（73.7%）及び全身用抗ウイルス薬（73.1%）であった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の併用薬を表 2.7.4-付録-25 に示す。

MMY1002 試験（9 例）で使用割合が高かった併用薬（50%以上）は，その他の鎮痛薬と解熱薬，スルホンアミドとトリメトプリム及び直接作用型抗ウイルス薬が各 66.7%（6 例），全身用副腎皮質ステロイド（単味製剤）が 55.6%（5 例）であった。

2.7.4.2 有害事象

2.7.4.2.1 有害事象の解析

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験で認められた有害事象の概要を表 2.7.4-9 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

Vd 群では 95.4%，DVd 群では 98.8%の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は Vd 群が 42.2%，DVd 群が 46.1%，最悪 Grade が 4 であった有害事象を発現した被験者の割合は Vd 群が 15.2%，DVd 群が 24.7%，最悪 Grade が 5 であった有害事象を発現した被験者の割合は Vd 群が 5.9%，DVd 群が 5.3%であった。重篤な有害事象の発現割合は Vd 群が 33.8%，DVd 群が 42.0%であった。治験薬の投与中止に至った有害事象の発現割合は Vd 群が 9.3%，DVd 群が 7.4%であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Rd 群では 97.5%，DRd 群では 98.4%の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は Rd 群が 54.8%，DRd 群が 51.3%，最悪 Grade が 4 であった有害事象を発現した被験者の割合は Rd 群が 13.5%，DRd 群が 26.7%，最悪 Grade が 5 であった有害事象を発現した被験者の割合は Rd 群が 5.3%，DRd 群が 3.8%であった。重篤な有害事象の発現割合は Rd 群が 42.0%，DRd 群が 49.1%であった。治験薬の投与中止に至った有害事象の発現割合は Rd 群が 7.8%，DRd 群が 6.9%であった。

MMY1001 試験（DPd 療法）

DPd 群では 100%の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は 38.8%，最悪 Grade が 4 であった有害事象を発現した被験者の割合は 53.4%，最悪 Grade が 5 であった有害事象を発現した被験者の割合は 6.8%であった。重篤な有害事象の発現割合は 48.5%であった。治験薬の投与中止に至った有害事象の発現割合は 12.6%であった。

表 2.7.4-9 有害事象の概要［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Any TEAE	226 (95.4%)	240 (98.8%)	274 (97.5%)	313 (98.4%)	103 (100.0%)
At least one related[a]	196 (82.7%)	225 (92.6%)	233 (82.9%)	304 (95.6%)	100 (97.1%)
At least one related to daratumumab	1 (0.4%)	182 (74.9%)	0	245 (77.0%)	95 (92.2%)
Maximum severity of any TEAE					
Grade 1	17 (7.2%)	7 (2.9%)	14 (5.0%)	5 (1.6%)	0
Grade 2	59 (24.9%)	48 (19.8%)	53 (18.9%)	48 (15.1%)	1 (1.0%)
Grade 3	100 (42.2%)	112 (46.1%)	154 (54.8%)	163 (51.3%)	40 (38.8%)
Grade 4	36 (15.2%)	60 (24.7%)	38 (13.5%)	85 (26.7%)	55 (53.4%)
Grade 5	14 (5.9%)	13 (5.3%)	15 (5.3%)	12 (3.8%)	7 (6.8%)
Any serious TEAE	80 (33.8%)	102 (42.0%)	118 (42.0%)	156 (49.1%)	50 (48.5%)
At least one related[a]	37 (15.6%)	50 (20.6%)	54 (19.2%)	97 (30.5%)	23 (22.3%)
At least one related to daratumumab	0	28 (11.5%)	0	49 (15.4%)	17 (16.5%)
Treatment discontinuation due to TEAE[b]	22 (9.3%)	18 (7.4%)	22 (7.8%)	22 (6.9%)	13 (12.6%)
At least one related to any drug	12 (5.1%)	8 (3.3%)	12 (4.3%)	14 (4.4%)	7 (6.8%)
At least one related to daratumumab	0	6 (2.5%)	0	9 (2.8%)	3 (2.9%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Keys: TEAE = treatment-emergent adverse event.
[a] TEAEs related to at least 1 of the combination regimen.
[b]Treatment discontinuation due to adverse event on the end of treatment CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE01A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE01A.SAS] 01JUN2016, 15:10

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた有害事象の概要を表 2.7.4-10 に示す。

治験薬投与を受けた被験者（8 例）では 100%（8 例）の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は 62.5%（5 例），最悪 Grade が 4 であった

有害事象を発現した被験者の割合は 37.5%（3 例）であり，最悪 Grade が 5 であった有害事象を発現した被験者はいなかった。重篤な有害事象の発現割合は 37.5%（3 例）であった。本剤の投与中止に至った有害事象の発現割合は 12.5%（1 例）であった。その他の治験薬の投与中止に至った有害事象の発現割合は，ボルテゾミブが 12.5%（1 例），デキサメタゾンが 12.5%（1 例）であった。

表 2.7.4-10 有害事象の概要［MMY1005 試験，安全性解析対象集団］

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: Safety	8
Any TEAEs	8 (100.0%)
At least one related[a]	8 (100.0%)
At least one related to bortezomib	8 (100.0%)
At least one related to dexamethasone	8 (100.0%)
At least one related to daratumumab	7 (87.5%)
Maximum toxicity grade	
Grade 1	0
Grade 2	0
Grade 3	5 (62.5%)
Grade 4	3 (37.5%)
Grade 5	0
Any serious TEAE	3 (37.5%)
At least one related[a]	2 (25.0%)
At least one related to bortezomib	2 (25.0%)
At least one related to dexamethasone	2 (25.0%)
At least one related to daratumumab	2 (25.0%)
TEAE leading to discontinuation of bortezomib	1 (12.5%)
At least one related to bortezomib	0
TEAE leading to discontinuation of dexamethasone	1 (12.5%)
At least one related to dexamethasone	0
TEAE leading to discontinuation of daratumumab	1 (12.5%)
At least one related to daratumumab	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
[a] TEAEs related to at least 1 of the 3 study treatment: bortezomib, dexamethasone or daratumumab.
Note: Percentages calculated with the number of subjects in safety population as denominator.
Note: Adverse events related to study treatments are adverse events with a relationship to study treatments of very likely, probably or possible.

[TSFAE01.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE01.SAS] 28SEP2016, 04:12

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の有害事象の概要を表 2.7.4-11 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）では，100%の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は Rd 群が 53.3%，DRd 群が 55.0%，最悪 Grade が 4 であった有害事象を発現した被験者の割合は Rd 群が 20.0%，DRd 群が 40.0%，最悪 Grade が 5 であった有害事象を発現した被験者の割合は Rd 群のみ 6.7%であった。重篤な有害事象の発現割合は Rd 群が 20.0%，DRd 群が 35.0%であった。DRd 群で本剤の投与中止に至った有害事象の発現割合は 15.0%であった。その他の治験薬の投与中止に至った有害事象の発現割合は，レナリドミドでは DRd 群のみ 15.0%，デキサメタゾンでは DRd 群のみ 15.0%であった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では，100%の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は Rd 群が 59.1%，DRd 群が 58.8%，最悪 Grade が 4 であった有害事象を発現した被験者の割合は Rd 群が 15.9%，DRd 群が 27.5%，最悪 Grade が 5 であった有害事象を発現した被験者の割合は Rd 群が 4.5%，DRd 群が 3.9%であった。重篤な有害事象の発現割合は Rd 群が 40.9%，DRd 群が 35.3%であった。DRd 群で本剤の投与中止に至った有害事象の発現割合は 9.8%であった。その他の治験薬の投与中止に至った有害事象の発現割合は，レナリドミドでは Rd 群 2.3%，DRd 群 9.8%，デキサメタゾンでは Rd 群 2.3%，DRd 群 9.8%であった。

表 2.7.4-11 有害事象の概要［MMY3003 試験（日本人，東アジア人，全体），安全性解析対象集団］

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283
Any TEAE	15 (100.0%)	44 (100.0%)	274 (97.5%)	20 (100.0%)	51 (100.0%)	278 (98.2%)
At least one related[c]	15 (100.0%)	30 (68.2%)	233 (82.9%)	20 (100.0%)	48 (94.1%)	269 (95.1%)
At least one related to lenalidomide	14 (93.3%)	28 (63.6%)	218 (77.6%)	20 (100.0%)	47 (92.2%)	257 (90.8%)
At least one related to dexamethasone	15 (100.0%)	27 (61.4%)	202 (71.9%)	16 (80.0%)	32 (62.7%)	223 (78.8%)
At least one related to daratumumab	0	0	0	15 (75.0%)	39 (76.5%)	215 (76.0%)
Maximum toxicity grade						
Grade 1	0	4 (9.1%)	14 (5.0%)	0	0	5 (1.8%)
Grade 2	3 (20.0%)	5 (11.4%)	53 (18.9%)	1 (5.0%)	5 (9.8%)	44 (15.5%)
Grade 3	8 (53.3%)	26 (59.1%)	154 (54.8%)	11 (55.0%)	30 (58.8%)	143 (50.5%)
Grade 4	3 (20.0%)	7 (15.9%)	38 (13.5%)	8 (40.0%)	14 (27.5%)	75 (26.5%)
Grade 5	1 (6.7%)	2 (4.5%)	15 (5.3%)	0	2 (3.9%)	11 (3.9%)
Any serious TEAE	3 (20.0%)	18 (40.9%)	118 (42.0%)	7 (35.0%)	18 (35.3%)	138 (48.8%)
At least one related[c]	2 (13.3%)	3 (6.8%)	54 (19.2%)	4 (20.0%)	11 (21.6%)	86 (30.4%)
At least one related to lenalidomide	2 (13.3%)	3 (6.8%)	50 (17.8%)	3 (15.0%)	9 (17.6%)	72 (25.4%)
At least one related to dexamethasone	1 (6.7%)	1 (2.3%)	35 (12.5%)	4 (20.0%)	8 (15.7%)	56 (19.8%)
At least one related to daratumumab	0	0	0	2 (10.0%)	7 (13.7%)	43 (15.2%)
TEAE leading to discontinuation of lenalidomide	0	1 (2.3%)	27 (9.6%)	3 (15.0%)	5 (9.8%)	32 (11.3%)
At least one related to lenalidomide	0	0	13 (4.6%)	1 (5.0%)	3 (5.9%)	18 (6.4%)
TEAE leading to discontinuation of dexamethasone	0	1 (2.3%)	35 (12.5%)	3 (15.0%)	5 (9.8%)	29 (10.2%)
At least one related to dexamethasone	0	0	12 (4.3%)	2 (10.0%)	3 (5.9%)	15 (5.3%)
TEAE leading to discontinuation of daratumumab	0	0	0	3 (15.0%)	5 (9.8%)	25 (8.8%)
At least one related to daratumumab	0	0	0	1 (5.0%)	2 (3.9%)	9 (3.2%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
[c] TEAEs related to at least 1 of the 3 study treatment: lenalidomide, dexamethasone or daratumumab.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE01A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE01A_3003.SAS] 30JUN2016, 20:38

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた有害事象の概要を表 2.7.4-12 に示す。

16 mg/kg 群では 98.7%の被験者が有害事象を発現した。最悪 Grade が 3 であった有害事象を発現した被験者の割合は 37.8%，最悪 Grade が 4 であった有害事象を発現した被験者の割合は 12.2%，最悪 Grade が 5 であった有害事象を発現した被験者の割合は 6.4%であった。重篤な有害事象の発現割合は 32.1%であった。本剤の投与中止に至った有害事象の発現割合は 3.8%であった。

表 2.7.4-12 有害事象の概要

［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Any TEAE	22 (95.7%)	55 (100.0%)	154 (98.7%)	3 (100.0%)	234 (98.7%)
Drug-related	21 (91.3%)	48 (87.3%)	120 (76.9%)	3 (100.0%)	192 (81.0%)
Any serious TEAE	7 (30.4%)	20 (36.4%)	50 (32.1%)	2 (66.7%)	79 (33.3%)
Drug-related	4 (17.4%)	0	15 (9.6%)	1 (33.3%)	20 (8.4%)
Maximum severity of any TEAE					
Grade 1	1 (4.3%)	3 (5.5%)	10 (6.4%)	0	14 (5.9%)
Grade 2	12 (52.2%)	21 (38.2%)	56 (35.9%)	2 (66.7%)	91 (38.4%)
Grade 3	7 (30.4%)	21 (38.2%)	59 (37.8%)	1 (33.3%)	88 (37.1%)
Grade 4	1 (4.3%)	10 (18.2%)	19 (12.2%)	0	30 (12.7%)
Grade 5	1 (4.3%)	0	10 (6.4%)	0	11 (4.6%)
Treatment discontinuation due to TEAE[a]	4 (17.4%)	0	6 (3.8%)	1 (33.3%)	11 (4.6%)
Drug-related	4 (17.4%)	0	0	1 (33.3%)	5 (2.1%)
Death due to TEAE[b]	0	0	3 (1.9%)	0	3 (1.3%)
Drug-related	0	0	0	0	0

Keys: TEAE = treatment-emergent adverse event.
[a]Treatment discontinuation due to adverse event on the end of treatment CRF page.
[b]Death due to adverse event on the death CRF page.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE01.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae01.sas] 03APR2015, 12:27

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験で認められた有害事象の概要を表 2.7.4-13 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では 100%の被験者が有害事象を発現した。最悪 Grade が 3 以上の有害事象を発現した被験者の割合は 8 mg/kg 群が 75.0%（3 例），16 mg/kg 群が 100%（5 例）であった。重篤な有害事象の発現割合は 8 mg/kg 群が 25.0%（1 例），16 mg/kg 群が 40.0%（2 例）であった。投与中止に至った有害事象は認められなかった。

表 2.7.4-13 有害事象の概要［MMY1002 試験，全投与解析対象集団］

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Number of subjects with any TEAEs	4 (100.0%)	5 (100.0%)	9 (100.0%)
Number of subjects with any study drug related TEAEs[a]	4 (100.0%)	5 (100.0%)	9 (100.0%)
Number of subjects with any TEAEs of Toxicity Grade 3 or Higher	3 (75.0%)	5 (100.0%)	8 (88.9%)
Number of subjects with any serious TEAEs	1 (25.0%)	2 (40.0%)	3 (33.3%)
Number of subjects with any TEAEs leading to study drug discontinuation	0	0	0
Number of subjects with any TEAEs leading to death	0	0	0
Number of subjects with any infusion-related reactions	1 (25.0%)	3 (60.0%)	4 (44.4%)

Key: TEAEs = treatment-emergent adverse events
[a] Adverse events whose causal relationship to the investigational medication were judged as ("possible", "probable", or "very likely") by the investigator.

[TSFAE01.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae01.sas] 19FEB2016, 10:44

2.7.4.2.1.1 比較的よく見られる有害事象

(1) 併用療法試験

1) 有害事象の要約

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験において，いずれかの群で 10%以上に認められた有害事象を表 2.7.4-14 に示す。また，すべての有害事象を表 2.7.4-付録-26 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

Vd 群及び DVd 群で発現割合が高かった有害事象（いずれかの群で 30%以上）は，血小板減少症（Vd 群 43.9%，DVd 群 58.8%，以下同順），末梢性感覚ニューロパチー（37.6%，47.3%），下痢（22.4%，31.7%）及び貧血（31.2%，26.3%）であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Rd 群及び DRd 群で発現割合が高かった有害事象（いずれかの群で 30%以上）は，好中球減少症（Rd 群 43.1%，DRd 群 61.9%，以下同順），下痢（24.6%，42.8%），疲労（27.8%，35.2%），咳嗽（12.5%，31.1%），上気道感染（20.6%，30.8%）及び貧血（34.9%，30.5%）であった。

MMY1001 試験（DPd 療法）

DPd 群で発現割合が高かった有害事象（30%以上）は，好中球減少症（78.6%），貧血（52.4%），疲労（49.5%），血小板減少症（40.8%），下痢（37.9%），白血球減少症（36.9%），咳嗽（35.9%），便秘（33.0%），呼吸困難及び悪心（各 30.1%）であった。

表 2.7.4-14 10%以上に認められた有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with TEAE	226 (95.4%)	240 (98.8%)	274 (97.5%)	313 (98.4%)	103 (100.0%)
MedDRA system organ class / Preferred term					
感染症および寄生虫症	126 (53.2%)	164 (67.5%)	204 (72.6%)	265 (83.3%)	72 (69.9%)
上気道感染	43 (18.1%)	60 (24.7%)	58 (20.6%)	98 (30.8%)	26 (25.2%)
鼻咽頭炎	9 (3.8%)	17 (7.0%)	43 (15.3%)	76 (23.9%)	8 (7.8%)
気管支炎	13 (5.5%)	28 (11.5%)	34 (12.1%)	46 (14.5%)	10 (9.7%)
肺炎	28 (11.8%)	29 (11.9%)	37 (13.2%)	41 (12.9%)	11 (10.7%)
気道感染	3 (1.3%)	0	22 (7.8%)	33 (10.4%)	0
副鼻腔炎	3 (1.3%)	10 (4.1%)	10 (3.6%)	19 (6.0%)	13 (12.6%)
胃腸障害	110 (46.4%)	143 (58.8%)	164 (58.4%)	242 (76.1%)	81 (78.6%)
下痢	53 (22.4%)	77 (31.7%)	69 (24.6%)	136 (42.8%)	39 (37.9%)
便秘	37 (15.6%)	48 (19.8%)	71 (25.3%)	90 (28.3%)	34 (33.0%)
悪心	26 (11.0%)	34 (14.0%)	40 (14.2%)	77 (24.2%)	31 (30.1%)
嘔吐	9 (3.8%)	26 (10.7%)	15 (5.3%)	51 (16.0%)	22 (21.4%)
血液およびリンパ系障害	135 (57.0%)	163 (67.1%)	184 (65.5%)	231 (72.6%)	91 (88.3%)
好中球減少症	22 (9.3%)	43 (17.7%)	121 (43.1%)	197 (61.9%)	81 (78.6%)
貧血	74 (31.2%)	64 (26.3%)	98 (34.9%)	97 (30.5%)	54 (52.4%)
血小板減少症	104 (43.9%)	143 (58.8%)	77 (27.4%)	86 (27.0%)	42 (40.8%)
白血球減少症	11 (4.6%)	19 (7.8%)	17 (6.0%)	28 (8.8%)	38 (36.9%)
リンパ球減少症	9 (3.8%)	32 (13.2%)	15 (5.3%)	21 (6.6%)	22 (21.4%)
一般・全身障害および投与部位の状態	123 (51.9%)	131 (53.9%)	156 (55.5%)	226 (71.1%)	82 (79.6%)
疲労	58 (24.5%)	52 (21.4%)	78 (27.8%)	112 (35.2%)	51 (49.5%)
発熱	27 (11.4%)	38 (15.6%)	31 (11.0%)	67 (21.1%)	26 (25.2%)
末梢性浮腫	19 (8.0%)	40 (16.5%)	37 (13.2%)	54 (17.0%)	16 (15.5%)
無力症	37 (15.6%)	21 (8.6%)	36 (12.8%)	50 (15.7%)	15 (14.6%)
悪寒	3 (1.3%)	11 (4.5%)	9 (3.2%)	18 (5.7%)	21 (20.4%)
非心臓性胸痛	1 (0.4%)	1 (0.4%)	5 (1.8%)	11 (3.5%)	15 (14.6%)
疼痛	5 (2.1%)	9 (3.7%)	4 (1.4%)	4 (1.3%)	11 (10.7%)
呼吸器、胸郭および縦隔障害	77 (32.5%)	130 (53.5%)	114 (40.6%)	196 (61.6%)	80 (77.7%)
咳嗽	30 (12.7%)	58 (23.9%)	35 (12.5%)	99 (31.1%)	37 (35.9%)
呼吸困難	21 (8.9%)	45 (18.5%)	32 (11.4%)	56 (17.6%)	31 (30.1%)
鼻閉	3 (1.3%)	12 (4.9%)	4 (1.4%)	16 (5.0%)	16 (15.5%)
湿性咳嗽	3 (1.3%)	9 (3.7%)	8 (2.8%)	16 (5.0%)	12 (11.7%)
筋骨格系および結合組織障害	87 (36.7%)	111 (45.7%)	154 (54.8%)	187 (58.8%)	74 (71.8%)
筋痙縮	5 (2.1%)	19 (7.8%)	52 (18.5%)	90 (28.3%)	27 (26.2%)
背部痛	24 (10.1%)	33 (13.6%)	48 (17.1%)	57 (17.9%)	26 (25.2%)
関節痛	11 (4.6%)	23 (9.5%)	21 (7.5%)	26 (8.2%)	23 (22.3%)
四肢痛	16 (6.8%)	22 (9.1%)	30 (10.7%)	26 (8.2%)	15 (14.6%)
骨痛	14 (5.9%)	14 (5.8%)	12 (4.3%)	24 (7.5%)	13 (12.6%)
筋骨格系胸痛	5 (2.1%)	16 (6.6%)	17 (6.0%)	16 (5.0%)	13 (12.6%)
神経系障害	131 (55.3%)	153 (63.0%)	124 (44.1%)	160 (50.3%)	62 (60.2%)
頭痛	14 (5.9%)	25 (10.3%)	19 (6.8%)	43 (13.5%)	17 (16.5%)
末梢性感覚ニューロパチー	89 (37.6%)	115 (47.3%)	19 (6.8%)	31 (9.7%)	8 (7.8%)
振戦	8 (3.4%)	3 (1.2%)	24 (8.5%)	28 (8.8%)	20 (19.4%)
浮動性めまい	24 (10.1%)	24 (9.9%)	24 (8.5%)	24 (7.5%)	22 (21.4%)
神経痛	26 (11.0%)	33 (13.6%)	3 (1.1%)	4 (1.3%)	1 (1.0%)
代謝および栄養障害	66 (27.8%)	93 (38.3%)	95 (33.8%)	127 (39.9%)	49 (47.6%)
食欲減退	12 (5.1%)	22 (9.1%)	29 (10.3%)	34 (10.7%)	11 (10.7%)
低カリウム血症	11 (4.6%)	22 (9.1%)	22 (7.8%)	33 (10.4%)	16 (15.5%)
高血糖	18 (7.6%)	21 (8.6%)	19 (6.8%)	27 (8.5%)	13 (12.6%)

表 2.7.4-14 10%以上に認められた有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
皮膚および皮下組織障害	32 (13.5%)	49 (20.2%)	83 (29.5%)	125 (39.3%)	39 (37.9%)
発疹	7 (3.0%)	13 (5.3%)	29 (10.3%)	38 (11.9%)	3 (2.9%)
そう痒症	3 (1.3%)	5 (2.1%)	29 (10.3%)	29 (9.1%)	10 (9.7%)
精神障害	53 (22.4%)	67 (27.6%)	93 (33.1%)	106 (33.3%)	47 (45.6%)
不眠症	35 (14.8%)	41 (16.9%)	55 (19.6%)	60 (18.9%)	24 (23.3%)
不安	6 (2.5%)	3 (1.2%)	12 (4.3%)	18 (5.7%)	13 (12.6%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02I.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE02I.SAS] 01JUN2016, 10:36

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた有害事象を表 2.7.4-付録-27 に示す。

治験薬投与を受けた被験者（8 例）で発現割合が高かった有害事象（30%以上）は，血小板減少症（87.5%，7 例），リンパ球減少症（62.5%，5 例），貧血，白血球減少症，好中球減少症，疲労，高血糖，異常感覚，血中乳酸脱水素酵素増加及び体重減少（各 37.5%，3 例）であった。

日本人被験者で MMY3004 試験の DVd 群に比べて発現割合が 20%以上高かった有害事象は，血小板減少症（MMY1005 試験 87.5%，MMY3004 試験 58.8%，以下同順），リンパ球減少症（62.5%，13.2%），異常感覚（37.5%，0.8%），血中乳酸脱水素酵素増加（37.5%，1.2%），体重減少（37.5%，5.3%），白血球減少症（37.5%，7.8%），高血糖（37.5%，8.6%），低酸素症（25.0%，0%），脱水（25.0%，1.2%），胃炎（25.0%，1.6%），喘鳴（25.0%，2.1%）及び悪寒（25.0%，4.5%）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の有害事象を表 2.7.4-付録-28 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）で発現割合が高かった有害事象（いずれかの群で 30%以上）は，好中球減少症（Rd 群 40.0%，DRd 群 60.0%，以下同順），鼻咽頭炎（26.7%，45.0%），リンパ球減少症（53.3%，40.0%），便秘（33.3%，40.0%）及び血小板減少症（40.0%，15.0%）であった。日本人集団で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かった有害事象は，Rd 群ではリンパ球減少症（日本人集団 53.3%，全体集団 5.3%，以下同順），血小板減少症（40.0%，27.4%），鼻咽頭炎（26.7%，15.3%），末梢性感覚ニューロパチー（20.0%，6.8%），γ－グルタミルトランスフェラーゼ増加（13.3%，2.5%），高尿酸血症（13.3%，2.8%）及びしゃっくり（13.3%，3.2%），DRd 群では鼻咽頭炎（45.0%，24.0%），リンパ球減少症（40.0%，6.0%），便秘（40.0%，29.3%），ALT 増加（25.0%，5.3%），味覚異常（20.0%，7.4%），高血糖（20.0%，8.8%），血中アルカリホスファターゼ増加（15.0%，2.1%），しゃっ

くり（15.0%，2.8%），AST 増加（15.0%，3.2%），皮膚乾燥（15.0%，3.5%）及び末梢性ニューロパチー（15.0%，4.2%）であった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）で発現割合が高かった有害事象（いずれかの群で 30%以上）は，好中球減少症（Rd 群 43.2%，DRd 群 66.7%，以下同順），上気道感染（40.9%，43.1%），便秘（31.8%，41.2%），鼻咽頭炎（20.5%，33.3%）及び下痢（13.6%，31.4%）であった。東アジア人集団で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かった有害事象は，Rd 群では上気道感染（東アジア人集団 40.9%，全体集団 20.6%，以下同順），食欲減退（25.0%，10.3%）及びリンパ球減少症（18.2%，5.3%），DRd 群では上気道感染（43.1%，31.8%），便秘（41.2%，29.3%）及び白血球減少症（19.6%，7.4%）であった。

2) Grade 3 又は 4 の有害事象

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験において，いずれかの群で 5%以上に認められた Grade 3 又は 4 の有害事象を表 2.7.4-15 に示す。また，すべての Grade 3 又は 4 の有害事象を表 2.7.4-付録-29 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

Grade 3 又は 4 の有害事象の発現割合は，Vd 群が 62.4%，DVd 群が 76.1%であった。発現割合が高かった Grade 3 又は 4 の有害事象（いずれかの群で 10%以上）は，血小板減少症（Vd 群 32.9%，DVd 群 45.3%，以下同順），貧血（16.0%，14.4%）及び好中球減少症（4.2%，12.8%）であり，いずれも SOC が血液及びリンパ系障害であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Grade 3 又は 4 の有害事象の発現割合は，Rd 群が 73.3%，DRd 群が 81.8%であった。発現割合が高かった Grade 3 又は 4 の有害事象（いずれかの群で 10%以上）は，好中球減少症（Rd 群 37.0%，DRd 群 54.7%，以下同順），血小板減少症（13.5%，12.6%）及び貧血（19.6%，12.3%）であり，いずれも SOC が血液及びリンパ系障害であった。

MMY1001 試験（DPd 療法）

DPd 群で認められた Grade 3 又は 4 の有害事象の発現割合は 99.0%であった。発現割合が高かった Grade 3 又は 4 の有害事象（10%以上）は，好中球減少症（76.7%），貧血（27.2%），白血球減少症（24.3%），血小板減少症（17.5%）及びリンパ球減少症（13.6%）であり，いずれも SOC が血液及びリンパ系障害であった。

表 2.7.4-15 5%以上に認められた Grade 3 又は 4 の有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with toxicity grade 3 or 4 TEAE	148 (62.4%)	185 (76.1%)	206 (73.3%)	260 (81.8%)	102 (99.0%)
MedDRA system organ class/Preferred term					
血液およびリンパ系障害	94 (39.7%)	131 (53.9%)	145 (51.6%)	191 (60.1%)	87 (84.5%)
好中球減少症	10 (4.2%)	31 (12.8%)	104 (37.0%)	174 (54.7%)	79 (76.7%)
血小板減少症	78 (32.9%)	110 (45.3%)	38 (13.5%)	40 (12.6%)	18 (17.5%)
貧血	38 (16.0%)	35 (14.4%)	55 (19.6%)	39 (12.3%)	28 (27.2%)
リンパ球減少症	6 (2.5%)	23 (9.5%)	10 (3.6%)	19 (6.0%)	14 (13.6%)
発熱性好中球減少症	1 (0.4%)	4 (1.6%)	7 (2.5%)	17 (5.3%)	7 (6.8%)
白血球減少症	4 (1.7%)	5 (2.1%)	7 (2.5%)	11 (3.5%)	25 (24.3%)
感染症および寄生虫症	45 (19.0%)	52 (21.4%)	64 (22.8%)	86 (27.0%)	29 (28.2%)
肺炎	23 (9.7%)	20 (8.2%)	23 (8.2%)	23 (7.2%)	8 (7.8%)
代謝および栄養障害	24 (10.1%)	33 (13.6%)	27 (9.6%)	43 (13.5%)	16 (15.5%)
高血糖	6 (2.5%)	8 (3.3%)	9 (3.2%)	10 (3.1%)	6 (5.8%)
一般・全身障害および投与部位の状態	22 (9.3%)	19 (7.8%)	21 (7.5%)	36 (11.3%)	15 (14.6%)
疲労	8 (3.4%)	11 (4.5%)	7 (2.5%)	18 (5.7%)	10 (9.7%)
呼吸器、胸郭および縦隔障害	11 (4.6%)	27 (11.1%)	18 (6.4%)	27 (8.5%)	19 (18.4%)
呼吸困難	2 (0.8%)	9 (3.7%)	2 (0.7%)	9 (2.8%)	7 (6.8%)
胃腸障害	9 (3.8%)	18 (7.4%)	16 (5.7%)	26 (8.2%)	8 (7.8%)
下痢	3 (1.3%)	9 (3.7%)	9 (3.2%)	16 (5.0%)	3 (2.9%)
神経系障害	25 (10.5%)	23 (9.5%)	15 (5.3%)	21 (6.6%)	13 (12.6%)
末梢性感覚ニューロパチー	16 (6.8%)	11 (4.5%)	1 (0.4%)	2 (0.6%)	2 (1.9%)
血管障害	11 (4.6%)	21 (8.6%)	8 (2.8%)	19 (6.0%)	6 (5.8%)
高血圧	2 (0.8%)	16 (6.6%)	1 (0.4%)	12 (3.8%)	3 (2.9%)
筋骨格系および結合組織障害	12 (5.1%)	18 (7.4%)	18 (6.4%)	18 (5.7%)	18 (17.5%)
背部痛	3 (1.3%)	3 (1.2%)	4 (1.4%)	4 (1.3%)	6 (5.8%)
傷害、中毒および処置合併症	5 (2.1%)	7 (2.9%)	9 (3.2%)	5 (1.6%)	10 (9.7%)
転倒	0	0	1 (0.4%)	0	6 (5.8%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE03I.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE03I.SAS] 01JUN2016, 10:37

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた Grade 3 又は 4 の有害事象を表 2.7.4-付録-30 に示す。

治験薬投与を受けた被験者（8 例）で認められた Grade 3 又は 4 の有害事象の発現割合は 100%（8 例）であった。そのうち 2 例以上に認められた Grade 3 又は 4 の有害事象は，血小板減少症（75.0%，6 例），リンパ球減少症（62.5%，5 例），白血球減少症，好中球減少症，高血糖及び低カリウム血症（各 25.0%，2 例）であった。

日本人被験者で MMY3004 試験の DVd 群に比べて発現割合が 20%以上高かった Grade 3 又は 4 の有害事象は，血小板減少症（MMY1005 試験 75.0%，MMY3004 試験 45.3%，以下同順），リン

パ球減少症（62.5%，9.5%），白血球減少症（25.0%，2.1%），低カリウム血症（25.0%，2.5%）及び高血糖（25.0%，3.3%）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の Grade 3 又は 4 の有害事象を表 2.7.4-付録-31 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）で認められた Grade 3 又は 4 の有害事象の発現割合は，Rd 群が 80.0%，DRd 群が 95.0%であった。発現割合が高かった Grade 3 又は 4 の有害事象（いずれかの群で 10%以上）は，好中球減少症（Rd 群 26.7%，DRd 群 55.0%，以下同順），リンパ球減少症（46.7%，40.0%），ALT 増加（0%，15.0%），肺炎（13.3%，10.0%），高血糖及びγ－グルタミルトランスフェラーゼ増加（各 0%，各 10.0%），血小板減少症及び貧血（各 13.3%，各 5.0%）であった。日本人集団で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かった Grade 3 又は 4 の有害事象は，Rd 群ではリンパ球減少症（日本人集団 46.7%，全体集団 3.6%，以下同順），DRd 群ではリンパ球減少症（40.0%，5.3%）及び ALT 増加（15.0%，2.5%）であった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）で認められた Grade 3 又は 4 の有害事象の発現割合は，Rd 群が 79.5%，DRd 群が 90.2%であった。発現割合が高かった Grade 3 又は 4 の有害事象（いずれかの群で 10%以上）は，好中球減少症（Rd 群 38.6%，DRd 群 62.7%，以下同順），リンパ球減少症（15.9%，15.7%），血小板減少症（15.9%，9.8%）及び貧血（25.0%，7.8%）であり，いずれも SOC が血液及びリンパ系障害であった。東アジア人集団で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かった Grade 3 又は 4 の有害事象は，Rd 群ではリンパ球減少症（東アジア人集団 15.9%，全体集団 3.6%，以下同順），DRd 群では好中球減少症（62.7%，51.9%）及びリンパ球減少症（15.7%，5.3%）であった。

3) 治験薬と関連性がある有害事象

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験で認められた治験薬と関連性がある有害事象を表 2.7.4-付録-32 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

DVd 群で発現割合が高かった本剤と関連性がある有害事象（10%以上）は，血小板減少症（30.0%），呼吸困難（13.2%），咳嗽及び疲労（各 11.1%），リンパ球減少症（10.7%）であった。また，Vd 群及び DVd 群で発現割合が高かったその他の治験薬と関連性がある有害事象（いずれかの群で 25%以上）は，血小板減少症（Vd 群 33.8%，DVd 群 51.0%，以下同順）及び末梢性感覚ニューロパチー（35.4%，47.3%）であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

DRd 群で発現割合が高かった本剤と関連性がある有害事象（10%以上）は，好中球減少症（18.9%），咳嗽（13.5%），疲労（12.3%），呼吸困難及び下痢（各 10.7%）であった。また，Rd 群及び DRd 群で発現割合が高かったその他の治験薬と関連性がある有害事象（いずれかの群

で 25%以上）は，好中球減少症（Rd 群 38.1%，DRd 群 57.9%，以下同順），疲労（19.9%，28.6%）及び下痢（10.7%，28.6%）であった。

MMY1001 試験（DPd 療法）

DPd 群で発現割合が高かった本剤と関連性がある有害事象（25%以上）は，好中球減少症（43.7%），貧血（31.1%），血小板減少症（26.2%），白血球減少症及び疲労（各 25.2%）であった。また，発現割合が高かったその他の治験薬と関連性がある有害事象（25%以上）は，好中球減少症（75.7%），貧血（41.7%），疲労（40.8%），白血球減少症（35.9%）及び血小板減少症（32.0%）であった。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた治験薬と関連性がある有害事象を表 2.7.4-付録-33 に示す。

治験薬投与を受けた被験者（8 例）で発現割合が高かった本剤と関連性がある有害事象（30%以上）は，血小板減少症（75.0%，6 例），リンパ球減少症（62.5%，5 例），白血球減少症及び好中球減少症（各 37.5%，3 例）であった。

日本人被験者で MMY3004 試験の DVd 群に比べて発現割合が 20%以上高かった本剤と関連性がある有害事象は，血小板減少症（MMY1005 試験 75.0%，MMY3004 試験 30.0%，以下同順），リンパ球減少症（62.5%，10.7%），白血球減少症（37.5%，4.1%），好中球減少症（37.5%，7.0%），低酸素症（25.0%，0%），異常感覚（25.0%，0%），体重減少（25.0%，1.2%），喘鳴（25.0%，2.1%）及び悪寒（25.0%，4.1%）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）で認められた治験薬と関連性がある有害事象を表 2.7.4-付録-34 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）において，DRd 群で発現割合が高かった本剤と関連性がある有害事象（15%以上）は，好中球減少症及びリンパ球減少症（各 20.0%），ALT 増加（15.0%）であった。日本人集団の DRd 群で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かった本剤と関連性がある有害事象は，リンパ球減少症（日本人集団 20.0%，全体集団 2.5%，以下同順）及び ALT 増加（15.0%，1.8%）であった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）において，DRd 群で発現割合が高かった本剤と関連性がある有害事象（15%以上）は，好中球減少症（19.6%）及び白血球減少症（15.7%）であった。東アジア人集団の DRd 群で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かった本剤と関連性がある有害事象は，白血球減少症（東アジア人集団 15.7%，全体集団 3.9%）であった。

(2) 単剤療法試験

1) 有害事象の要約

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合において，16 mg/kg 群で 10%以上に認められた有害事象（全 Grade，Grade 3 又は 4）を表 2.7.4-16 に示す。また，すべての有害事象を表 2.7.4-付録-35，Grade 別（すべての Grade）の有害事象を表 2.7.4-付録-36，初回発現までの期間別（≤6 カ月，>6 カ月）の有害事象を表 2.7.4-付録-37 に示す。

16 mg/kg 群で発現割合が高かった有害事象（20%以上）は，疲労（37.8%），悪心（25.6%），貧血（25.0%），好中球減少症（21.8%）及び背部痛（21.2%）であった。

表 2.7.4-16 10%以上に認められた有害事象［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with TEAEs	22 (95.7%)	8 (34.8%)	55 (100.0%)	31 (56.4%)	154 (98.7%)	87 (55.8%)	3 (100.0%)	1 (33.3%)	234 (98.7%)	127 (53.6%)
MedDRA system organ class/Preferred term										
一般・全身障害および投与部位の状態	11 (47.8%)	0	36 (65.5%)	6 (10.9%)	106 (67.9%)	10 (6.4%)	0	0	153 (64.6%)	16 (6.8%)
疲労	2 (8.7%)	0	20 (36.4%)	1 (1.8%)	59 (37.8%)	3 (1.9%)	0	0	81 (34.2%)	4 (1.7%)
発熱	8 (34.8%)	0	20 (36.4%)	1 (1.8%)	29 (18.6%)	2 (1.3%)	0	0	57 (24.1%)	3 (1.3%)
悪寒	0	0	9 (16.4%)	1 (1.8%)	16 (10.3%)	0	0	0	25 (10.5%)	1 (0.4%)
呼吸器、胸郭および縦隔障害	8 (34.8%)	1 (4.3%)	32 (58.2%)	1 (1.8%)	95 (60.9%)	8 (5.1%)	2 (66.7%)	0	137 (57.8%)	10 (4.2%)
咳嗽	5 (21.7%)	0	12 (21.8%)	0	31 (19.9%)	0	1 (33.3%)	0	49 (20.7%)	0
鼻閉	0	0	5 (9.1%)	0	25 (16.0%)	0	1 (33.3%)	0	31 (13.1%)	0
呼吸困難	1 (4.3%)	0	11 (20.0%)	0	22 (14.1%)	1 (0.6%)	0	0	34 (14.3%)	1 (0.4%)
筋骨格系および結合組織障害	6 (26.1%)	1 (4.3%)	30 (54.5%)	5 (9.1%)	89 (57.1%)	12 (7.7%)	1 (33.3%)	0	126 (53.2%)	18 (7.6%)
背部痛	1 (4.3%)	0	8 (14.5%)	3 (5.5%)	33 (21.2%)	3 (1.9%)	1 (33.3%)	0	43 (18.1%)	6 (2.5%)
関節痛	2 (8.7%)	0	5 (9.1%)	0	25 (16.0%)	0	0	0	32 (13.5%)	0
四肢痛	1 (4.3%)	0	1 (1.8%)	0	23 (14.7%)	1 (0.6%)	0	0	25 (10.5%)	1 (0.4%)
筋骨格系胸痛	0	0	5 (9.1%)	0	16 (10.3%)	2 (1.3%)	0	0	21 (8.9%)	2 (0.8%)
胃腸障害	9 (39.1%)	0	27 (49.1%)	1 (1.8%)	85 (54.5%)	3 (1.9%)	2 (66.7%)	0	123 (51.9%)	4 (1.7%)
悪心	3 (13.0%)	0	10 (18.2%)	1 (1.8%)	40 (25.6%)	0	0	0	53 (22.4%)	1 (0.4%)
下痢	2 (8.7%)	0	13 (23.6%)	0	24 (15.4%)	0	1 (33.3%)	0	40 (16.9%)	0
便秘	1 (4.3%)	0	6 (10.9%)	0	22 (14.1%)	0	0	0	29 (12.2%)	0
嘔吐	1 (4.3%)	0	8 (14.5%)	1 (1.8%)	20 (12.8%)	0	1 (33.3%)	0	30 (12.7%)	1 (0.4%)
感染症および寄生虫症	7 (30.4%)	0	32 (58.2%)	4 (7.3%)	85 (54.5%)	15 (9.6%)	1 (33.3%)	1 (33.3%)	125 (52.7%)	20 (8.4%)
上気道感染	0	0	12 (21.8%)	0	27 (17.3%)	1 (0.6%)	0	0	39 (16.5%)	1 (0.4%)
鼻咽頭炎	2 (8.7%)	0	9 (16.4%)	0	18 (11.5%)	0	1 (33.3%)	0	30 (12.7%)	0
血液およびリンパ系障害	9 (39.1%)	2 (8.7%)	21 (38.2%)	16 (29.1%)	76 (48.7%)	53 (34.0%)	0	0	106 (44.7%)	71 (30.0%)
貧血	4 (17.4%)	1 (4.3%)	12 (21.8%)	6 (10.9%)	39 (25.0%)	27 (17.3%)	0	0	55 (23.2%)	34 (14.3%)
好中球減少症	1 (4.3%)	1 (4.3%)	3 (5.5%)	1 (1.8%)	34 (21.8%)	19 (12.2%)	0	0	38 (16.0%)	21 (8.9%)
血小板減少症	3 (13.0%)	2 (8.7%)	10 (18.2%)	8 (14.5%)	31 (19.9%)	22 (14.1%)	0	0	44 (18.6%)	32 (13.5%)
代謝および栄養障害	2 (8.7%)	0	16 (29.1%)	7 (12.7%)	64 (41.0%)	13 (8.3%)	0	0	82 (34.6%)	20 (8.4%)
食欲減退	1 (4.3%)	0	5 (9.1%)	0	23 (14.7%)	1 (0.6%)	0	0	29 (12.2%)	1 (0.4%)
高カルシウム血症	0	0	4 (7.3%)	2 (3.6%)	18 (11.5%)	5 (3.2%)	0	0	22 (9.3%)	7 (3.0%)

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

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MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験で認められた Grade 別の有害事象を表 2.7.4-付録-38，8 mg/kg 群及び 16 mg/kg 群での初回発現までの期間別の有害事象をそれぞれ表 2.7.4-付録-39 及び表 2.7.4-付録-40 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で発現割合が高かった有害事象（いずれかの群で 2 例以上）は，リンパ球減少症［8 mg/kg 群：100%（4 例），16 mg/kg 群：100%（5 例）］，好中球減少症［8 mg/kg 群：50%（2 例），16 mg/kg 群：100%（5 例）］，発熱［8 mg/kg 群：25.0%（1 例），16 mg/kg 群：60.0%（3 例）］及び白血球減少症［8 mg/kg 群：0%（0 例），16 mg/kg 群：60.0%（3 例）］であった。

2) Grade 3 又は 4 の有害事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた有害事象（全 Grade，Grade 3 又は 4）を表 2.7.4-付録-41 に示す。

16 mg/kg 群で認められた Grade 3 又は 4 の有害事象の発現割合は 55.8%（87 例）であった。発現割合が高かった Grade 3 又は 4 の有害事象（10%以上）は，貧血（17.3%），血小板減少症（14.1%）及び好中球減少症（12.2%）であり，いずれも SOC が血液及びリンパ系障害であった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で認められた Grade 3 又は 4 の有害事象の発現割合は 8 mg/kg 群が 75.0%（3 例），16 mg/kg 群が 100%（5 例）であった。発現割合が高かった Grade 3 又は 4 の有害事象（いずれかの群で 2 例以上）は，リンパ球減少症［8 mg/kg 群：50%（2 例），16 mg/kg 群：100%（5 例）］，好中球減少症［8 mg/kg 群：0%（0 例），16 mg/kg 群：80.0%（4 例）］及び白血球減少症［8 mg/kg 群：0%（0 例），16 mg/kg 群：60.0%（3 例）］であった（表 2.7.4-付録-38）。

3) 本剤と関連性がある有害事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた本剤と関連性がある有害事象を表 2.7.4-付録-42 に示す。

16 mg/kg 群で発現割合が高かった本剤と関連性がある有害事象（10%以上）は，疲労（19.2%），悪心（14.1%），貧血（12.2%），鼻閉，好中球減少症及び血小板減少症（各 10.9%）であった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験で認められた本剤と関連性がある有害事象を表 2.7.4-付録-43 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で発現割合が高かった本剤と関連性がある有害事象（いずれかの群で 2 例以上）は，リンパ球減少症［8 mg/kg 群：100%（4 例），16 mg/kg 群：100%（5 例）］，好中球減少症［8 mg/kg 群：0%（0 例），16 mg/kg 群：100%（5 例）］，発熱［8 mg/kg 群：25.0%（1 例），16 mg/kg 群：60.0%（3 例）］，白血球減少症［8 mg/kg 群：0%（0 例），16 mg/kg 群：60.0%（3 例）］であった。

2.7.4.2.1.2 死亡

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験で認められた死亡例及び主な死因の概要を表 2.7.4-17 に示す。また，各試験で認められた死亡例の一覧を表 2.7.4-付録-44 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

治験薬の最終投与後 30 日以内に死亡した被験者の割合は，Vd 群が 5.5%（13 例），DVd 群が 5.3%（13 例）であった。有害事象による死亡は Vd 群が 4.2%（10 例），DVd 群が 4.5%（11 例）であり，疾患進行による死亡は Vd 群が 1.3%（3 例），DVd 群が 0.8%（2 例）であった。治験薬の初回投与後 60 日以内に死亡した被験者の割合は，Vd 群が 3.8%（9 例），DVd 群が 2.9%（7 例）であった。死因は両群とも有害事象が最も多く，Vd 群が 2.1%（5 例），DVd 群が 2.9%（7 例）であった。

死亡に至った有害事象を発現した被験者の割合は，Vd 群が 5.9%（14 例），DVd 群が 5.3%（13 例）であった（表 2.7.4-付録-45）。そのうち 2 例以上に認められた死亡に至った有害事象は，Vd 群では全身健康状態低下（3 例）及び肺炎（2 例），DVd 群では呼吸不全及び虚血性脳卒中（各 2 例）であり，それ以外の事象はすべて 1 例のみで認められた（表 2.7.4-付録-45，表 2.7.4-付録-46）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

治験薬の最終投与後 30 日以内に死亡した被験者の割合は，Rd 群が 5.7%（16 例），DRd 群が 4.1%（13 例）であった。有害事象による死亡は Rd 群が 4.3%（12 例），DRd 群が 3.8%（12 例）であり，疾患進行による死亡は Rd 群が 1.4%（4 例），DRd 群が 0.3%（1 例）であった。治験薬の初回投与後 60 日以内に死亡した被験者の割合は，Rd 群が 2.5%（7 例），DRd 群が 0.9%（3 例）であった。死因は両群とも有害事象が最も多く，Rd 群が 2.1%（6 例），DRd 群が 0.9%（3 例）であった。

死亡に至った有害事象を発現した被験者の割合は，Rd 群が 5.3%（15 例），DRd 群が 3.8%（12 例）であった（表 2.7.4-付録-45）。そのうち 2 例以上に認められた死亡に至った有害事象は，Rd 群では急性腎不全（3 例）及び肺炎（2 例），DRd 群では敗血症性ショック（3 例）及び肺炎（2 例）であり，それ以外の事象はすべて 1 例のみで認められた（表 2.7.4-付録-45，表 2.7.4-付録-46）。

MMY1001 試験（DPd 療法）

DPd 群で治験薬の最終投与後 30 日以内に死亡した被験者の割合は 6.8%（7 例）であり，有害事象による死亡は 4.9%（5 例），疾患進行による死亡は 1.9%（2 例）であった。治験薬の初回投与後 60 日以内に死亡した被験者の割合は 6.8%（7 例）であり，死因は有害事象 4.9%（5 例）が最も多かった。

DPd 群で死亡に至った有害事象を発現した被験者の割合は 6.8%（7 例）であった（表 2.7.4-付録-45）。そのうち 2 例以上に認められた死亡に至った有害事象はなく，すべて 1 例のみで認められた（表 2.7.4-付録-45，表 2.7.4-付録-46）。

表 2.7.4-17 死亡例及び主な死因の概要［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects who died within 30 days of last study treatment dose	13 (5.5%)	13 (5.3%)	16 (5.7%)	13 (4.1%)	7 (6.8%)
Adverse events	10 (4.2%)	11 (4.5%)	12 (4.3%)	12 (3.8%)	5 (4.9%)
Disease progression	3 (1.3%)	2 (0.8%)	4 (1.4%)	1 (0.3%)	2 (1.9%)
Other	0	0	0	0	0
Total number of subjects who died within 60 days of first study treatment dose	9 (3.8%)	7 (2.9%)	7 (2.5%)	3 (0.9%)	7 (6.8%)
Adverse events	5 (2.1%)	7 (2.9%)	6 (2.1%)	3 (0.9%)	5 (4.9%)
Disease progression	4 (1.7%)	0	1 (0.4%)	0	2 (1.9%)
Other	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: Percentages are calculated with the number of subjects in each group as denominator.

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日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）で死亡した被験者はいなかった（表 2.7.4-付録-47）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の死亡例及び主な死因の概要を表 2.7.4-付録-48 に示す。

日本人の ITT 集団（Rd 群 15 例，DRd 群 21 例）で治験薬の最終投与後 30 日以内に死亡した被験者の割合は，Rd 群の 6.7%（1 例）のみであった（表 2.7.4-付録-48）。日本人の安全性解析対象集団（Rd 群 15 例，DRd 群 20 例）で認められた死亡に至った有害事象は，Rd 群の急性腎不全（1 例）のみであった（表 2.7.4-付録-49）。当該被験者は，前述の治験薬の最終投与後 30 日以内に死亡した被験者であり，主な死因は疾患進行であった（表 2.7.4-付録-46）。

東アジア人の ITT 集団（Rd 群 44 例，DRd 群 52 例）で治験薬の最終投与後 30 日以内に死亡した被験者の割合は，Rd 群が 4.5%（2 例），DRd 群が 3.8%（2 例）であった。治験薬の初回投与後 60 日以内に死亡した被験者の割合は，Rd 群の 2.3%（1 例）のみであった（表 2.7.4-付録-48）。

東アジア人の安全性解析対象集団（Rd 群 44 例，DRd 群 51 例）で認められた死亡に至った有害事象は，Rd 群では急性腎不全及び敗血症（各 1 例），DRd 群では肺炎及び多臓器不全（各 1 例）であった（表 2.7.4-付録-49）。

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた死亡例及び主な死因の概要を表 2.7.4-18 に示す。また，MMY2002 試験及び GEN501 試験で認められた死亡例の一覧を表 2.7.4-付録-50 に示す。

16 mg/kg 群で本剤の最終投与後 30 日以内に死亡した被験者の割合は 9.0%（14 例）であり，疾患進行による死亡は 7.1%（11 例），有害事象による死亡は 1.9%（3 例）であった。

16 mg/kg 群で死亡に至った有害事象を発現した被験者の割合は 6.4%（10 例）であった（表 2.7.4-付録-51）。そのうち 2 例以上に認められた死亡に至った有害事象は全身健康状態低下（5 例）であり，それ以外の事象はすべて 1 例のみで認められた（表 2.7.4-付録-51）。

表 2.7.4-18 死亡例及び主な死因の概要

［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Total number of subjects died	1 (4.3%)	15 (27.3%)	40 (25.6%)	0	56 (23.6%)
Adverse event	0	0	3 (1.9%)	0	3 (1.3%)
Progressive disease	1 (4.3%)	10 (18.2%)	35 (22.4%)	0	46 (19.4%)
Other	0	5 (9.1%)	2 (1.3%)	0	7 (3.0%)
Death within 30 days of last dose	0	1 (1.8%)	14 (9.0%)	0	15 (6.3%)
Adverse event	0	0	3 (1.9%)	0	3 (1.3%)
Progressive disease	0	1 (1.8%)	11 (7.1%)	0	12 (5.1%)
Other	0	0	0	0	0

Percentages are calculated with the number of subjects in each group as denominator.

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MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，治験期間中に死亡した被験者はいなかった（表 2.7.4-付録-52）。

2.7.4.2.1.3 重篤な有害事象

(1) 併用療法試験

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験において，いずれかの群で 3%以上に認められた重篤な有害事象を表 2.7.4-19 に示す。また，すべての重篤な有害事象を表 2.7.4-付録-53，各試験で認められた重篤な有害事象の一覧を表 2.7.4-付録-54 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

重篤な有害事象の発現割合は，Vd 群が 33.8%，DVd 群が 42.0%であった。発現割合が最も高かった重篤な有害事象は，SOC 別では両群とも感染症及び寄生虫症（Vd 群 18.1%，DVd 群 19.8%），PT 別では両群とも肺炎（Vd 群 9.3%，DVd 群 7.8%）であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

重篤な有害事象の発現割合は，Rd 群が 42.0%，DRd 群が 49.1%であった。発現割合が最も高かった重篤な有害事象は，SOC 別では両群とも感染症及び寄生虫症（Rd 群 22.8%，DRd 群 29.6%），PT 別では両群とも肺炎（Rd 群 8.5%，DRd 群 7.5%）であった。

MMY1001 試験（DPd 療法）

DPd 群で認められた重篤な有害事象の発現割合は 48.5%であった。発現割合が最も高かった重篤な有害事象は，SOC 別では感染症及び寄生虫症（20.4%），PT 別では肺炎（6.8%）であった。

表 2.7.4-19 3%以上に認められた重篤な有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with serious TEAE	80 (33.8%)	102 (42.0%)	118 (42.0%)	156 (49.1%)	50 (48.5%)
MedDRA system organ class/Preferred term					
感染症および寄生虫症	43 (18.1%)	48 (19.8%)	64 (22.8%)	94 (29.6%)	21 (20.4%)
肺炎	22 (9.3%)	19 (7.8%)	24 (8.5%)	24 (7.5%)	7 (6.8%)
敗血症	2 (0.8%)	2 (0.8%)	5 (1.8%)	2 (0.6%)	4 (3.9%)
血液およびリンパ系障害	2 (0.8%)	15 (6.2%)	11 (3.9%)	21 (6.6%)	8 (7.8%)
発熱性好中球減少症	0	2 (0.8%)	4 (1.4%)	12 (3.8%)	4 (3.9%)
貧血	1 (0.4%)	8 (3.3%)	2 (0.7%)	3 (0.9%)	3 (2.9%)
一般・全身障害および投与部位の状態	12 (5.1%)	9 (3.7%)	8 (2.8%)	16 (5.0%)	4 (3.9%)
発熱	4 (1.7%)	4 (1.6%)	4 (1.4%)	10 (3.1%)	0
傷害、中毒および処置合併症	5 (2.1%)	7 (2.9%)	8 (2.8%)	8 (2.5%)	7 (6.8%)
転倒	0	0	1 (0.4%)	0	4 (3.9%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

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日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の重篤な有害事象を表 2.7.4-付録-55，重篤な有害事象の一覧を表 2.7.4-付録-56 に示す。

治験薬投与を受けた被験者（8 例）では，重篤な有害事象の発現割合は 37.5%（3 例）であり，その内訳は帯状疱疹，鼻咽頭炎及び前立腺癌が各 12.5%（1 例）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の重篤な有害事象を表 2.7.4-付録-57 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）で認められた重篤な有害事象の発現割合は，Rd 群が 20.0%（3 例），DRd 群が 35.0%（7 例）であった。そのうち 2 例以上に認められた重篤な有害事象は DRd 群の肺炎（10.0%，2 例）であり，それ以外の事象はすべて 1 例のみで認められた。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）で認められた重篤な有害事象の発現割合は，Rd 群が 40.9%，DRd 群が 35.3%であった。発現割合が最も高かった重篤な有害事象は，SOC 別では両群とも感染症及び寄生虫症（Rd 群 25.0%，DRd 群 13.7%），PT 別では両群とも肺炎（Rd 群 9.1%，DRd 群 5.9%）であった。

(2) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合において，1%以上に認められた重篤な有害事象を表 2.7.4-20 に示す。また，すべての重篤な有害事象を表 2.7.4-付録-58，MMY2002 試験及び GEN501 試験で認められた重篤な有害事象の一覧を表 2.7.4-付録-59 に示す。

16 mg/kg 群で認められた重篤な有害事象の発現割合は 32.1%であった。発現割合が最も高かった重篤な有害事象は，肺炎（5.8%）であり，次いで全身健康状態低下及び発熱（各 3.2%），高カルシウム血症（2.6%）であった。それ以外の事象はすべて 2%未満であった。

表 2.7.4-20 1%以上に認められた重篤な有害事象

［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Total number of subjects with serious TEAEs	7 (30.4%)	20 (36.4%)	50 (32.1%)	2 (66.7%)	79 (33.3%)
MedDRA system organ class / Preferred term					
感染症および寄生虫症	0	6 (10.9%)	19 (12.2%)	1 (33.3%)	26 (11.0%)
肺炎	0	3 (5.5%)	9 (5.8%)	0	12 (5.1%)
帯状疱疹	0	0	2 (1.3%)	0	2 (0.8%)
大葉性肺炎	0	0	2 (1.3%)	0	2 (0.8%)
水痘	0	0	2 (1.3%)	0	2 (0.8%)
一般・全身障害および投与部位の状態	1 (4.3%)	4 (7.3%)	13 (8.3%)	0	18 (7.6%)
全身健康状態低下	0	1 (1.8%)	5 (3.2%)	0	6 (2.5%)
発熱	1 (4.3%)	2 (3.6%)	5 (3.2%)	0	8 (3.4%)
代謝および栄養障害	0	1 (1.8%)	6 (3.8%)	0	7 (3.0%)
高カルシウム血症	0	0	4 (2.6%)	0	4 (1.7%)
筋骨格系および結合組織障害	0	2 (3.6%)	6 (3.8%)	0	8 (3.4%)
筋骨格系胸痛	0	0	2 (1.3%)	0	2 (0.8%)
臨床検査	1 (4.3%)	1 (1.8%)	4 (2.6%)	0	6 (2.5%)
交差適合試験不適合	0	0	3 (1.9%)	0	3 (1.3%)
血液およびリンパ系障害	1 (4.3%)	3 (5.5%)	3 (1.9%)	0	7 (3.0%)
貧血	1 (4.3%)	1 (1.8%)	2 (1.3%)	0	4 (1.7%)
傷害、中毒および処置合併症	1 (4.3%)	1 (1.8%)	3 (1.9%)	0	5 (2.1%)
脊椎圧迫骨折	1 (4.3%)	0	2 (1.3%)	0	3 (1.3%)
神経系障害	0	2 (3.6%)	3 (1.9%)	0	5 (2.1%)
頭痛	0	0	2 (1.3%)	0	2 (0.8%)

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

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MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の重篤な有害事象を表 2.7.4-付録-60，重篤な有害事象の一覧を表 2.7.4-付録-61 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，重篤な有害事象の発現割合は 8 mg/kg 群が 25.0%（1 例），16 mg/kg 群が 40.0%（2 例）であり，その内訳は 8 mg/kg 群の 1 例が血小板減少症，16 mg/kg 群の 1 例が肺炎，残りの 1 例が頭痛及び発熱であった。

2.7.4.2.1.4 その他の重要な有害事象

(1) 併用療法試験

1) 投与調節に至った有害事象

a) 本剤の投与調節に至った有害事象

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の本剤併用群における本剤の投与調節に至った有害事象を表 2.7.4-付録-62，本剤の投与調節の内訳を表 2.7.4-付録-63 に示す。治験実施計画書では本剤の用量調節は許容されていないため，本剤の投与調節では，投与

に関する処置が投与延期又は休薬であった有害事象を集計した。なお，GEN503 試験は投与調節に関連する情報を収集していないため，DRd 群の併合解析から除外した。

また，本剤持続静脈内投与中に投与調節に至った IRR については，2.7.4.2.1.5(1)1)a)③(i) に記載した。

MMY3004 試験（DVd 療法）

DVd 群では，本剤の投与調節に至った有害事象の発現割合は 35.8%であり，発現割合が高かった事象は血小板減少症（11.5%）及び肺炎（4.5%）であった。

MMY3003 試験（DRd 療法）

DRd 群では，本剤の投与調節に至った有害事象の発現割合は 37.1%であり，発現割合が高かった事象は好中球減少症（10.2%）及び肺炎（3.5%）であった。

MMY1001 試験（DPd 療法）

DPd 群では，本剤の投与調節に至った有害事象の発現割合は 48.5%であり，発現割合が高かった事象は好中球減少症（23.3%）及び血小板減少症（8.7%）であった。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の本剤の投与調節に至った有害事象を表 2.7.4-付録-64，投与調節の内訳を表 2.7.4-付録-65 に示す。

治験薬投与を受けた被験者（8 例）で本剤の投与調節に至った有害事象の発現割合は 50.0%（4 例）であった。そのうち 2 例以上に認められた本剤の投与調節に至った有害事象は血小板減少症（25.0%，2 例）であり，それ以外の事象はすべて 1 例のみで認められた。

MMY3003 試験（DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の本剤の投与調節に至った有害事象を表 2.7.4-付録-66，投与調節の内訳を表 2.7.4-付録-67 に示す。

日本人集団の DRd 群（20 例）で本剤の投与調節に至った有害事象の発現割合は 45.0%（9 例）であった。そのうち 2 例以上に認められた本剤の投与調節に至った有害事象は好中球減少症（10.0%，2 例）であり，それ以外の事象はすべて 1 例のみで認められた。

東アジア人集団の DRd 群（51 例）で本剤の投与調節に至った有害事象の発現割合は 33.3%（17 例）であった。そのうち 2 例以上に認められた本剤の投与調節に至った有害事象は好中球減少症（13.7%，7 例）及び血小板減少症（3.9%，2 例）であり，それ以外の事象はすべて 1 例のみで認められた。

b) その他の治験薬の投与調節に至った有害事象

全体集団

その他の治験薬の投与調節では，投与に関する処置に関して，ボルテゾミブでは投与延期，休薬，投与スケジュールの変更又は減量，レナリドミドでは投与延期，休薬又は減量，ポマリドミドでは投与延期，休薬，再増量又は減量，デキサメタゾンでは投与延期，休薬又は減量に至った有害事象を集計した。なお，GEN503 試験は投与調節に関する情報を収集していないため，DRd 群の併合解析から除外した。

MMY3004 試験（Vd 療法 vs DVd 療法）

ボルテゾミブの投与調節に至った有害事象の発現割合は，Vd 群が 54.4%，DVd 群が 63.8%であり，発現割合が最も高かった有害事象は末梢性感覚ニューロパチー（Vd 群 23.2%，DVd 群 31.7%）であった（表 2.7.4-付録-68）。デキサメタゾンの投与調節に至った有害事象の発現割合は Vd 群が 39.2%，DVd 群が 45.7%であり，いずれかの群で 4%以上に認められた有害事象は上気道感染（Vd 群 4.6%，DVd 群 3.3%）であった（表 2.7.4-付録-69）。

MMY3003 試験（Rd 療法 vs DRd 療法）

レナリドミドの投与調節に至った有害事象の発現割合は Rd 群が 54.4%，DRd 群が 70.7%であり，発現割合が最も高かった有害事象は好中球減少症（Rd 群 22.4%，DRd 群 34.3%）であった（表 2.7.4-付録-70）。デキサメタゾンの投与調節に至った有害事象の発現割合は Rd 群が 44.5%，DRd 群が 58.3%であり，いずれかの群で 5%以上に認められた有害事象は好中球減少症（Rd 群 4.3%，DRd 群 7.1%）であった（表 2.7.4-付録-71）。

MMY1001 試験（DPd 療法）

DPd 群では，ポマリドミドの投与調節に至った有害事象の発現割合は 72.8%であり，発現割合が最も高かった有害事象は好中球減少症（47.6%）であった（表 2.7.4-付録-72）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験のボルテゾミブの投与調節に至った有害事象を表 2.7.4-付録-73，デキサメタゾンの投与調節に至った有害事象を表 2.7.4-付録-74 に示す。

治験薬投与を受けた被験者（8 例）では，ボルテゾミブの投与調節に至った有害事象の発現割合は 100%（8 例）であり，2 例以上に認められた事象は血小板減少症（50.0%，4 例）及び疲労（25.0%，2 例）であった。デキサメタゾンの投与調節に至った有害事象の発現割合は 87.5%（7 例）であり，2 例以上に認められた事象は高血糖（25.0%，2 例）であった。

日本人被験者で MMY3004 試験の DVd 群に比べて発現割合が 20%以上高かったボルテゾミブの投与調節に至った有害事象は，血小板減少症（MMY1005 試験 50.0%，MMY3004 試験 13.2%，以下同順）及び疲労（25.0%，2.1%）であり，日本人被験者で MMY3004 試験の DVd 群に比べて発現割合が 20%以上高かったデキサメタゾンの投与調節に至った有害事象は，高血糖（25.0%，2.5%）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）のレナリドミドの投与調節に至った有害事象を表 2.7.4-付録-75，デキサメタゾンの投与調節に至った有害事象を表 2.7.4-付録-76 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）では，レナリドミドの投与調節に至った有害事象の発現割合は Rd 群が 60.0%，DRd 群が 90.0%であり，発現割合が高かった事象は好中球減少症（Rd 群 26.7%，DRd 群 35.0%）であった。デキサメタゾンの投与調節に至った有害事象の発現割合は Rd 群が 46.7%，DRd 群が 40.0%であり，いずれかの群で 2 例以上に認められた有害事象は DRd 群の高血糖（10.0%，2 例）であった。日本人集団で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かったレナリドミドの投与調節に至った有害事象は，DRd 群の ALT 増加（日本人集団 15.0%，全体集団 2.8%）であった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では，レナリドミドの投与調節に至った有害事象の発現割合は Rd 群が 54.5%，DRd 群が 72.5%であり，発現割合が高かった事象は好中球減少症（Rd 群 36.4%，DRd 群 45.1%）であった。デキサメタゾンの投与調節に至った有害事象の発現割合は Rd 群が 25.0%，DRd 群が 27.5%であり，いずれかの群で 5%以上に認められた有害事象は DRd 群の高血糖（5.9%，3 例）であった。東アジア人集団で MMY3003 試験の全体集団に比べて発現割合が 10%以上高かったレナリドミドの投与調節に至った有害事象は，Rd 群では好中球減少症（東アジア人集団 36.4%，全体集団 22.4%，以下同順），DRd 群では好中球減少症（45.1%，34.3%）であった。

2) 治験薬の投与中止に至った有害事象

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験で認められた治験薬の投与中止に至った有害事象を表 2.7.4-21 に示す。なお，治験薬の投与中止に至った有害事象は，CRF の「治験薬投与中止」ページの主な中止理由に入力された有害事象を集計した。

また，CRF の「有害事象」ページで本剤の投与処置が中止と入力された有害事象を本剤の投与が中止となった有害事象として集計し，更に本剤のみ投与中止（その他の治験薬は継続）となった有害事象も集計した。本剤併用群で本剤の投与が中止となった有害事象を表 2.7.4-付録-77，本剤のみ投与中止（その他の治験薬は継続）となった有害事象を表 2.7.4-付録-78 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

治験薬の投与中止に至った有害事象の発現割合は Vd 群が 9.3%，DVd 群が 7.4%であった。DVd 群で発現割合が最も高かった治験薬の投与中止に至った有害事象は肺炎（1.2%）であった。全体で 2 例以上に認められた治験薬の投与中止に至った有害事象は，肺炎（Vd 群 1 例，DVd 群 3 例，以下同順），うっ血性心不全（0 例，2 例），末梢性感覚ニューロパチー（6 例，1 例），心停止（1 例，1 例）及び起立性低血圧（2 例，0 例）であった。

DVd 群で本剤の投与が中止となった有害事象の発現割合は 9.5%であった。そのうち 2 例以上に認められた本剤の投与が中止となった有害事象は，肺炎（4 例），虚血性脳卒中（2 例）及び気管支痙攣（2 例）であり，それ以外の事象はすべて 1 例のみで認められた。また，本剤のみ投

与中止（その他の治験薬は継続）となった有害事象の発現割合は 1.6%（4 例）であり，その内訳は気管支痙攣，気管支炎，胃腸炎及び肺炎（各 1 例）であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

治験薬の投与中止に至った有害事象の発現割合は Rd 群が 7.8%，DRd 群が 6.9%であった。DRd 群で発現割合が最も高かった治験薬の投与中止に至った有害事象は肺炎及び全身健康状態低下（各 0.9%）であった。全体で 2 例以上に認められた治験薬の投与中止に至った有害事象は，肺炎（Rd 群 2 例，DRd 群 3 例，以下同順），全身健康状態低下（0 例，3 例），敗血症性ショック（0 例，2 例），腎不全（2 例，1 例），脳梗塞（1 例，1 例）及び肺塞栓症（3 例，0 例）であった。

DRd 群で本剤の投与が中止となった有害事象の発現割合は 9.1%であった。そのうち 2 例以上に認められた本剤の投与が中止となった有害事象は，肺炎（4 例），敗血症性ショック（3 例），全身健康状態低下（3 例），喉頭浮腫（2 例）及び高カルシウム血症（2 例）であり，それ以外の事象はすべて 1 例のみで認められた。また，本剤のみ投与中止（その他の治験薬は継続）となった有害事象の発現割合は 0.6%（2 例）であり，その内訳は発声障害，呼吸困難，喉頭浮腫，呼吸不全及び喘鳴（各 1 例）であった。

MMY1001 試験（DPd 療法）

DPd 群では治験薬の投与中止に至った有害事象の発現割合は 12.6%であり，2 例以上に認められた事象はなかった。SOC 別では感染症及び寄生虫症による治験薬の投与中止が 4.9%（5 例）と最も多かった。

DPd 群で本剤の投与が中止となった有害事象の発現割合は 15.5%であった。そのうち 2 例以上に認められた本剤の投与が中止となった有害事象はなく，すべて 1 例のみで認められた。また，本剤のみ投与中止（その他の治験薬は継続）となった有害事象は認められなかった。

表 2.7.4-21 治験薬の投与中止に至った有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with TEAE leading to discontinuation of study treatment [a]	22 (9.3%)	18 (7.4%)	22 (7.8%)	22 (6.9%)	13 (12.6%)
MedDRA system organ class/Preferred term					
感染症および寄生虫症	5 (2.1%)	6 (2.5%)	5 (1.8%)	8 (2.5%)	5 (4.9%)
肺炎	1 (0.4%)	3 (1.2%)	2 (0.7%)	3 (0.9%)	1 (1.0%)
敗血症性ショック	1 (0.4%)	0	0	2 (0.6%)	0
細菌性気管支炎	0	0	0	1 (0.3%)	0
細菌性肺炎	0	0	0	1 (0.3%)	0
ウイルス性肺炎	0	0	0	1 (0.3%)	0
気管支肺炎	0	1 (0.4%)	0	0	0
壊疽	1 (0.4%)	0	0	0	0
胃腸炎	0	1 (0.4%)	0	0	0
感染	0	0	1 (0.4%)	0	0
乳腺炎	0	0	0	0	1 (1.0%)
壊死性筋膜炎	0	0	1 (0.4%)	0	0
ノカルジア症	1 (0.4%)	0	0	0	0
進行性多巣性白質脳症	0	0	0	0	1 (1.0%)
敗血症	0	1 (0.4%)	1 (0.4%)	0	1 (1.0%)
上気道感染	1 (0.4%)	0	0	0	0
尿路感染	0	0	0	0	1 (1.0%)
一般・全身障害および投与部位の状態	2 (0.8%)	0	0	3 (0.9%)	0
全身健康状態低下	1 (0.4%)	0	0	3 (0.9%)	0
無力症	1 (0.4%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.4%)	3 (1.1%)	3 (0.9%)	0
急性単球性白血病	0	0	0	1 (0.3%)	0
胃腺癌	0	0	0	1 (0.3%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.3%)	0
肺腺癌	0	0	1 (0.4%)	0	0
前立腺癌	0	0	1 (0.4%)	0	0
直腸腺癌	0	0	1 (0.4%)	0	0
移行上皮癌	0	1 (0.4%)	0	0	0
神経系障害	10 (4.2%)	3 (1.2%)	2 (0.7%)	2 (0.6%)	0
脳梗塞	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
認知障害	0	0	0	1 (0.3%)	0
自律神経ニューロパチー	1 (0.4%)	0	0	0	0
脳出血	0	0	1 (0.4%)	0	0
脳血管発作	1 (0.4%)	0	0	0	0
認知症	1 (0.4%)	0	0	0	0
味覚異常	0	1 (0.4%)	0	0	0
虚血性脳卒中	0	1 (0.4%)	0	0	0
神経痛	1 (0.4%)	0	0	0	0
錯感覚	1 (0.4%)	0	0	0	0
末梢性感覚ニューロパチー	6 (2.5%)	1 (0.4%)	0	0	0
失神寸前の状態	0	1 (0.4%)	0	0	0

表 2.7.4-21 治験薬の投与中止に至った有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
心臓障害	2 (0.8%)	4 (1.6%)	2 (0.7%)	1 (0.3%)	2 (1.9%)
心肺不全	0	0	0	1 (0.3%)	0
急性心筋梗塞	0	1 (0.4%)	0	0	0
狭心症	0	0	0	0	1 (1.0%)
心房細動	0	1 (0.4%)	0	0	0
心停止	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
うっ血性心不全	0	2 (0.8%)	0	0	1 (1.0%)
心筋梗塞	1 (0.4%)	0	0	0	0
心膜炎	0	0	1 (0.4%)	0	0
胃腸障害	0	1 (0.4%)	0	1 (0.3%)	0
憩室穿孔	0	0	0	1 (0.3%)	0
十二指腸潰瘍	0	1 (0.4%)	0	0	0
代謝および栄養障害	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
高カルシウム血症	0	0	0	1 (0.3%)	0
体液貯留	1 (0.4%)	0	0	0	0
代謝性アシドーシス	0	1 (0.4%)	0	0	0
精神障害	0	0	0	1 (0.3%)	0
うつ病	0	0	0	1 (0.3%)	0
腎および尿路障害	0	0	2 (0.7%)	1 (0.3%)	0
腎不全	0	0	2 (0.7%)	1 (0.3%)	0
呼吸器、胸郭および縦隔障害	1 (0.4%)	5 (2.1%)	5 (1.8%)	1 (0.3%)	4 (3.9%)
喉頭浮腫	0	1 (0.4%)	0	1 (0.3%)	0
急性呼吸不全	0	0	1 (0.4%)	0	0
気管支痙攣	0	1 (0.4%)	0	0	0
呼吸困難	0	1 (0.4%)	0	0	1 (1.0%)
労作性呼吸困難	0	1 (0.4%)	0	0	0
胸水症	0	1 (0.4%)	0	0	0
低酸素症	0	0	0	0	1 (1.0%)
間質性肺疾患	0	0	0	0	1 (1.0%)
肺塞栓症	1 (0.4%)	0	3 (1.1%)	0	0
肺水腫	0	0	1 (0.4%)	0	0
呼吸不全	0	1 (0.4%)	0	0	1 (1.0%)
皮膚および皮下組織障害	0	1 (0.4%)	0	1 (0.3%)	0
全身性皮疹	0	0	0	1 (0.3%)	0
発疹	0	1 (0.4%)	0	0	0
血液およびリンパ系障害	0	0	3 (1.1%)	0	1 (1.0%)
貧血	0	0	1 (0.4%)	0	0
好中球減少症	0	0	1 (0.4%)	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0
血小板減少症	0	0	1 (0.4%)	0	1 (1.0%)
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	0	0	0
脊椎骨折	0	1 (0.4%)	0	0	0
硬膜下血腫	1 (0.4%)	0	0	0	0
筋骨格系および結合組織障害	1 (0.4%)	0	1 (0.4%)	0	0
筋力低下	1 (0.4%)	0	0	0	0
脊柱管狭窄症	0	0	1 (0.4%)	0	0

表 2.7.4-21 治験薬の投与中止に至った有害事象［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
血管障害	2 (0.8%)	0	1 (0.4%)	0	1 (1.0%)
大動脈解離	0	0	0	0	1 (1.0%)
深部静脈血栓症	0	0	1 (0.4%)	0	0
起立性低血圧	2 (0.8%)	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
[a] Includes those subjects indicated as having discontinued treatment due to an adverse event on the end of treatment CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

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日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の治験薬の投与中止に至った有害事象を表 2.7.4-付録-79，本剤の投与が中止となった有害事象を表 2.7.4-付録-80 に示す。

治験薬投与を受けた被験者（8 例）では，12.5%（1 例）の被験者が治験薬の投与中止に至った有害事象（前立腺癌）を発現した。本剤の投与が中止となった有害事象の発現割合は 12.5%（1 例）であり，その内訳は前立腺癌（1 例）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）の治験薬の投与中止に至った有害事象を表 2.7.4-付録-81，DRd 群で本剤の投与が中止となった有害事象を表 2.7.4-付録-82 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）で治験薬の投与中止に至った有害事象の発現割合は DRd 群のみ 10.0%（2 例：エプスタイン・バーウイルス関連リンパ増殖性障害及び脳梗塞が各 1 例）であった。DRd 群で本剤の投与が中止となった有害事象の発現割合は 15.0%（3 例）であり，その内訳は肺炎，エプスタイン・バーウイルス関連リンパ増殖性障害及び脳梗塞（各 1 例）であった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）で治験薬の投与中止に至った有害事象の発現割合は Rd 群が 2.3%（1 例：敗血症），DRd 群が 5.9%（3 例：肺炎，エプスタイン・バーウイルス関連リンパ増殖性障害及び脳梗塞が各 1 例）であった。DRd 群で本剤の投与が中止となった有害事象の発現割合は 9.8%（5 例）であり，その内訳は肺炎（2 例），多臓器不全，エプスタイン・バーウイルス関連リンパ増殖性障害及び脳梗塞（各 1 例）であった。

(2) 単剤療法試験

1) 本剤の投与延期に至った有害事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の本剤の投与延期に至った有害事象を表 2.7.4-付録-83 に示す。

16 mg/kg 群では，本剤の投与延期に至った有害事象の発現割合は 15.4%であり，発現割合が高かった事象は，上気道感染及び肺炎（各 1.9%）であった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の本剤の投与延期に至った有害事象を表 2.7.4-付録-84 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，本剤の投与延期に至った有害事象の発現割合は 8 mg/kg 群が 25.0%（1 例）であり，上気道感染が認められた。

2) 本剤の投与中断に至った有害事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の本剤持続静脈内投与中に投与中断に至った有害事象を表 2.7.4-付録-85 に示す。

16 mg/kg 群では，本剤持続静脈内投与中に投与中断に至った有害事象の発現割合は 39.7%であり，発現割合が高かった本剤の投与中断に至った有害事象（5%以上）は，鼻閉（7.7%），悪寒（7.1%），アレルギー性鼻炎（6.4%），咳嗽（5.8%）及び呼吸困難（5.1%）であった。本剤の投与中断に至った有害事象のほとんど（62 例のうち 59 例）が IRR と判断された（2.7.4.2.1.5(1)1)b)④(i) 参照）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験の本剤持続静脈内投与中に投与中断に至った有害事象を表 2.7.4-付録-86 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，本剤持続静脈内投与中に投与中断に至った有害事象の発現割合は 8 mg/kg 群が 25.0%（1 例），16 mg/kg 群が 20.0%（1 例）であり，その内訳は 8 mg/kg 群の 1 例が発熱，16 mg/kg 群の 1 例が悪寒，頭痛，低酸素症，口腔咽頭痛及び発熱であった。いずれの事象も IRR であった。

3) 本剤の投与中止に至った有害事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の本剤の投与中止に至った有害事象を表 2.7.4-22 に示す。なお，本剤の投与中止に至った有害事象は，CRF の「治験薬投与中止」ページの主な中止理由に入力された有害事象を集計した。

16 mg/kg 群では，本剤の投与中止に至った有害事象の発現割合は 3.8%（6 例）であった。2 例以上に認められた本剤の投与中止に至った有害事象は全身健康状態低下（2 例）であり，それ以外の事象はすべて 1 例のみで認められた。

表 2.7.4-22 本剤の投与中止に至った有害事象［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with TEAEs leading to treatment discontinuation	4 (17.4%)	4 (17.4%)	0	0	6 (3.8%)	0	1 (33.3%)	1 (33.3%)	11 (4.6%)	5 (2.1%)
Preferred term										
全身健康状態低下	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
高カルシウム血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
肺炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脊髄圧迫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
気管支痙攣	1 (4.3%)	1 (4.3%)	0	0	0	0	1 (33.3%)	1 (33.3%)	2 (0.8%)	2 (0.8%)
サイトカイン放出症候群	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
潮紅	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
肝機能異常	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
過敏症	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events reported as the reason for treatment discontinuation on the end of treatment CRF page are summarized.

[TSFAE07.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae07.sas] 16MAR2015, 12:04

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，本剤の投与中止に至った有害事象は認められなかった（表 2.7.4-付録-87）。

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

(1) 特に注目すべき有害事象

IRR，好中球減少症，感染症及び寄生虫症，血小板減少症及び出血関連事象，溶血，間接クームス試験への干渉及び輸血への影響，心イベント，肝胆道系障害及び二次性悪性腫瘍を特に注目すべき有害事象とし，それぞれ評価した（評価方法は 2.7.4.1.1.2(5) 参照）。

1) Infusion related reaction（IRR）

a) 併用療法試験

① Infusion related reaction（IRR）

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の本剤併用群で認められた IRR（全 Grade，Grade 3 又は 4）を表 2.7.4-23 に示す。なお，いずれの試験でも Grade 4 の IRR は認められなかった。

MMY3004 試験（DVd 療法）

DVd 群で認められた IRR の発現割合は 45.3%であった。認められた IRR は呼吸器，胸郭及び縦隔障害（SOC）が最も多く，PT 別で発現割合が高かった事象は呼吸困難（10.7%），気管支痙攣（9.1%），咳嗽（7.0%），咽喉刺激感（4.9%）及び鼻閉（4.1%）であった。発現割合が高かったその他の IRR は悪寒（4.1%）であった。認められた IRR の多くは Grade 1 又は 2 であった。Grade 3 の IRR の発現割合は 8.6%（21 例）であり，主な事象は気管支痙攣及び高血圧（各 2.5%，6 例），呼吸困難（2.1%，5 例）であった。

MMY3003 試験及び GEN503 試験併合（DRd 療法）

DRd 群で認められた IRR の発現割合は 48.4%であった。認められた IRR は呼吸器，胸郭及び縦隔障害（SOC）が最も多く，PT 別で発現割合が高かった事象は咳嗽（10.1%），呼吸困難（8.2%）及び気管支痙攣（4.4%）であった。発現割合が高かったその他の IRR は嘔吐（6.0%），悪心（5.3%）及び悪寒（4.1%）であった。認められた IRR の多くは Grade 1 又は 2 であった。Grade 3 の IRR の発現割合は 5.3%（17 例）であり，主な事象は高血圧（0.9%，3 例），呼吸困難，喘鳴及び喉頭浮腫（各 0.6%，2 例）であった。

MMY1001 試験（DPd 療法）

DPd 群で認められた IRR の発現割合は 49.5%であった。認められた IRR は呼吸器，胸郭及び縦隔障害（SOC）が最も多く，PT 別で発現割合が高かった事象は呼吸困難及び咳嗽（各 10.7%），咽喉刺激感及び鼻閉（各 6.8%）及びくしゃみ（4.9%）であった。発現割合が高かったその他の

IRR は悪寒（14.6%），悪心（8.7%）及び発熱（4.9%）であった。認められた IRR の多くは Grade 1 又は 2 であった。Grade 3 の IRR の発現割合は 3.9%（4 例）であり，その内訳は高血圧（1.9%，2 例），低酸素症及び血圧上昇（各 1.0%，1 例）であった。

表 2.7.4-23 Infusion related reaction（IRR）

［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

	MMY3004 DVd		MMY3003+GEN503 DRd		MMY1001 DPd		Total Dara Combined	
	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]
Analysis set: safety	243		318		103		664	
Total number of subjects with infusion related reactions	110 (45.3%)	21 (8.6%)	154 (48.4%)	17 (5.3%)	51 (49.5%)	4 (3.9%)	315 (47.4%)	42 (6.3%)
Total number of subjects with infusion related reactions in more than 1 infusion	4 (1.6%)	1 (0.4%)	16 (5.0%)	3 (0.9%)	1 (1.0%)	0	21 (3.2%)	4 (0.6%)
MedDRA system organ class/Preferred term								
呼吸器、胸郭および縦隔障害	83 (34.2%)	13 (5.3%)	101 (31.8%)	7 (2.2%)	37 (35.9%)	1 (1.0%)	221 (33.3%)	21 (3.2%)
呼吸困難	26 (10.7%)	5 (2.1%)	26 (8.2%)	2 (0.6%)	11 (10.7%)	0	63 (9.5%)	7 (1.1%)
咳嗽	17 (7.0%)	0	32 (10.1%)	0	11 (10.7%)	0	60 (9.0%)	0
気管支痙攣	22 (9.1%)	6 (2.5%)	14 (4.4%)	1 (0.3%)	0	0	36 (5.4%)	7 (1.1%)
咽喉刺激感	12 (4.9%)	0	9 (2.8%)	0	7 (6.8%)	0	28 (4.2%)	0
鼻閉	10 (4.1%)	1 (0.4%)	9 (2.8%)	0	7 (6.8%)	0	26 (3.9%)	1 (0.2%)
アレルギー性鼻炎	3 (1.2%)	0	9 (2.8%)	0	1 (1.0%)	0	13 (2.0%)	0
喘鳴	4 (1.6%)	0	6 (1.9%)	2 (0.6%)	3 (2.9%)	0	13 (2.0%)	2 (0.3%)
喉頭浮腫	2 (0.8%)	2 (0.8%)	7 (2.2%)	2 (0.6%)	2 (1.9%)	0	11 (1.7%)	4 (0.6%)
鼻漏	4 (1.6%)	0	6 (1.9%)	0	0	0	10 (1.5%)	0
くしゃみ	0	0	2 (0.6%)	0	5 (4.9%)	0	7 (1.1%)	0
低酸素症	0	0	4 (1.3%)	1 (0.3%)	2 (1.9%)	1 (1.0%)	6 (0.9%)	2 (0.3%)
咽喉絞扼感	4 (1.6%)	0	1 (0.3%)	0	1 (1.0%)	0	6 (0.9%)	0
発声障害	0	0	4 (1.3%)	1 (0.3%)	0	0	4 (0.6%)	1 (0.2%)
湿性咳嗽	1 (0.4%)	0	2 (0.6%)	0	1 (1.0%)	0	4 (0.6%)	0
アレルギー性咳嗽	2 (0.8%)	0	0	0	1 (1.0%)	0	3 (0.5%)	0
鼻閉塞	1 (0.4%)	0	2 (0.6%)	0	0	0	3 (0.5%)	0
口腔咽頭痛	1 (0.4%)	0	1 (0.3%)	0	1 (1.0%)	0	3 (0.5%)	0
アレルギー性呼吸器症状	0	0	2 (0.6%)	0	0	0	2 (0.3%)	0
喉頭刺激感	0	0	1 (0.3%)	0	1 (1.0%)	0	2 (0.3%)	0
窒息	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
喘息	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
喀血	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0

表 2.7.4-23 Infusion related reaction（IRR）

［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004 DVd		MMY3003+GEN503 DRd		MMY1001 DPd		Total Dara Combined	
	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]
喉頭不快感	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
喉頭狭窄	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
鼻部不快感	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
口腔咽頭不快感	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
口腔咽頭腫脹	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.2%)	1 (0.2%)
副鼻腔不快感	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
咽頭浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.2%)	1 (0.2%)
呼気延長	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
肺水腫	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
気道うっ血	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
低音性連続性ラ音	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
副鼻腔うっ血	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
副鼻腔障害	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
上気道性喘鳴	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
窒息感	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
上気道咳症候群	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
一般・全身障害および投与部位の状態	21 (8.6%)	1 (0.4%)	34 (10.7%)	1 (0.3%)	22 (21.4%)	0	77 (11.6%)	2 (0.3%)
悪寒	10 (4.1%)	0	13 (4.1%)	1 (0.3%)	15 (14.6%)	0	38 (5.7%)	1 (0.2%)
発熱	4 (1.6%)	0	6 (1.9%)	0	5 (4.9%)	0	15 (2.3%)	0
胸部不快感	2 (0.8%)	0	5 (1.6%)	0	2 (1.9%)	0	9 (1.4%)	0
冷感	0	0	5 (1.6%)	1 (0.3%)	1 (1.0%)	0	6 (0.9%)	1 (0.2%)
非心臓性胸痛	0	0	1 (0.3%)	0	3 (2.9%)	0	4 (0.6%)	0
疲労	1 (0.4%)	0	2 (0.6%)	0	0	0	3 (0.5%)	0
高熱	0	0	1 (0.3%)	0	1 (1.0%)	0	2 (0.3%)	0
インフルエンザ様疾患	1 (0.4%)	0	1 (0.3%)	0	0	0	2 (0.3%)	0
溢出	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
注入部位そう痒感	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
注入部位発疹	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
倦怠感	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
粘膜浮腫	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
疼痛	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.2%)	1 (0.2%)

表 2.7.4-23 Infusion related reaction（IRR）

［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004 DVd		MMY3003+GEN503 DRd		MMY1001 DPd		Total Dara Combined	
	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]
分泌物分泌	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
苦悶感	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
胃腸障害	21 (8.6%)	2 (0.8%)	37 (11.6%)	1 (0.3%)	10 (9.7%)	0	68 (10.2%)	3 (0.5%)
悪心	6 (2.5%)	0	17 (5.3%)	0	9 (8.7%)	0	32 (4.8%)	0
嘔吐	9 (3.7%)	0	19 (6.0%)	1 (0.3%)	4 (3.9%)	0	32 (4.8%)	1 (0.2%)
下痢	4 (1.6%)	0	0	0	1 (1.0%)	0	5 (0.8%)	0
腹痛	0	0	3 (0.9%)	0	1 (1.0%)	0	4 (0.6%)	0
嚥下障害	1 (0.4%)	0	2 (0.6%)	0	0	0	3 (0.5%)	0
口唇腫脹	1 (0.4%)	1 (0.4%)	1 (0.3%)	0	0	0	2 (0.3%)	1 (0.2%)
口の錯感覚	0	0	2 (0.6%)	0	0	0	2 (0.3%)	0
上腹部痛	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.2%)	1 (0.2%)
消化不良	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
口唇そう痒症	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
嚥下痛	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
口蓋浮腫	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
舌そう痒症	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
血管障害	14 (5.8%)	7 (2.9%)	19 (6.0%)	4 (1.3%)	6 (5.8%)	2 (1.9%)	39 (5.9%)	13 (2.0%)
高血圧	8 (3.3%)	6 (2.5%)	6 (1.9%)	3 (0.9%)	2 (1.9%)	2 (1.9%)	16 (2.4%)	11 (1.7%)
潮紅	2 (0.8%)	0	5 (1.6%)	0	3 (2.9%)	0	10 (1.5%)	0
低血圧	3 (1.2%)	1 (0.4%)	6 (1.9%)	1 (0.3%)	0	0	9 (1.4%)	2 (0.3%)
ほてり	1 (0.4%)	0	2 (0.6%)	0	1 (1.0%)	0	4 (0.6%)	0
血管拡張	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
皮膚および皮下組織障害	9 (3.7%)	1 (0.4%)	26 (8.2%)	1 (0.3%)	2 (1.9%)	0	37 (5.6%)	2 (0.3%)
そう痒症	3 (1.2%)	0	8 (2.5%)	1 (0.3%)	0	0	11 (1.7%)	1 (0.2%)
多汗症	1 (0.4%)	1 (0.4%)	5 (1.6%)	0	1 (1.0%)	0	7 (1.1%)	1 (0.2%)
蕁麻疹	1 (0.4%)	0	4 (1.3%)	0	0	0	5 (0.8%)	0
発疹	1 (0.4%)	0	3 (0.9%)	0	0	0	4 (0.6%)	0
紅斑	0	0	3 (0.9%)	0	0	0	3 (0.5%)	0
アレルギー性皮膚炎	2 (0.8%)	0	0	0	0	0	2 (0.3%)	0
冷汗	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
多形紅斑	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
アレルギー性そう痒症	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0

表 2.7.4-23 Infusion related reaction（IRR）

［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004 DVd		MMY3003+GEN503 DRd		MMY1001 DPd		Total Dara Combined	
	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]
紅斑性皮疹	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
斑状丘疹状皮疹	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
そう痒性皮疹	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
顔面腫脹	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
眼障害	11 (4.5%)	2 (0.8%)	11 (3.5%)	0	4 (3.9%)	0	26 (3.9%)	2 (0.3%)
流涙増加	5 (2.1%)	1 (0.4%)	6 (1.9%)	0	2 (1.9%)	0	13 (2.0%)	1 (0.2%)
結膜浮腫	3 (1.2%)	1 (0.4%)	0	0	0	0	3 (0.5%)	1 (0.2%)
眼刺激	0	0	2 (0.6%)	0	1 (1.0%)	0	3 (0.5%)	0
眼部腫脹	0	0	2 (0.6%)	0	0	0	2 (0.3%)	0
眼のアレルギー	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
眼脂	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
眼の障害	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
眼そう痒症	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
眼瞼浮腫	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
眼充血	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
神経系障害	5 (2.1%)	0	12 (3.8%)	1 (0.3%)	4 (3.9%)	0	21 (3.2%)	1 (0.2%)
頭痛	2 (0.8%)	0	7 (2.2%)	0	1 (1.0%)	0	10 (1.5%)	0
浮動性めまい	2 (0.8%)	0	1 (0.3%)	0	1 (1.0%)	0	4 (0.6%)	0
錯感覚	1 (0.4%)	0	2 (0.6%)	0	1 (1.0%)	0	4 (0.6%)	0
味覚異常	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
会話障害	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
失神	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
心臓障害	5 (2.1%)	0	9 (2.8%)	1 (0.3%)	3 (2.9%)	0	17 (2.6%)	1 (0.2%)
洞性頻脈	3 (1.2%)	0	2 (0.6%)	1 (0.3%)	1 (1.0%)	0	6 (0.9%)	1 (0.2%)
頻脈	0	0	5 (1.6%)	0	1 (1.0%)	0	6 (0.9%)	0
狭心症	0	0	1 (0.3%)	0	1 (1.0%)	0	2 (0.3%)	0
上室性頻脈	1 (0.4%)	0	1 (0.3%)	0	0	0	2 (0.3%)	0
徐脈	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
動悸	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
筋骨格系および結合組織障害	5 (2.1%)	0	5 (1.6%)	2 (0.6%)	2 (1.9%)	0	12 (1.8%)	2 (0.3%)
背部痛	4 (1.6%)	0	1 (0.3%)	0	1 (1.0%)	0	6 (0.9%)	0
筋骨格系胸痛	0	0	3 (0.9%)	1 (0.3%)	0	0	3 (0.5%)	1 (0.2%)

表 2.7.4-23 Infusion related reaction（IRR）

［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］（続き）

	MMY3004 DVd		MMY3003+GEN503 DRd		MMY1001 DPd		Total Dara Combined	
	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]	All grades	Grade 3 or 4[a]
骨痛	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
筋骨格痛	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
筋肉痛	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
臨床検査	0	0	3 (0.9%)	0	1 (1.0%)	1 (1.0%)	4 (0.6%)	1 (0.2%)
血圧上昇	0	0	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	2 (0.3%)	1 (0.2%)
心電図ＱＴ延長	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
心拍数増加	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
酸素飽和度低下	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
耳および迷路障害	2 (0.8%)	0	0	0	1 (1.0%)	0	3 (0.5%)	0
耳そう痒症	1 (0.4%)	0	0	0	1 (1.0%)	0	2 (0.3%)	0
回転性めまい	1 (0.4%)	0	0	0	0	0	1 (0.2%)	0
感染症および寄生虫症	0	0	3 (0.9%)	0	0	0	3 (0.5%)	0
結膜炎	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
鼻咽頭炎	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
上気道感染	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
免疫系障害	0	0	1 (0.3%)	0	1 (1.0%)	0	2 (0.3%)	0
サイトカイン放出症候群	0	0	0	0	1 (1.0%)	0	1 (0.2%)	0
薬物過敏症	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
血液およびリンパ系障害	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
貧血	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
血小板減少症	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
傷害、中毒および処置合併症	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
注入に伴う反応	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
精神障害	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0
うつ病	0	0	1 (0.3%)	0	0	0	1 (0.2%)	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.
[a]Grade 3 only; no Grade 4 infusion-related reactions were reported.

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた IRR を表 2.7.4-付録-88 に示す。

治験薬投与を受けた被験者（8 例）で認められた IRR の発現割合は 62.5%（5 例）であった。認められた IRR は呼吸器，胸郭及び縦隔障害（SOC）が最も多く，PT 別で 2 例以上に認められた事象は低酸素症及び喘鳴（各 25.0%，2 例）であった。2 例以上に認められたその他の IRR は悪寒（25.0%，2 例）であった。すべての IRR は Grade 1 又は 2 であった。

MMY3003 試験（DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の DRd 群で認められた人種別（日本人，東アジア人，全体）の IRR（全 Grade，Grade 3，Grade 4，Grade 5）を表 2.7.4-付録-89 に示す。

日本人集団の DRd 群（20 例）で認められた IRR の発現割合は 40.0%（8 例）であった。2 例以上に認められた IRR は呼吸困難（2 例）であり，それ以外はすべて 1 例のみで認められた。Grade 3 の IRR は呼吸困難（1 例）のみであった。

東アジア人集団の DRd 群（51 例）で認められた IRR の発現割合は 51.0%（26 例）であった。3 例以上に認められた IRR は呼吸困難（5 例），低血圧（4 例），低酸素症，悪寒及び冷感（各 3 例）であった。Grade 3 の IRR の発現割合は 11.8%（6 例）であり，その内訳は呼吸困難，喘鳴，低酸素症，肺水腫，悪寒，冷感，低血圧，筋骨格系胸痛（各 1 例）であった。

② 発現時期別 infusion related reaction（IRR）

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の本剤併用群で認められた発現時期別（初回，2 回目，3 回目以降の投与時）の IRR を表 2.7.4-付録-90，発現時期別の IRR 発現までの時間の要約を表 2.7.4-付録-91 に示す。

MMY3004 試験（DVd 療法）

DVd 群では 45.3%（110 例）に IRR が認められ，発現時期別では，初回投与時に 98.2%（108/110 例），2 回目投与時に 1.8%（2/110 例），3 回目以降の投与時に 3.6%（4/110 例）の被験者が IRR を発現した。投与開始から IRR 発現までの時間の中央値は 80.0 分（範囲：15～1695 分）であった。遅発性の IRR が 1 例に認められ，本剤の初回投与（サイクル 1，Day 1）から約 1 日後に Grade 2 の発熱を発現し，17 時間後に回復した。

MMY3003 試験及び GEN503 試験併合（DRd 療法）

DRd 群では 48.4%（154 例）に IRR が認められ，発現時期別では，初回投与時に 96.1%（148/154 例），2 回目投与時に 3.9%（6/154 例），3 回目以降の投与時に 11.0%（17/154 例）の被験者が IRR を発現した。投与開始から IRR 発現までの時間の中央値は 90.0 分（範囲：5～4370 分）であった。遅発性の IRR が 1 例に認められ，本剤の初回投与（サイクル 1，Day 1）から約 3 日後に Grade 1 のそう痒症を発現し，25 時間以内に回復した。

MMY1001 試験（DPd 療法）

DPd 群では 49.5%（51 例）に IRR が認められ，発現時期別では，初回投与時に 100%（51/51 例），2 回目投与時に 2.0%（1/51 例）の被験者が IRR を発現した。3 回目以降の投与時に IRR は認められなかった。投与開始から IRR 発現までの時間の中央値は 76.0 分（範囲：7～1200 分）であった。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた発現時期別（初回，2 回目，3 回目以降の投与時）の IRR を表 2.7.4-付録-92，発現時期別の IRR 発現までの時間の要約を表 2.7.4-付録-93 に示す。

治験薬投与を受けた被験者（8 例）では 62.5%（5 例）に IRR が認められ，初回投与時に 100%（5/5 例）の被験者が IRR を発現した。2 回目及び 3 回目以降の投与時に IRR は認められなかった。投与開始から IRR 発現までの時間の中央値は 85.0 分（範囲：20～184 分）であった。

MMY3003 試験（DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の DRd 群で認められた人種別（日本人，東アジア人，全体）及び発現時期別（初回，2 回目，3 回目以降の投与時）の IRR を表 2.7.4-付録-94，人種別及び発現時期別の IRR 発現までの時間の要約を表 2.7.4-付録-95 に示す。

日本人集団の DRd 群（20 例）では 40.0%（8 例）に IRR が認められ，発現時期別では，初回投与時に 75.0%（6/8 例），2 回目投与時に 12.5%（1/8 例），3 回目以降の投与時に 37.5%（3/8 例）の被験者が IRR を発現した。投与開始から IRR 発現までの時間の中央値は 86.5 分（範囲：23～138 分）であった。

東アジア人集団の DRd 群（51 例）では 51.0%（26 例）に IRR が認められ，発現時期別では，初回投与時に 92.3%（24/26 例），2 回目投与時に 7.7%（2/26 例），3 回目以降の投与時に 19.2%（5/26 例）の被験者が IRR を発現した。投与開始から IRR 発現までの時間の中央値は 120.0 分（範囲：23～540 分）であった。

③ Infusion related reaction（IRR）による投与の調節

(i) 本剤の投与調節に至った infusion related reaction（IRR）

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の本剤併用群で認められた本剤の投与調節（投与中断，投与中止又は減速）に至った IRR を表 2.7.4-付録-96 に示す。

MMY3004 試験（DVd 療法）

DVd 群で IRR を発現した 110 例のうち，本剤の投与調節に至った IRR の発現割合は 94.5%（104/110 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（72.7%，80/110 例）。

MMY3003 試験及び GEN503 試験併合（DRd 療法）

DRd 群で IRR を発現した 154 例のうち，本剤の投与調節に至った IRR の発現割合は 83.8%（129/154 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（57.8%，89/154 例）。

MMY1001 試験（DPd 療法）

DPd 群で IRR を発現した 51 例のうち，本剤の投与調節に至った IRR の発現割合は 92.2%（47/51 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（68.6%，35/51 例）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた本剤の投与調節に至った IRR を表 2.7.4-付録-97 に示す。

治験薬投与を受けた被験者（8 例）で IRR を発現した 5 例のうち，本剤の投与調節に至った IRR の発現割合は 100%（5/5 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（80.0%，4/5 例）。

MMY3003 試験（DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の DRd 群で認められた人種別（日本人，東アジア人，全体）の本剤の投与調節に至った IRR を表 2.7.4-付録-98 に示す。

日本人集団の DRd 群で IRR を発現した 8 例のうち，本剤の投与調節に至った IRR の発現割合は 87.5%（7/8 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（75.0%，6/8 例）。

東アジア人集団の DRd 群で IRR を発現した 26 例のうち，本剤の投与調節に至った IRR の発現割合は 84.6%（22/26 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（61.5%，16/26 例）。

(ii) 本剤の投与中止に至った infusion related reaction（IRR）

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の本剤併用群で認められた本剤の投与中止に至った IRR を表 2.7.4-付録-99 に示す。

MMY3004 試験（DVd 療法）

DVd 群で IRR を発現した 110 例のうち，1.8%（2/110 例）が本剤の投与を中止した。その内訳は 1 例が気管支痙攣，喉頭浮腫及び発疹，残りの 1 例が気管支痙攣であった。

MMY3003 試験及び GEN503 試験併合（DRd 療法）

DRd 群で IRR を発現した 154 例のうち，1.3%（2/154 例）が本剤の投与を中止した。その内訳は 1 例が喉頭浮腫，発声障害，呼吸困難，喘鳴及び消化不良，残りの 1 例が喉頭浮腫であった。

MMY1001 試験（DPd 療法）

DPd 群で IRR を発現した 51 例のうち，2.0%（1/51 例）が低酸素症のため本剤の投与を中止した。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験で認められた本剤の投与中止に至った IRR を表 2.7.4-付録-100 に示す。

治験薬投与を受けた被験者（8 例）では，本剤の投与中止に至った IRR は認められなかった。

MMY3003 試験（DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の DRd 群で認められた人種別（日本人，東アジア人，全体）の本剤の投与中止に至った IRR を表 2.7.4-付録-101 に示す。

日本人集団及び東アジア人集団ともに，DRd 群で本剤の投与中止に至った IRR は認められなかった。

④ Infusion related reaction（IRR）の管理

前投薬

IRR の管理のため，本剤の投与前に前投薬として副腎皮質ステロイド，解熱鎮痛剤及び抗ヒスタミン剤の使用を治験実施計画書で規定していた。

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験の本剤併用群（664 例）の全例が全身用抗ヒスタミン剤（ジフェンヒドラミン，クロルフェニラミンマレイン酸塩，*d*-クロルフェニラミンマレイン酸塩又はクレマスチンフマル酸塩等）の前投薬を受けた。また，DVd 群の 2 例及び DRd 群の 1 例を除いた全例が解熱鎮痛剤（アセトアミノフェン／paracetamol）の前投薬を受けた。なお，デキサメタゾン又は等価の副腎皮質ステロイドの前投薬に関しては，治験薬の一部として治験実施計画書で規定されていたため，前投薬の集計から除外した（表 2.7.4-付録-102）。

MMY1005 試験では，IRR の管理を目的として使用した前投薬は副腎皮質ステロイド（デキサメタゾン），解熱鎮痛剤（アセトアミノフェン／paracetamol）及び全身用抗ヒスタミン剤（ジフェンヒドラミン等）であり，治験薬投与を受けた被験者（8 例）の全例がこれらの前投薬を受けた（表 2.7.4-付録-103）。

MMY3003 試験の DRd 群では，日本人集団（20 例）及び東アジア人集団（51 例）の全例が解熱鎮痛剤（アセトアミノフェン／paracetamol）及び全身用抗ヒスタミン剤（ジフェンヒドラミン，クロルフェニラミンマレイン酸塩又は *d*-クロルフェニラミンマレイン酸塩等）の前投薬を受けた（表 2.7.4-付録-104）。

後投薬

いずれの試験においても，治験実施計画書で呼吸器系合併症のリスクが高い被験者に対する後投薬の検討を規定していた。

本剤併用群では，後投薬を受けた被験者の割合は DVd 群が 8.6%，DRd 群が 9.4%であり，DPd 群で後投薬を受けた被験者はいなかった。DVd 群及び DRd 群で使用した主な後投薬は，全身用抗ヒスタミン剤（DVd 群 5.8%，DRd 群 6.9%，以下同順）及び閉塞性気道障害用薬（サルブタモール硫酸塩等）（2.5%，1.9%）であった（表 2.7.4-付録-105）。

MMY1005 試験では，治験薬投与を受けた被験者（8 例）のうち 12.5%（1 例）が全身用抗ヒスタミン剤（ジフェンヒドラミン）及び閉塞性気道障害用薬（サルブタモール硫酸塩）の後投薬を受けた（表 2.7.4-付録-106）。

MMY3003 試験の DRd 群では，日本人集団（20 例）及び東アジア人集団（51 例）で後投薬を受けた被験者はいなかった（表 2.7.4-付録-107）。

b) 単剤療法試験

① Infusion related reaction（IRR）関連事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた IRR（全 Grade，Grade 3 又は 4）を表 2.7.4-24 に示す。なお，いずれの試験でも Grade 4 の IRR は認められなかった。

16 mg/kg 群で認められた IRR の発現割合は 51.3%であった。認められた IRR は呼吸器，胸郭及び縦隔障害（SOC）が最も多く，PT 別で発現割合が高かった事象は鼻閉（10.9%），咳嗽（7.7%），アレルギー性鼻炎（6.4%），咽喉刺激感（5.8%）及び呼吸困難（5.1%）であった。発現割合が高かったその他の IRR は悪寒（7.1%）及び悪心（5.1%）であった。認められた IRR の多くは Grade 1 又は 2 であった。Grade 3 の IRR の発現割合は 3.8%（6 例）であり，その内訳は気管支痙攣及び高血圧（各 1.3%，2 例），呼吸困難，低酸素症及び貧血（各 0.6%，1 例）であった。

表 2.7.4-24 Infusion related reaction（IRR）［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with infusion related reactions	15 (65.2%)	2 (8.7%)	30 (54.5%)	2 (3.6%)	80 (51.3%)	6 (3.8%)	3 (100.0%)	0	128 (54.0%)	10 (4.2%)
MedDRA system organ class/Preferred term										
呼吸器、胸郭および縦隔障害	3 (13.0%)	1 (4.3%)	24 (43.6%)	0	55 (35.3%)	4 (2.6%)	2 (66.7%)	0	84 (35.4%)	5 (2.1%)
鼻閉	0	0	3 (5.5%)	0	17 (10.9%)	0	1 (33.3%)	0	21 (8.9%)	0
咳嗽	0	0	6 (10.9%)	0	12 (7.7%)	0	1 (33.3%)	0	19 (8.0%)	0
アレルギー性鼻炎	1 (4.3%)	0	12 (21.8%)	0	10 (6.4%)	0	0	0	23 (9.7%)	0
咽喉刺激感	0	0	0	0	9 (5.8%)	0	0	0	9 (3.8%)	0
呼吸困難	1 (4.3%)	0	3 (5.5%)	0	8 (5.1%)	1 (0.6%)	0	0	12 (5.1%)	1 (0.4%)
気管支痙攣	1 (4.3%)	1 (4.3%)	1 (1.8%)	0	4 (2.6%)	2 (1.3%)	1 (33.3%)	0	7 (3.0%)	3 (1.3%)
くしゃみ	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
咽喉絞扼感	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
低酸素症	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
口腔咽頭痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
喘鳴	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
アレルギー性咳嗽	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
喉頭浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
アレルギー性喉頭炎	0	0	3 (5.5%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
鼻部障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
発声障害	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
一般・全身障害および投与部位の状態	9 (39.1%)	0	9 (16.4%)	1 (1.8%)	20 (12.8%)	0	0	0	38 (16.0%)	1 (0.4%)
悪寒	0	0	5 (9.1%)	1 (1.8%)	11 (7.1%)	0	0	0	16 (6.8%)	1 (0.4%)
発熱	6 (26.1%)	0	4 (7.3%)	0	5 (3.2%)	0	0	0	15 (6.3%)	0
胸部不快感	0	0	2 (3.6%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
胸痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
疲労	2 (8.7%)	0	0	0	1 (0.6%)	0	0	0	3 (1.3%)	0
インフルエンザ様疾患	3 (13.0%)	0	0	0	1 (0.6%)	0	0	0	4 (1.7%)	0
注入部位内出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
疼痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
非心臓性胸痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0

表 2.7.4-24 Infusion related reaction（IRR）［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］（続き）

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]
胃腸障害	3 (13.0%)	0	7 (12.7%)	0	11 (7.1%)	0	1 (33.3%)	0	22 (9.3%)	0
悪心	2 (8.7%)	0	3 (5.5%)	0	8 (5.1%)	0	0	0	13 (5.5%)	0
嘔吐	0	0	5 (9.1%)	0	7 (4.5%)	0	1 (33.3%)	0	13 (5.5%)	0
上腹部痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
下痢	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口の錯感覚	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口内乾燥	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
消化不良	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
口唇浮腫	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
皮膚および皮下組織障害	1 (4.3%)	0	3 (5.5%)	0	6 (3.8%)	0	0	0	10 (4.2%)	0
そう痒症	1 (4.3%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	5 (2.1%)	0
発疹	1 (4.3%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
斑状皮疹	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
蕁麻疹	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
多汗症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
眼障害	0	0	0	0	5 (3.2%)	0	0	0	5 (2.1%)	0
眼そう痒症	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
霧視	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
白内障	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋骨格系および結合組織障害	0	0	2 (3.6%)	0	4 (2.6%)	0	0	0	6 (2.5%)	0
背部痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
鼡径部痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋肉痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
側腹部痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
筋骨格痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
血管障害	4 (17.4%)	0	4 (7.3%)	1 (1.8%)	4 (2.6%)	2 (1.3%)	0	0	12 (5.1%)	3 (1.3%)
高血圧	1 (4.3%)	0	2 (3.6%)	1 (1.8%)	3 (1.9%)	2 (1.3%)	0	0	6 (2.5%)	3 (1.3%)
潮紅	2 (8.7%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
低血圧	2 (8.7%)	0	1 (1.8%)	0	0	0	0	0	3 (1.3%)	0
血液およびリンパ系障害	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
貧血	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
赤血球凝集	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

表 2.7.4-24 Infusion related reaction（IRR）［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］（続き）

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]	Any Grade	Grade 3 or 4[a]
心臓障害	3 (13.0%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	7 (3.0%)	0
動悸	1 (4.3%)	0	0	0	1 (0.6%)	0	0	0	2 (0.8%)	0
洞性頻脈	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
頻脈	2 (8.7%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
神経系障害	3 (13.0%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	7 (3.0%)	0
頭痛	1 (4.3%)	0	0	0	3 (1.9%)	0	0	0	4 (1.7%)	0
浮動性めまい	2 (8.7%)	0	1 (1.8%)	0	0	0	0	0	3 (1.3%)	0
精神障害	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
不安	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
譫妄	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
免疫系障害	3 (13.0%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	0	0	0	6 (2.5%)	2 (0.8%)
サイトカイン放出症候群	1 (4.3%)	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	3 (1.3%)	1 (0.4%)
季節性アレルギー	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
過敏症	2 (8.7%)	1 (4.3%)	0	0	0	0	0	0	2 (0.8%)	1 (0.4%)
感染症および寄生虫症	0	0	0	0	0	0	1 (33.3%)	0	1 (0.4%)	0
鼻咽頭炎	0	0	0	0	0	0	1 (33.3%)	0	1 (0.4%)	0

[a] Grade 3 only; no Grade 4 infusion-related reactions were reported.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
Modified from Appendix TSFAE20

MMY2002 試験及び GEN501 試験で認められた気管支痙攣の IRR の一覧を表 2.7.4-付録-109 に示す。

気管支痙攣は臨床的に特に懸念される IRR であり，いずれも本剤と関連性があると判断された。

MMY2002 試験（124 例）では，16 mg/kg 群の 4 例が気管支痙攣を発現した。4 例すべてが初回投与中に急性の気管支痙攣を発現し，本剤の投与を中断した後，すべての被験者が回復した。その後 2 例が投与を再開し，初回投与を完了した。初回投与中に気管支痙攣を発現した 4 例は，いずれも 2 回目以降の投与では気管支痙攣を再発しなかった。

GEN501 試験 Part 1（32 例）では，2 例が遅発性の気管支痙攣を発現した。その内訳は 2 mg/kg 群の 1 例が Grade 3 の事象を 1 件（投与 2 日後），24 mg/kg 群の 1 例が Grade 2 の事象を 2 件（2 回目投与約 24 時間後，及び 3 回目投与約 24 時間後）であった（2.7.4.2.1.5(1)1)b)② 参照）。遅発性の気管支痙攣が最初に認められた後に治験実施計画書を改訂し，後投薬としてすべての被験者に本剤投与の翌日から 2 日間，経口ステロイドを投与することとした。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験で認められた IRR の一覧を表 2.7.4-付録-110 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で認められた IRR の発現割合は，8 mg/kg 群が 25.0%（1 例），16 mg/kg 群が 60.0%（3 例）であった。発現割合が高かった IRR は発熱［8 mg/kg 群：25.0%（1 例），16 mg/kg 群：60.0%（3 例）］であり，それ以外の事象はすべて 1 例のみで認められた。すべての IRR は Grade 1 又は 2 であった。

② 発現時期別 infusion related reaction（IRR）

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群で認められた発現時期別（初回，2 回目，3 回目以降の投与時）の IRR の要約を表 2.7.4-付録-111 に示す。

16 mg/kg 群では 51.3%（80 例）に IRR が認められ，発現時期別では，初回投与時に 91.3%（73/80 例），2 回目投与時に 11.3%（9/80 例），3 回目以降の投与時に 12.5%（10/80 例）の被験者が IRR を発現した。投与開始から IRR 発現までの時間の中央値は 90.00 分（範囲：1.0～557.0 分）であった。

遅発性の IRR が 4 例に認められた。その内訳は，気管支痙攣が 2 例，発熱が 2 例であった。遅発性の気管支痙攣を発現した GEN501 試験 Part 1 の 2 例は，以降の投与時にも再発したため，いずれも本剤の投与を中止した（表 2.7.4-22）。一方，遅発性の発熱が MMY1002 試験の 2 例に認められた。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で認められた IRR（8 mg/kg 群：1 例，16 mg/kg 群：3 例）のうち，発現時期別では，初回投与時に 8 mg/kg 群の 100%（1/1 例），16 mg/kg 群の 66.7%（2/3 例）の被験者が IRR を発現し，2 回目以降の投与時に 16 mg/kg 群の 33.3%（1/3 例）の被験者が IRR を発現した。（表 2.7.4-付録-110）。

遅発性の IRR（発熱）が 16 mg/kg 群の 2 例に認められた。そのうち 1 例は本剤の初回投与 2 日後に発熱を発現し，残りの 1 例は 2 回目以降の投与時に発熱が 6 件（5 件は投与 2～3 日後，残り 1 件は投与 10 日後に発現）認められた。すべての発熱は発現後 1～3 日以内に回復した（表 2.7.4-付録-110）。

③ 製剤別 infusion related reaction（IRR）

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群で認められた製剤別（第 II 相試験用製剤，第 III 相試験用製剤）の IRR（初回，2 回目，3 回目以降の投与時）を表 2.7.4-付録-112 に示す。

第 II 相試験用製剤（64 例）で認められた IRR の発現割合は 46.9%（30/64 例），第 III 相試験用製剤（92 例）で認められた IRR の発現割合は 54.3%（50/92 例）であり，16 mg/kg 群で認められた IRR の発現割合（51.3%，80/156 例）と同程度であった。また，認められた製剤別の有害事象の種類及び発現割合も同程度であった。

いずれの製剤も IRR は初回投与時の発現割合が最も高かった。第 II 相試験用製剤では 30 例に IRR が認められ，発現時期別では，初回投与時に 90.0%（27/30 例），2 回目投与時に 13.3%（4/30 例），3 回目以降の投与時に 16.7%（5/30 例）の被験者が IRR を発現した。第 III 相試験用製剤では 50 例に IRR が認められ，発現時期別では，初回投与時に 92.0%（46/50 例），2 回目投与時に 10.0%（5/50 例），3 回目以降の投与時に 10.0%（5/50 例）の被験者が IRR を発現した。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，全例に第 III 相試験用製剤を投与した（IRR の発現割合は 2.7.4.2.1.5(1)1)b)①，発現時期別の IRR は 2.7.4.2.1.5(1)1)b)② 参照）。

④ Infusion related reaction（IRR）による投与の調節

(i) 本剤の投与中断に至った infusion related reaction（IRR）

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の本剤の投与中断に至った IRR を表 2.7.4-付録-113 に示す。

16 mg/kg 群で IRR を発現した 80 例のうち，本剤の投与中断に至った IRR の発現割合は 73.8%（59/80 例）であり，SOC 別では呼吸器，胸郭及び縦隔障害の事象が最も多かった（55.0%，44/80 例）。なお，本剤の投与中断に至った有害事象のほとんど（62 例のうち 59 例）が IRR と判断された（2.7.4.2.1.4(2)2) 参照）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で認められた IRR（8 mg/kg 群：1 例，16 mg/kg 群：3 例）のうち，8 mg/kg 群の 100%（1/1 例），16 mg/kg 群の 33.3%（1/3 例）の被験者が本剤の投与を中断した。全体で 2 例以上に認められた本剤の投与中断に至った IRR は発熱［8 mg/kg 群：100%（1/1 例），16 mg/kg 群：33.3%（1/3 例）］であった（表 2.7.4-付録-110）。

(ii) 本剤の投与中止に至った infusion related reaction（IRR）

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合の本剤の投与中止に至った IRR を表 2.7.4-付録-114 に示す。

16 mg/kg 群では，本剤の投与中止に至った IRR は認められなかった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，本剤の投与中止に至った IRR は認められなかった（表 2.7.4-付録-110）。

⑤ Infusion related reaction（IRR）の管理

前投薬

IRR の管理のため，本剤の投与前に前投薬として副腎皮質ステロイド，解熱鎮痛剤及び抗ヒスタミン剤の使用を治験実施計画書で規定していた。

16 mg/kg 群の全例が副腎皮質ステロイド，解熱鎮痛剤（アセトアミノフェン／paracetamol）及び抗ヒスタミン剤の前投薬を受けた（表 2.7.4-付録-115）。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では全例が前投薬［副腎皮質ステロイド（メチルプレドニゾロン），解熱鎮痛剤（アセトアミノフェン／paracetamol）及び抗ヒスタミン剤（ジフェンヒドラミン）］を受けた（表 2.7.4-付録-116）。

後投薬

後投薬として副腎皮質ステロイドの経口投与を実施することを治験実施計画書で規定していた。なお，GEN501 試験 Part 1 初期の時点では，後投薬は治験実施計画書に規定していなかった（2.7.4.2.1.5(1)1)b)① 参照）。また，治験実施計画書で呼吸器系合併症のリスクが高い被験者に対する後投薬の検討を規定していた。

16 mg/kg 群で使用した後投薬は，副腎皮質ステロイド（96.2%）が最も多く，次いで抗ヒスタミン剤（14.1%），解熱鎮痛剤（1.9%）であった（表 2.7.4-付録-117）。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では全例が後投薬（副腎皮質ステロイド）を受けた（表 2.7.4-付録-116）。

2) 好中球減少症

a) 併用療法試験

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

好中球減少症の発現割合は Vd 群が 9.3%（Grade 3 又は 4 が 4.2%），DVd 群が 17.7%（Grade 3 又は 4 が 12.8%）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。DVd 群の好中球減少症の発現割合は，サイクル 8 までは 17.3%であったが，本剤のみの投与となるサイクル 9 以降は 1.8%に減少した。3 サイクル目までの Grade 3 又は 4 の好中球減少症の発現割合は，Vd 群が 3.0%，DVd 群が 10.7%であった。

Vd 群では 5.1%，DVd 群では 7.4%の被験者に免疫賦活薬（主にフィルグラスチム）が投与された（表 2.7.4-付録-118）。投与サイクルの遅延又は投与調節に至った好中球減少症の発現割合は Vd 群が 0.4%（1 例），DVd 群が 2.5%（6 例）であった。また，重篤な好中球減少症が DVd 群のみ 0.8%（2 例），いずれかの治験薬の投与が中止となった好中球減少症が DVd 群のみ 0.4%（1 例）に認められた（表 2.7.4-付録-53，表 2.7.4-付録-119）。

発熱性好中球減少症の発現割合は Vd 群が 0.4%（1 例），DVd 群が 1.6%（4 例）であった（表 2.7.4-付録-26）。重篤な発熱性好中球減少症が DVd 群のみ 0.8%（2 例）に認められた（表 2.7.4-付録-53）。いずれかの治験薬の投与が中止となった発熱性好中球減少症は認められなかった（表 2.7.4-付録-119）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

好中球減少症の発現割合は Rd 群が 43.1%（Grade 3 又は 4 が 37.0%），DRd 群が 61.9%（Grade 3 又は 4 が 54.7%）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。MMY3003 試験では，最初の 2 サイクルで認められた好中球減少症の発現割合は，Rd 群が 25.6%，DRd 群が 48.4%であった。その後の発現割合はサイクル 3～6 では Rd 群が 29.3%，DRd 群が 29.4%，サイクル 7 以降では Rd 群が 27.2%，DRd 群が 29.9%であった。2 サイクル目までの Grade 3 又は 4 の好中球減少症の発現割合は，Rd 群が 20.3%，DRd 群が 41.3%であった。

Rd 群では 28.5%，DRd 群では 48.4%の被験者に免疫賦活薬（主にフィルグラスチム）が投与された（表 2.7.4-付録-118）。MMY3003 試験で投与サイクルの遅延又は投与調節に至った好中球減少症の発現割合は，Rd 群が 28.8%，DRd 群が 37.8%であった。また，重篤な好中球減少症が DRd 群のみ 1.6%（5 例），いずれかの治験薬の投与が中止となった好中球減少症が Rd 群の 0.4%（1 例），DRd 群の 0.3%（1 例）に認められた（表 2.7.4-付録-53，表 2.7.4-付録-119）。

発熱性好中球減少症の発現割合は Rd 群が 2.5%（7 例），DRd 群が 5.3%（17 例）であった（表 2.7.4-付録-26）。重篤な発熱性好中球減少症が Rd 群の 1.4%（4 例），DRd 群の 3.8%（12 例）に認められた（表 2.7.4-付録-53）。いずれかの治験薬の投与が中止となった発熱性好中球減少症は認められなかった（表 2.7.4-付録-119）。

MMY1001 試験（DPd 療法）

DPd 群では好中球減少症の発現割合は 78.6%（Grade 3 又は 4 が 76.7%）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。最初の 8 週間で Grade 3 又は 4 の好中球減少症が認められた被験者の割合は 70.9%であった。

57.3%の被験者に免疫賦活薬（主にフィルグラスチム）が投与された（表 2.7.4-付録-118）。投与サイクルの遅延又は投与調節に至った好中球減少症の発現割合は 23.3%であった。また，重篤な好中球減少症が 1.0%（1 例）に認められた（表 2.7.4-付録-53）。いずれかの治験薬の投与が中止となった好中球減少症は認められなかった（表 2.7.4-付録-119）。

DPd 群では発熱性好中球減少症の発現割合は 6.8%（7 例）であった（表 2.7.4-付録-26）。重篤な発熱性好中球減少症が 3.9%（4 例）に認められた（表 2.7.4-付録-53）。いずれかの治験薬の投与が中止となった発熱性好中球減少症は認められなかった（表 2.7.4-付録-119）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）では，好中球減少症の発現割合は 37.5%（3 例）であり，Grade 3 が 25.0%（2 例）であった。Grade 4 の好中球減少症は認められなかった（表 2.7.4-付録-120）。免疫賦活薬を投与された被験者はいなかった（表 2.7.4-付録-121）。投与サイクルの遅延又は投与調節に至った好中球減少症及び重篤な好中球減少症は認められず（表 2.7.4-付録-122，表 2.7.4-付録-55），いずれかの治験薬の投与が中止となった好中球減少症も認められなかった（表 2.7.4-付録-123）。また，発熱性好中球減少症は認められなかった（表 2.7.4-付録-120）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）の好中球減少症の発現割合は Rd 群が 40.0%（Grade 3 又は 4 が 26.7%），DRd 群が 60.0%（Grade 3 又は 4 が 55.0%）であった（表 2.7.4-付録-28，表 2.7.4-付録-31）。投与サイクルの遅延又は投与調節に至った好中球減少症の発現割合は Rd 群が 26.7%，DRd 群が 35.0%であった（表 2.7.4-付録-124）。また，重篤な好中球減少症及びいずれかの治験薬の投与が中止となった好中球減少症は認められなかった（表 2.7.4-付録-57，表 2.7.4-付録-125）。発熱性好中球減少症は認められなかった（表 2.7.4-付録-28）。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）の好中球減少症の発現割合は Rd 群が 43.2%（Grade 3 又は 4 が 38.6%），DRd 群が 66.7%（Grade 3 又は 4 が 62.7%）であった（表 2.7.4-付録-28，表 2.7.4-付録-31）。投与サイクルの遅延又は投与調節に至った好中球減少症の発現割合は Rd 群が 36.4%，DRd 群が 47.1%であった（表 2.7.4-付録-124）。また，重篤な好中球減少症が DRd 群のみ 3.9%（2 例）に認められた（表 2.7.4-付録-57）。いずれかの治験薬の投与が中止となった好中球減少症は認められなかった（表 2.7.4-付録-125）。発熱性好中球減少症の発現割合は Rd 群が 2.3%（1 例），DRd 群が 3.9%（2 例）であった（表 2.7.4-付録-28）。重篤な発熱性好中球減少症が DRd 群のみ 2.0%（1 例）に認められた（表 2.7.4-付録-57）。いずれかの治験薬の投与が中止となった発熱性好中球減少症は認められなかった（表 2.7.4-付録-125）。

b) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では好中球減少症の発現割合は 21.8%（Grade 3 が 9.6%，Grade 4 が 2.6%）であった（表 2.7.4-付録-35，表 2.7.4-付録-36）。15.4%の被験者に免疫賦活薬（主にフィルグラスチム）が投与された（表 2.7.4-付録-126）。また，重篤な好中球減少症が 0.6%（1 例）に認められた（表 2.7.4-付録-58）。本剤の投与中止に至った好中球減少症は認められなかった（表 2.7.4-22）。発熱性好中球減少症は認められなかった（表 2.7.4-付録-35）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）の好中球減少症の発現割合は 8 mg/kg 群が 50.0%（2 例），16 mg/kg 群が 100.0%（5 例）であり，Grade 3 が 16 mg/kg 群のみ 80.0%（4 例）に認められた。Grade 4 の好中球減少症は認められなかった（表 2.7.4-付録-38）。16 mg/kg 群の

20.0%（1 例）の被験者に免疫賦活薬（フィルグラスチム）が投与された（表 2.7.4-付録-127）。また，重篤な好中球減少症及び本剤の投与中止に至った好中球減少症は認められなかった（表 2.7.4-付録-60，表 2.7.4-付録-87）。発熱性好中球減少症は認められなかった（表 2.7.4-付録-38）。

3) 感染症及び寄生虫症

a) 併用療法試験

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

感染症及び寄生虫症（SOC）の発現割合は，Vd 群が 53.2%，DVd 群が 67.5%であった。発現割合が高かった感染症及び寄生虫症（いずれかの群で 10%以上）は，上気道感染（Vd 群 18.1%，DVd 群 24.7%，以下同順），肺炎（11.8%，11.9%）及び気管支炎（5.5%，11.5%）であった。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は Vd 群が 19.0%，DVd 群が 21.4%であり，いずれかの群で 3%以上に認められた事象は肺炎（Vd 群 9.7%，DVd 群 8.2%）であった（表 2.7.4-付録-128）。DVd 群では本剤のみの投与となるサイクル 9 以降に Grade 3 又は 4 の感染症及び寄生虫症は認められなかった。重篤な感染症及び寄生虫症の発現割合は Vd 群が 18.1%，DVd 群が 19.8%であった（表 2.7.4-付録-53）。

DVd 群では，初回発現までの期間別の感染症及び寄生虫症の発現割合は，≤6 カ月が 66.3%，>6 カ月が 27.5%であり，経時的な発現割合の減少が認められた（表 2.7.4-付録-129）。>6 カ月で発現した Grade 3 又は 4 の感染症及び寄生虫症の発現割合は 0.7%（1 例）であった（表 2.7.4-付録-130）。

日和見感染の発現に関して，いずれかの群で 1%以上に認められた事象は，帯状疱疹（Vd 群 3.0%，DVd 群 5.3%，以下同順），口腔カンジダ症（2.1%，1.6%）及びカンジダ感染（1.3%，0.8%）であった（表 2.7.4-付録-128）。

いずれかの治験薬の投与が中止となった感染症及び寄生虫症の発現割合は Vd 群が 2.5%（6 例），DVd 群が 3.7%（9 例）であった（表 2.7.4-付録-119）。死亡に至った感染症及び寄生虫症の発現割合は Vd 群が 1.7%（4 例，うち肺炎が 2 例，敗血症性ショック及び気管気管支炎が各 1 例），DVd 群が 0.8%（2 例，うち肺炎及び肺敗血症が各 1 例）であった（表 2.7.4-付録-45）。

肺炎の発現割合は Vd 群が 11.8%（28 例），DVd 群が 11.9%（29 例）であった。肺炎は Grade 3 又は 4 の感染症及び寄生虫症のうち最も発現割合が高く［Vd 群 9.7%（23 例），DVd 群 8.2%（20 例）］，重篤な感染症及び寄生虫症のうちでも最も発現割合が高かった［Vd 群 9.3%（22 例），DVd 群 7.8%（19 例）］（表 2.7.4-付録-128，表 2.7.4-付録-53）。治験薬の投与中止に至った肺炎の発現割合は Vd 群が 0.4%（1 例），DVd 群が 1.2%（3 例）であり，死亡に至った肺炎の発現割合は Vd 群が 0.8%（2 例），DVd 群が 0.4%（1 例）であった（表 2.7.4-21，表 2.7.4-付録-45）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

感染症及び寄生虫症（SOC）の発現割合は，Rd 群が 72.6%，DRd 群が 83.3%であった。発現割合が高かった感染症及び寄生虫症（いずれかの群で 10%以上）は，上気道感染（Rd 群 20.6%，

DRd 群 30.8%，以下同順），鼻咽頭炎（15.3%，23.9%），気管支炎（12.1%，14.5%），肺炎（13.2%，12.9%）及び気道感染（7.8%，10.4%）であった。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は Rd 群が 22.8%，DRd 群が 27.0%であり，いずれかの群で 3%以上に認められた事象は肺炎（Rd 群 8.2%，DRd 群 7.2%）であった（表 2.7.4-付録-128）。重篤な感染症及び寄生虫症の発現割合は Rd 群が 22.8%，DRd 群が 29.6%であった（表 2.7.4-付録-53）。

MMY3003 試験の DRd 群では，初回発現までの期間別の感染症及び寄生虫症の発現割合は，≤6 カ月が 72.8%，6～≤12 カ月が 58.3%，>12 カ月が 36.4%であり，経時的な発現割合の減少が認められた（表 2.7.4-付録-131）。同様に，Grade 3 又は 4 の感染症及び寄生虫症も経時的な発現割合の減少（≤6 カ月が 18.4%，6～≤12 カ月が 12.7%，>12 カ月が 4.6%）が認められた（表 2.7.4-付録-132）。

日和見感染の発現に関して，いずれかの群で 1%以上に認められた事象は，帯状疱疹（Rd 群 1.8%，DRd 群 2.8%，以下同順），口腔ヘルペス（0.7%，2.5%），口腔カンジダ症（1.4%，1.9%），口腔真菌感染（1.8%，1.6%），真菌感染（0.4%，1.3%），ヘルペスウイルス感染（0%，1.3%）及び皮膚カンジダ（1.1%，0%）であった（表 2.7.4-付録-128）。

いずれかの治験薬の投与が中止となった感染症及び寄生虫症の発現割合は Rd 群が 2.5%（7 例），DRd 群が 3.1%（10 例）であった（表 2.7.4-付録-119）。死亡に至った感染症及び寄生虫症の発現割合は Rd 群が 1.4%（4 例，うち肺炎が 2 例，敗血症性ショック及び敗血症が各 1 例），DRd 群が 2.2%（7 例，うち敗血症性ショックが 3 例，肺炎が 2 例，細菌性肺炎及びウイルス性肺炎が各 1 例）であった（表 2.7.4-付録-45）。

肺炎の発現割合は Rd 群が 13.2%（37 例），DRd 群が 12.9%（41 例）であった。肺炎は Grade 3 又は 4 の感染症及び寄生虫症のうち最も発現割合が高く［Rd 群 8.2%（23 例），DRd 群 7.2%（23 例）］，重篤な感染症及び寄生虫症のうちでも最も発現割合が高かった［Rd 群 8.5%（24 例），DRd 群 7.5%（24 例）］（表 2.7.4-付録-128，表 2.7.4-付録-53）。治験薬の投与中止に至った肺炎の発現割合は Rd 群が 0.7%（2 例），DRd 群が 0.9%（3 例）であり，死亡に至った肺炎の発現割合は Rd 群が 0.7%（2 例），DRd 群が 0.6%（2 例）であった（表 2.7.4-21，表 2.7.4-付録-45）。

MMY1001 試験（DPd 療法）

DPd 群では，感染症及び寄生虫症（SOC）の発現割合は 69.9%であった。発現割合が高かった感染症及び寄生虫症（10%以上）は，上気道感染（25.2%），副鼻腔炎（12.6%）及び肺炎（10.7%）であった。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は 28.2%であり，3%以上に認められた事象は肺炎（7.8%）であった（表 2.7.4-付録-128）。重篤な感染症及び寄生虫症の発現割合は 20.4%であった（表 2.7.4-付録-53）。また，日和見感染の発現に関して，認められた事象は帯状疱疹及び陰部ヘルペス（各 1.9%），口腔ヘルペス，シュードモナス性敗血症及び癜風（各 1.0%）であった（表 2.7.4-付録-128）。

いずれかの治験薬の投与が中止となった感染症及び寄生虫症の発現割合は 4.9%（5 例）であり，死亡に至った感染症及び寄生虫症の発現割合は 1.9%（2 例，うち進行性多巣性白質脳症及び敗血症が各 1 例）であった（表 2.7.4-付録-119，表 2.7.4-付録-45）。進行性多巣性白質脳症を発現した 1 例は，リツキシマブ及び幹細胞移植を含む 5 レジメンの前治療歴があった。Day 8 の本剤投

与後に Grade 3 の進行性多巣性白質脳症が認められた。治験担当医師は本事象と治験薬との関連性について，デキサメタゾンと関連性があり（「可能性小」），ポマリドミドとは関連性がなく（「多分なし」），本剤とも関連性がない（「関連なし」）と判断した。当該被験者は投与を中止し，Day 31 に進行性多巣性白質脳症のため死亡した。

肺炎の発現割合は 10.7%（11 例）であった。肺炎は Grade 3 又は 4 の感染症及び寄生虫症のうち最も発現割合が高く（7.8%，8 例），重篤な感染症及び寄生虫症のうちでも最も発現割合が高かった（6.8%，7 例）（表 2.7.4-付録-128，表 2.7.4-付録-53）。治験薬の投与中止に至った肺炎の発現割合は 1.0%（1 例）であり，死亡に至った肺炎は認められなかった（表 2.7.4-21，表 2.7.4-付録-45）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）では，感染症及び寄生虫症（SOC）の発現割合は 62.5%（5 例）であり，その内訳は鼻咽頭炎が 25.0%（2 例），気管支炎，帯状疱疹及びインフルエンザが各 12.5%（1 例）であった。そのうち帯状疱疹及び鼻咽頭炎の各 1 例が Grade 3 であり，いずれも重篤な有害事象であった（表 2.7.4-付録-120，表 2.7.4-付録-55）。Grade 4 の感染症及び寄生虫症は認められなかった。Grade 3 の鼻咽頭炎はサイクル 1～3，Grade 3 の帯状疱疹はサイクル 4～8 の時点で発現した（表 2.7.4-付録-133）。日和見感染の発現に関して，帯状疱疹が 12.5%（1 例）に認められた（表 2.7.4-付録-120）。いずれかの治験薬の投与が中止となった感染症及び寄生虫症，並びに死亡に至った感染症及び寄生虫症は認められなかった（表 2.7.4-付録-123，表 2.7.4-付録-47）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）では感染症及び寄生虫症（SOC）の発現割合は Rd 群が 86.7%，DRd 群が 85.0%であった。発現割合が高かった感染症及び寄生虫症（いずれかの群で 10%以上）は，鼻咽頭炎（Rd 群 26.7%，DRd 群 45.0%，以下同順），上気道感染（20.0%，15.0%）及び肺炎（20.0%，10.0%）であった。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は Rd 群が 13.3%（2 例），DRd 群が 25.0%（5 例）であり，いずれかの群で 2 例以上に認められた事象は肺炎［Rd 群 13.3%（2 例），DRd 群 10.0%（2 例）］であった（表 2.7.4-付録-134）。重篤な感染症及び寄生虫症の発現割合は Rd 群が 6.7%（1 例），DRd 群が 20.0%（4 例）であった（表 2.7.4-付録-57）。また，日和見感染の発現に関して，帯状疱疹が Rd 群の 6.7%（1 例），サイトメガロウイルス感染が DRd 群の 5.0%（1 例）に認められた（表 2.7.4-付録-134）。いずれかの治験薬の投与が中止となった感染症及び寄生虫症が DRd 群の 5.0%（1 例，肺炎）に認められた（表 2.7.4-付録-125）。死亡に至った感染症及び寄生虫症は認められなかった（表 2.7.4-付録-49）。

日本人集団の肺炎の発現割合は Rd 群が 20.0%（3 例），DRd 群が 10.0%（2 例）であった。Grade 3 又は 4 の肺炎の発現割合は Rd 群が 13.3%（2 例），DRd 群が 10.0%（2 例），重篤な肺炎の発現割合は Rd 群が 6.7%（1 例），DRd 群が 10.0%（2 例）であった（表 2.7.4-付録-134，表 2.7.4-付録-57）。治験薬の投与中止に至った肺炎は認められなかった（表 2.7.4-付録-81）。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では感染症及び寄生虫症（SOC）の発現割合は Rd 群が 86.4%，DRd 群が 86.3%であった。発現割合が高かった感染症及び寄生虫症（いずれかの群で 10%以上）は，上気道感染（Rd 群 40.9%，DRd 群 43.1%，以下同順），鼻咽頭炎（20.5%，33.3%）及び肺炎（13.6%，9.8%）であった。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は Rd 群が 25.0%（11 例），DRd 群が 19.6%（10 例）であり，いずれかの群で 2 例以上に認められた事象は肺炎［Rd 群 9.1%（4 例），DRd 群 5.9%（3 例）］であった（表 2.7.4-付録-134）。重篤な感染症及び寄生虫症の発現割合は Rd 群が 25.0%（11 例），DRd 群が 13.7%（7 例）であった（表 2.7.4-付録-57）。また，日和見感染の発現に関して，認められた事象は帯状疱疹［Rd 群 9.1%（4 例），DRd 群 7.8%（4 例）］，単純ヘルペス及び肺結核［Rd 群のみ各 2.3%（1 例）］，サイトメガロウイルス感染［DRd 群のみ 2.0%（1 例）］であった（表 2.7.4-付録-134）。いずれかの治験薬の投与が中止となった感染症及び寄生虫症が Rd 群の 2.3%（1 例，敗血症），DRd 群の 3.9%（2 例，いずれも肺炎），死亡に至った感染症及び寄生虫症が DRd 群のみ 2.0%（1 例，肺炎）に認められた（表 2.7.4-付録-125，表 2.7.4-付録-49）。

東アジア人集団の肺炎の発現割合は Rd 群が 13.6%（6 例），DRd 群が 9.8%（5 例）であった。Grade 3 又は 4 の肺炎の発現割合は Rd 群が 9.1%（4 例），DRd 群が 5.9%（3 例），重篤な肺炎の発現割合は Rd 群が 9.1%（4 例），DRd 群が 5.9%（3 例）であった（表 2.7.4-付録-134，表 2.7.4-付録-57）。治験薬の投与中止に至った肺炎が DRd 群のみ 2.0%（1 例）に認められた（表 2.7.4-付録-81）。

① 帯状疱疹

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

帯状疱疹の発現割合は Vd 群が 3.0%（7 例，うち 1 例は予防的な抗ウイルス療法を受けた），DVd 群が 5.3%（13 例，うち 8 例は予防的な抗ウイルス療法を受けた）であった。Grade 3 又は 4 の帯状疱疹の発現割合は Vd 群が 0.4%（1 例），DVd 群が 1.6%（4 例）であった（表 2.7.4-付録-128）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

帯状疱疹の発現割合は Rd 群が 1.8%（5 例），DRd 群が 2.8%（9 例）であった。Grade 3 又は 4 の帯状疱疹は Rd 群のみ 0.4%（1 例）に認められた（表 2.7.4-付録-128）。MMY3003 試験では，帯状疱疹が発現した被験者のうち，予防的な抗ウイルス療法を受けたのは Rd 群の 2/5 例，DRd 群の 2/6 例であった。

MMY1001 試験（DPd 療法）

DPd 群では，帯状疱疹の発現割合は 1.9%（2 例，うち 1 例は予防的な抗ウイルス療法を受けた）であり，いずれも Grade 3 又は 4 であった（表 2.7.4-付録-128）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）では，12.5%（1 例，予防的な抗ウイルス療法を受けた）が Grade 3 の重篤な帯状疱疹を発現した（表 2.7.4-付録-135，表 2.7.4-付録-136）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）では Rd 群の 6.7%（1 例）が帯状疱疹を発現した。Grade 3 又は 4 の帯状疱疹は認められなかった（表 2.7.4-付録-137）。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では，Rd 群の 9.1%（4 例），DRd 群の 7.8%（4 例）が帯状疱疹を発現し，Rd 群の 2.3%（1 例）が Grade 3 であった（表 2.7.4-付録-137）。

b) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では，感染症及び寄生虫症（SOC）の発現割合は 54.5%であった。発現割合が高かった感染症及び寄生虫症（10%以上）は，上気道感染（17.3%）及び鼻咽頭炎（11.5%）であった（表 2.7.4-付録-35）。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は 9.6%であり，3%以上に認められた事象は肺炎（5.1%）であった（表 2.7.4-付録-41）。重篤な感染症及び寄生虫症の発現割合は 12.2%であり，最も発現割合が高かった事象は肺炎（5.8%，9 例）であった（表 2.7.4-付録-58）。初回発現までの期間別の感染症及び寄生虫症の発現割合は，≤6 カ月が 50.6%，>6 カ月が 38.5%であった（表 2.7.4-付録-138）。また，日和見感染の発現に関して，認められた事象は帯状疱疹及び口腔カンジダ症（各 1.9%），カンジダ感染，単純ヘルペス及び水痘（各 1.3%），サイトメガロウイルス性脈絡網膜炎，眼部単純ヘルペス及び口腔ヘルペス（各 0.6%）であった（表 2.7.4-付録-138）。本剤の投与中止に至った感染症及び寄生虫症は H1N1 インフルエンザ及び肺炎（各 0.6%，1 例）であった（表 2.7.4-22）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，感染症及び寄生虫症（SOC）の発現割合は 8 mg/kg 群が 50.0%（2 例），16 mg/kg 群が 60.0%（3 例）であった。全体で 2 例以上に認められた感染症及び寄生虫症は鼻咽頭炎［8 mg/kg 群：25.0%（1 例），16 mg/kg 群：20.0%（1 例）］であり，それ以外の事象はすべて 1 例のみで認められた。16 mg/kg 群で発現した肺炎の 1 例が Grade 3 であり，かつ重篤な有害事象であった（表 2.7.4-付録-38，表 2.7.4-付録-60）。日和見感染は認められなかった（表 2.7.4-付録-38）。本剤の投与中止に至った感染症及び寄生虫症は認められなかった（表 2.7.4-付録-87）。

① 帯状疱疹

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では，帯状疱疹の発現割合は 1.9%（3 例）であり，1.3%（2 例）が Grade 3 であった（表 2.7.4-付録-36）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，帯状疱疹は認められなかった（表 2.7.4-付録-38）。

4) 血小板減少症及び出血関連事象

a) 併用療法試験

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

血小板減少症の発現割合は Vd 群が 43.9%（Grade 3 又は 4 が 32.9%），DVd 群が 58.8%（Grade 3 又は 4 が 45.3%）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。血小板減少症の発現割合は，本剤を 1 週間隔で投与するサイクル 1～3 では Vd 群が 40.5%，DVd 群が 56.4%であり，サイクル 4～8 では Vd 群が 16.3%，DVd 群が 20.7%であった。DVd 群では本剤のみの投与となるサイクル 9 以降の発現割合は 1.8%であった。3 サイクル目までの Grade 3 又は 4 の血小板減少症の発現割合は，Vd 群が 30.4%，DVd 群が 43.6%であった。投与サイクルの遅延又は投与調節に至った血小板減少症の発現割合は Vd 群が 11.8%，DVd 群が 16.9%であった。また，いずれかの治験薬の投与が中止となった血小板減少症が Vd 群の 0.4%（1 例），DVd 群の 0.8%（2 例）に認められた（表 2.7.4-付録-119）。

Vd 群の 9.7%，DVd 群の 15.2%の被験者に血小板輸血を実施した。

出血関連事象の発現割合は Vd 群が 3.8%（9 例，うち Grade 3 又は 4 が 2 例），DVd 群が 7.0%（17 例，うち Grade 3 又は 4 が 3 例）であった（表 2.7.4-付録-139）。なお，該当事象を追加して集計した 2016 年 6 月 30 日クリニカルカットオフ時の集計では，出血関連事象の発現割合は Vd 群が 8.9%（21 例，うち Grade 3 又は 4 が 2 例），DVd 群が 11.1%（27 例，うち Grade 3 又は 4 が 4 例）であった（表 2.7.4-付録-140）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

血小板減少症の発現割合は Rd 群が 27.4%（Grade 3 又は 4 が 13.5%），DRd 群が 27.0%（Grade 3 又は 4 が 12.6%）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。投与サイクルの遅延又は投与調節に至った血小板減少症の発現割合は Rd 群が 7.8%，DRd 群が 7.8%であった。また，いずれかの治験薬の投与が中止となった血小板減少症が Rd 群のみ 0.7%（2 例）に認められた（表 2.7.4-付録-119）。

MMY3003 試験では，Rd 群の 8.2%，DRd 群の 7.1%の被験者に血小板輸血を実施した。

出血関連事象の発現割合は Rd 群が 3.9%（11 例，うち Grade 3 又は 4 が 1 例），DRd 群が 4.7%（15 例，うち Grade 3 又は 4 が 1 例）であった（表 2.7.4-付録-139）。なお，該当事象を追加して集計した 2016 年 6 月 30 日クリニカルカットオフ時の集計では，出血関連事象の発現割合は Rd 群が 9.6%（27 例，うち Grade 3 又は 4 が 1 例），DRd 群が 11.9%（38 例，うち Grade 3 又は 4 が 2 例）であった（表 2.7.4-付録-140）。

MMY1001 試験（DPd 療法）

DPd 群では血小板減少症の発現割合は 40.8%（Grade 3 又は 4 が 17.5%）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。投与サイクルの遅延又は投与調節に至った血小板減少症の発現割合は 8.7%であった。また，いずれかの治験薬の投与が中止となった血小板減少症が 1.0%（1 例）に認められた（表 2.7.4-付録-119）。

DPd 群の 12.6%の被験者に血小板輸血を実施した。

出血関連事象の発現割合は 6.8%（7 例，うち Grade 3 又は 4 が 1 例）であった（表 2.7.4-付録-139）。なお，該当事象を追加して集計した 2016 年 6 月 30 日クリニカルカットオフ時の集計では，出血関連事象の発現割合は 15.5%（16 例，うち Grade 3 又は 4 が 1 例）であった（表 2.7.4-付録-140）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）では，血小板減少症の発現割合は 87.5%（7 例）であり，Grade 3 が 37.5%（3 例），Grade 4 が 37.5%（3 例）であった（表 2.7.4-付録-120）。投与サイクルの遅延又は投与調節に至った血小板減少症の発現割合は 50.0%（4 例）であった（表 2.7.4-付録-122）。いずれかの治験薬の投与が中止となった血小板減少症は認められなかった（表 2.7.4-付録-123）。

12.5%（1 例）の被験者に血小板輸血を実施した（表 2.7.4-付録-141）。当該被験者は Grade 3 の出血を伴う血小板減少症（thrombocytopenia with bleeding）が認められ，DLT として報告された。

出血関連事象の発現割合は 12.5%（1 例）であり，その内訳は Grade 1 の皮下出血であった（表 2.7.4-付録-142，表 2.7.4-付録-143）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）では血小板減少症の発現割合は Rd 群が 40.0%（Grade 3 又は 4 が 13.3%），DRd 群が 15.0%（Grade 3 又は 4 が 5.0%）であった（表 2.7.4-付録-28，表 2.7.4-付録-31）。投与サイクルの遅延又は投与調節に至った血小板減少症の発現割合は Rd 群が 6.7%（1 例），DRd 群が 5.0%（1 例）であった（表 2.7.4-付録-124）。いずれかの治験薬の投与が中止となった血小板減少症は認められなかった（表 2.7.4-付録-125）。Rd 群の 6.7%（1 例）の被験者に血小板輸血を実施した（表 2.7.4-付録-144）。また，出血関連事象は認められなかった（表 2.7.4-付録-145）。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では血小板減少症の発現割合は Rd 群が 29.5%（Grade 3 又は 4 が 15.9%），DRd 群が 23.5%（Grade 3 又は 4 が 9.8%）であった（表 2.7.4-付録-28，表 2.7.4-付録-31）。投与サイクルの遅延又は投与調節に至った血小板減少症の発現割合は Rd 群が 2.3%（1 例），DRd 群が 3.9%（2 例）であった（表 2.7.4-付録-124）。いずれかの治験薬の投与が中止となった血小板減少症は認められなかった（表 2.7.4-付録-125）。Rd 群の 11.4%（5 例），DRd 群の 5.9%（5 例）の被験者に血小板輸血を実施した（表 2.7.4-付録-144）。また，出血関連事象の発現割合は Rd 群が 9.1%（4 例），DRd 群が 5.9%（3 例）であった。Grade 3 又は 4 の出血関連事象は認められなかった（表 2.7.4-付録-145）。

b) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では血小板減少症の発現割合は 19.9%（Grade 3 が 8.3%，Grade 4 が 5.8%）であった（表 2.7.4-付録-35，表 2.7.4-付録-36）。本剤の投与中止に至った血小板減少症は認められなかった（表 2.7.4-22）。

9.6%の被験者に血小板輸血を実施した（表 2.7.4-付録-146）。

出血関連事象の発現割合は 11.5%（18 例，うち Grade 3 又は 4 が 2 例）であった（表 2.7.4-付録-147）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，血小板減少症の発現割合は 8 mg/kg 群が 25.0%（1 例），16 mg/kg 群が 20.0%（1 例）であり，いずれも Grade 4 であった（表 2.7.4-付録-38）。本剤の投与中止に至った血小板減少症は認められなかった（表 2.7.4-付録-87）。

8 mg/kg 群の 25.0%（1 例），16 mg/kg 群の 20.0%（1 例）の被験者に血小板輸血を実施した（表 2.7.4-付録-148）。

出血関連事象は認められなかった（表 2.7.4-付録-149）。

5) 溶血

a) 併用療法試験

MMY3004 試験，MMY3003 試験（全体，日本人及び東アジア人集団），GEN503 試験及び MMY1005 試験（日本人）では，有害事象として溶血は認められなかった（表 2.7.4-付録-26，表 2.7.4-付録-27，表 2.7.4-付録-28）。

MMY1001 試験（DPd 群）の 1 例が Day 70 に末梢血液塗抹検査で分裂赤血球が確認され，Grade 1 の溶血と判断された。当該事象は，最後の輸血処置から 13 日後かつ本剤の最終投与の 12 日後に発現した。また，貧血の進行は認められなかった。

b) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では有害事象として溶血は認められなかった（表 2.7.4-付録-35）。

MMY2002 試験（124 例）では，16 mg/kg 群の 1 例に赤血球凝集が認められた。当該被験者の既往歴は狭心症，高血圧及び疼痛であった。Day 16 に Grade 1 の非重篤な赤血球凝集が認められ，本剤と関連性がある（「可能性大」）と判断された。その後本剤の投与を継続し，当該事象は軽快した。

GEN501 試験の Part 1 で溶血解析を実施した 32 例のうち，3 例に溶血が認められ，すべて 1 mg/kg 以下の投与群であった。重症度はいずれも Grade 1 であり，すべての事象は回復した。臨床的に意味のある 1 g/dL を超えるヘモグロビン減少（本剤の投与前から投与後 12 時間まで）は

認められなかった。GEN501 試験 Part 1 の対象集団全体では溶血解析結果に一貫した傾向は認められなかった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，有害事象として溶血は認められなかった（表 2.7.4-付録-38）。

6) 間接クームス試験への干渉及び輸血への影響

a) 併用療法試験

併用療法試験では，本剤初回投与前のみ間接クームス試験を実施し，投与後の評価は実施しなかった。本剤の投与による輸血の判断への影響は報告されなかった。

b) 単剤療法試験

① 直接及び間接クームス試験

GEN501 試験

GEN501 試験 Part 1（32 例）では，本剤の投与前及び投与後 2 時間の時点に治験実施医療機関でクームス試験を実施した。試験初期の段階（改訂第 7 版，2011 年 2 月）では間接クームス試験のみを実施した。改訂第 9 版（2011 年 6 月）では直接クームス試験も可能としたが，CRF が適切に更新されなかったことから，直接クームス試験と間接クームス試験の結果を比較できなかった。また，GEN501 試験 Part 2（72 例）では，16 mg/kg 群の 3 例に交差適合試験不適合が重篤な有害事象として報告されたものの，赤血球輸血の実施に関連した有害事象は認められず，その後も合併症を発現することなく輸血の継続が可能であった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，すべての被験者に対してベースライン及び本剤投与後に直接及び間接クームス試験を実施した。間接クームス試験では，ベースラインで既に陽性であった 16 mg/kg 群の 1 例を除き，ベースライン陰性であった被験者 8 例が本剤の初回投与後 5 時間以内の時点で陽性となった。また，直接クームス試験では，16 mg/kg 群の 4 例が本剤の初回投与後 5 時間以内の時点で陽性となった。

本剤の投与による輸血の判断への影響は報告されなかった。

② 輸血及び赤血球輸血関連事象

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では，30.8%の被験者に輸血を 208 件実施し，28.8%の被験者に赤血球を輸血した（表 2.7.4-付録-146）。貧血に対して濃厚赤血球を投与された 1 例に Grade 1 の非重篤な赤血球凝集が認められたが，本事象発現後も本剤に対する処置（投与延期，投与中断）を実施することなく，本剤の投与継続が可能であった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，8 mg/kg 群の 25.0%（1 例）に輸血を 1 件，16 mg/kg 群の 20.0%（1 例）に輸血を 8 件実施した。16 mg/kg 群の 20.0%（1 例）に赤血球輸血を 2 件実施した（表 2.7.4-付録-148）。赤血球輸血の実施に関連した有害事象は認められなかった（表 2.7.4-付録-38）。

7) 心イベント

a) 併用療法試験

① 心房細動

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

心房細動の発現割合は Vd 群が 1.7%（4 例，うち Grade 3 又は 4 が 2 例），DVd 群が 4.5%（11 例，うち Grade 3 又は 4 が 4 例）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。DVd 群では，心房細動を発現した 11 例のうち既往歴として心房細動を 4 例，高血圧を 7 例が有しており，うち 1 例は心房細動及び高血圧の両方の既往歴を有していた。一方 Vd 群では，心房細動を発現した 4 例のうち既往歴として心房細動を 1 例，高血圧を 2 例の被験者が有していた。重篤な心房細動が DVd 群のみ 2.1%（5 例），治験薬の投与中止に至った心房細動が DVd 群のみ 0.4%（1 例）に認められた（表 2.7.4-付録-53，表 2.7.4-21）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

心房細動の発現割合は Rd 群が 2.5%（7 例，うち Grade 3 又は 4 が 3 例），DRd 群が 3.1%（10 例，うち Grade 3 又は 4 が 3 例）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。重篤な心房細動が Rd 群の 0.7%（2 例），DRd 群の 0.6%（2 例）に認められた（表 2.7.4-付録-53）。治験薬の投与中止に至った心房細動は認められなかった（表 2.7.4-21）。

MMY1001 試験（DPd 療法）

DPd 群では心房細動の発現割合は 6.8%（7 例，うち Grade 3 又は 4 が 1 例）であった（表 2.7.4-付録-26，表 2.7.4-付録-29）。心房細動を発現した 7 例のうち既往歴として心房細動を 2 例，高血圧を 2 例，冠動脈疾患を 1 例が有していた。重篤な心房細動が 1.0%（1 例）に認められた（表 2.7.4-付録-53）。治験薬の投与中止に至った心房細動は認められなかった（表 2.7.4-21）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）では心房細動は認められなかった（表 2.7.4-付録-120）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）では，DRd 群のみ 5.0%（1 例）に心房細動が認められた（表 2.7.4-付録-28）。Grade 3 又は 4 の心房細動は認められず（表 2.7.4-付録-31），治験薬の投与中止に至った心房細動も認められなかった（表 2.7.4-付録-81）。

日本人集団で認められた心房細動以外に，東アジア人集団（Rd 群 44 例，DRd 群 51 例）で心房細動は認められなかった。

② QT 延長

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

両群とも心電図 QT 延長は認められなかった（表 2.7.4-付録-150）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Rd 群及び DRd 群で認められた心電図 QT 延長の発現割合は，Rd 群が 0.4%（1 例），DRd 群が 1.9%（6 例）であった（表 2.7.4-付録-150）。Grade 3 又は 4 の心電図 QT 延長は認められなかった（表 2.7.4-付録-29）。QTcF が 500 msec を超えたのは DRd 群の 1 例のみであった。当該被験者は心不全の既往歴を有しており，Day 50 に QTcF の実測値が 532 msec となり心電図 QT 延長が認められた。ベースラインの心電図は正常であった。治験担当医師は本事象と治験薬との関連性について，レナリドミドと関連性があり（「ほぼ確実」），本剤及びデキサメタゾンとは関連性がない（「関連なし」）と判断した。治験薬の投与は継続し，心電図 QT 延長は発現から 7 日後に回復し，その後再発しなかった。

MMY1001 試験（DPd 療法）

DPd 群では心電図 QT 延長は認められなかった（表 2.7.4-付録-150）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）では心電図 QT 延長は認められなかった（表 2.7.4-付録-151）。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）では心電図 QT 延長は認められなかった（表 2.7.4-付録-28）。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では，DRd 群の 2.0%（1 例）に心電図 QT 延長が認められた（表 2.7.4-付録-28）。当該被験者は Day 142 に心電図 QT 延長を発現し，治験担当医師は本事象と治験薬とは関連性がない（「関連なし」）と判断した。当該被験者は治験薬の投与を継続し，クリニカルカットオフ時点では回復していなかった。

b) 単剤療法試験

① 心房細動

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では心房細動は認められなかった（表 2.7.4-付録-35）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では心房細動は認められなかった（表 2.7.4-付録-38）。

② QT 延長

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では心電図 QT 延長の発現割合は 0.6%（1 例）であった。また，併合データの対象集団全体では，≤4 mg/kg 群の 5 例（Grade 3 が 1 例）に心電図 QT 延長が認められた（表 2.7.4-付録-152，表 2.7.4-付録-36）。

MMY2002 試験（124 例）では，16 mg/kg 群の 1 例が Day 22 に Grade 1 の QT 延長を発現した（ベースライン値は正常）。QT 延長は発現日の翌日に回復した。認められた有害事象は本剤と関連性がない（「多分なし」）と判断された。当該被験者は本剤の投与を継続し，その後の心電図評価では正常であった。

GEN501 試験 Part 1（32 例）では，0.005～1 mg/kg のコホートの 5 例に QT 延長が認められた。2 mg/kg 以上の投与を受けた被験者では QT 延長は認められなかった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では QT 延長関連事象は認められなかった（表 2.7.4-付録-153）。また，QTcF が 500 msec を超えた被験者はいなかった。

8) 肝胆道系障害

a) 併用療法試験

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

肝胆道系障害（SOC）の発現割合は，Vd 群が 2.1%（5 例），DVd 群が 3.7%（9 例）であった。このうち，Vd 群で認められた PT 別の有害事象は高ビリルビン血症（0.8%，2 例），胆汁うっ滞，肝アミロイドーシス，虚血性肝炎及び門脈域の炎症（各 0.4%，1 例）であった（表 2.7.4-付録-26）。Vd 群で肝アミロイドーシス及び門脈域の炎症を発現した 1 例の既往歴は，胆嚢切除並びに臨床検査値上のアルカリフォスファターゼ高値及び ALT 高値であった。DVd 群で認められた PT 別の有害事象は高ビリルビン血症（2.1%，5 例），胆嚢炎（1.2%，3 例），慢性胆嚢炎及び胆嚢障害（各 0.4%，1 例）であった（表 2.7.4-付録-26）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

肝胆道系障害（SOC）の発現割合は，Rd 群が 2.5%（7 例），DRd 群が 3.5%（11 例）であった。このうち，Rd 群で認められた PT 別の有害事象は肝障害（1.1%，3 例），高ビリルビン血症（0.7%，2 例），脂肪肝，胆管結石及び肝腫瘤（各 0.4%，1 例）であった（表 2.7.4-付録-26）。DRd 群で認められた PT 別の有害事象は高ビリルビン血症（1.3%，4 例），肝機能異常及び肝細胞損傷（各 0.6%，2 例），胆石症，脂肪肝及び肝障害（各 0.3%，1 例）であった（表 2.7.4-付録-26）。また，DRd 群で認められた 11 例のうち 7 例は肝胆道系障害と関連する既往歴を有していた。そのうち 1 例は疾患進行と同時に乳酸脱水素酵素増加を併発し，肝障害ではなく悪性腫瘍が原因であることが示唆された。

MMY1001 試験（DPd 療法）

DPd 群では肝胆道系障害（SOC）の発現割合は 5.8%（6 例）であった。このうち，認められた PT 別の有害事象は高ビリルビン血症（4.9%，5 例），胆石症（1.0%，1 例）であった（表 2.7.4-付録-26）。これら 6 例のうち 2 例は高ビリルビン血症，2 例は肝機能検査異常の既往歴を有していた。肝機能検査異常の既往歴を有する 2 例のうち 1 例は，Grade 3 の ALT 増加及び AST 増加と同時に Grade 2 の高ビリルビン血症を併発し，すべての事象は治験担当医師により本剤と関連性がない（「関連なし」）と判断された。また，肝障害の既往歴がなかった 1 例は疾患進行が認められ，Grade 3 のアルカリフォスファターゼ増加並びに Grade 2 の ALT 増加及び AST 増加と同時に Grade 3 の高ビリルビン血症を併発した。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）で，肝胆道系障害（SOC）に分類される有害事象（PT）は，薬物性肝障害（12.5%，1 例）であった（表 2.7.4-付録-120）。当該被験者は既往歴として薬物性肝障害を有していた。当該被験者は Grade 2 の薬物性肝障害を 2 件，及び本剤の投与中断に至った Grade 3 の薬物性肝障害を 1 件発現し，いずれも本剤と関連性がある（「可能性小」）と判断された。いずれの薬物性肝障害も回復した。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）で，肝胆道系障害（SOC）に分類される有害事象（PT）は，DRd 群の肝機能異常（10.0%，2 例）であった（表 2.7.4-付録-28）。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）で，肝胆道系障害（SOC）に分類される有害事象（PT）は，Rd 群の高ビリルビン血症（2.3%，1 例），DRd 群の肝機能異常（3.9%，2 例）であった（表 2.7.4-付録-28）。

b) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

16 mg/kg 群では肝胆道系障害（SOC）の発現割合は 5.1%（8 例）であった。このうち，認められた PT 別の有害事象は肝機能異常（3.8%，6 例），肝不全，高ビリルビン血症及び黄疸（各 0.6%，1 例）であった（表 2.7.4-付録-35）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では肝胆道系障害（SOC）は認められなかった（表 2.7.4-付録-38）。

9) 二次性悪性腫瘍

a) 併用療法試験

全体集団

MMY3004 試験（Vd 療法 vs DVd 療法）

二次性悪性腫瘍の発現割合は，Vd 群が 0.4%（1 例），DVd 群が 2.5%（6 例）であった。造血器悪性腫瘍は認められなかった。DVd 群では，0.4%（1 例）に皮膚有棘細胞癌が発現し，それ以外はすべて皮膚以外の浸潤性の悪性腫瘍であった（表 2.7.4-付録-154）。移行上皮癌（膀胱癌）を発現した DVd 群の 1 例は治験薬の投与を中止し（表 2.7.4-21），その他の二次性悪性腫瘍に関しては，発現後も治験実施計画書の規定に従い治験薬の投与を継続した。二次性悪性腫瘍を発現した被験者はいずれもクリニカルカットオフ時点で生存していた（表 2.7.4-付録-155）。

二次性悪性腫瘍が認められた 7 例（Vd 群 1 例，DVd 群 6 例）のうち，Vd 群の 1 例及び DVd 群の 4 例は投与開始から 6 カ月以内に二次性悪性腫瘍が認められた。また，7 例の前治療歴に関して，IMiD が 5 例（いずれも DVd 群），アルキル化剤が 7 例（Vd 群 1 例，DVd 群 6 例）であった（表 2.7.4-付録-155）。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

二次性悪性腫瘍の発現割合は，Rd 群が 3.6%（10 例），DRd 群が 3.1%（10 例）であった。発現した二次性悪性腫瘍のほぼ半数が非浸潤性の皮膚悪性腫瘍［Rd 群 1.8%（5 例），DRd 群 1.9%（6 例）］であった（表 2.7.4-付録-154）。DRd 群の 3 例（皮膚有棘細胞癌，基底細胞癌及びボーエン病の各 1 例）は既往歴の悪性腫瘍が再発したものであった。

Rd 群では 1 例が造血器悪性腫瘍（鉄芽球性貧血）を発現した。DRd 群では 2 例が造血器悪性腫瘍（急性単球性白血病及びエプスタイン・バーウイルス関連リンパ増殖性障害）を発現し（表 2.7.4-付録-155），いずれも治験薬の投与を中止した（表 2.7.4-21）。そのうち急性単球性白血病を発現した 1 例は異形成変化（dysplastic change）の既往歴を有していた。

皮膚以外の浸潤性の二次性悪性腫瘍に関して，Rd 群では 3 例（肺腺癌，前立腺癌及び直腸腺癌）が治験薬の投与を中止し（表 2.7.4-21），1 例（膀胱移行上皮癌）は治験薬の投与を継続した。DRd 群では 1 例（胃腺癌）が治験薬の投与を中止し（表 2.7.4-21），1 例（皮膚転移）は治験薬の投与中止に至った肺炎の発現と同時期に報告された。

MMY1001 試験（DPd 療法）

DPd 群では二次性悪性腫瘍は認められなかった（表 2.7.4-付録-154）。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

治験薬投与を受けた被験者（8 例）で認められた二次性悪性腫瘍は Grade 3 の前立腺癌（12.5%, 1 例）であり（表 2.7.4-付録-120），治験薬の投与を中止した（表 2.7.4-付録-79）。当該被験者は Day 103 の MRI により前立腺癌が疑われ，Day 167 の前立腺生検の結果，前立腺癌と報告された。当該被験者は，治験組入れのスクリーニング前に FDG-PET にて前立腺の異常を指摘されていた。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

日本人集団（Rd 群 15 例，DRd 群 20 例）では，DRd 群の 10.0%（2 例）に二次性悪性腫瘍が認められた。ボーエン病を発現した 1 例は治験薬の投与を継続し，エプスタイン・バーウイルス関連リンパ増殖性障害を発現した 1 例は治験薬の投与を中止した（表 2.7.4-付録-81）。

二次性悪性腫瘍以外に，東アジア人（Rd 群 44 例，DRd 群 51 例）では，DRd 群の 5.9%（3 例）に二次性悪性腫瘍が認められた。日本人集団で認められた 2 例以外に，前述の皮膚転移が 1 例に認められた。

b) 単剤療法試験

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

MMY2002 試験及び MMY1002 試験では，二次性悪性腫瘍は認められなかった（表 2.7.4-付録-156）。GEN501 試験 Part 2（72 例）では，16 mg/kg 群の 1 例が疾患進行による本剤投与中止後に基底細胞癌を発現した。当該被験者は，最初は皮膚癌と報告されたものの，データベースロック後に治験担当医師により基底細胞癌に修正された。また，GEN501 試験 Part 2 の 8 mg/kg 群の 1 例が二次性悪性腫瘍を発現した。Day 189 の疾患進行による治験中止から約 1 カ月後の身体所見で肝転移が疑われたが，原発性悪性腫瘍はみつからなかった。その後の肝生検により腺癌と診断され，免疫組織化学検査から原発部位は結腸であることが示唆された。当該被験者は治験中止から約 2 カ月後に肝転移の腺癌のため死亡した。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では二次性悪性腫瘍は認められなかった（表 2.7.4-付録-38）。

2.7.4.2.2 個別有害事象の文章による説明

投与期間中及び最終投与後 30 日目までの期間に認められた死亡，重篤な有害事象，治験薬の投与中止に至った有害事象，Grade 3 又は 4 の IRR，Grade 3 又は 4 の感染症及び寄生虫症（SOC），全 Grade の気管支痙攣，並びに二次性悪性腫瘍を発現した被験者に関する叙述は，各試験の治験総括報告書（併用療法：【CTD 5.3.5.1.2-1】MMY3004/CSR，【CTD 5.3.5.1.1-1】

MMY3003/CSR，【CTD 5.3.5.4.1-1】GEN503/CSR，【CTD 5.3.5.4.2-1】MMY1001/CSR，【CTD 5.3.5.2.4-1】MMY1005/CSR，単剤療法：【CTD 5.3.5.2.1-1】MMY2002/CSR，【CTD 5.3.5.2.2-1】GEN501/CSR，【CTD 5.3.5.2.3-1】MMY1002/CSR），及び安全性更新情報（併用療法：【CTD 5.3.5.3.1】2016 年 6 月 30 日クリニカルカットオフ，単剤療法：【CTD 5.3.5.3.3】2015 年 6 月 30 日クリニカルカットオフ）に記載した。

2.7.4.3 臨床検査値の評価

2.7.4.3.1 併用療法試験

2.7.4.3.1.1 血液学的検査

(1) 血液学的検査値異常

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験で認められた Grade 別の血液学的検査値異常を表 2.7.4-付録-157 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

Vd 群及び DVd 群で認められた主な Grade 3 又は 4 の血液学的検査値異常は，リンパ球数低値（Vd 群 29.8%，DVd 群 50.8%，以下同順）及び血小板数低値（35.9%，48.3%）であった。Grade 3 のヘモグロビン低値の発現割合は Vd 群が 15.6%，DVd 群が 16.6%であり，Grade 4 は認められなかった。Grade 3 又は 4 の好中球数低値の発現割合は，Vd 群が 5.9%，DVd 群が 16.2%であった。Grade 3 又は 4 の白血球数低値の発現割合は，Vd 群が 5.9%（Grade 3 のみ），DVd 群が 14.5%であった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Rd 群及び DRd 群で認められた主な Grade 3 又は 4 の血液学的検査値異常は，好中球数低値（Rd 群 40.7%，DRd 群 54.9%，以下同順），リンパ球数低値（40.1%，53.3%）及び白血球数低値（24.6%，42.9%）であった。Grade 3 又は 4 の血小板数低値の発現割合は，Rd 群が 15.7%，DRd 群が 13.6%であった。Grade 3 のヘモグロビン低値の発現割合は Rd 群が 20.6%，DRd 群が 13.6%であり，Grade 4 は認められなかった。

MMY1001 試験（DPd 療法）

DPd 群で認められた主な Grade 3 又は 4 の血液学的検査値異常は，好中球数低値（82.4%），リンパ球数低値（72.5%）及び白血球数低値（65.7%）であった。Grade 3 のヘモグロビン低値の発現割合は 32.4%であり，Grade 4 は認められなかった。Grade 3 又は 4 の血小板数低値の発現割合は 19.6%であった。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の Grade 別の血液学的検査値異常を表 2.7.4-付録-158 に示す。

治験薬投与を受けた被験者（8 例）で認められた Grade 3 又は 4 の血液学的検査値異常は，血小板数低値［75.0%（6 例），うち Grade 3 及び 4 が各 3 例］，リンパ球数低値［75.0%（6 例），うち Grade 3 が 5 例，Grade 4 が 1 例］，好中球数低値及び白血球数低値［各 25.0%（2 例），いずれも Grade 3］であった。Grade 3 又は 4 のヘモグロビン低値は認められなかった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）で認められた Grade 別の血液学的検査値異常を表 2.7.4-付録-159 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）で認められた主な Grade 3 又は 4 の血液学的検査値異常は，リンパ球数低値（Rd 群 53.3%，DRd 群 60.0%，以下同順），好中球数低値（26.7%，55.0%）及び白血球数低値［20.0%（Grade 3 のみ），35.0%］であった。Grade 3 又は 4 の血小板数低値の発現割合は Rd 群が 13.3%（2 例），DRd 群が 5.0%（1 例，Grade 4）であった。Grade 3 のヘモグロビン低値の発現割合は Rd 群が 13.3%（2 例），DRd 群が 5.0%（1 例）であり，Grade 4 は認められなかった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）で認められた主な Grade 3 又は 4 の血液学的検査値異常は，好中球数低値（Rd 群 47.7%，DRd 群 62.7%，以下同順），リンパ球数低値（34.1%，49.0%）及び白血球数低値［27.3%（Grade 3 のみ），43.1%］であった。Grade 3 又は 4 の血小板数低値の発現割合は Rd 群が 20.5%（9 例），DRd 群が 9.8%（5 例）であった。Grade 3 のヘモグロビン低値の発現割合は Rd 群が 25.0%（11 例），DRd 群が 9.8%（5 例）であり，Grade 4 は認められなかった。

(2) 血液学的検査値のベースラインからの変化

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験での血液学的検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-160 に示す。また，各投与群の好中球数，リンパ球数及び血小板数の平均値の経時的な推移（サイクル 8 まで）をそれぞれ図 2.7.4-付録-1，図 2.7.4-付録-2 及び図 2.7.4-付録-3 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

ベースラインで認められた Grade 3 のリンパ球数低値は Vd 群 8 例，DVd 群 8 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 のリンパ球数低値が Vd 群 70 例，DVd 群 121 例に認められた。ベースラインで認められた Grade 3 又は 4 の血小板数低値は Vd 群 3 例，DVd 群 3 例であったが，治験薬投与後では Grade 3 又は 4 の血小板数低値が Vd 群 85 例，DVd 群 116 例に認められた。ベースラインで認められた Grade 3 のヘモグロビン低値は Vd 群 5 例，DVd 群 10 例であったが，治験薬投与後では Grade 3 のヘモグロビン低値が Vd 群 37 例，DVd 群 40 例に認められ，ベースラインを含め Grade 4 は認められなかった。ベースラインで認められた Grade 3

の好中球数低値は Vd 群 1 例，DVd 群 2 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の好中球数低値が Vd 群 14 例，DVd 群 39 例に認められた。ベースラインで認められた Grade 3 の白血球数低値は Vd 群 2 例，DVd 群 1 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の白血球数低値が Vd 群 14 例，DVd 群 35 例に認められ，このうち Vd 群では Grade 4 は認められなかった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

ベースラインで認められた Grade 3 又は 4 の好中球数低値は Rd 群 2 例（Grade 4 なし），DRd 群 5 例であったが，治験薬投与後では Grade 3 又は 4 の好中球数低値が Rd 群 114 例，DRd 群 174 例に認められた。ベースラインで認められた Grade 3 又は 4 のリンパ球数低値は Rd 群 7 例（Grade 4 なし），DRd 群 14 例であったが，治験薬投与後では Grade 3 又は 4 のリンパ球数低値が Rd 群 112 例，DRd 群 169 例に認められた。ベースラインで認められた Grade 3 の白血球数低値は Rd 群 0 例，DRd 群 1 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の白血球数低値が Rd 群 69 例，DRd 群 136 例に認められた。ベースラインで認められた Grade 3 の血小板数低値は Rd 群 1 例，DRd 群 2 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の血小板数低値が Rd 群 44 例，DRd 群 43 例に認められた。ベースラインで認められた Grade 3 のヘモグロビン低値は Rd 群 7 例，DRd 群 8 例であったが，治験薬投与後では Grade 3 のヘモグロビン低値が Rd 群 58 例，DRd 群 43 例に認められ，ベースラインを含め Grade 4 は認められなかった。

MMY1001 試験（DPd 療法）

DPd 群では，ベースラインでは Grade 3 又は 4 の好中球数低値は認められなかったが，治験薬投与後では Grade 3 又は 4 の好中球数低値が 84 例に認められた。ベースラインで認められた Grade 3 又は 4 のリンパ球数低値は 11 例であったが，治験薬投与後では Grade 3 又は 4 のリンパ球数低値が 74 例に認められた。ベースラインでは Grade 3 又は 4 の白血球数低値は認められなかったが，治験薬投与後では Grade 3 又は 4 の白血球数低値が 67 例に認められた。ベースラインで認められた Grade 3 のヘモグロビン低値は 3 例であったが，治験薬投与後では Grade 3 のヘモグロビン低値が 33 例に認められ，ベースラインを含め Grade 4 は認められなかった。ベースラインで認められた Grade 3 の血小板数低値は 2 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の血小板数低値が 20 例に認められた。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験での血液学的検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-161 に示す。また，血液学的検査項目の平均値の経時的な推移を図 2.7.4-付録-4 に示す。

治験薬投与を受けた被験者（8 例）の全例が，すべての血液学的検査項目でベースラインに Grade 2 以下であった。治験薬投与後では Grade 3 又は 4 の血小板数低値が 6 例，Grade 3 又は 4 のリンパ球数低値が 6 例に認められた。治験薬投与後では Grade 3 の好中球数低値が 2 例，白血

球数低値が 2 例に認められ，いずれも Grade 4 は認められなかった。治験薬投与後では Grade 3 又は 4 のヘモグロビン低値は認められなかった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）での血液学的検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-162 に示す。また，日本人集団の Rd 群及び DRd 群での好中球数，リンパ球数及び血小板数の平均値の経時的な推移をそれぞれ図 2.7.4-付録-5，図 2.7.4-付録-6 及び図 2.7.4-付録-7，東アジア人集団の Rd 群及び DRd 群での好中球数，リンパ球数及び血小板数の平均値の経時的な推移をそれぞれ図 2.7.4-付録-8，図 2.7.4-付録-9 及び図 2.7.4-付録-10 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）の全例が，すべての血液学的検査項目でベースラインに Grade 2 以下であった。治験薬投与後では Grade 3 又は 4 のリンパ球数低値が Rd 群 8 例，DRd 群 12 例に認められた。治験薬投与後では Grade 3 又は 4 の好中球数低値が Rd 群 4 例，DRd 群 11 例に認められた。治験薬投与後では Grade 3 又は 4 の白血球数低値が Rd 群 3 例，DRd 群 7 例に認められ，このうち Rd 群では Grade 4 は認められなかった。治験薬投与後では Grade 3 又は 4 の血小板数低値が Rd 群 2 例，DRd 群 1 例（Grade 4）に認められた。治験薬投与後では Grade 3 のヘモグロビン低値が Rd 群 2 例，DRd 群 1 例に認められ，Grade 4 は認められなかった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）では，ベースラインで認められた Grade 3 の好中球数低値は Rd 群 1 例，DRd 群 0 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の好中球数低値が Rd 群 21 例，DRd 群 32 例に認められた。ベースラインでは Grade 3 又は 4 のリンパ球数低値は認められなかったが，治験薬投与後では Grade 3 又は 4 のリンパ球数低値が Rd 群 15 例，DRd 群 25 例に認められた。ベースラインでは Grade 3 又は 4 の白血球数低値は認められなかったが，治験薬投与後では Grade 3 又は 4 の白血球数低値が Rd 群 12 例，DRd 群 22 例に認められ，このうち Rd 群では Grade 4 は認められなかった。ベースラインで認められた Grade 3 の血小板数低値は Rd 群 1 例，DRd 群 0 例であったが（Grade 4 なし），治験薬投与後では Grade 3 又は 4 の血小板数低値が Rd 群 9 例，DRd 群 5 例に認められた。ベースラインで認められた Grade 3 のヘモグロビン低値は Rd 群 2 例，DRd 群 1 例であったが，治験薬投与後では Grade 3 のヘモグロビン低値が Rd 群 11 例，DRd 群 5 例に認められ，ベースラインを含め Grade 4 は認められなかった。

2.7.4.3.1.2 血液生化学検査

全体集団

MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験で認められた Grade 別の血液生化学検査値異常を表 2.7.4-付録-157，血液生化学検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-163 に示す。また，各投与群のクレアチニン濃度及び CrCL の平均値の経時的な推移（サイクル 8 まで）をそれぞれ図 2.7.4-付録-11 及び図 2.7.4-付録-12 に示す。

MMY3004 試験（Vd 療法 vs DVd 療法）

Vd 群及び DVd 群のいずれかで 5%以上に認められた Grade 4 の血液生化学検査値異常はなかった。5%以上に認められた Grade 3 の血液生化学検査値異常はリン酸低値（5.2%，9.4%，以下同順）及びナトリウム低値（5.6%，5.0%）であった。

ALT 高値の発現割合は，Grade 3 では Vd 群が 0.4%（1 例），DVd 群が 2.1%（5 例）であり，Grade 4 では Vd 群が 0.4%（1 例），DVd 群が 0.4%（1 例）であった。AST 高値の発現割合は，Grade 3 では Vd 群が 0%，DVd 群が 0.8%（2 例）であり，Grade 4 では Vd 群が 0.4%（1 例），DVd 群が 0.4%（1 例）であった。Grade 3 のビリルビン高値の発現割合は Vd 群が 0.4%（1 例），DVd 群が 0%であり，Grade 4 は認められなかった。

MMY3003 試験及び GEN503 試験併合（Rd 療法 vs DRd 療法）

Rd 群及び DRd 群のいずれかで 5%以上に認められた Grade 4 の血液生化学検査値異常はなかった。5%以上に認められた Grade 3 の血液生化学検査値異常はリン酸低値（Rd 群 10.9%，DRd 群 11.7%，以下同順）及びカリウム低値（3.3%，5.4%）であった。

Grade 4 の ALT 高値，AST 高値及びビリルビン高値は認められなかった。Grade 3 の ALT 高値の発現割合は Rd 群が 1.8%（5 例），DRd 群が 2.5%（8 例）であった。Grade 3 の AST 高値の発現割合は Rd 群が 0%，DRd 群が 1.0%（3 例）であった。Grade 3 のビリルビン高値の発現割合は Rd 群が 0.4%（1 例），DRd 群が 0.6%（2 例）であった。

MMY1001 試験（DPd 療法）

DPd 群で 5%以上に認められた Grade 4 の血液生化学検査値異常は補正カルシウム高値（9.2%）であった。5%以上に認められた Grade 3 の血液生化学検査値異常はナトリウム低値（11.2%）及びリン酸低値（10.3%）であった。

Grade 4 の ALT 高値，AST 高値及びビリルビン高値は認められなかった。Grade 3 の ALT 高値，AST 高値及びビリルビン高値の発現割合はそれぞれ 3.1%（3 例），3.1%（3 例）及び 2.0%（2 例）であった。

日本人及び東アジア人

MMY1005 試験（DVd 療法）：国内試験

MMY1005 試験の Grade 別の血液生化学検査値異常を表 2.7.4-付録-158，血液生化学検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-161 に示す。また，ALT，AST 及びクレアチニンの平均値の経時的な推移を図 2.7.4-付録-4 に示す。

治験薬投与を受けた被験者（8 例）では Grade 4 の血液生化学検査値異常は認められなかった。Grade 3 の血液生化学検査値異常はカリウム低値（25.0%，2 例），AST 高値及び ALT 高値（各 12.5%，1 例）であった。

MMY3003 試験（Rd 療法 vs DRd 療法）：日本人集団及び東アジア人集団

MMY3003 試験の人種別（日本人，東アジア人，全体）及び Grade 別の血液生化学検査値異常を表 2.7.4-付録-159，血液生化学検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-164 に示す。

日本人集団（Rd 群 15 例，DRd 群 20 例）のいずれかの群で 5%以上に認められた Grade 4 の血液生化学検査値異常は，補正カルシウム高値［Rd 群 6.7%（1 例），DRd 群 5.0%（1 例），以下同順］及びクレアチニン高値［6.7%（1 例），0%］であった。5%以上に認められた Grade 3 の血液生化学検査値異常は，ALT 高値［0%，15.0%（3 例）］，リン酸低値［13.3%（2 例），10.0%（2 例）］及び AST 高値［0%，5.0%（1 例）］であった。Grade 3 又は 4 のビリルビン高値は認められなかった。

東アジア人集団（Rd 群 44 例，DRd 群 51 例）のいずれかの群で 5%以上に認められた Grade 4 の血液生化学検査値異常はなかった。5%以上に認められた Grade 3 の血液生化学検査値異常は，リン酸低値［Rd 群 4.8%（2 例），DRd 群 10.0%（5 例），以下同順］及び ALT 高値［2.3%（1 例），5.9%（3 例）］であった。Grade 3 の AST 高値の発現割合は Rd 群が 0%，DRd 群が 2.0%（1 例）であり，Grade 4 は認められなかった。Grade 3 又は 4 のビリルビン高値は認められなかった。

2.7.4.3.2 単剤療法試験

2.7.4.3.2.1 血液学的検査

(1) 血液学的検査値異常

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた Grade 別の血液学的検査値異常（ベースラインの Grade から悪化した被験者のみ集計）を表 2.7.4-付録-165 に示す。

16 mg/kg 群で発現割合が最も高かった Grade 3 又は 4 に悪化した血液学的検査値異常は，リンパ球数低値（39.1%）であった。その他の Grade 3 又は 4 に悪化した血液学的検査値異常の発現割合は，好中球数低値が 20.5%，ヘモグロビン低値が 19.2%，白血球数低値が 18.6%，血小板数低値が 18.1%であった。これらの項目のうち，ヘモグロビン低値に関して Grade 4 への悪化は認められなかった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験での血液学的検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-166 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）で発現割合が最も高かった Grade 3 又は 4 に悪化した血液学的検査値異常は，リンパ球数低値［8 mg/kg 群：50.0%（2 例），16 mg/kg 群：100%（5 例）］であった。Grade 3 に悪化した好中球数低値の発現割合は 8 mg/kg 群が 0%，16 mg/kg 群が 80.0%（4 例）であり，Grade 4 への悪化は認められなかった。Grade 3 に悪化した白血球数低値の発現割合は 8 mg/kg 群が 0%，16 mg/kg 群が 60.0%（3 例）であり，Grade 4 への悪化は認められなかった。Grade 3 又は 4 に悪化した血小板数低値の発現割合は 8 mg/kg 群が

25.0%（1 例），16 mg/kg 群が 20.0%（1 例）であり，いずれも Grade 4 への悪化であった。Grade 3 に悪化したヘモグロビン低値の発現割合は 8 mg/kg 群が 25.0%（1 例），16 mg/kg 群が 20.0%（1 例）であり，Grade 4 への悪化は認められなかった。

(2) 血液学的検査値のベースラインからの変化

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合での血液学的検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-167 に示す。

16 mg/kg 群では，ベースラインに Grade 4 の血液学的検査項目は認められなかった。ベースラインで認められた Grade 3 のリンパ球数低値は 18 例であったが，治験薬投与後では Grade 3 又は 4 のリンパ球数低値が 69 例に認められた。ベースラインで認められた Grade 3 のヘモグロビン低値は 8 例であったが，治験薬投与後では Grade 3 のヘモグロビン低値が 36 例に認められ，Grade 4 は認められなかった。ベースラインで認められた Grade 3 の好中球数低値は 1 例であったが，治験薬投与後では Grade 3 又は 4 の好中球数低値が 32 例に認められた。ベースラインで認められた Grade 3 の白血球数低値は 2 例であったが，治験薬投与後では Grade 3 又は 4 の白血球数低値が 30 例に認められた。ベースラインで認められた Grade 3 の血小板数低値は 2 例であったが，治験薬投与後では Grade 3 又は 4 の血小板数低値が 29 例に認められた。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，ベースラインに Grade 4 の血液学的検査項目は認められなかった。ベースラインで認められた Grade 3 のリンパ球数低値は 8 mg/kg 群 1 例，16 mg/kg 群 0 例であったが，治験薬投与後では Grade 3 又は 4 のリンパ球数低値が 8 mg/kg 群 2 例（Grade 4 のみ），16 mg/kg 群 5 例に認められた。ベースラインで認められた Grade 3 の好中球数低値は 8 mg/kg 群 1 例，16 mg/kg 群 0 例であったが，治験薬投与後では Grade 3 の好中球数低値が 8 mg/kg 群 0 例，16 mg/kg 群 4 例に認められ，Grade 4 は認められなかった。ベースラインで認められた Grade 3 の白血球数低値は 8 mg/kg 群 0 例，16 mg/kg 群 1 例であったが，治験薬投与後では Grade 3 の白血球数低値が 8 mg/kg 群 0 例，16 mg/kg 群 4 例に認められ，Grade 4 は認められなかった。ベースラインでは Grade 3 の血小板数低値は認められなかったが，治験薬投与後では Grade 3 又は 4 の血小板数低値は 8 mg/kg 群 1 例，16 mg/kg 群 1 例であり，いずれも Grade 4 であった。ベースラインでは Grade 3 のヘモグロビン低値は認められなかったが，治験薬投与後では Grade 3 のヘモグロビン低値が 8 mg/kg 群 1 例，16 mg/kg 群 1 例に認められ，Grade 4 は認められなかった（表 2.7.4-付録-166）。

2.7.4.3.2.2 血液生化学検査

(1) 血液生化学検査値異常

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合で認められた Grade 別の血液生化学検査値異常（ベースラインの Grade から悪化した被験者のみ集計）を表 2.7.4-付録-168 に示す。

認められた血液生化学検査値異常の多くは Grade 1 又は 2 であった。16 mg/kg 群では，Grade 4 に悪化した血液生化学検査値異常のうち 3%以上に認められたのは尿酸高値（4.2%）であった。Grade 3 に悪化した血液生化学検査値異常のうち 3%以上に認められたのはリン酸低値（5.9%），ナトリウム低値（4.0%），補正カルシウム高値（3.9%）及びアルブミン低値（3.3%）であった。

16 mg/kg 群の AST 高値及びビリルビン高値に関して，Grade 4 への悪化は認められなかった。Grade 3 に悪化した AST 高値の発現割合は 1.3%（2 例），Grade 3 に悪化したビリルビン高値の発現割合は 1.3%（2 例）であった。Grade 3 又は 4 の ALT 高値は認められなかった。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験での血液生化学検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-166 に示す。

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）では，Grade 3 又は 4 に悪化した血液生化学検査値異常は認められなかった。

(2) 血液生化学検査値のベースラインからの変化

MMY2002 試験，GEN501 試験及び MMY1002 試験併合

単剤 3 試験併合での血液生化学検査値のベースラインの Grade から最悪 Grade への推移を表 2.7.4-付録-169 に示す。

16 mg/kg 群では，ベースラインで認められた Grade 3 又は 4 の補正カルシウム高値は 5 例であったが，治験薬投与後では Grade 3 又は 4 の補正カルシウム高値が 12 例に認められた。ベースラインで認められた Grade 3 又は 4 の尿酸高値は 5 例（Grade 4 のみ）であったが，治験薬投与後では Grade 3 又は 4 の尿酸高値は 7 例であり，いずれも Grade 4 であった。ベースラインで認められた Grade 3 のリン酸低値は 1 例であったが，治験薬投与後では Grade 3 のリン酸低値が 6 例に認められ，ベースラインを含め Grade 4 は認められなかった。ベースラインで認められた Grade 3 のナトリウム低値は 1 例であったが，治験薬投与後では Grade 3 のナトリウム低値が 6 例に認められ，ベースラインを含め Grade 4 は認められなかった。その他の血液生化学検査項目は，治験薬投与後に Grade 3 又は 4 であった被験者が 5 例以下であった。

また，肝機能に関して，Hy’s Law（Guidance for industry. Drug-Induced Liver Injury: premarketing Clinical Evaluation. U.S. Department of Health and Human Services, Food and Drug Administration）[5)] の基準に該当した被験者はいなかった（表 2.7.4-付録-170）。

MMY1002 試験（最終解析結果）：国内試験

MMY1002 試験（8 mg/kg 群 4 例，16 mg/kg 群 5 例）の全例が，すべての血液生化学検査項目でベースラインに Grade 2 以下であった。治験薬投与後では Grade 3 又は 4 の血液生化学検査項目は認められなかった（表 2.7.4-付録-166）。

2.7.4.4 バイタルサイン，身体的所見及び安全性に関連する他の観察項目

2.7.4.4.1 併用療法試験

2.7.4.4.1.1 バイタルサイン

MMY3004 試験，MMY3003 試験（全体，日本人及び東アジア人集団），GEN503 試験及び MMY1001 試験では，安全性が懸念されるバイタルサインの異常は認められなかった。

MMY1005 試験（国内試験）では臨床的に重要なバイタルサインの異常は認められなかった。

2.7.4.4.1.2 腫瘍崩壊症候群

MMY3003 試験（全体，日本人及び東アジア人集団），GEN503 試験，MMY1001 試験及び MMY1005 試験（国内試験）では，有害事象として腫瘍崩壊症候群は認められなかった（表 2.7.4-付録-26，表 2.7.4-付録-27，表 2.7.4-付録-28）。

MMY3004 試験の DVd 群の 1 例に Grade 3 の重篤な腫瘍崩壊症候群が有害事象として認められた。本事象に対する治験薬の処置は実施せず，ラスブリカーゼ及び静脈内輸液による治療を実施し，発現翌日に回復した。

2.7.4.4.2 単剤療法試験

2.7.4.4.2.1 バイタルサイン

単剤 3 試験併合では，安全性が懸念されるバイタルサインの変動は認められなかった。

MMY1002 試験（国内試験）では，8 及び 16 mg/kg 群のいずれも臨床的に重要なバイタルサインの異常は認められなかった。

2.7.4.4.2.2 腫瘍崩壊症候群

単剤 3 試験併合では，有害事象として腫瘍崩壊症候群は認められなかった（表 2.7.4-付録-35）。

MMY1002 試験（国内試験）では，8 及び 16 mg/kg 群のいずれも有害事象として腫瘍崩壊症候群は認められなかった（表 2.7.4-付録-38）。

2.7.4.5 安全性更新情報

2.7.4.5.1 併用療法試験

2.7.4.5.1.1 2016 年 6 月 30 日クリニカルカットオフ時の安全性更新情報

対象とした被験者数は，MMY3004 試験，MMY3003 試験，GEN503 試験及び MMY1001 試験で治験薬を投与された 1,182 例（本剤併用群：664 例，本剤非併用群：518 例）であり，前回の併用療法試験の解析時と同じであった。2016 年 6 月 30 日のクリニカルカットオフ時点で更新された併用療法試験の安全性情報を以下に記載した。

全般的な曝露状況

・ 治験薬を投与された被験者（1,182 例）のうち，更に 65 例が疾患進行により投与を中止し，更に 13 例が有害事象により投与を中止した。2016 年 6 月 30 日のクリニカルカットオフ時点で 43.4%（513 例）が投与継続中であった（【CTD 5.3.5.3.1】TSIDS01）。

・ 投与期間の中央値は DVd 群で 4.6 カ月間，Rd 群で 2.6 カ月間，DRd 群で 3.5 カ月間，DPd 群で 0.7 カ月間延長した。Vd 群の投与期間は 5.2 カ月であり，前回の併用療法試験の解析時と変わらなかった。本剤の総投与回数の中央値は DVd 群が 16.0 回から 20.0 回，DRd 群が 24.0 回から 28.0 回，DPd 群が 14.0 回から 16.0 回に増加した（【CTD 5.3.5.3.1】TSIEXP01）。

有害事象の解析

・ 有害事象の発現割合は前回の併用療法試験の解析時と同程度であり，Vd 群及び DVd 群では血小板減少症，Rd 群，DRd 群及び DPd 群では好中球減少症の発現割合が最も高かった。また，発現割合が 10%以上の有害事象に関して，前回の併用療法試験の解析時から 5%以上変化した事象はなかった。（【CTD 5.3.5.3.1】TSFAE02IC）

・ Grade 3 又は 4 の有害事象の発現割合に関して特筆すべき新たな懸念は認められず，発現割合が 5%以上の Grade 3 又は 4 の有害事象に関して，前回の併用療法試験の解析時から 2%以上変化した事象はなかった（【CTD 5.3.5.3.1】TSFAE03I）。

・ 投与後 30 日以内の死亡が新たに 8 例に認められたものの，死亡した被験者の割合は各投与群で 5.3～8.7%であり，前回の併用療法試験の解析時（4.1～6.8%）と同程度であった。死亡に至った有害事象が新たに 9 例に認められ，その内訳は，DVd 群が敗血症性ショック，Rd 群が冠動脈不全，DRd 群がインフルエンザ，レジオネラ感染，心不全，心突然死及びエプスタイン・バーウイルス関連リンパ増殖性障害，DPd 群が心停止及び突然死であった（【CTD 5.3.5.3.1】TSFAE16）。

・ 重篤な有害事象を新たに発現した被験者数は，本剤非併用群と比較して本剤併用群で多かったものの（Vd 群：1 例，DVd 群：16 例，Rd 群：8 例，DRd 群：18 例），発現割合が 3%以上の重篤な有害事象に関して，前回の併用療法試験の解析時から 2%以上変化した事象はなかった（【CTD 5.3.5.3.1】TSFAE05A）。

・ 治験薬の投与中止に至った有害事象が新たに 13 例に認められた（【CTD 5.3.5.3.1】TSFAE14）。

器官別又は症候群別有害事象の解析

・ DRd 群で IRR が新たに 2 例に認められた。その他の投与群では前回の併用療法試験の解析時から IRR を新たに発現した被験者はいなかった（【CTD 5.3.5.3.1】TSFAE06A）。

・ 感染症及び寄生虫症（SOC）を新たに発現した被験者数は，本剤非併用群と比較して本剤併用群で多かったものの（Vd 群：3 例，DVd 群：13 例，Rd 群：3 例，DRd 群：11 例），ほとんどの事象が Grade 1 又は 2 であった（【CTD 5.3.5.3.1】TSFAE17）。各投与群で感染症及び寄生虫症により治験薬の投与中止又は死亡に至った被験者の割合（治験薬の投与中

止：1.8～4.9%，死亡：1.2～2.8%）は，前回の併用療法試験の解析時（治験薬の投与中止：1.8～4.9%，死亡：0.8～2.2%）と同程度であった（【CTD 5.3.5.3.1】TSFAE14，TSFAE16）。

・ 前回の併用療法試験の解析時以降，DVd 群で新たに 4 例に二次性悪性腫瘍が発現した［基底細胞癌及び扁平上皮癌（1 例），皮膚有棘細胞癌（1 例），前立腺癌（1 例）及び骨髄異形成症候群（1 例）］。Vd 群では，二次性悪性腫瘍を新たに発現した被験者はいなかった。DVd 群は本剤の投与を継続しているため，Vd 群と比較して投与期間が長い（DVd 群 11.1 カ月，Vd 群 5.2 カ月）ことが要因と考えられる。この 4 例はいずれも IMiD 及びアルキル化剤の前治療歴を有していた。その他の投与群では，Rd 群で新たに 2 例（胃腺癌，胸膜中皮腫が各 1 例），DRd 群で新たに 4 例（扁平上皮癌，喉頭扁平上皮癌，前立腺癌及び移行上皮癌が各 1 例）に二次性悪性腫瘍が発現した。DPd 群では二次性悪性腫瘍は認められなかった。各投与群間で，2016 年 6 月 30 日のクリニカルカットオフ時点までに発現した腫瘍の種類に一定の傾向は認められなかった（皮膚悪性腫瘍 15 例，皮膚以外の浸潤性の悪性腫瘍 18 例，造血器悪性腫瘍 4 例）（【CTD 5.3.5.3.1】TSFSPM01）。

2.7.4.5.2 単剤療法試験

2.7.4.5.2.1 2015 年 6 月 30 日クリニカルカットオフ時の安全性更新情報

対象とした被験者数は 2015 年 1 月 9 日（MMY1002 試験は 2015 年 2 月 6 日）をクリニカルカットオフ日とした前回の単剤療法試験の併合解析時と同じであった（併合データの対象集団全体が 237 例，うち 16 mg/kg 群が 156 例）。2015 年 6 月 30 日のクリニカルカットオフ時点で更新された単剤療法試験の安全性情報を以下に記載した。

全般的な曝露状況

・ 16 mg/kg 群（156 例）のうち，更に 10 例が疾患進行により投与を中止した。有害事象により投与を中止した被験者数は変わらなかった。2015 年 6 月 30 日のクリニカルカットオフ時点で 14.7%（23 例）が投与継続中であった（【CTD 5.3.5.3.3】TSIDS01M）。

・ 16 mg/kg 群の投与期間の中央値は前回の単剤療法試験の併合解析時と同じ 3.253 カ月であったが，最長投与期間は 14.19 カ月間から 20.04 カ月間に延長した。本剤の総投与回数の中央値は 11.0 回から 11.5 回に増加した（【CTD 5.3.5.3.3】TSIEXP01M）。

有害事象の解析

・ 有害事象の発現割合は前回の単剤療法試験の併合解析時と同程度であり，疲労，悪心，貧血，好中球減少症，背部痛，咳嗽及び血小板減少症の発現割合が最も高かった（【CTD 5.3.5.3.3】TSFAE01M，TSFAE02M1）。また，発現割合が 10%以上の有害事象に関して，前回の単剤療法試験の併合解析時から 5%以上変化した事象はなかった（【CTD 5.3.5.3.3】TSFAE02M2）。

・ 新たに 3 件の Grade 3 又は 4 の有害事象が 16 mg/kg 群の 3 例に発現した（Grade 3 の気道感染，Grade 3 の下痢，Grade 4 の細菌性敗血症）（【CTD 5.3.5.3.3】TSFAE04M，

TSFAE02M2）。そのうち 2 例は前回の単剤療法試験の併合解析時にも Grade 3 又は 4 の有害事象を発現しており，1 例は新たに Grade 3 又は 4 の有害事象を発現した。

・ 新たに認められた投与後 30 日以内の死亡又は有害事象による死亡はなかった（【CTD 5.3.5.3.3】TSFDTH01MA）。

・ 重篤な有害事象の発現割合は前回の単剤療法試験の併合解析時と同程度であった（【CTD 5.3.5.3.3】TSFAE03M2）。新たに 3 件の重篤な有害事象が 2 例に発現した。1 例は重篤な有害事象（Grade 3 の気道感染）を新たに発現した。残りの 1 例は前回の単剤療法試験の併合解析時にも重篤な有害事象（肺炎）を発現しており，今回新たに Grade 2 の帯状疱疹及び Grade 4 の細菌性敗血症を発現した。

・ 本剤の投与延期に至った有害事象，又は本剤の投与中断に至った有害事象を新たに発現した被験者はおらず（【CTD 5.3.5.3.3】TSFAE06M，TSFAE07M），本剤の投与中止に至った有害事象を新たに発現した被験者もいなかった（【CTD 5.3.5.3.3】TSFAE05M）。

器官別又は症候群別有害事象の解析

・ IRR を新たに発現した被験者はいなかった。16 mg/kg 群では 48.1%の被験者に IRR が認められ，前回の単剤療法試験の併合解析時（51.3%）よりもわずかに低下した（【CTD 5.3.5.3.3】TSFAE09M）。これは，前回の単剤療法試験の併合解析時で IRR と報告された被験者のうち，7 例（貧血が 3 例，高血圧が 2 例，白内障及び発疹が各 1 例）の内容が更新され，そのうち 5 例が IRR ではないと報告されたためであった。

・ 16 mg/kg 群の感染症及び寄生虫症（SOC）の発現割合は 59.0%であり，前回の単剤療法試験の併合解析時（54.5%）から 7 例増加した（【CTD 5.3.5.3.3】TSFAE11M）。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は 10.3%であり，新たに Grade 4 の細菌性敗血症が 1 例に発現した（【CTD 5.3.5.3.3】TSFAE04M，TSFAE03M2）。

・ 新たに認められた二次性悪性腫瘍はなかった（【CTD 5.3.5.3.3】LSFAE01M）。

2.7.4.5.2.2 2015 年 12 月 31 日クリニカルカットオフ時の安全性更新情報

対象とした被験者数は GEN501 試験 Part 2 及び MMY2002 試験の本剤 16 mg/kg 群の 148 例（GEN501 試験 Part 2：42 例，MMY2002 試験：106 例）であった [6)]。2015 年 12 月 31 日のクリニカルカットオフ時点での安全性情報の概要を以下に示す。

全般的な曝露状況

・ 16 mg/kg 群（148 例）のうち，83.1%が疾患進行により投与を中止した。有害事象により投与を中止した被験者は 4.1%であった。2015 年 12 月 31 日のクリニカルカットオフ時点で 8.1%（12 例）が投与継続中であった。

・ 投与期間の中央値は 3.4 カ月（範囲：0.03～26.0 カ月）であり，本剤の総投与回数の中央値は 12 回（範囲：1～40 回）であった。

有害事象の解析

・ 3 例が有害事象（H1N1 インフルエンザ，肺炎及び誤嚥性肺炎）により死亡した。

・ 発現割合が 20%以上の有害事象は，疲労（41.9%），悪心（29.7%），貧血（28.4%），背部痛（27.0%），咳嗽（25.7%），血小板減少症及び上気道感染（各 21.6%），好中球減少症（20.9%）であった。

器官別又は症候群別有害事象の解析

・ 48%の被験者に IRR が認められた。発現割合が 5%以上の IRR は，鼻閉（11.5%），咳嗽（8.1%），アレルギー性鼻炎及び悪寒（各 6.8%），咽喉刺激感（6.1%），呼吸困難及び悪心（各 5.4%）であった。

・ 2.7%（4 例）の被験者が Grade 3 以上の IRR を発現し，その内訳は気管支痙攣が 2 例，呼吸困難，低酸素症及び高血圧が各 1 例であった。本剤の投与中止に至った IRR は認められなかった。

・ 発現割合が 20%以上の感染症及び寄生虫症（SOC）の有害事象は上気道感染（21.6%）であった。Grade 3 の上気道感染の発現割合は 0.7%（1 例）であった。

2.7.4.5.2.3 [redacted] 年 [redacted] 月 [redacted] 日クリニカルカットオフ時の安全性更新情報

対象とした被験者数は GEN501 試験 Part 2 及び MMY2002 試験の本剤 16 mg/kg 群の 148 例（GEN501 試験 Part 2：42 例，MMY2002 試験：106 例）であり，2015 年 12 月 31 日をクリニカルカットオフ日とした前回の 2 試験併合解析時と同じであった。[redacted] 年 [redacted] 月 [redacted] 日のクリニカルカットオフ時点での安全性情報の概要を以下に示す。

全般的な曝露状況

・ 16 mg/kg 群（148 例）のうち，95.3%が投与を中止した。中止理由は疾患進行（86.5%）が最も多く，次いで有害事象（4.1%）であった。4.7%（7 例）の被験者が投与継続中であった（【CTD 5.3.5.3.6】TSIDS01M）。

・ 投与期間の中央値は 3.351 カ月（範囲：0.03～36.53 カ月）であり，本剤の総投与回数の中央値は 12.0 回（範囲：1～51 回）であった（【CTD 5.3.5.3.6】TSIEXP01M）。

有害事象の解析

・ 発現割合が 20%以上の有害事象は，疲労（41.9%），悪心（29.7%），貧血（28.4%），背部痛（27.0%），咳嗽（25.7%），上気道感染（22.3%），血小板減少症及び好中球減少症（各 20.9%）であった（【CTD 5.3.5.3.6】TSFAE02M）。

・ 発現割合が 10%以上の Grade 3 又は 4 の有害事象は，貧血（17.6%），血小板減少症（14.2%）及び好中球減少症（10.1%）であった（【CTD 5.3.5.3.6】TSFAE02M）。

・ 投与後 30 日以内の有害事象による死亡は 3 例であり，前回の 2 試験併合解析時と同じ例数であった（【CTD 5.3.5.3.6】TSFDTH01M）。

・ 発現割合が最も高かった重篤な有害事象は，肺炎（4.7%）であり，次いで全身健康状態低下（3.4%），高カルシウム血症（2.7%），帯状疱疹，発熱及び交差適合試験不適合（各2.0%）であった。それ以外の事象はすべて 2%未満であった（【CTD 5.3.5.3.6】TSFAE03M）。

・ 発現割合が高かった有害事象及び Grade 3 又は 4 の有害事象に関して，前回の 2 試験併合解析時から発現割合が明らかに変化した事象はなく，特筆すべき安全性上の懸念は認められなかった。

2.7.4.6 特別な患者集団及び状況下における安全性

2.7.4.6.1 部分集団解析

2.7.4.6.1.1 併用療法試験

MMY3004 試験，MMY3003 試験，GEN503 試験併合及び MMY1001 試験の本剤併用群（DVd 群，DRd 群及び DPd 群）で認められた有害事象を部分集団別（内因性要因：年齢，性別，人種，ベースラインの腎機能，ベースラインの肝機能，外因性要因：地域）に解析した。

本剤併用群（664 例）で認められた部分集団別の有害事象の概要を表 2.7.4-25 に示す。

ベースラインの腎機能を除くすべての部分集団で，有害事象，重篤な有害事象，Grade 3 又は 4 の有害事象，治験薬の投与中止に至った有害事象及び死亡に至った有害事象の発現割合はおおむね同様（10%未満の差）であった。ベースラインの腎機能（CrCL 値）が中等度（30～<60 mL/min）の集団の重篤な有害事象の発現割合は 58.5%（93/159 例）であり，全体の 46.4%（308/664 例）よりも高かった。また，高度（<30 mL/min）の集団に関しては被験者数が少ないため（12 例），意味のある比較はできなかった。

表 2.7.4-25 本剤併用群で認められた部分集団別の有害事象の概要［MMY3004 試験，MMY3003 試験及び GEN503 試験併合，MMY1001 試験，安全性解析対象集団］

		Dara Combined					
		N	TEAE	Serious TEAE	Grade 3 or 4 TEAE	TD due to TEAE[a]	TEAE with outcome Death[b]
All subjects		664	656 (98.8%)	308 (46.4%)	547 (82.4%)	53 (8.0%)	32 (4.8%)
Age:	18 to < 65 years	336	332 (98.8%)	140 (41.7%)	270 (80.4%)	16 (4.8%)	15 (4.5%)
	65 to < 75 years	269	266 (98.9%)	135 (50.2%)	227 (84.4%)	28 (10.4%)	15 (5.6%)
	>= 75 years	59	58 (98.3%)	33 (55.9%)	50 (84.7%)	9 (15.3%)	2 (3.4%)
Sex:	Male	382	378 (99.0%)	191 (50.0%)	317 (83.0%)	36 (9.4%)	21 (5.5%)
	Female	282	278 (98.6%)	117 (41.5%)	230 (81.6%)	17 (6.0%)	11 (3.9%)
Race:	White	527	519 (98.5%)	253 (48.0%)	430 (81.6%)	45 (8.5%)	28 (5.3%)
	Other	137	137 (100.0%)	55 (40.1%)	117 (85.4%)	8 (5.8%)	4 (2.9%)
Renal Impairment (Creatinine Clearance)	Normal (CrCl >= 90 mL/min)	240	238 (99.2%)	99 (41.3%)	194 (80.8%)	16 (6.7%)	12 (5.0%)
	Mild (CrCl 60 to < 90 mL/min)	249	245 (98.4%)	104 (41.8%)	202 (81.1%)	17 (6.8%)	9 (3.6%)
	Moderate (CrCl 30 to < 60 mL/min)	159	157 (98.7%)	93 (58.5%)	135 (84.9%)	17 (10.7%)	11 (6.9%)
	Severe (CrCl < 30 mL/min)	12	12 (100.0%)	10 (83.3%)	12 (100.0%)	3 (25.0%)	0
Hepatic Function[c]	Normal	570	563 (98.8%)	263 (46.1%)	470 (82.5%)	47 (8.2%)	29 (5.1%)
	Impaired	86	85 (98.8%)	39 (45.3%)	70 (81.4%)	6 (7.0%)	3 (3.5%)
Geographic Region:	West EU+NA+CAN	398	396 (99.5%)	190 (47.7%)	342 (85.9%)	32 (8.0%)	18 (4.5%)
	Other Regions	266	260 (97.7%)	118 (44.4%)	205 (77.1%)	21 (7.9%)	14 (5.3%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event. TD = treatment discontinuation.
Note: Percentages are calculated with the number of subjects in each subgroup as denominator.
[a]Treatment discontinuation due to adverse event on the end of treatment CRF page.
[b]TEAE with outcome death on the AE CRF page.
[c]Hepatic function is classified as normal and impaired groups. The impaired group includes subjects of 82 mildly, 3 moderately and 1 severely hepatic impairment per NCI Organ Dysfunction criteria.
West EU+US+CAN includes Belgium, Denmark, Greece, Netherlands, France, Great Britain, Sweden, Italy, Spain, USA, and Canada. Other region includes Australia, Israel, Japan, South Korea, Turkey, Taiwan, Poland, Brazil, Czech Republic, Hungary, Mexico, Russia, and Ukraine.

[TSFAE01S3.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE01S3.SAS] 12JUL2016, 12:48

2.7.4.6.1.2 単剤療法試験

単剤療法の 16 mg/kg 群で認められた有害事象を部分集団別（内因性要因：年齢，性別，人種，ベースラインの腎機能，ベースラインの肝機能，外因性要因：地域，製剤剤）に解析した。

単剤 3 試験併合の 16 mg/kg 群（156 例）で認められた部分集団別の有害事象の概要を表 2.7.4-26 に示す。

16 mg/kg 群で認められた部分集団別の有害事象の発現割合は，おおむね同様（10%未満の差）であった。年齢が≥75 歳の被験者の有害事象による死亡の発現割合は 12.5%（2/16 例）であり，全体の 1.9%（3/156 例）よりも高かったが，≥75 歳の被験者数が少ないため（16 例），意味のある比較はできなかった。また，腎機能別の部分集団では，ベースラインの CrCL が<30 mL/min の

被験者数が少ないため（5 例），意味のある比較はできなかった。ベースラインで軽度の肝機能障害を有する被験者での有害事象の発現割合は，重篤な有害事象が 42.9%（9/21 例），Grade 3 以上の有害事象が 71.4%（15/21 例），本剤の投与中止に至った有害事象が 19.0%（4/21 例）であり，16 mg/kg 群全体での発現割合（重篤な有害事象が 32.1%，Grade 3 以上の有害事象が 56.4%，本剤の投与中止に至った有害事象が 3.8%）よりも高い傾向にあったが，正常な肝機能を有する被験者との比較で明らかな傾向は認められなかった。

表 2.7.4-26 16 mg/kg 群で認められた部分集団別の有害事象の概要
［MMY2002 試験，GEN501 試験及び MMY1002 試験併合，全投与解析対象集団］

		16 mg/kg					
		N	TEAE	Serious TEAE	Grade 3 or Higher TEAE	TD due to TEAE[a]	Death due to TEAE[b]
All subjects		156	154 (98.7%)	50 (32.1%)	88 (56.4%)	6 (3.8%)	3 (1.9%)
Age:	18 to <65 years	86	86 (100.0%)	26 (30.2%)	45 (52.3%)	3 (3.5%)	1 (1.2%)
	65 to <75 years	54	52 (96.3%)	20 (37.0%)	35 (64.8%)	1 (1.9%)	0
	>=75 years	16	16 (100.0%)	4 (25.0%)	8 (50.0%)	2 (12.5%)	2 (12.5%)
Sex:	Male	84	82 (97.6%)	24 (28.6%)	42 (50.0%)	2 (2.4%)	2 (2.4%)
	Female	72	72 (100.0%)	26 (36.1%)	46 (63.9%)	4 (5.6%)	1 (1.4%)
Race:	White	119	117 (98.3%)	40 (33.6%)	64 (53.8%)	6 (5.0%)	3 (2.5%)
	Other	37	37 (100.0%)	10 (27.0%)	24 (64.9%)	0	0
Renal Impairment (Creatinine Clearance)	>=60 ml/min	95	94 (98.9%)	29 (30.5%)	48 (50.5%)	2 (2.1%)	2 (2.1%)
	30– <60 ml/min	56	56 (100.0%)	19 (33.9%)	37 (66.1%)	4 (7.1%)	1 (1.8%)
	<30 ml/min	5	4 (80.0%)	2 (40.0%)	3 (60.0%)	0	0
Hepatic Function[c]	Normal	134	132 (98.5%)	40 (29.9%)	72 (53.7%)	2 (1.5%)	1 (0.7%)
	Mildly Impaired	21	21 (100.0%)	9 (42.9%)	15 (71.4%)	4 (19.0%)	2 (9.5%)
Geographic Region:	EU	40	39 (97.5%)	15 (37.5%)	12 (30.0%)	3 (7.5%)	1 (2.5%)
	North America + Japan[d]	116	115 (99.1%)	35 (30.2%)	76 (65.5%)	3 (2.6%)	2 (1.7%)
Drug Products:	Phase 2 Product	64	63 (98.4%)	17 (26.6%)	34 (53.1%)	1 (1.6%)	1 (1.6%)
	Phase 3 Product	92	91 (98.9%)	33 (35.9%)	54 (58.7%)	5 (5.4%)	2 (2.2%)

Keys: TEAE = treatment-emergent adverse event. TD = treatment discontinuation.
Note: Percentages are calculated with the number of subjects in each subgroup as denominator.
[a]Treatment discontinuation due to adverse event on the end of treatment CRF page.
[b]Death due to adverse event on the death CRF page.
[c]Hepatic function is classified into 4 levels per NCI Organ Dysfunction criteria: Normal: total bilirubin ≤ ULN and AST ≤ ULN; Mildly Impaired: (total bilirubin ≤ ULN and AST > ULN) or (ULN < total bilirubin ≤ 1.5×ULN); Moderately Impaired: 1.5×ULN < total bilirubin ≤ 3×ULN; and Severely Impaired: total bilirubin > 3×ULN.
[d] Five subjects from Japanese Study MMY1002 were combined with the North American subgroup.
Modified from Appendix TSFAE01S

2.7.4.6.2 薬物相互作用

本剤の薬剤相互作用を検討した試験は実施していない。本剤は内因性免疫グロブリン G と同様に生体内の非特異的な異化経路を介して小ペプチド，さらにはアミノ酸レベルに分解されると予想され，腎排泄や肝酵素が介在する代謝が本剤の主要な排泄経路である可能性は低い。そのため，患者の腎機能，肝機能又は薬物代謝酵素活性の違いは本剤の排泄に影響を及ぼさないと考えられる（【CTD 2.7.2】）。また，ダラツムマブ（遺伝子組換え）はモノクローナル抗体であり，細

胞表面の CD38 上のエピトープと特異的に結合することから，本剤は薬物代謝酵素の活性に直接的な影響を及ぼさないと考えられる（【CTD 2.7.2】）。

MMY1001 試験では，併用療法下における低分子薬（ボルテゾミブ，ポマリドミド及びサリドマイド）及び daratumumab の PK プロファイルについて検討した。その結果，本剤とこれらの併用薬との間に薬物動態学的相互作用は認められなかった（【CTD 2.7.2】）。

2.7.4.6.3 妊娠及び授乳時の使用

妊婦に本剤が投与されたという報告はない。また，本剤の投与による発生異常又は胎児及び新生児への毒性を検討する非臨床試験は実施していない。

妊娠可能な女性に本剤を投与する場合，投与期間中及び投与終了後 3 カ月まで有効な避妊法を用いることとした。3 カ月のウォッシュアウト期間は，血清中 daratumumab 濃度の推定半減期（約 18 日，単剤療法）に基づいて設定された期間である（【CTD 2.7.2】）。また，理論上，本剤は半減期の約 5 倍の期間（90 日間）で体内から排泄されると予想される。妊娠可能な女性に投与終了後 3 カ月まで避妊を推奨することは，かなり保守的な手段である。

本剤が動物又はヒトの乳汁中に分泌されるかどうか，また乳汁産生に影響を及ぼすかは不明である。授乳婦に本剤を投与することによる乳児への影響を検討した試験は実施していない。母体のイムノグロブリン G は乳汁中に移行するものの，乳汁中の抗体は新生児及び乳児の体内でほとんど循環することがないことが示唆されている[7)]。

2.7.4.6.4 過量投与

いずれの試験においても，本剤の過量投与は起こらなかった。GEN501 試験では本剤を 24 mg/kg の用量まで単剤投与したが，最大耐量に到達しなかった。

本剤の過量投与に対する特異的な解毒剤はない。過量投与が認められた場合は，患者に有害作用の徴候又は症状がないかをモニタリングするとともに，適切な対症療法を直ちに開始すること。

2.7.4.6.5 薬物乱用

各医療機関で患者に投与するため，本剤は医療提供者のコントロール下に置かれる。本剤の薬物乱用は起こらないと考えられる。

2.7.4.6.6 離脱症状及び反跳現象

本剤の離脱症状及び反眺現象を検討する試験は実施していない。本剤の投与期間は疾患進行が認められるまでとした。

2.7.4.6.7 自動車運転及び機械操作に対する影響又は精神機能の障害

本剤による自動車運転及び機械操作に対する影響や精神機能の障害に関する情報はない。

自動車運転及び機械操作に対する影響や精神機能の障害に関して，本剤の影響を検討する試験は実施していない。しかし，併合解析で認められた疲労等の有害事象が，自動車運転及び機械操作に影響を及ぼす可能性が考えられる。

2.7.4.7 市販後データ

本剤に関するすべての市販後データは自発的に収集，蓄積される。2016 年 5 月 15 日までに得られたすべての有害事象は Global Medical Safety で審査され，global safety database に蓄積された。その結果，市販後の安全性プロファイルは，単剤療法試験で再発又は難治性の MM 患者に対して認められた既知の安全性プロファイルとおおむね同様であった。

回収された global safety database 中の計 289 例のデータのうち，266 例について安全性解析を実施した。人口統計学的特性は，男性が 52%，年齢が 38～88 歳（平均値 64.4 歳，中央値 65 歳）であった。51.9%（138/266 例）が重篤な有害事象，48.1%（128/266 例）が非重篤な有害事象を発現したが，92.1%（245/266 例）の転帰は致死性ではなかった。

138 例に認められた重篤な有害事象の発現件数は 366 件であった。発現割合が高かった有害事象は，IRR（9.6%，35/366 件），血小板数減少又は血小板減少症（5.2%，19/366 件），呼吸困難（4.4%，16/366 件）及び死亡（4.1%，15/366 件）であった。報告された有害事象の多くは企業中核データシート（Company Core Data Sheet）に掲載された事象であった。

138 例に認められた重篤な有害事象のうち，致死性の転帰を示した 21 例に関して更に解析した。21 例のうち 13 例が原因不明の死亡であり，残りの 8 例の致死性の有害事象は，死亡，汎血球減少症，形質細胞性骨髄腫及び敗血症（各 2 例），急性呼吸不全，無力症，心障害，うっ血性心不全，中枢神経系壊死，脳血管発作，疾患進行，発熱性好中球減少症，白血球増加症，白質脳症，代謝性アシドーシス，形質芽球性リンパ腫，頻脈，頻呼吸（各 1 例）であった。

また，2007 年 10 月 12 日（国際誕生日）から 2016 年 5 月 15 日までに報告された重篤な有害事象の一覧を【CTD 5.3.6】に示す。

参考文献

1） レブラミド®カプセル 2.5 mg／レブラミド®カプセル 5 mg　添付文書（第 13 版，2016 年 1 月改訂）. セルジーン株式会社.

2） Terpos E, et al. European myeloma network guidelines for the management of multiple myeloma-related complications. Haematologica. 2015;100:1254-66.

3） ベルケイド®注射用 3 mg　添付文書（第 9 版，2015 年 6 月改訂）. ヤンセンファーマ株式会社.

4） Areethamsirikul N, et al. The risk of secondary primary malignancies after therapy for multiple myeloma. Leuk Lymphoma. 2015;56:3012-21.

5） Food and Drug Administration. Guidance for industry drug-induced liver injury: premarketing clinical evaluation. July 2009.

6） Usmani SZ, et al. Clinical efficacy of daratumumab monotherapy in patients with heavily pretreated relapsed or refractory multiple myeloma. Blood. 2016;128:37-44

7） Van de Perre P. Transfer of antibody via mother's milk (Review). Vaccine. 2003;21:3374-6.

2.7.4.8 付録

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Adverse Events of Clinical Interest

The following terms were included in the assessments of adverse events of clinical interest. All adverse events included in the analysis were treatment emergent. Unless otherwise specified, the same terms were used for the assessments regardless of studies.

Infusion Related Reactions (Infusion Related Adverse Events)

For all studies except Study GEN501 (ie, Studies MMY3004, MMY3003, GEN503, MMY1001, MMY1005, MMY2002, and MMY1002), adverse events were considered as IRRs when determined so by the investigators. For Study GEN501, adverse events were considered as IRRs based on the retrospective review of adverse events that occurred within 48 hours of the daratumumab infusion.

Neutropenia

Adverse events coded to the preferred term of neutropenia and febrile neutropenia were examined.

Infections and Infestations

Adverse events in the SOC of infections and infestations were examined. For combination therapy studies (Studies MMY3004, MMY3003, GEN503, MMY1001, and MMY1005), opportunistic infections include adverse events coded to the following preferred terms: herpes zoster, oral herpes, oral candidiasis, oral fungal infection, fungal infection, herpes virus infection, fungal skin infection, balanitis candida, candida infection, cytomegalovirus infection, pneumonia legionella, pneumonia klebsiella, pneumonia streptococcal, pseudomonas infection, eye infection fungal, fungal oesophagitis, genital herpes, genital herpes simplex, genital infection fungal, herpes simplex, nasal herpes, oesophageal candidiasis, ophthalmic herpes simplex, pneumocystis jirovecii pneumonia, pneumonia cytomegaloviral, pseudomonal sepsis, pulmonary tuberculosis, skin candida, tinea infection, tinea cruris, tinea versicolour, tongue fungal infection, varicella, varicella zoster virus infection. For monotherapy studies (Studies MMY2002, GEN501, and MMY1002), opportunistic infections include adverse events coded to the following preferred terms: herpes zoster, oral candidiasis, candida infection, herpes simplex, varicella, cytomegalovirus chorioretinitis, ophthalmic herpes simplex, oral herpes, and vulvovaginal candidiasis.

Thrombocytopenia and Bleeding

Adverse events coded to the preferred term of thrombocytopenia were examined.

At the first clinical cutoff for the primary analysis for combination therapy studies (Studies MMY3004, MMY3003, GEN503, and MMY1001), the bleeding events include adverse events coded to the following preferred terms: anal haemorrhage, haematuria, subdural

haematoma, urinary bladder haemorrhage, uterine haemorrhage, conjunctival haemorrhage, haemarthrosis, haematoma, haemoptysis, haemorrhoidal haemorrhage, pulmonary alveolar haemorrhage, pulmonary haemorrhage, subarachnoid haemorrhage. For monotherapy studies (Studies MMY2002, GEN501, and MMY1002) and later analysis of combination therapy, the bleeding events include adverse events coded to the following preferred terms: anal haemorrhage, haematuria, subdural haematoma, urinary bladder haemorrhage, uterine haemorrhage, conjunctival haemorrhage, haemarthrosis, haematoma, haemoptysis, haemorrhoidal haemorrhage, pulmonary alveolar haemorrhage, pulmonary haemorrhage, subarachnoid haemorrhage, cerebral haemorrhage, epistaxis, gingival bleeding, haematochezia, haemorrhage subcutaneous, lip haemorrhage, lower gastrointestinal haemorrhage, mouth haemorrhage, petechiae, rectal haemorrhage, skin haemorrhage, subdural haemorrhage, vaginal haemorrhage.

Hemolysis
Adverse events coded to the preferred term of haemolysis were examined.

Cardiac Events (Atrial Fibrillation and QT Prolongation)
Adverse events coded to the preferred term of atrial fibrillation were examined. Adverse events with potential link to QT prolongation includes adverse events coded to the following preferred terms: electrocardiogram QT interval abnormal, Electrocardiogram QT prolonged, long QT syndrome, long QT syndrome congenital, torsade de pointes, ventricular tachycardia, cardiac arrest, cardiac death, cardiac fibrillation, cardio-respiratory arrest, electrocardiogram repolarisation abnormality, electrocardiogram U-wave abnormality, loss of consciousness, sudden cardiac death, sudden death, syncope, ventricular arrhythmia, ventricular fibrillation, ventricular flutter, ventricular tachyarrhythmia.

Hepatobiliary Disorders
Adverse events in the SOC of hepatobiliary disorders were examined.

Second Primary Malignancies
Adverse events of secondary primary malignancy were identified through the modified Standardized MedDRA Query (SMQ) as following: applicable events were selected from MALIGNANT OR UNSPECIFIED TUMOURS (SMQ) for Studies MMY3004, MMY3003, GEN503 and MMY1001, or from BREAST NEOPLASMS, MALIGNANT AND UNSPECIFIED (SMQ), MALIGNANCIES (SMQ), MALIGNANT LYMPHOMAS (SMQ), MYELODYSPLASTIC SYNDROME (SMQ), OVARIAN NEOPLASMS, MALIGNANT AND UNSPECIFIED (SMQ), PREMALIGNANT DISORDERS (SMQ), PROSTATE NEOPLASMS, MALIGNANT AND UNSPECIFIED (SMQ), SKIN NEOPLASMS, MALIGNANT AND UNSPECIFIED (SMQ), UTERINE AND FALLOPIAN TUBE NEOPLASMS, MALIGNANT AND UNSPECIFIED (SMQ) for Study MMY1005 and monotherapy studies (Studies MMY2002, GEN501, and MMY1002).

表 2.7.4-付録-2 Study Disposition; All-treated Analysis Set (Study 54767414MMY1005)

TSIDS01: Study Disposition; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Subjects ongoing	8 (100.0%)
Subjects ongoing treatment	7 (87.5%)
Subjects who discontinued treatment	1 (12.5%)
Reason for discontinuation	
Adverse event	1 (12.5%)
Death	0
Lost to follow-up	0
Physician decision	0
Study terminated by sponsor	0
Withdrawal by subject	0
Pregnancy	0
Progressive disease	0
Other	0
Completed study participation	0
Subjects who discontinued study	0
Reason for discontinuation	
Adverse event	0
Death	0
Lost to follow-up	0
Physician decision	0
Study terminated by sponsor	0
Withdrawal by subject	0
Pregnancy	0
Progressive disease	0
Screen Failure	0
Other	0

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.
Cutoff date: 03JUN2016.

[TSIDS01.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIDS01.SAS] 28SEP2016, 04:35

表 2.7.4-付録-3 Summary of Subject Disposition; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

TSIDS01_3003: Summary of Subject Disposition; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: intent-to-treat	15	44	283	21	52	286	36	96	569
Subjects randomized but not treated[c]	0	0	2 (0.7%)	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Subjects treated[c]	15 (100.0%)	44 (100.0%)	281 (99.3%)	20 (95.2%)	51 (98.1%)	283 (99.0%)	35 (97.2%)	95 (99.0%)	564 (99.1%)
Subjects who discontinued treatment[d]	7 (46.7%)	22 (50.0%)	132 (47.0%)	6 (30.0%)	16 (31.4%)	66 (23.3%)	13 (37.1%)	38 (40.0%)	198 (35.1%)
Reason for discontinuation									
Progressive disease	7 (46.7%)	21 (47.7%)	96 (34.2%)	2 (10.0%)	10 (19.6%)	40 (14.1%)	9 (25.7%)	31 (32.6%)	136 (24.1%)
Adverse event	0	1 (2.3%)	23 (8.2%)	2 (10.0%)	3 (5.9%)	19 (6.7%)	2 (5.7%)	4 (4.2%)	42 (7.4%)
Non-compliance with study drug[e]	0	0	5 (1.8%)	1 (5.0%)	1 (2.0%)	1 (0.4%)	1 (2.9%)	1 (1.1%)	6 (1.1%)
Withdrawal by subject	0	0	5 (1.8%)	0	0	1 (0.4%)	0	0	6 (1.1%)
Physician decision	0	0	2 (0.7%)	1 (5.0%)	1 (2.0%)	3 (1.1%)	1 (2.9%)	1 (1.1%)	5 (0.9%)
Death	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)	0	1 (1.1%)	3 (0.5%)
Subjects who discontinued study[c]	4 (26.7%)	10 (22.7%)	55 (19.4%)	1 (4.8%)	7 (13.5%)	34 (11.9%)	5 (13.9%)	17 (17.7%)	89 (15.6%)
Reason for discontinuation									
Death	3 (20.0%)	8 (18.2%)	44 (15.5%)	0	6 (11.5%)	30 (10.5%)	3 (8.3%)	14 (14.6%)	74 (13.0%)
Withdrawal by subject	1 (6.7%)	2 (4.5%)	9 (3.2%)	0	0	3 (1.0%)	1 (2.8%)	2 (2.1%)	12 (2.1%)
Lost to follow-up	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Progressive disease	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
[c] Percentages are based on number of subjects randomized.
[d] Percentages are based on number of subjects treated.
[e] Based on reason ‘ Subject refused to further study treatment′ on ‘End of Treatment′ CRF page.

[TSIDS01_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSIDS01_3003.SAS] 30JUN2016, 22:46

表 2.7.4-付録-4 Subject Disposition; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSIDS01: Subject Disposition; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Discontinued from treatment	14 (60.9%)	49 (89.1%)	123 (78.8%)	1 (33.3%)	187 (78.9%)
Progressive disease	10 (43.5%)	49 (89.1%)	108 (69.2%)	0	167 (70.5%)
Adverse event	4 (17.4%)	0	6 (3.8%)	1 (33.3%)	11 (4.6%)
Physician decision	0	0	4 (2.6%)	0	4 (1.7%)
Withdrawal of consent	0	0	3 (1.9%)	0	3 (1.3%)
Non-compliance with study drug	0	0	1 (0.6%)	0	1 (0.4%)
Protocol violation	0	0	1 (0.6%)	0	1 (0.4%)
Death	0	0	0	0	0
Lost to follow-up	0	0	0	0	0
Other	0	0	0	0	0
Pregnancy	0	0	0	0	0
Study terminated by sponsor	0	0	0	0	0

Percentages are calculated with the number of subjects in each group as denominator.

[TSIDS01.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsids01.sas] 16MAR2015, 12:12

表 2.7.4-付録-5 Summary of Subject Disposition and Number of Subjects Who Discontinued Study Drug and/or Study Participation; All Screened Subjects (Study 54767414MMY1002)

TSIDS01: Summary of Subject Disposition and Number of Subjects Who Discontinued Study Drug and/or Study Participation; All Screened Subjects (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Number of subjects			
Screened			13
Treated	4 (100.0%)	5 (100.0%)	9 (100.0%)
Ongoing at the date of cutoff	0	0	0
Discontinuation for study drug	4 (100.0%)	5 (100.0%)	9 (100.0%)
NON-COMPLIANCE WITH STUDY DRUG	0	1 (20.0%)	1 (11.1%)
PROGRESSIVE DISEASE	4 (100.0%)	3 (60.0%)	7 (77.8%)
PROTOCOL VIOLATION	0	1 (20.0%)	1 (11.1%)

Cutoff date: 25SEP2015

[TSIDS01.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsids01.sas] 18FEB2016, 15:22

表 2.7.4-付録-6 Summary of Duration of Study Treatment and Dose Intensity; All-treated Analysis Set (Study 54767414MMY1005)

TSIEXP02: Summary of Duration of Study Treatment and Dose Intensity; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)
Analysis set: All-treated	8
Duration of study treatment (months)	
N	8
Mean (SD)	5.73 (1.458)
Median	5.34
Range	(4.3; 8.9)
Bortezomib dose intensity (mg/m^2/cycle)[a]	
N	8
Mean (SD)	3.61 (0.597)
Median	3.72
Range	(2.9; 4.4)
Dexamethasone dose intensity (mg/cycle)[b]	
N	8
Mean (SD)	74.53 (43.852)
Median	71.72
Range	(17.2; 160.0)
Daratumumab dose intensity (Cycles 1- 3, mg/kg/cycle)[c]	
N	8
Mean (SD)	43.74 (6.103)
Median	45.10
Range	(32.5; 50.3)
Daratumumab dose intensity (Cycles 4 - 8, mg/kg/cycle)[c]	
N	8
Mean (SD)	16.53 (0.548)
Median	16.61
Range	(15.3; 17.0)
Daratumumab dose intensity (Cycle ≥9, mg/kg/cycle)[c]	
N	3
Mean (SD)	16.33 (1.035)
Median	16.64
Range	(15.2; 17.2)
Number of daratumumab infusions	
N	8
Mean (SD)	13.6 (1.69)
Median	13.0
Range	(12; 17)

Key: Vd = bortezomib-dexamethasone.
[a] Dose intensity (mg/m^2/cycle) is calculated as the sum of total doses (mg/m^2) received in all cycles divided by the number of treatment cycles on bortezomib.
[b] Dose intensity (mg/cycle) is calculated as the sum of total doses (mg) received in all cycles divided by the number of treatment cycles on dexamethasone.
[c] Dose intensity (mg/kg/cycle) is calculated as the sum of total doses (mg/kg) received in all cycles divided by the number of treatment cycles on daratumumab.

[TSIEXP02.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIEXP02.SAS] 28SEP2016, 04:37

表 2.7.4-付録-7 Summary of Exposure to Study Treatment by Cycle; All-treated Analysis Set (Study 54767414MMY1005)

TSIEXP04: Summary of Exposure to Study Treatment by Cycle; All-treated Analysis Set (Study 54767414MMY1005)

	Treatment Cycle									
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8	Cycle 9+	Total
Analysis set: All-treated	8	8	8	8	8	8	7	6	3	8
Treatment group: Vd + Daratumumab (16 mg/kg)										
Bortezomib (mg/m^2)										
N	8	8	8	8	8	8	7	6	0	8
Mean (SD)	5.22 (0.073)	4.09 (1.275)	3.32 (1.032)	3.64 (0.938)	3.24 (0.682)	2.88 (1.083)	3.13 (0.848)	2.98 (0.863)	-	27.36 (4.290)
Median	5.23	4.56	3.15	3.95	2.95	2.67	2.71	2.65	-	25.66
Range	(5.1; 5.3)	(2.6; 5.3)	(2.0; 5.2)	(2.6; 5.3)	(2.6; 4.1)	(1.1; 4.1)	(2.0; 4.1)	(1.9; 4.1)	-	(23.3; 34.9)
Dexamethasone (mg)										
N	8	8	8	8	8	8	7	6	0	8
Mean (SD)	127.78 (54.671)	99.63 (59.504)	82.71 (57.186)	64.18 (49.469)	49.18 (45.950)	49.18 (45.950)	53.37 (47.948)	54.30 (53.458)	-	560.06 (336.145)
Median	159.60	109.30	84.80	39.80	39.80	39.80	39.80	39.80	-	535.30
Range	(39.6; 160.0)	(20.0; 160.0)	(13.2; 160.0)	(14.6; 160.0)	(14.6; 160.0)	(14.6; 160.0)	(14.6; 160.0)	(6.6; 160.0)	-	(137.8; 1280.0)
Daratumumab (mg/kg)										
N	8	8	8	8	8	8	7	6	3	8
Mean (SD)	44.14 (7.578)	40.34 (11.950)	46.75 (5.901)	16.50 (0.620)	16.36 (0.670)	16.75 (0.537)	16.58 (0.602)	16.33 (0.770)	37.05 (22.010)	221.49 (24.725)
Median	47.77	46.47	49.14	16.70	16.52	16.80	16.80	16.35	33.28	214.64
Range	(31.3; 49.3)	(16.6; 50.9)	(32.7; 50.8)	(15.2; 17.0)	(15.1; 17.0)	(15.7; 17.3)	(15.3; 17.2)	(15.1; 17.2)	(17.2; 60.7)	(189.2; 261.7)

Key: Vd = bortezomib-dexamethasone.

[TSIEXP04.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIEXP04.SAS] 28SEP2016, 04:38

表 2.7.4-付録-8 Summary of Relative Dose Intensity; All-treated Analysis Set (Study 54767414MMY1005)

TSIEXP03: Summary of Relative Dose Intensity; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)
Analysis set: All-treated	8
Bortezomib (mg/m^2) relative dose intensity (%)	
N	8
Mean (SD)	71.55 (14.245)
Median	72.19
Range	(55.9; 95.2)
Dexamethasone (mg) relative dose intensity (%)	
N	8
Mean (SD)	61.13 (25.317)
Median	48.16
Range	(34.2; 100.0)
Daratumumab (mg/kg) relative dose intensity (%)	
N	8
Mean (SD)	95.91 (8.008)
Median	97.12
Range	(83.4; 105.4)
Daratumumab (mg/kg) relative dose intensity (Cycles 1 - 3, %)	
N	8
Mean (SD)	91.13 (12.715)
Median	93.97
Range	(67.8; 104.9)
Daratumumab (mg/kg) relative dose intensity (Cycles 4 - 8, %)	
N	8
Mean (SD)	103.29 (3.424)
Median	103.81
Range	(95.6; 106.3)
Daratumumab (mg/kg) relative dose intensity (Cycle ≥9, %)	
N	3
Mean (SD)	102.07 (6.467)
Median	104.01
Range	(94.9; 107.3)

Key: Vd = bortezomib-dexamethasone.

[TSIEXP03.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIEXP03.SAS] 28SEP2016, 04:37

表 2.7.4-付録-9 Summary of Duration of Study Treatment and Dose Intensity; Safety Analysis Set (Study 54767414MMY3003)

TSIEXP02_3003: Summary of Duration of Study Treatment and Dose Intensity; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283	35	95	564
Duration of study treatment (months)									
N	15	44	281	20	51	283	35	95	564
Mean (SD)	7.87 (2.579)	9.71 (4.696)	10.59 (4.921)	8.77 (3.073)	11.16 (4.203)	12.31 (4.263)	8.38 (2.866)	10.49 (4.473)	11.45 (4.679)
Median	8.77	9.68	12.29	9.89	11.27	13.14	9.00	10.48	12.75
Range	(2.5; 11.1)	(0.2; 17.3)	(0.2; 20.1)	(2.6; 12.6)	(1.5; 19.1)	(0.0; 20.7)	(2.5; 12.6)	(0.2; 19.1)	(0.0; 20.7)
Lenalidomide dose intensity (mg/cycle)[c]									
N	15	44	280	20	51	282	35	95	562
Mean (SD)	363.75 (163.476)	388.14 (148.032)	414.71 (127.758)	279.62 (144.314)	326.58 (145.404)	373.81 (134.059)	315.68 (156.291)	355.09 (149.071)	394.19 (132.432)
Median	475.00	478.58	479.83	302.71	322.31	381.61	311.00	344.00	439.32
Range	(85.0; 525.0)	(70.0; 526.8)	(65.0; 537.5)	(50.0; 527.3)	(50.0; 527.3)	(50.0; 528.3)	(50.0; 527.3)	(50.0; 527.3)	(50.0; 537.5)
Dexamethasone dose intensity (mg/cycle)[c]									
N	15	44	281	20	51	283	35	95	564
Mean (SD)	138.86 (25.230)	142.51 (29.865)	132.73 (33.017)	129.06 (37.753)	136.01 (31.686)	129.47 (32.437)	133.26 (32.906)	139.02 (30.865)	131.10 (32.739)
Median	149.09	152.57	149.33	149.06	151.25	144.00	149.09	152.00	146.67
Range	(80.0; 160.0)	(20.0; 160.0)	(20.0; 165.7)	(58.3; 160.0)	(58.3; 160.0)	(20.0; 178.1)	(58.3; 160.0)	(20.0; 160.0)	(20.0; 178.1)
Daratumumab dose intensity (Cycles 1- 2, mg/kg/cycle)[d]									
N	0	0	0	20	51	283	20	51	283
Mean (SD)				60.30 (7.053)	61.67 (5.650)	60.18 (8.719)	60.30 (7.053)	61.67 (5.650)	60.18 (8.719)
Median				64.17	64.00	63.92	64.17	64.00	63.92
Range				(41.0; 66.1)	(41.0; 66.1)	(1.4; 66.5)	(41.0; 66.1)	(41.0; 66.1)	(1.4; 66.5)
Daratumumab dose intensity (Cycles 3 - 6, mg/kg/cycle)[d]									
N	0	0	0	20	50	270	20	50	270

TSIEXP02_3003: Summary of Duration of Study Treatment and Dose Intensity; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Mean (SD)				31.41 (2.542)	31.56 (2.330)	31.12 (2.629)	31.41 (2.542)	31.56 (2.330)	31.12 (2.629)
Median				32.32	32.20	32.00	32.32	32.20	32.00
Range				(24.9; 34.9)	(24.0; 34.9)	(15.8; 34.9)	(24.9; 34.9)	(24.0; 34.9)	(15.8; 34.9)
Daratumumab dose intensity (Cycle ≥7, mg/kg/cycle)[d]									
N	0	0	0	16	46	252	16	46	252
Mean (SD)				15.88 (0.599)	15.94 (0.548)	16.01 (0.383)	15.88 (0.599)	15.94 (0.548)	16.01 (0.383)
Median				15.69	15.98	16.00	15.69	15.98	16.00
Range				(15.1; 16.9)	(14.9; 17.2)	(14.9; 17.2)	(15.1; 16.9)	(14.9; 17.2)	(14.9; 17.2)
Number of daratumumab infusions									
N	0	0	0	20	51	283	20	51	283
Mean (SD)				18.5 (4.24)	21.5 (5.31)	22.3 (6.00)	18.5 (4.24)	21.5 (5.31)	22.3 (6.00)
Median				20.0	21.0	24.0	20.0	21.0	24.0
Range				(10; 24)	(7; 30)	(1; 32)	(10; 24)	(7; 30)	(1; 32)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
[c] Dose intensity (mg/cycle) is calculated as the sum of total doses (mg) received in all cycles divided by the number of treatment cycles on lenalidomide and dexamethasone, respectively.
[d] Dose intensity (mg/kg/cycle) is calculated as the sum of total doses (mg/kg) received in all cycles divided by the number of treatment cycles on daratumumab.

表 2.7.4-付録-10 Summary of Exposure to Study Treatment by Cycle; Safety Analysis Set (Study 54767414MMY3003)

TSIEXP03_3003: Summary of Exposure to Study Treatment by Cycle; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Cycle							
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycles 7+	Total
Total[a]								
Treatment group: Rd								
Analysis set: safety	281	268	266	257	239	228	217	281
Lenalidomide (mg)								
N	280	268	265	254	238	227	217	280
Mean (SD)	448.00 (135.949)	448.92 (131.276)	440.79 (140.461)	437.30 (138.394)	430.88 (135.854)	427.20 (140.884)	3239.72 (1808.150)	4914.93 (2760.079)
Median	525.00	525.00	525.00	525.00	525.00	525.00	3150.00	4767.50
Range	(70.0; 550.0)	(70.0; 550.0)	(30.0; 700.0)	(50.0; 550.0)	(60.0; 550.0)	(45.0; 550.0)	(160.0; 8100.0)	(70.0; 11050.0)
Dexamethasone (mg)								
N	281	268	265	257	238	227	217	281
Mean (SD)	145.14 (30.348)	145.72 (30.641)	142.63 (33.677)	140.74 (35.495)	137.99 (37.016)	137.72 (37.165)	960.96 (512.854)	1517.57 (786.570)
Median	160.00	160.00	160.00	160.00	160.00	160.00	1020.00	1520.00
Range	(20.0; 161.9)	(20.0; 161.9)	(20.0; 166.1)	(20.0; 170.2)	(16.0; 170.2)	(20.0; 170.2)	(60.0; 2160.0)	(20.0; 3120.0)
Treatment group: DRd								
Analysis set: safety	283	277	272	265	261	256	254	283
Lenalidomide (mg)								
N	282	275	266	260	254	249	248	282
Mean (SD)	425.66 (140.655)	413.02 (146.037)	397.88 (151.524)	393.90 (154.434)	390.93 (155.906)	386.29 (153.273)	3025.87 (1707.022)	4921.13 (2589.923)
Median	525.00	525.00	525.00	525.00	525.00	525.00	2817.50	4702.50
Range	(80.0; 550.0)	(70.0; 550.0)	(35.0; 550.0)	(25.0; 550.0)	(15.0; 550.0)	(25.0; 660.0)	(20.0; 7350.0)	(90.0; 10500.0)
Dexamethasone (mg)								
N	283	277	271	264	259	253	253	283
Mean (SD)	147.10 (27.829)	147.37 (30.088)	139.04 (34.611)	139.75 (35.698)	137.45 (37.967)	136.61 (36.760)	1039.54 (522.671)	1732.11 (746.433)
Median	160.00	160.00	160.00	160.00	160.00	160.00	1040.00	1792.00
Range	(20.0; 240.0)	(40.0; 280.0)	(20.0; 200.0)	(16.0; 180.0)	(16.0; 180.0)	(8.0; 180.0)	(40.0; 2580.0)	(20.0; 3460.0)
Daratumumab (mg/kg)								
N	283	275	270	263	259	253	252	283
Mean (SD)	59.38 (10.127)	61.93 (7.353)	31.23 (3.850)	31.68 (2.679)	31.09 (3.948)	30.88 (4.326)	137.65 (47.665)	357.45 (96.638)

TSIEXP03_3003: Summary of Exposure to Study Treatment by Cycle; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Cycle							
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycles 7+	Total
Median	64.00	64.00	32.00	32.00	32.00	32.00	143.63	383.33
Range	(1.4; 67.6)	(16.0; 69.6)	(15.8; 34.9)	(16.0; 35.1)	(15.1; 34.3)	(15.1; 35.5)	(16.0; 272.0)	(1.4; 509.5)
Japanese								
Treatment group: Rd								
Analysis set: safety	15	15	15	14	13	13	11	15
Lenalidomide (mg)								
N	15	15	15	14	12	12	11	15
Mean (SD)	389.33 (158.935)	386.33 (175.718)	361.00 (190.237)	349.64 (167.659)	393.75 (162.455)	334.17 (182.431)	1709.09 (848.575)	3298.67 (1981.693)
Median	500.00	525.00	525.00	315.00	512.50	332.50	1575.00	3770.00
Range	(80.0; 525.0)	(100.0; 525.0)	(70.0; 525.0)	(65.0; 525.0)	(140.0; 525.0)	(45.0; 525.0)	(280.0; 3150.0)	(340.0; 6300.0)
Dexamethasone (mg)								
N	15	15	15	14	13	13	11	15
Mean (SD)	141.33 (29.729)	141.33 (29.729)	149.33 (28.149)	142.86 (34.065)	143.23 (32.286)	136.92 (38.163)	581.09 (217.837)	1234.27 (487.024)
Median	160.00	160.00	160.00	160.00	160.00	160.00	560.00	1400.00
Range	(80.0; 160.0)	(80.0; 160.0)	(80.0; 160.0)	(80.0; 160.0)	(80.0; 160.0)	(60.0; 160.0)	(320.0; 1000.0)	(440.0; 1960.0)
Treatment group: DRd								
Analysis set: safety	20	20	20	18	17	17	16	20
Lenalidomide (mg)								
N	20	19	19	16	16	15	15	20
Mean (SD)	327.75 (151.079)	322.37 (171.483)	281.32 (167.944)	290.00 (183.703)	288.44 (165.899)	307.67 (156.546)	1462.67 (720.582)	2691.75 (1781.014)
Median	300.00	315.00	210.00	262.50	315.00	315.00	1260.00	2650.00
Range	(110.0; 550.0)	(70.0; 525.0)	(35.0; 525.0)	(25.0; 525.0)	(15.0; 525.0)	(100.0; 525.0)	(450.0; 2625.0)	(150.0; 5800.0)
Dexamethasone (mg)								
N	20	20	20	18	17	17	16	20
Mean (SD)	138.41 (35.276)	137.26 (33.578)	131.80 (37.546)	130.50 (44.102)	135.84 (38.362)	135.38 (39.241)	589.90 (234.545)	1227.37 (510.465)
Median	159.20	159.20	159.60	159.60	159.60	159.60	620.00	1436.20
Range	(79.2; 160.0)	(79.2; 160.0)	(59.6; 160.0)	(19.8; 160.0)	(72.0; 160.0)	(64.0; 160.0)	(159.8; 958.8)	(237.8; 1915.6)
Daratumumab (mg/kg)								
N	20	20	20	18	17	17	16	20
Mean (SD)	60.21 (10.320)	60.40 (9.184)	31.53 (5.249)	31.80 (3.886)	31.66 (4.012)	30.39 (5.318)	81.12 (25.111)	298.39 (67.147)

TSIEXP03_3003: Summary of Exposure to Study Treatment by Cycle; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Cycle							
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycles 7+	Total
Median	64.00	65.17	33.15	32.92	32.65	32.08	79.66	323.69
Range	(32.0; 66.0)	(34.0; 66.9)	(16.4; 34.9)	(16.6; 34.0)	(16.5; 33.9)	(15.6; 33.8)	(16.9; 121.6)	(162.6; 380.7)
East Asian[b]								
Treatment group: Rd								
Analysis set: safety	44	43	43	42	36	35	32	44
Lenalidomide (mg)								
N	44	43	43	42	35	34	32	44
Mean (SD)	412.95 (156.351)	438.72 (142.633)	410.12 (163.734)	409.05 (158.965)	394.43 (161.381)	376.76 (171.451)	2795.94 (1757.258)	4271.25 (2644.919)
Median	525.00	525.00	525.00	525.00	525.00	512.50	2512.50	4130.00
Range	(70.0; 525.0)	(100.0; 525.0)	(70.0; 525.0)	(65.0; 525.0)	(100.0; 525.0)	(45.0; 525.0)	(280.0; 6615.0)	(70.0; 9590.0)
Dexamethasone (mg)								
N	44	43	43	42	36	35	32	44
Mean (SD)	146.73 (31.351)	149.30 (26.313)	151.63 (23.997)	147.62 (28.611)	143.43 (30.998)	142.86 (33.657)	1030.63 (569.404)	1562.26 (820.104)
Median	160.00	160.00	160.00	160.00	160.00	160.00	964.00	1536.00
Range	(20.0; 160.0)	(60.0; 160.0)	(80.0; 160.0)	(80.0; 160.0)	(80.0; 160.0)	(60.0; 160.0)	(160.0; 1960.0)	(20.0; 2900.0)
Treatment group: DRd								
Analysis set: safety	51	51	50	48	47	47	46	51
Lenalidomide (mg)								
N	51	50	49	46	46	45	45	51
Mean (SD)	385.20 (148.007)	364.10 (160.931)	355.10 (175.153)	357.28 (174.552)	345.00 (167.136)	335.67 (164.312)	2338.33 (1740.086)	4076.18 (2529.238)
Median	405.00	350.00	350.00	315.00	315.00	315.00	1980.00	3735.00
Range	(110.0; 550.0)	(70.0; 525.0)	(35.0; 525.0)	(25.0; 525.0)	(15.0; 525.0)	(60.0; 525.0)	(100.0; 6825.0)	(150.0; 9975.0)
Dexamethasone (mg)								
N	51	51	50	48	47	47	46	51
Mean (SD)	144.08 (30.869)	140.69 (32.140)	137.12 (33.599)	138.94 (35.321)	142.75 (32.129)	141.31 (33.790)	966.09 (573.534)	1683.12 (748.432)
Median	160.00	160.00	160.00	160.00	160.00	160.00	880.00	1613.20
Range	(79.2; 160.0)	(79.2; 160.0)	(59.6; 160.0)	(19.8; 160.0)	(72.0; 160.0)	(64.0; 160.0)	(40.0; 2260.0)	(237.8; 3200.0)
Daratumumab (mg/kg)								
N	51	51	50	48	47	47	46	51

TSIEXP03_3003: Summary of Exposure to Study Treatment by Cycle; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Cycle							
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycles 7+	Total
Mean (SD)	60.88 (8.564)	62.46 (6.947)	31.44 (4.549)	31.47 (4.106)	31.99 (2.540)	31.31 (4.199)	116.61 (58.126)	347.29 (85.064)
Median	64.00	64.30	32.54	32.51	32.21	32.06	119.35	340.30
Range	(32.0; 66.0)	(34.0; 69.6)	(16.1; 34.9)	(16.0; 34.7)	(16.5; 34.1)	(15.4; 35.5)	(16.0; 227.9)	(110.8; 473.6)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.

[TSIEXP03_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSIEXP03_3003.SAS] 02JUL2016, 00:06

表 2.7.4-付録-11 Summary of Relative Dose Intensity; Safety Analysis Set (Study 54767414MMY3003)

TSIEXP05_3003: Summary of Relative Dose Intensity; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283	35	95	564
Lenalidomide (mg) relative dose intensity (%)									
N	15	44	280	20	51	282	35	95	562
Mean (SD)	81.14 (29.027)	82.16 (23.055)	85.90 (18.417)	64.19 (25.451)	70.76 (26.641)	77.67 (22.944)	71.46 (27.953)	76.04 (25.560)	81.77 (21.198)
Median	95.71	94.35	95.77	61.37	69.88	85.21	80.31	84.29	92.77
Range	(16.8; 100.0)	(16.8; 100.0)	(16.8; 100.0)	(13.2; 100.0)	(13.2; 100.0)	(13.2; 100.0)	(13.2; 100.0)	(13.2; 100.0)	(13.2; 100.0)
Dexamethasone (mg) relative dose intensity (%)									
N	15	44	281	20	51	283	35	95	564
Mean (SD)	99.69 (0.949)	99.90 (0.567)	99.38 (4.253)	99.18 (1.638)	99.16 (3.493)	99.00 (4.290)	99.40 (1.391)	99.50 (2.603)	99.19 (4.272)
Median	100.00	100.00	100.00	99.74	100.00	100.00	99.99	100.00	100.00
Range	(96.4; 100.0)	(96.4; 100.4)	(50.0; 104.2)	(92.7; 100.0)	(75.9; 100.0)	(63.9; 111.3)	(92.7; 100.0)	(75.9; 100.4)	(50.0; 111.3)
Daratumumab (mg/kg) relative dose intensity (%)									
N	0	0	0	20	51	283	20	51	283
Mean (SD)	-	-	-	97.41 (5.516)	98.07 (5.275)	96.28 (10.584)	97.41 (5.516)	98.07 (5.275)	96.28 (10.584)
Median	-	-	-	98.44	99.53	99.65	98.44	99.53	99.65
Range	-	-	-	(80.4; 103.9)	(80.4; 104.3)	(1.7; 104.9)	(80.4; 103.9)	(80.4; 104.3)	(1.7; 104.9)
Daratumumab (mg/kg) relative dose intensity (Cycles 1 - 2, %)									
N	0	0	0	20	51	283	20	51	283
Mean (SD)	-	-	-	94.22 (11.020)	96.36 (8.828)	94.49 (12.793)	94.22 (11.020)	96.36 (8.828)	94.49 (12.793)
Median	-	-	-	100.27	100.00	99.93	100.27	100.00	99.93
Range	-	-	-	(64.1; 103.3)	(64.1; 103.3)	(1.7; 103.9)	(64.1; 103.3)	(64.1; 103.3)	(1.7; 103.9)
Daratumumab (mg/kg) relative dose intensity (Cycles 3 - 6, %)									

TSIEXP05_3003: Summary of Relative Dose Intensity; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
N	0	0	0	20	50	270	20	50	270
Mean (SD)	-	-	-	100.09 (5.773)	99.40 (6.455)	97.52 (8.115)	100.09 (5.773)	99.40 (6.455)	97.52 (8.115)
Median	-	-	-	101.98	100.90	100.00	101.98	100.90	100.00
Range	-	-	-	(88.6; 109.0)	(75.0; 109.0)	(49.4; 109.0)	(88.6; 109.0)	(75.0; 109.0)	(49.4; 109.0)
Daratumumab (mg/kg) relative dose intensity (Cycles ≥7, %)									
N	0	0	0	16	46	252	16	46	252
Mean (SD)	-	-	-	99.24 (3.741)	99.43 (3.787)	99.73 (3.422)	99.24 (3.741)	99.43 (3.787)	99.73 (3.422)
Median	-	-	-	98.04	99.85	100.00	98.04	99.85	100.00
Range	-	-	-	(94.2; 105.4)	(88.5; 107.4)	(71.4; 107.4)	(94.2; 105.4)	(88.5; 107.4)	(71.4; 107.4)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.

表 2.7.4-付録-12 Summary of Study Medications; All Treated Analysis Population (Study 54767414MMY1002)

TSIEXP01: Summary of Study Medications; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Duration of study drug treatment (days)			
N	4	5	9
Mean (SD)	181.8 (124.94)	121.0 (136.08)	148.0 (127.03)
Median	190.5	72.0	169.0
Range	(22; 324)	(1; 289)	(1; 324)
Categories of study drug treatment (days)			
1-35	1 (25.0%)	2 (40.0%)	3 (33.3%)
36-56	0	0	0
57-182	1 (25.0%)	1 (20.0%)	2 (22.2%)
≥183	2 (50.0%)	2 (40.0%)	4 (44.4%)
Duration of study drug treatment (months)			
N	4	5	9
Mean (SD)	5.97 (4.105)	3.98 (4.471)	4.86 (4.174)
Median	6.26	2.37	5.55
Range	(0.7; 10.6)	(0.0; 9.5)	(0.0; 10.6)

Note: Duration of study drug treatment (days) is derived as the date of the last study drug administration minus the date of the first study drug administration plus 1.

[TSIEXP01.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsiexp01.sas] 18FEB2016, 15:25

表 2.7.4-付録-13 Summary of Cumulative Dose of Daratumumab and Dose Intensities; All Treated Analysis Population (Study 54767414MMY1002)

TSIEXP02: Summary of Cumulative Dose of Daratumumab and Dose Intensities; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Cumulative dose of Daratumumab (mg/kg)			
N	4	5	9
Mean (SD)	113.14 (69.860)	147.60 (138.664)	132.28 (108.507)
Median	127.10	122.68	122.68
Range	(16.3; 182.1)	(16.2; 309.7)	(16.2; 309.7)
Total number of Daratumumab infusion			
N	4	5	9
Mean (SD)	13.5 (7.94)	9.6 (9.07)	11.3 (8.31)
Median	16.0	8.0	15.0
Range	(2; 20)	(1; 20)	(1; 20)
Relative dose intensity (%)			
N	4	5	9
Mean (SD)	103.55 (6.930)	98.68 (4.239)	100.84 (5.793)
Median	100.62	96.78	99.45
Range	(99.2; 113.8)	(94.7; 104.7)	(94.7; 113.8)
<95	0	1 (20.0%)	1 (11.1%)
≥95	4 (100.0%)	4 (80.0%)	8 (88.9%)

Note: Interrupted and/or incomplete infusions are also included.
Note: Total cumulative dose is the sum of received doses (mg/kg).
Note: Relative dose intensity (%) is calculated as 100 x Total cumulative dose/Planned total cumulative dose.

[TSIEXP02.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsiexp02.sas] 18FEB2016, 15:26

表 2.7.4-付録-14 Summary of Demographics; All-treated Analysis Set (Study 54767414MMY1005)

TSIDEM01: Summary of Demographics; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)
Analysis set: All-treated	8
Age (years)	
N	8
Mean (SD)	73.4 (8.65)
Median	74.5
Range	(54; 82)
< 65	1 (12.5%)
65 - 74	3 (37.5%)
≥75	4 (50.0%)
Sex	
N	8
Male	6 (75.0%)
Female	2 (25.0%)
Ethnicity	
N	8
Hispanic or Latino	0
Not Hispanic or Latino	8 (100.0%)
Unknown	0
Not Reported	0
Race	
N	8
White	0
Black or African American	0
Asian	8 (100.0%)
American Indian or Alaska Native	0
Native Hawaiian or other Pacific Islander	0
Other	0
Unknown	0
Not Reported	0
Weight (kg)	
N	8
Mean (SD)	57.40 (10.281)
Median	57.15
Range	(45.0; 71.7)
Height (cm)	
N	8
Mean (SD)	157.8 (9.57)
Median	159.9
Range	(145; 169)
BMI (kg/m^2)	
N	8
Mean (SD)	22.896 (2.0575)
Median	22.786
Range	(19.87; 26.19)
BSA (m^2)	
N	8
Mean (SD)	1.583 (0.1859)
Median	1.596
Range	(1.36; 1.83)
Baseline ECOG score	
N	8
0	6 (75.0%)
1	2 (25.0%)
≥2	0

TSIDEM01: Summary of Demographics; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)

Keys: Vd = bortezomib-dexamethasone; kg = kilogram, m = meter, BMI = body mass index, BSA = body surface area.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSIDEM01.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIDEM01.SAS] 28SEP2016, 04:31

表 2.7.4-付録-15 Summary of Baseline Characteristics; All-treated Analysis Set (Study 54767414MMY1005)

TSIDEM02: Summary of Baseline Characteristics; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)
Analysis set: All-treated	8
Type of myeloma by immunofixation	
N	8
IgG	4 (50.0%)
IgA	2 (25.0%)
IgM	0
IgD	0
IgE	0
Light chain	2 (25.0%)
Kappa	2 (25.0%)
Lambda	0
Biclonal	0
Negative immunofixation	0
Type of measurable disease[a]	
N	8
IgG	3 (37.5%)
IgA	2 (25.0%)
Other[b]	0
Urine only	1 (12.5%)
Serum FLC only	2 (25.0%)
Stage for multiple myeloma[c]	
N	8
I	7 (87.5%)
II	1 (12.5%)
III	0
Number of prior lines of therapy, n (%)	
N	8
1	2 (25.0%)
2	6 (75.0%)
3	0
>3	0
Prior bortezomib treatment, n (%)	
N	8
No	4 (50.0%)
Yes	4 (50.0%)
Time from MM diagnosis (years)	
N	8
Mean (SD)	4.60 (2.924)
Median	3.74
Range	(2.3; 11.5)
Number of lytic bone lesions	
N	8
None	1 (12.5%)
1-3	4 (50.0%)
4-10	2 (25.0%)
More than 10	1 (12.5%)
Presence of diffuse myeloma-related osteopenia	
N	8
Yes	4 (50.0%)
No	4 (50.0%)
Number of extramedullary plasmacytomas	
N	8
0	8 (100.0%)
≥ 1	0

TSIDEM02: Summary of Baseline Characteristics; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)
Presence of evaluable bone marrow assessment	
N	8
Yes	8 (100.0%)
No	0
% Plasma cells, bone marrow aspirate	
N	8
<10	3 (37.5%)
10-30	3 (37.5%)
>30	2 (25.0%)
% Plasma cells, bone marrow biopsy/aspirate	
N	8
<10	3 (37.5%)
10-30	3 (37.5%)
>30	2 (25.0%)
Any cytogenetic abnormality[d]	
N	8
Standard risk	5 (62.5%)
High risk	3 (37.5%)
Del17p	2 (25.0%)
T(4;14)	3 (37.5%)
T(14;16)	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; FLC = serum free light chain; ISS = International staging system.
[a] Includes subjects without measurable disease in serum and urine.
[b] Includes IgD, IgM, IgE and biclonal.
[c] ISS staging is derived based on the combination of serum ß2-microglobulin and albumin.
[d] Cytogenetic abnormalities are based on FISH or karyotype testing.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSIDEM02.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIDEM02.SAS] 28SEP2016, 04:32

表 2.7.4-付録-16 Summary of Demographics and Baseline Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

TSIDEM02_3003: Summary of Demographics and Baseline Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: intent-to-treat	15	44	283	21	52	286	36	96	569
Age, years									
N	15	44	283	21	52	286	36	96	569
Category, n (%)									
< 65	4 (26.7%)	21 (47.7%)	140 (49.5%)	6 (28.6%)	28 (53.8%)	133 (46.5%)	10 (27.8%)	49 (51.0%)	273 (48.0%)
65 - 74	9 (60.0%)	19 (43.2%)	108 (38.2%)	12 (57.1%)	18 (34.6%)	124 (43.4%)	21 (58.3%)	37 (38.5%)	232 (40.8%)
≥75	2 (13.3%)	4 (9.1%)	35 (12.4%)	3 (14.3%)	6 (11.5%)	29 (10.1%)	5 (13.9%)	10 (10.4%)	64 (11.2%)
Mean (SD)	67.1 (7.93)	64.3 (8.08)	64.3 (8.84)	66.6 (9.94)	63.7 (9.59)	64.4 (9.03)	66.8 (9.03)	64.0 (8.89)	64.4 (8.93)
Median	67.0	65.0	65.0	68.0	64.0	65.0	68.0	64.0	65.0
Range	(50; 81)	(44; 85)	(42; 87)	(45; 80)	(34; 80)	(34; 89)	(45; 81)	(34; 85)	(34; 89)
Sex, n (%)									
N	15	44	283	21	52	286	36	96	569
Male	9 (60.0%)	27 (61.4%)	164 (58.0%)	11 (52.4%)	26 (50.0%)	173 (60.5%)	20 (55.6%)	53 (55.2%)	337 (59.2%)
Female	6 (40.0%)	17 (38.6%)	119 (42.0%)	10 (47.6%)	26 (50.0%)	113 (39.5%)	16 (44.4%)	43 (44.8%)	232 (40.8%)
Ethnicity, n (%)									
N	15	44	283	21	52	286	36	96	569
Hispanic or Latino	0	0	3 (1.1%)	0	0	1 (0.3%)	0	0	4 (0.7%)
Not Hispanic or Latino	15 (100.0%)	44 (100.0%)	238 (84.1%)	21 (100.0%)	52 (100.0%)	258 (90.2%)	36 (100.0%)	96 (100.0%)	496 (87.2%)
Unknown	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Not Reported	0	0	41 (14.5%)	0	0	25 (8.7%)	0	0	66 (11.6%)
Race, n (%)									
N	15	44	283	21	52	286	36	96	569
White	0	0	186 (65.7%)	0	0	207 (72.4%)	0	0	393 (69.1%)
Black or African American	0	0	11 (3.9%)	0	0	5 (1.7%)	0	0	16 (2.8%)
Asian	15 (100.0%)	44 (100.0%)	46 (16.3%)	21 (100.0%)	52 (100.0%)	54 (18.9%)	36 (100.0%)	96 (100.0%)	100 (17.6%)
American Indian or Alaska Native	0	0	0	0	0	0	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0	0	0	0	0	0	0
Other	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Unknown	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Not Reported	0	0	36 (12.7%)	0	0	18 (6.3%)	0	0	54 (9.5%)

TSIDEM02_3003: Summary of Demographics and Baseline Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Weight (kg)									
N	0	0	2	20	50	280	20	50	282
Mean (SD)	-	-	64.00 (5.657)	54.52 (9.874)	57.46 (12.923)	73.69 (16.268)	54.52 (9.874)	57.46 (12.923)	73.62 (16.234)
Median	-	-	64.00	57.15	57.15	73.00	57.15	57.15	73.00
Range	-	-	(60.0; 68.0)	(37.6; 73.0)	(37.0; 123.0)	(37.0; 132.0)	(37.6; 73.0)	(37.0; 123.0)	(37.0; 132.0)
Height (cm)									
N	15	44	279	21	52	282	36	96	561
Mean (SD)	158.2 (9.88)	160.8 (8.03)	166.0 (10.59)	156.8 (9.74)	157.4 (9.32)	165.8 (10.54)	157.4 (9.68)	159.0 (8.87)	165.9 (10.56)
Median	156.0	162.0	166.0	156.7	158.5	165.8	156.6	159.6	166.0
Range	(137; 178)	(137; 178)	(137; 201)	(132; 175)	(132; 183)	(132; 195)	(132; 178)	(132; 183)	(132; 201)
Baseline ECOG score, n (%)									
N	15	44	283	21	52	286	36	96	569
0	10 (66.7%)	21 (47.7%)	150 (53.0%)	14 (66.7%)	25 (48.1%)	139 (48.6%)	24 (66.7%)	46 (47.9%)	289 (50.8%)
1	4 (26.7%)	22 (50.0%)	118 (41.7%)	7 (33.3%)	25 (48.1%)	136 (47.6%)	11 (30.6%)	47 (49.0%)	254 (44.6%)
2	1 (6.7%)	1 (2.3%)	15 (5.3%)	0	2 (3.8%)	11 (3.8%)	1 (2.8%)	3 (3.1%)	26 (4.6%)
>2	0	0	0	0	0	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.

[TSIDEM02_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSIDEM02_3003.SAS] 30JUN2016, 22:20

表 2.7.4-付録-17 Summary of Baseline Disease Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

TSIDEM03_3003: Summary of Baseline Disease Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: intent-to-treat	15	44	283	21	52	286	36	96	569
Type of myeloma by immunofixation, n (%)									
N	15	44	283	21	52	286	36	96	569
IgG	8 (53.3%)	23 (52.3%)	167 (59.0%)	16 (76.2%)	31 (59.6%)	164 (57.3%)	24 (66.7%)	54 (56.3%)	331 (58.2%)
IgA	4 (26.7%)	13 (29.5%)	56 (19.8%)	0	9 (17.3%)	55 (19.2%)	4 (11.1%)	22 (22.9%)	111 (19.5%)
IgM	0	0	0	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
IgD	1 (6.7%)	2 (4.5%)	6 (2.1%)	0	2 (3.8%)	5 (1.7%)	1 (2.8%)	4 (4.2%)	11 (1.9%)
IgE	0	0	0	0	0	0	0	0	0
Light chain	1 (6.7%)	5 (11.4%)	46 (16.3%)	3 (14.3%)	7 (13.5%)	55 (19.2%)	4 (11.1%)	12 (12.5%)	101 (17.8%)
Kappa	1 (6.7%)	3 (6.8%)	32 (11.3%)	1 (4.8%)	4 (7.7%)	34 (11.9%)	2 (5.6%)	7 (7.3%)	66 (11.6%)
Lambda	0	2 (4.5%)	14 (4.9%)	2 (9.5%)	3 (5.8%)	21 (7.3%)	2 (5.6%)	5 (5.2%)	35 (6.2%)
Biclonal	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Negative immunofixation	1 (6.7%)	1 (2.3%)	8 (2.8%)	1 (4.8%)	2 (3.8%)	4 (1.4%)	2 (5.6%)	3 (3.1%)	12 (2.1%)
Type of measurable disease[c], n (%)									
N	15	44	283	21	52	286	36	96	569
IgG	8 (53.3%)	23 (52.3%)	158 (55.8%)	16 (76.2%)	31 (59.6%)	151 (52.8%)	24 (66.7%)	54 (56.3%)	309 (54.3%)
IgA	4 (26.7%)	12 (27.3%)	51 (18.0%)	0	9 (17.3%)	49 (17.1%)	4 (11.1%)	21 (21.9%)	100 (17.6%)
Other[d]	0	1 (2.3%)	2 (0.7%)	1 (4.8%)	2 (3.8%)	5 (1.7%)	1 (2.8%)	3 (3.1%)	7 (1.2%)
Urine only	2 (13.3%)	5 (11.4%)	37 (13.1%)	2 (9.5%)	5 (9.6%)	41 (14.3%)	4 (11.1%)	10 (10.4%)	78 (13.7%)
Serum FLC only	1 (6.7%)	2 (4.5%)	33 (11.7%)	2 (9.5%)	5 (9.6%)	39 (13.6%)	3 (8.3%)	7 (7.3%)	72 (12.7%)
NE	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
ISS staging[e], n (%)									
N	15	44	283	21	52	286	36	96	569
I	11 (73.3%)	24 (54.5%)	140 (49.5%)	13 (61.9%)	31 (59.6%)	137 (47.9%)	24 (66.7%)	55 (57.3%)	277 (48.7%)
II	2 (13.3%)	10 (22.7%)	86 (30.4%)	5 (23.8%)	15 (28.8%)	93 (32.5%)	7 (19.4%)	25 (26.0%)	179 (31.5%)
III	2 (13.3%)	10 (22.7%)	57 (20.1%)	3 (14.3%)	6 (11.5%)	56 (19.6%)	5 (13.9%)	16 (16.7%)	113 (19.9%)
Time from MM diagnosis to randomization(years)									
N	15	44	283	21	52	286	36	96	569
Mean (SD)	4.01 (3.922)	3.87 (3.303)	4.82 (3.607)	5.35 (5.654)	4.53 (3.869)	4.56 (3.607)	4.79 (4.987)	4.23 (3.617)	4.69 (3.606)
Median	2.97	2.58	3.95	3.43	3.91	3.48	3.00	3.32	3.64
Range	(0.9; 13.5)	(0.9; 13.5)	(0.4; 21.7)	(0.9; 27.0)	(0.8; 27.0)	(0.4; 27.0)	(0.9; 27.0)	(0.8; 27.0)	(0.4; 27.0)

TSIDEM03_3003: Summary of Baseline Disease Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Number of lytic bone lesions, n (%)									
N	15	44	280	21	52	278	36	96	558
None	3 (20.0%)	12 (27.3%)	74 (26.4%)	8 (38.1%)	13 (25.0%)	68 (24.5%)	11 (30.6%)	25 (26.0%)	142 (25.4%)
1-3	4 (26.7%)	9 (20.5%)	58 (20.7%)	6 (28.6%)	13 (25.0%)	55 (19.8%)	10 (27.8%)	22 (22.9%)	113 (20.3%)
4-10	2 (13.3%)	9 (20.5%)	51 (18.2%)	5 (23.8%)	13 (25.0%)	71 (25.5%)	7 (19.4%)	22 (22.9%)	122 (21.9%)
More than 10	6 (40.0%)	14 (31.8%)	97 (34.6%)	2 (9.5%)	13 (25.0%)	84 (30.2%)	8 (22.2%)	27 (28.1%)	181 (32.4%)
Presence of diffuse myeloma-related osteopenia, n (%)									
N	15	44	283	21	52	283	36	96	566
Yes	11 (73.3%)	21 (47.7%)	127 (44.9%)	11 (52.4%)	27 (51.9%)	134 (47.3%)	22 (61.1%)	48 (50.0%)	261 (46.1%)
No	4 (26.7%)	23 (52.3%)	156 (55.1%)	10 (47.6%)	25 (48.1%)	149 (52.7%)	14 (38.9%)	48 (50.0%)	305 (53.9%)
Number of extramedullary plasmacytomas, n (%)									
N	15	44	283	21	52	286	36	96	569
0	15 (100.0%)	43 (97.7%)	278 (98.2%)	21 (100.0%)	47 (90.4%)	277 (96.9%)	36 (100.0%)	90 (93.8%)	555 (97.5%)
≥1	0	1 (2.3%)	5 (1.8%)	0	5 (9.6%)	9 (3.1%)	0	6 (6.3%)	14 (2.5%)
Presence of evaluable bone marrow assessment									
N	15	44	283	21	52	286	36	96	569
Yes	15 (100.0%)	44 (100.0%)	281 (99.3%)	21 (100.0%)	52 (100.0%)	281 (98.3%)	36 (100.0%)	96 (100.0%)	562 (98.8%)
No	0	0	2 (0.7%)	0	0	5 (1.7%)	0	0	7 (1.2%)
% Plasma cells, bone marrow biopsy									
N	0	17	119	1	18	130	1	35	249
<10	0	1 (5.9%)	16 (13.4%)	0	4 (22.2%)	24 (18.5%)	0	5 (14.3%)	40 (16.1%)
10-30	0	7 (41.2%)	49 (41.2%)	1 (100.0%)	7 (38.9%)	58 (44.6%)	1 (100.0%)	14 (40.0%)	107 (43.0%)
>30	0	9 (52.9%)	54 (45.4%)	0	7 (38.9%)	48 (36.9%)	0	16 (45.7%)	102 (41.0%)
% Plasma cells, bone marrow aspirate									
N	15	43	259	20	51	253	35	94	512
<10	4 (26.7%)	9 (20.9%)	67 (25.9%)	9 (45.0%)	22 (43.1%)	77 (30.4%)	13 (37.1%)	31 (33.0%)	144 (28.1%)
10-30	8 (53.3%)	16 (37.2%)	115 (44.4%)	3 (15.0%)	13 (25.5%)	103 (40.7%)	11 (31.4%)	29 (30.9%)	218 (42.6%)
>30	3 (20.0%)	18 (41.9%)	77 (29.7%)	8 (40.0%)	16 (31.4%)	73 (28.9%)	11 (31.4%)	34 (36.2%)	150 (29.3%)

TSIDEM03_3003: Summary of Baseline Disease Characteristics; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
% Plasma cells, bone marrow biopsy/aspirate									
N	15	44	281	21	52	281	36	96	562
<10	4 (26.7%)	8 (18.2%)	58 (20.6%)	9 (42.9%)	17 (32.7%)	61 (21.7%)	13 (36.1%)	25 (26.0%)	119 (21.2%)
10-30	8 (53.3%)	16 (36.4%)	122 (43.4%)	4 (19.0%)	16 (30.8%)	119 (42.3%)	12 (33.3%)	32 (33.3%)	241 (42.9%)
>30	3 (20.0%)	20 (45.5%)	101 (35.9%)	8 (38.1%)	19 (36.5%)	101 (35.9%)	11 (30.6%)	39 (40.6%)	202 (35.9%)
Any cytogenetic abnormality[f]									
N	15	42	211	20	50	228	35	92	439
Standard risk	10 (66.7%)	35 (83.3%)	176 (83.4%)	17 (85.0%)	46 (92.0%)	193 (84.6%)	27 (77.1%)	81 (88.0%)	369 (84.1%)
High risk	5 (33.3%)	7 (16.7%)	35 (16.6%)	3 (15.0%)	4 (8.0%)	35 (15.4%)	8 (22.9%)	11 (12.0%)	70 (15.9%)
del(17p)	3 (20.0%)	3 (7.1%)	20 (9.5%)	3 (15.0%)	3 (6.0%)	25 (11.0%)	6 (17.1%)	6 (6.5%)	45 (10.3%)
t(4;14)	4 (26.7%)	6 (14.3%)	15 (7.1%)	0	1 (2.0%)	10 (4.4%)	4 (11.4%)	7 (7.6%)	25 (5.7%)
t(14;16)	1 (6.7%)	1 (2.4%)	6 (2.8%)	0	0	2 (0.9%)	1 (2.9%)	1 (1.1%)	8 (1.8%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Key: FLC = serum free light chain; ISS = International staging system.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
[c] Includes subjects without measurable disease in serum and urine.
[d] Includes IgD, IgM, IgE and bioclonal.
[e] ISS staging is derived based on the combination of serum β2-microglobulin and albumin.
[f] Cytogenetic abnormalities are based on FISH or karyotype testing. Percentages calculated with the number of subjects in each treatment group as denominator.

[TSIDEM03_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSIDEM03_3003.SAS] 30JUN2016, 22:35

表 2.7.4-付録-18 Demographics and Baseline Characteristics; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSIDEM01: Demographics and Baseline Characteristics; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Age (years)					
N	23	55	156	3	237
Category, n (%)					
18 - <65	13 (56.5%)	32 (58.2%)	86 (55.1%)	2 (66.7%)	133 (56.1%)
65 - <75	9 (39.1%)	20 (36.4%)	54 (34.6%)	1 (33.3%)	84 (35.4%)
>=75	1 (4.3%)	3 (5.5%)	16 (10.3%)	0	20 (8.4%)
Mean (SD)	62.0 (8.65)	61.2 (9.20)	62.9 (9.50)	59.0 (9.54)	62.4 (9.33)
Median	64.0	62.0	63.0	58.0	63.0
Range	(42; 76)	(38; 76)	(31; 84)	(50; 69)	(31; 84)
Sex, n (%)					
N	23	55	156	3	237
Male	14 (60.9%)	38 (69.1%)	84 (53.8%)	3 (100.0%)	139 (58.6%)
Female	9 (39.1%)	17 (30.9%)	72 (46.2%)	0	98 (41.4%)
Race, n (%)					
N	23	55	156	3	237
White	23 (100.0%)	35 (63.6%)	119 (76.3%)	3 (100.0%)	180 (75.9%)
Black or African American	0	1 (1.8%)	16 (10.3%)	0	17 (7.2%)
Asian	0	4 (7.3%)	9 (5.8%)	0	13 (5.5%)
American Indian or Alaska Native	0	0	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0	0	0
Other	0	0	2 (1.3%)	0	2 (0.8%)
Unknown	0	0	1 (0.6%)	0	1 (0.4%)
Not reported	0	15 (27.3%)	9 (5.8%)	0	24 (10.1%)
Height (cm)					
N	23	55	154	3	235
Mean (SD)	171.74 (6.503)	171.99 (11.957)	168.02 (10.407)	179.00 (4.359)	169.45 (10.606)
Median	172.00	173.00	168.00	177.00	170.00
Range	(153.0; 182.0)	(137.4; 198.0)	(139.0; 196.0)	(176.0; 184.0)	(137.4; 198.0)
Weight (kg)					
N	23	55	156	3	237
Mean (SD)	81.35 (13.547)	79.42 (19.689)	75.90 (19.473)	77.33 (12.055)	77.26 (18.975)
Median	80.00	79.40	75.50	76.00	77.10
Range	(60.0; 117.0)	(46.2; 160.2)	(38.4; 141.8)	(66.0; 90.0)	(38.4; 160.2)
Baseline ECOG score, n (%)					
N	23	55	156	3	237
0	8 (34.8%)	18 (32.7%)	46 (29.5%)	2 (66.7%)	74 (31.2%)
1	14 (60.9%)	34 (61.8%)	100 (64.1%)	1 (33.3%)	149 (62.9%)
2	1 (4.3%)	3 (5.5%)	10 (6.4%)	0	14 (5.9%)

TSIDEM01: Demographics and Baseline Characteristics; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Geographic region, n (%)					
N	23	55	156	3	237
European Union	23 (100.0%)	30 (54.5%)	40 (25.6%)	3 (100.0%)	96 (40.5%)
Japan	0	4 (7.3%)	5 (3.2%)	0	9 (3.8%)
North America	0	21 (38.2%)	111 (71.2%)	0	132 (55.7%)
Baseline renal impairment, n (%)					
N	23	55	156	3	237
Stage 1	9 (39.1%)	16 (29.1%)	44 (28.2%)	2 (66.7%)	71 (30.0%)
Stage 2	12 (52.2%)	23 (41.8%)	51 (32.7%)	0	86 (36.3%)
Stage 3	2 (8.7%)	14 (25.5%)	56 (35.9%)	1 (33.3%)	73 (30.8%)
Stage 4	0	2 (3.6%)	4 (2.6%)	0	6 (2.5%)
Stage 5	0	0	1 (0.6%)	0	1 (0.4%)
Baseline hepatic function, n (%)					
N	23	55	155	3	236
Normal	15 (65.2%)	45 (81.8%)	134 (86.5%)	3 (100.0%)	197 (83.5%)
Mild	8 (34.8%)	10 (18.2%)	21 (13.5%)	0	39 (16.5%)

Note: Renal impairment is classified into 5 stages by creatinine clearance: Stage 1: ≥90 ml/min; Stage 2: 60 – <90 ml/min; Stage 3: 30 – <60 ml/min; Stage 4: 15 – <30 ml/min; and Stage 5: < 15 ml/min.
Hepatic function is classified into 4 levels per NCI Organ Dysfunction criteria: Normal: total bilirubin ≤ ULN and AST ≤ ULN; Mildly Impaired: (total bilirubin ≤ ULN and AST > ULN) or (ULN < total bilirubin ≤ 1.5×ULN); Moderately Impaired: 1.5×ULN < total bilirubin ≤ 3×ULN; and Severely Impaired: total bilirubin > 3×ULN.

[TSIDEM01.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsidem01.sas] 16MAR2015, 12:12

表 2.7.4-付録-19 Summary of Demographics at Baseline; All Treated Analysis Population (Study 54767414MMY1002)

TSIDEM01: Summary of Demographics at Baseline; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Sex			
N	4	5	9
Male	2 (50.0%)	2 (40.0%)	4 (44.4%)
Female	2 (50.0%)	3 (60.0%)	5 (55.6%)
Race			
N	4	5	9
White	0	0	0
Black or African American	0	0	0
Asian	4 (100.0%)	5 (100.0%)	9 (100.0%)
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Not Reported	0	0	0
Unknown	0	0	0
Multiple	0	0	0
Other	0	0	0
Age (years)			
N	4	5	9
Mean (SD)	67.3 (3.95)	60.8 (9.18)	63.7 (7.71)
Median	66.0	61.0	65.0
Range	(64; 73)	(47; 72)	(47; 73)
< 65	1 (25.0%)	3 (60.0%)	4 (44.4%)
>= 65	3 (75.0%)	2 (40.0%)	5 (55.6%)
Screening Weight (kg)			
N	4	5	9
Mean (SD)	54.30 (4.681)	59.10 (9.974)	56.97 (8.023)
Median	54.65	59.60	58.20
Range	(48.4; 59.5)	(43.9; 71.6)	(43.9; 71.6)
Screening Height (cm)			
N	4	5	9
Mean (SD)	160.35 (2.575)	159.20 (8.635)	159.71 (6.335)
Median	160.15	162.70	162.20
Range	(157.5; 163.6)	(143.8; 164.0)	(143.8; 164.0)
Screening BSA (m^2)			
N	4	5	9
Mean (SD)	1.556 (0.0717)	1.604 (0.1724)	1.583 (0.1320)
Median	1.553	1.647	1.617
Range	(1.48; 1.64)	(1.31; 1.77)	(1.31; 1.77)

[TSIDEM01.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsidem01.sas] 18FEB2016, 15:23

表 2.7.4-付録-20 Summary of Disease Characteristics at Baseline; All Treated Analysis Population (Study 54767414MMY1002)

TSIDEM02: Summary of Disease Characteristics at Baseline; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
ECOG			
N	4	5	9
0	3 (75.0%)	4 (80.0%)	7 (77.8%)
1	1 (25.0%)	1 (20.0%)	2 (22.2%)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
Stage for MM			
N	4	5	9
I	2 (50.0%)	2 (40.0%)	4 (44.4%)
II	2 (50.0%)	2 (40.0%)	4 (44.4%)
III	0	1 (20.0%)	1 (11.1%)
Involved types of myeloma			
N	4	5	9
IgG	3 (75.0%)	2 (40.0%)	5 (55.6%)
IgA	0	1 (20.0%)	1 (11.1%)
IgM	0	0	0
IgD	0	0	0
IgE	0	0	0
Light Chain, Free (only)	1 (25.0%)	2 (40.0%)	3 (33.3%)
Kappa	1 (25.0%)	1 (20.0%)	2 (22.2%)
Lambda	0	1 (20.0%)	1 (11.1%)
Serum calcium (corrected; mg/dL)			
N	4	5	9
<11.5	4 (100.0%)	5 (100.0%)	9 (100.0%)
≥11.5	0	0	0
Serum creatinine (mg/dL)			
N	4	5	9
<2	4 (100.0%)	5 (100.0%)	9 (100.0%)
≥2	0	0	0
Hemoglobin (g/dL)			
N	4	5	9
<10	0	1 (20.0%)	1 (11.1%)
≥10	4 (100.0%)	4 (80.0%)	8 (88.9%)
Presence of Lytic Bone Lesions			
N	4	5	9
Present	4 (100.0%)	5 (100.0%)	9 (100.0%)
Not present	0	0	0
Presence of Osteopenia			
N	4	5	9
Present	0	5 (100.0%)	5 (55.6%)
Not present	4 (100.0%)	0	4 (44.4%)
Presence of Lytic Bone Lesions or Osteopenia			
N	4	5	9
Present	4 (100.0%)	5 (100.0%)	9 (100.0%)
Not present	0	0	0
Bone marrow cytogenetic			
N	4	5	9
t(4;14)(p16;q32)	2 (50.0%)	1 (20.0%)	3 (33.3%)
t(14;16)(q32;q23)	0	0	0
Del(17p13)	0	2 (40.0%)	2 (22.2%)
Normal	2 (50.0%)	2 (40.0%)	4 (44.4%)
Time since initial diagnosis (months)			
N	4	5	9
Mean (SD)	37.79 (36.511)	77.98 (35.077)	60.12 (39.545)
Median	27.84	69.91	62.85
Range	(7.5; 88.0)	(47.8; 138.5)	(7.5; 138.5)
Time since last progression or relapse (months)			
N	3	5	8

TSIDEM02: Summary of Disease Characteristics at Baseline; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Mean (SD)	0.78 (0.083)	2.06 (1.595)	1.58 (1.376)
Median	0.79	1.84	0.94
Range	(0.7; 0.9)	(0.2; 4.1)	(0.2; 4.1)
Screening IgG (g/L)			
N	4	5	9
Mean (SD)	32.490 (21.8117)	16.712 (21.2067)	23.724 (21.7353)
Median	36.845	3.790	23.380
Range	(3.51; 52.76)	(1.52; 51.17)	(1.52; 52.76)
Screening IgA (g/L)			
N	4	5	9
Mean (SD)	0.225 (0.2484)	3.882 (8.4459)	2.257 (6.2773)
Median	0.130	0.090	0.090
Range	(0.05; 0.59)	(0.05; 18.99)	(0.05; 18.99)

[TSIDEM02.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsidem02.sas] 07MAR2016, 10:34

表 2.7.4-付録-21 Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects who received concomitant medications	228 (96.2%)	237 (97.5%)	279 (99.3%)	313 (98.4%)	103 (100.0%)
Therapeutic class/pharmacologic class/preferred term					
Antibacterials for systemic use	171 (72.2%)	181 (74.5%)	229 (81.5%)	264 (83.0%)	76 (73.8%)
Beta-lactam antibacterials, penicillins	55 (23.2%)	70 (28.8%)	119 (42.3%)	159 (50.0%)	38 (36.9%)
Augmentin /00756801/	22 (9.3%)	23 (9.5%)	38 (13.5%)	58 (18.2%)	17 (16.5%)
Amoxicillin	10 (4.2%)	13 (5.3%)	50 (17.8%)	57 (17.9%)	10 (9.7%)
Pip/tazo	14 (5.9%)	16 (6.6%)	30 (10.7%)	46 (14.5%)	12 (11.7%)
Spektramox	6 (2.5%)	14 (5.8%)	15 (5.3%)	21 (6.6%)	0
Amoxi-clavulanico	5 (2.1%)	9 (3.7%)	8 (2.8%)	14 (4.4%)	4 (3.9%)
Phenoxymethylpenicillin	0	2 (0.8%)	14 (5.0%)	11 (3.5%)	4 (3.9%)
Flucloxacillin	0	0	3 (1.1%)	10 (3.1%)	0
Amoxicillin w/clavulanate potassium	1 (0.4%)	11 (4.5%)	2 (0.7%)	6 (1.9%)	2 (1.9%)
Benzylpenicillin	0	2 (0.8%)	4 (1.4%)	5 (1.6%)	1 (1.0%)
Sultamicillin	0	0	2 (0.7%)	5 (1.6%)	0
Piperacillin w/tazobactam /01606301/	1 (0.4%)	1 (0.4%)	2 (0.7%)	4 (1.3%)	1 (1.0%)
Amoxicilina + clavulanico	1 (0.4%)	1 (0.4%)	3 (1.1%)	3 (0.9%)	0
Piperacillin	2 (0.8%)	3 (1.2%)	1 (0.4%)	3 (0.9%)	1 (1.0%)
Unacid /00917901/	2 (0.8%)	0	0	3 (0.9%)	0
Cloxacillin	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
Ampicillin	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
Clavulanic acid	1 (0.4%)	2 (0.8%)	0	1 (0.3%)	0
Dicloxacillin	0	0	1 (0.4%)	1 (0.3%)	0
Mecillinam	0	0	0	1 (0.3%)	0
Pivampicillin	0	0	0	1 (0.3%)	0
Pivmecillinam	0	0	0	1 (0.3%)	0
Temocillin	0	0	0	1 (0.3%)	0
Augmentin sr	0	0	1 (0.4%)	0	0
Duocid /00892601/	0	0	1 (0.4%)	0	0
Mezlocillin	1 (0.4%)	0	0	0	0
Pheneticillin	0	1 (0.4%)	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Tazobactam	0	0	1 (0.4%)	0	0
Quinolone antibacterials	66 (27.8%)	84 (34.6%)	88 (31.3%)	133 (41.8%)	41 (39.8%)
Ciprofloxacin	27 (11.4%)	35 (14.4%)	29 (10.3%)	64 (20.1%)	18 (17.5%)
Levofloxacin	35 (14.8%)	42 (17.3%)	52 (18.5%)	54 (17.0%)	27 (26.2%)
Moxifloxacin	15 (6.3%)	13 (5.3%)	11 (3.9%)	24 (7.5%)	4 (3.9%)
Ofloxacin	2 (0.8%)	2 (0.8%)	5 (1.8%)	7 (2.2%)	0
Norfloxacin	1 (0.4%)	3 (1.2%)	3 (1.1%)	2 (0.6%)	0
Fluoroquinolones	0	0	0	1 (0.3%)	0
Garenoxacin	0	0	0	1 (0.3%)	0
Pefloxacin	0	0	0	1 (0.3%)	0
Tosufloxacin	0	0	0	1 (0.3%)	0
Gemifloxacin	1 (0.4%)	0	0	0	0
Pipemidic acid	0	0	1 (0.4%)	0	0
Other beta-lactam antibacterials	56 (23.6%)	57 (23.5%)	79 (28.1%)	102 (32.1%)	28 (27.2%)
Ceftriaxone	14 (5.9%)	18 (7.4%)	21 (7.5%)	33 (10.4%)	5 (4.9%)
Cefuroxime	13 (5.5%)	13 (5.3%)	18 (6.4%)	23 (7.2%)	2 (1.9%)
Meropenem	14 (5.9%)	8 (3.3%)	13 (4.6%)	20 (6.3%)	5 (4.9%)
Cefalexin	6 (2.5%)	7 (2.9%)	11 (3.9%)	10 (3.1%)	4 (3.9%)
Cefepime	8 (3.4%)	5 (2.1%)	4 (1.4%)	6 (1.9%)	9 (8.7%)
Cefpodoxime	1 (0.4%)	2 (0.8%)	0	6 (1.9%)	2 (1.9%)
Cefazolin	1 (0.4%)	6 (2.5%)	7 (2.5%)	5 (1.6%)	2 (1.9%)
Cefditoren	4 (1.7%)	2 (0.8%)	4 (1.4%)	4 (1.3%)	0
Cefixime	0	1 (0.4%)	2 (0.7%)	3 (0.9%)	0
Cefaclor	0	0	2 (0.7%)	2 (0.6%)	0
Cefadroxil	0	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
Cefcapene	0	0	1 (0.4%)	2 (0.6%)	0
Cefdinir	0	0	1 (0.4%)	2 (0.6%)	0
Cefotaxime	1 (0.4%)	3 (1.2%)	3 (1.1%)	2 (0.6%)	1 (1.0%)
Imipenem	0	1 (0.4%)	2 (0.7%)	2 (0.6%)	1 (1.0%)
Cefmetazole	0	0	1 (0.4%)	1 (0.3%)	0
Cefoperazone	0	2 (0.8%)	0	1 (0.3%)	0
Cefotiam	0	0	0	1 (0.3%)	0
Cefozopran	0	0	1 (0.4%)	1 (0.3%)	0
Ceftaroline fosamil	0	0	0	1 (0.3%)	0
Ceftazidime	4 (1.7%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	0
Ceftibuten	1 (0.4%)	0	2 (0.7%)	1 (0.3%)	0
Doripenem	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Ertapenem	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Flomoxef	0	0	2 (0.7%)	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Aztreonam	1 (0.4%)	0	1 (0.4%)	0	1 (1.0%)
Cefalotin	0	0	1 (0.4%)	0	0
Cefradine	0	0	1 (0.4%)	0	0
Ceftizoxime	0	1 (0.4%)	0	0	0
Cephalosporin nos	0	0	0	0	1 (1.0%)
Primaxin	1 (0.4%)	3 (1.2%)	3 (1.1%)	0	0
Sulfonamides and trimethoprim	74 (31.2%)	88 (36.2%)	99 (35.2%)	102 (32.1%)	25 (24.3%)
Bactrim	72 (30.4%)	86 (35.4%)	92 (32.7%)	88 (27.7%)	24 (23.3%)
Co-trimoxazole	1 (0.4%)	2 (0.8%)	8 (2.8%)	14 (4.4%)	0
Sulfamethoxazole	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Trimethoprim	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Macrolides, lincosamides and streptogramins	38 (16.0%)	52 (21.4%)	54 (19.2%)	89 (28.0%)	31 (30.1%)
Azithromycin	16 (6.8%)	29 (11.9%)	29 (10.3%)	54 (17.0%)	25 (24.3%)
Clarithromycin	20 (8.4%)	18 (7.4%)	15 (5.3%)	21 (6.6%)	2 (1.9%)
Roxithromycin	1 (0.4%)	3 (1.2%)	7 (2.5%)	12 (3.8%)	1 (1.0%)
Clindamycin	6 (2.5%)	3 (1.2%)	2 (0.7%)	8 (2.5%)	5 (4.9%)
Pristinamycin	0	0	3 (1.1%)	4 (1.3%)	1 (1.0%)
Erythromycin	0	1 (0.4%)	1 (0.4%)	3 (0.9%)	0
Josamycin	0	0	0	1 (0.3%)	0
Spiramycin	0	0	3 (1.1%)	1 (0.3%)	2 (1.9%)
Tetracyclines	4 (1.7%)	9 (3.7%)	21 (7.5%)	23 (7.2%)	2 (1.9%)
Doxycycline	2 (0.8%)	8 (3.3%)	20 (7.1%)	21 (6.6%)	2 (1.9%)
Minocycline	1 (0.4%)	0	0	1 (0.3%)	0
Oxytetracycline	0	0	0	1 (0.3%)	0
Tetracycline	0	0	2 (0.7%)	1 (0.3%)	0
Chinoxalindimethanol dioxide	0	1 (0.4%)	0	0	0
Tigecycline	1 (0.4%)	0	0	0	0
Other antibacterials	9 (3.8%)	13 (5.3%)	15 (5.3%)	14 (4.4%)	19 (18.4%)
Vancomycin	7 (3.0%)	7 (2.9%)	6 (2.1%)	5 (1.6%)	18 (17.5%)
Nitrofurantoin	1 (0.4%)	0	4 (1.4%)	3 (0.9%)	0
Teicoplanin	2 (0.8%)	2 (0.8%)	3 (1.1%)	3 (0.9%)	0
Daptomycin	0	0	0	2 (0.6%)	0
Linezolid	2 (0.8%)	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
Fosfomycin	0	3 (1.2%)	2 (0.7%)	1 (0.3%)	1 (1.0%)
Methenamine	0	0	0	1 (0.3%)	0
Akritoin	0	1 (0.4%)	0	0	0
Colistin	1 (0.4%)	0	0	0	0
Nitroxoline	0	1 (0.4%)	0	0	0
Polymyxin b	1 (0.4%)	0	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Aminoglycoside antibacterials	8 (3.4%)	6 (2.5%)	14 (5.0%)	12 (3.8%)	5 (4.9%)
Amikacin	2 (0.8%)	0	5 (1.8%)	8 (2.5%)	0
Gentamicin	2 (0.8%)	4 (1.6%)	6 (2.1%)	3 (0.9%)	2 (1.9%)
Tobramycin	4 (1.7%)	1 (0.4%)	2 (0.7%)	2 (0.6%)	4 (3.9%)
Isepamicin	0	1 (0.4%)	1 (0.4%)	0	0
Combinations of antibacterials	0	2 (0.8%)	4 (1.4%)	5 (1.6%)	0
Sulperazon	0	1 (0.4%)	1 (0.4%)	3 (0.9%)	0
Cefoperazone w/sulbactam	0	1 (0.4%)	3 (1.1%)	2 (0.6%)	0
Amphenicols	3 (1.3%)	4 (1.6%)	6 (2.1%)	3 (0.9%)	0
Chloramphenicol	3 (1.3%)	4 (1.6%)	5 (1.8%)	3 (0.9%)	0
Thiamphenicol	0	0	1 (0.4%)	0	0
Uncoded	1 (0.4%)	1 (0.4%)	0	3 (0.9%)	1 (1.0%)
Antibiotics	1 (0.4%)	1 (0.4%)	0	3 (0.9%)	0
D-mannose	0	0	0	0	1 (1.0%)
Analgesics	95 (40.1%)	133 (54.7%)	226 (80.4%)	257 (80.8%)	82 (79.6%)
Other analgesics and antipyretics	72 (30.4%)	102 (42.0%)	215 (76.5%)	244 (76.7%)	66 (64.1%)
Acetylsalicylic acid	8 (3.4%)	12 (4.9%)	160 (56.9%)	187 (58.8%)	40 (38.8%)
Paracetamol	43 (18.1%)	61 (25.1%)	99 (35.2%)	115 (36.2%)	39 (37.9%)
Metamizole	18 (7.6%)	23 (9.5%)	12 (4.3%)	14 (4.4%)	0
Pregabalin	20 (8.4%)	30 (12.3%)	17 (6.0%)	14 (4.4%)	5 (4.9%)
Carbasalate	1 (0.4%)	0	1 (0.4%)	5 (1.6%)	0
Lenoltec with codeine no 1	0	0	0	3 (0.9%)	2 (1.9%)
Pa	0	0	1 (0.4%)	3 (0.9%)	0
Medinite	0	0	1 (0.4%)	2 (0.6%)	0
Nefopam	0	0	4 (1.4%)	2 (0.6%)	3 (2.9%)
Propacetamol	0	0	1 (0.4%)	2 (0.6%)	0
Solpadeine /00154101/	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Dolo mobilat /00544301/	0	1 (0.4%)	0	1 (0.3%)	0
Dozol	0	1 (0.4%)	0	1 (0.3%)	0
Flupirtine	0	0	0	1 (0.3%)	0
Magnyl /02350501/	0	1 (0.4%)	0	1 (0.3%)	0
New lulu a	0	0	0	1 (0.3%)	0
Tylenol sinus medication	0	0	2 (0.7%)	1 (0.3%)	0
Aminophenazone	0	1 (0.4%)	0	0	0
Anilides	0	0	1 (0.4%)	0	0
Benylin 4 flu /01328001/	0	0	1 (0.4%)	0	0
Coricidin /01142901/	0	0	0	0	1 (1.0%)
Cotylenol	0	0	1 (0.4%)	0	0
Fervex /00959901/	0	1 (0.4%)	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Neo citran /00438101/	1 (0.4%)	0	0	0	0
Salicylic acid	0	0	1 (0.4%)	0	0
Topiramate	0	0	1 (0.4%)	0	0
Vicks formula 44m /01056501/	0	0	1 (0.4%)	0	0
Vicks nyquil cold and flu multi-symptom	0	0	1 (0.4%)	0	0
Opioids	55 (23.2%)	82 (33.7%)	96 (34.2%)	90 (28.3%)	50 (48.5%)
Tramadol	18 (7.6%)	29 (11.9%)	24 (8.5%)	29 (9.1%)	8 (7.8%)
Morphine	16 (6.8%)	25 (10.3%)	31 (11.0%)	27 (8.5%)	12 (11.7%)
Oxycodone	15 (6.3%)	15 (6.2%)	27 (9.6%)	27 (8.5%)	23 (22.3%)
Fentanyl	17 (7.2%)	16 (6.6%)	21 (7.5%)	20 (6.3%)	11 (10.7%)
Panadeine co	4 (1.7%)	5 (2.1%)	14 (5.0%)	9 (2.8%)	2 (1.9%)
Ultracet	3 (1.3%)	8 (3.3%)	18 (6.4%)	9 (2.8%)	1 (1.0%)
Hydromorphone	1 (0.4%)	3 (1.2%)	5 (1.8%)	8 (2.5%)	10 (9.7%)
Oxycocet	2 (0.8%)	3 (1.2%)	4 (1.4%)	6 (1.9%)	2 (1.9%)
Pethidine	1 (0.4%)	2 (0.8%)	4 (1.4%)	5 (1.6%)	6 (5.8%)
Targin	6 (2.5%)	4 (1.6%)	6 (2.1%)	5 (1.6%)	0
Lamaline /01708901/	0	0	0	3 (0.9%)	1 (1.0%)
Buprenorphine	0	0	0	1 (0.3%)	0
Myprodol	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Procet /01554201/	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
Vicodin	0	2 (0.8%)	2 (0.7%)	1 (0.3%)	0
Codenong	1 (0.4%)	1 (0.4%)	0	0	0
Dihydrocodeine	0	1 (0.4%)	2 (0.7%)	0	0
Ketobemidone	0	0	1 (0.4%)	0	0
Nalbuphine	0	0	1 (0.4%)	0	0
Naloxone w/oxycodone	0	2 (0.8%)	0	0	0
Oxymorphone	0	0	0	0	1 (1.0%)
Paracetamol w/tramadol	0	1 (0.4%)	0	0	0
Pentazocine	0	0	1 (0.4%)	0	0
Piritramide	0	2 (0.8%)	1 (0.4%)	0	0
Tapentadol	1 (0.4%)	0	0	0	0
Trimeperidine	0	1 (0.4%)	0	0	0
Tylox /00446701/	0	0	0	0	3 (2.9%)
Valoron n /00628301/	0	3 (1.2%)	0	0	0
Antimigraine preparations	0	0	0	0	1 (1.0%)
Zolmitriptan	0	0	0	0	1 (1.0%)
Uncoded	0	0	0	0	1 (1.0%)
Analgesics	0	0	0	0	1 (1.0%)
Drugs for acid related disorders	110 (46.4%)	128 (52.7%)	133 (47.3%)	165 (51.9%)	47 (45.6%)

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Drugs for peptic ulcer and gastro-oesophageal reflux disease (gord)	104 (43.9%)	124 (51.0%)	117 (41.6%)	144 (45.3%)	42 (40.8%)
Omeprazole	46 (19.4%)	57 (23.5%)	62 (22.1%)	49 (15.4%)	8 (7.8%)
Pantoprazole	30 (12.7%)	42 (17.3%)	14 (5.0%)	27 (8.5%)	10 (9.7%)
Esomeprazole	7 (3.0%)	4 (1.6%)	16 (5.7%)	23 (7.2%)	8 (7.8%)
Famotidine	11 (4.6%)	11 (4.5%)	8 (2.8%)	18 (5.7%)	17 (16.5%)
Ranitidine	5 (2.1%)	16 (6.6%)	14 (5.0%)	18 (5.7%)	5 (4.9%)
Lansoprazole	12 (5.1%)	10 (4.1%)	8 (2.8%)	13 (4.1%)	0
Rabeprazole	2 (0.8%)	0	0	6 (1.9%)	0
Sucralfate	1 (0.4%)	2 (0.8%)	1 (0.4%)	5 (1.6%)	2 (1.9%)
Proton pump inhibitors	0	0	0	2 (0.6%)	0
Rebamipide	2 (0.8%)	0	1 (0.4%)	2 (0.6%)	0
Lafutidine	0	0	0	1 (0.3%)	0
Nizatidine	0	0	0	1 (0.3%)	0
Polaprezinc	0	0	0	1 (0.3%)	0
Albis	0	1 (0.4%)	0	0	0
Alginic acid	0	1 (0.4%)	0	0	0
Gualenic acid	0	0	2 (0.7%)	0	0
Irsogladine	0	0	1 (0.4%)	0	0
Other drugs for peptic ulcer and gastro-oesop	0	0	1 (0.4%)	0	0
Sulpiride	1 (0.4%)	0	1 (0.4%)	0	0
Teprenone	1 (0.4%)	2 (0.8%)	2 (0.7%)	0	0
Antacids	16 (6.8%)	15 (6.2%)	35 (12.5%)	54 (17.0%)	12 (11.7%)
Magnesium oxide	1 (0.4%)	1 (0.4%)	17 (6.0%)	20 (6.3%)	4 (3.9%)
Magnesium carbonate	0	1 (0.4%)	1 (0.4%)	10 (3.1%)	2 (1.9%)
Calcium carbonate	8 (3.4%)	4 (1.6%)	10 (3.6%)	8 (2.5%)	6 (5.8%)
Magnesium hydroxide	2 (0.8%)	3 (1.2%)	4 (1.4%)	8 (2.5%)	1 (1.0%)
Aludrox /00082501/	0	1 (0.4%)	1 (0.4%)	4 (1.3%)	0
Almagate	0	1 (0.4%)	4 (1.4%)	2 (0.6%)	0
Diovol /00018101/	0	0	0	2 (0.6%)	0
Gaviscon /01405501/	0	1 (0.4%)	0	2 (0.6%)	1 (1.0%)
Magaldrate	0	0	0	1 (0.3%)	0
Magnesia komp n	1 (0.4%)	0	0	1 (0.3%)	0
Simeco /00416501/	0	0	0	1 (0.3%)	1 (1.0%)
Topal	0	0	1 (0.4%)	1 (0.3%)	0
Algeldrate	0	1 (0.4%)	0	0	0
Aluminium hydroxide	1 (0.4%)	1 (0.4%)	0	0	0
Aluminium phosphate	1 (0.4%)	0	0	0	0
Antacids with antiflatulents	0	0	1 (0.4%)	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Antacids, other combinations	1 (0.4%)	0	0	0	0
Calcium glycerophosphate	0	1 (0.4%)	0	0	0
Hydrotalcite	0	1 (0.4%)	1 (0.4%)	0	0
Mucaine /00115701/	2 (0.8%)	1 (0.4%)	0	0	0
Novaluzid	1 (0.4%)	1 (0.4%)	0	0	0
Rani-q /01722401/	0	0	1 (0.4%)	0	0
Topaal /00894301/	0	0	1 (0.4%)	0	0
Antivirals for systemic use	151 (63.7%)	154 (63.4%)	116 (41.3%)	158 (49.7%)	28 (27.2%)
Direct acting antivirals	151 (63.7%)	154 (63.4%)	116 (41.3%)	158 (49.7%)	28 (27.2%)
Aciclovir	102 (43.0%)	102 (42.0%)	67 (23.8%)	90 (28.3%)	9 (8.7%)
Valaciclovir	45 (19.0%)	51 (21.0%)	41 (14.6%)	47 (14.8%)	15 (14.6%)
Oseltamivir	12 (5.1%)	5 (2.1%)	16 (5.7%)	29 (9.1%)	3 (2.9%)
Zanamivir	0	0	2 (0.7%)	4 (1.3%)	0
Famciclovir	6 (2.5%)	4 (1.6%)	2 (0.7%)	3 (0.9%)	1 (1.0%)
Lamivudine	0	1 (0.4%)	0	2 (0.6%)	0
Ganciclovir	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
Imidazolyl ethanamide pentandioic acid	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Peramivir	0	0	0	1 (0.3%)	0
Valganciclovir	0	1 (0.4%)	0	1 (0.3%)	0
Entecavir	0	0	0	0	1 (1.0%)
Ribavirin	0	1 (0.4%)	0	0	0
Umifenovir	0	2 (0.8%)	0	0	0
Immunostimulants	13 (5.5%)	19 (7.8%)	80 (28.5%)	155 (48.7%)	59 (57.3%)
Immunostimulants	13 (5.5%)	19 (7.8%)	80 (28.5%)	155 (48.7%)	59 (57.3%)
Filgrastim	11 (4.6%)	18 (7.4%)	66 (23.5%)	116 (36.5%)	50 (48.5%)
Granulocyte colony stimulating factor	1 (0.4%)	1 (0.4%)	6 (2.1%)	19 (6.0%)	1 (1.0%)
Lenograstim	0	0	8 (2.8%)	18 (5.7%)	5 (4.9%)
Pegfilgrastim	0	0	2 (0.7%)	12 (3.8%)	13 (12.6%)
Lipegfilgrastim	0	0	2 (0.7%)	1 (0.3%)	0
Tilorone	0	0	0	1 (0.3%)	0
Interferon alfa-2b	0	1 (0.4%)	0	0	0
Interferon gamma	1 (0.4%)	0	0	0	0
Antihistamines for systemic use	21 (8.9%)	73 (30.0%)	63 (22.4%)	135 (42.5%)	45 (43.7%)
Antihistamines for systemic use	21 (8.9%)	73 (30.0%)	63 (22.4%)	135 (42.5%)	45 (43.7%)
Diphenhydramine	6 (2.5%)	19 (7.8%)	14 (5.0%)	32 (10.1%)	33 (32.0%)
Chlorphenamine	3 (1.3%)	7 (2.9%)	9 (3.2%)	22 (6.9%)	0
Clemastine	2 (0.8%)	13 (5.3%)	0	20 (6.3%)	0
Fexofenadine	0	2 (0.8%)	9 (3.2%)	18 (5.7%)	0
Dexchlorpheniramine	3 (1.3%)	2 (0.8%)	3 (1.1%)	14 (4.4%)	2 (1.9%)

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Cetirizine	1 (0.4%)	6 (2.5%)	10 (3.6%)	10 (3.1%)	2 (1.9%)
Loratadine	3 (1.3%)	5 (2.1%)	1 (0.4%)	9 (2.8%)	4 (3.9%)
Promethazine	1 (0.4%)	6 (2.5%)	0	7 (2.2%)	3 (2.9%)
Desloratadine	0	0	2 (0.7%)	6 (1.9%)	0
Levocetirizine	0	0	7 (2.5%)	6 (1.9%)	4 (3.9%)
Cyclizine	0	1 (0.4%)	4 (1.4%)	4 (1.3%)	0
Dimetindene	0	6 (2.5%)	3 (1.1%)	4 (1.3%)	0
Piprinhydrinate	0	2 (0.8%)	0	3 (0.9%)	0
Dimenhydrinate	1 (0.4%)	0	3 (1.1%)	2 (0.6%)	0
Ebastine	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Olopatadine	1 (0.4%)	0	0	2 (0.6%)	0
Oxomemazine	0	0	0	2 (0.6%)	0
Bepotastine	0	0	1 (0.4%)	1 (0.3%)	0
Cyproheptadine	0	0	1 (0.4%)	1 (0.3%)	0
Pheniramine	0	3 (1.2%)	0	1 (0.3%)	0
Acrivastine	0	1 (0.4%)	0	0	0
Alimemazine	0	0	1 (0.4%)	0	0
Astemizole	0	1 (0.4%)	1 (0.4%)	0	0
Azelastine	0	0	0	0	1 (1.0%)
Bisulepin	0	4 (1.6%)	0	0	0
Chloropyramine	0	2 (0.8%)	0	0	0
Difenidol	0	0	1 (0.4%)	0	0
Doxylamine	1 (0.4%)	0	0	0	0
Mequitazine	0	0	2 (0.7%)	0	0
Vertigo-vomex n	0	1 (0.4%)	0	0	0
Antithrombotic agents	35 (14.8%)	52 (21.4%)	98 (34.9%)	117 (36.8%)	27 (26.2%)
Antithrombotic agents	35 (14.8%)	52 (21.4%)	98 (34.9%)	117 (36.8%)	27 (26.2%)
Enoxaparin	21 (8.9%)	30 (12.3%)	49 (17.4%)	50 (15.7%)	15 (14.6%)
Dalteparin	3 (1.3%)	4 (1.6%)	15 (5.3%)	24 (7.5%)	0
Tinzaparin	1 (0.4%)	1 (0.4%)	16 (5.7%)	18 (5.7%)	4 (3.9%)
Heparin	5 (2.1%)	4 (1.6%)	10 (3.6%)	11 (3.5%)	4 (3.9%)
Nadroparin	4 (1.7%)	12 (4.9%)	3 (1.1%)	8 (2.5%)	0
Warfarin	0	3 (1.2%)	8 (2.8%)	7 (2.2%)	5 (4.9%)
Heparinoid	1 (0.4%)	0	2 (0.7%)	5 (1.6%)	0
Clopidogrel	0	2 (0.8%)	2 (0.7%)	4 (1.3%)	0
Fondaparinux	0	2 (0.8%)	3 (1.1%)	4 (1.3%)	1 (1.0%)
Rivaroxaban	3 (1.3%)	3 (1.2%)	6 (2.1%)	4 (1.3%)	4 (3.9%)
Bemiparin	0	0	3 (1.1%)	3 (0.9%)	0
Apixaban	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	1 (1.0%)

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Dipyridamole	0	0	0	1 (0.3%)	0
Edoxaban	0	0	0	1 (0.3%)	0
Fluindione	0	0	3 (1.1%)	1 (0.3%)	1 (1.0%)
Phenprocoumon	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
Prasugrel	0	0	0	1 (0.3%)	0
Tirofiban	0	0	0	1 (0.3%)	0
Acenocoumarol	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0
Alteplase	0	0	0	0	3 (2.9%)
Parnaparin	1 (0.4%)	0	0	0	0
Ticagrelor	0	0	1 (0.4%)	0	0
Mineral supplements	40 (16.9%)	60 (24.7%)	71 (25.3%)	95 (29.9%)	38 (36.9%)
Potassium	27 (11.4%)	37 (15.2%)	39 (13.9%)	53 (16.7%)	22 (21.4%)
Potassium	23 (9.7%)	35 (14.4%)	39 (13.9%)	50 (15.7%)	22 (21.4%)
Neutra-phos-k /00599901/	0	0	1 (0.4%)	3 (0.9%)	0
Kalinor-acid	0	0	0	1 (0.3%)	0
Ascorbic acid w/potassium bicarbonate	1 (0.4%)	0	0	0	0
Kalinor-brausetabletten	0	1 (0.4%)	0	0	0
Potassium aspartate	0	1 (0.4%)	0	0	0
Potassium citrate	1 (0.4%)	0	1 (0.4%)	0	0
Potassium phosphate dibasic	0	1 (0.4%)	0	0	0
Potassium phosphate monobasic	3 (1.3%)	0	1 (0.4%)	0	1 (1.0%)
Potassium-sandoz	0	0	1 (0.4%)	0	0
Swiss-kal eff	1 (0.4%)	1 (0.4%)	0	0	0
Calcium	18 (7.6%)	20 (8.2%)	22 (7.8%)	31 (9.7%)	5 (4.9%)
Lekovit ca	6 (2.5%)	5 (2.1%)	8 (2.8%)	17 (5.3%)	0
Calcium gluconate	9 (3.8%)	5 (2.1%)	3 (1.1%)	6 (1.9%)	1 (1.0%)
Calcium	1 (0.4%)	6 (2.5%)	8 (2.8%)	4 (1.3%)	2 (1.9%)
Calcium sandoz /02293601/	0	0	0	3 (0.9%)	0
Calcium sandoz forte d	0	0	0	2 (0.6%)	0
Calcet /00637401/	0	0	0	1 (0.3%)	0
Calcium citrate w/colecalciferol	0	1 (0.4%)	0	1 (0.3%)	0
Homeopatics nos	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	0
Calcifort /01767901/	0	0	1 (0.4%)	0	0
Calcite d	0	1 (0.4%)	0	0	0
Calcium carbonate w/vitamin d nos	0	0	0	0	1 (1.0%)
Calcium chloride	1 (0.4%)	0	0	0	0
Calcium d3 /01483701/	1 (0.4%)	4 (1.6%)	0	0	0
Calcium phosphate	0	1 (0.4%)	0	0	0
Calcium picken	0	1 (0.4%)	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Calcium w/magnesium	0	0	0	0	1 (1.0%)
Calcium w/vitamin d nos	0	2 (0.8%)	2 (0.7%)	0	0
Other mineral supplements	12 (5.1%)	20 (8.2%)	30 (10.7%)	30 (9.4%)	20 (19.4%)
Magnesium	3 (1.3%)	14 (5.8%)	20 (7.1%)	15 (4.7%)	5 (4.9%)
Magnesium sulfate	7 (3.0%)	2 (0.8%)	11 (3.9%)	8 (2.5%)	9 (8.7%)
Magnesium citrate	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	2 (1.9%)
Copper	0	0	0	1 (0.3%)	1 (1.0%)
Dynamag	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
K-phos neutral	0	0	0	1 (0.3%)	0
Magnesium chelate	0	0	0	1 (0.3%)	0
Other mineral products	0	0	0	1 (0.3%)	0
Magnesium chloride	0	0	0	0	1 (1.0%)
Magnesium verla /00648601/	1 (0.4%)	0	0	0	0
Magnosolv	1 (0.4%)	1 (0.4%)	0	0	0
Phos-nak	0	1 (0.4%)	0	0	1 (1.0%)
Phosphate-sandoz	0	0	1 (0.4%)	0	0
Phosphoneurol	0	0	0	0	1 (1.0%)
Sodium fluoride	0	1 (0.4%)	0	0	0
Zinc	0	0	0	0	1 (1.0%)
Uncoded	0	0	1 (0.4%)	1 (0.3%)	0
Fosetamine	0	0	0	1 (0.3%)	0
Mineral supplements	0	0	1 (0.4%)	0	0
Blood substitutes and perfusion solutions	37 (15.6%)	52 (21.4%)	54 (19.2%)	85 (26.7%)	26 (25.2%)
Irrigating solutions	30 (12.7%)	40 (16.5%)	45 (16.0%)	58 (18.2%)	22 (21.4%)
Sodium chloride	24 (10.1%)	35 (14.4%)	37 (13.2%)	52 (16.4%)	18 (17.5%)
Sodium bicarbonate	7 (3.0%)	7 (2.9%)	10 (3.6%)	9 (2.8%)	4 (3.9%)
Colyte /00751601/	0	0	2 (0.7%)	1 (0.3%)	0
Sodium citrate	0	0	0	1 (0.3%)	0
Ringer /01179901/	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
Salt solutions	1 (0.4%)	0	0	0	0
I.v. solutions	4 (1.7%)	12 (4.9%)	15 (5.3%)	18 (5.7%)	3 (2.9%)
Lactec /00490001/	0	0	0	3 (0.9%)	0
Smoflipid	0	2 (0.8%)	2 (0.7%)	3 (0.9%)	0
Amino acids nos w/electrolytes nos/glucose	0	0	0	2 (0.6%)	0
Electrolytes nos	0	2 (0.8%)	0	2 (0.6%)	0
Ringer-lactate	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Amino acids nos w/electrolytes nos//07977301/	0	0	0	1 (0.3%)	0
El-4	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
Electrolytes nos w/glucose	1 (0.4%)	0	2 (0.7%)	1 (0.3%)	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Freamine	1 (0.4%)	0	0	1 (0.3%)	0
I.v. solutions	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
Jonosteril /00351401/	1 (0.4%)	0	0	1 (0.3%)	0
Mannitol	0	1 (0.4%)	0	1 (0.3%)	0
Olimel n5e	0	0	0	1 (0.3%)	0
Osmotan	0	0	0	1 (0.3%)	0
Smofkabiven perifer	0	0	0	1 (0.3%)	0
Solita-t1	0	0	0	1 (0.3%)	0
Solutions affecting the electrolyte balance	0	0	1 (0.4%)	1 (0.3%)	0
Amino acids nos w/carbohydrates nos/07403401/	1 (0.4%)	0	0	0	0
Aminofluid	0	0	1 (0.4%)	0	0
Dextrose and sodium chloride injection	0	0	3 (1.1%)	0	0
Dextrose w/potassium chloride	0	0	2 (0.7%)	0	0
Flebobag ring lact	0	0	3 (1.1%)	0	0
Glucose 1-phosphate disodium	0	0	0	0	1 (1.0%)
Medium-chain triglycerides	0	1 (0.4%)	0	0	0
Phosphate /01684601/	0	0	1 (0.4%)	0	0
Plasma lyte 148	0	0	0	0	1 (1.0%)
Sodium lactate	0	0	1 (0.4%)	0	0
Solutions for parenteral nutrition	0	0	3 (1.1%)	0	0
Solutions producing osmotic diuresis	0	0	1 (0.4%)	0	0
Sterofundin iso	1 (0.4%)	3 (1.2%)	0	0	0
I.v. solution additives	6 (2.5%)	10 (4.1%)	6 (2.1%)	11 (3.5%)	3 (2.9%)
Sodium phosphate	0	1 (0.4%)	5 (1.8%)	6 (1.9%)	3 (2.9%)
Electrolyte solutions /90010101/	0	0	0	2 (0.6%)	0
Phosphoric acid	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	0
Lysine	0	0	0	1 (0.3%)	0
Compound sodium chloride /06440701/	0	1 (0.4%)	0	0	0
Electrosol	0	1 (0.4%)	0	0	0
Reosorbilact	2 (0.8%)	4 (1.6%)	0	0	0
Ringer aguettant	3 (1.3%)	3 (1.2%)	0	0	0
Blood and related products	5 (2.1%)	3 (1.2%)	5 (1.8%)	6 (1.9%)	0
Blood, whole	0	0	0	3 (0.9%)	0
Albumin human	4 (1.7%)	2 (0.8%)	3 (1.1%)	1 (0.3%)	0
Dextran sulfate	0	0	0	1 (0.3%)	0
Infukoll hes	0	0	0	1 (0.3%)	0
Plasma	0	0	0	1 (0.3%)	0
Red blood cells	0	0	0	1 (0.3%)	0
Gelatin	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Hetastarch	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
Uncoded	0	0	0	4 (1.3%)	0
Carbohydrates nos w/potassium chloride/sodium	0	0	0	3 (0.9%)	0
Solacet f	0	0	0	1 (0.3%)	0
Hemodialytics and hemofiltrates	0	0	0	2 (0.6%)	0
Ringer-acetat	0	0	0	2 (0.6%)	0
Psycholeptics	37 (15.6%)	45 (18.5%)	73 (26.0%)	84 (26.4%)	30 (29.1%)
Hypnotics and sedatives	22 (9.3%)	27 (11.1%)	40 (14.2%)	44 (13.8%)	15 (14.6%)
Zopiclone	4 (1.7%)	4 (1.6%)	11 (3.9%)	12 (3.8%)	3 (2.9%)
Zolpidem	7 (3.0%)	8 (3.3%)	13 (4.6%)	10 (3.1%)	4 (3.9%)
Midazolam	3 (1.3%)	7 (2.9%)	9 (3.2%)	9 (2.8%)	4 (3.9%)
Brotizolam	0	0	3 (1.1%)	5 (1.6%)	0
Temazepam	7 (3.0%)	9 (3.7%)	4 (1.4%)	5 (1.6%)	3 (2.9%)
Estazolam	1 (0.4%)	0	2 (0.7%)	3 (0.9%)	0
Melatonin	3 (1.3%)	0	0	2 (0.6%)	1 (1.0%)
Alteril	0	0	0	1 (0.3%)	0
Flunitrazepam	0	0	1 (0.4%)	1 (0.3%)	0
Lormetazepam	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
Nitrazepam	0	0	0	1 (0.3%)	0
Rilmazafone	0	0	0	1 (0.3%)	0
Eszopiclone	0	0	1 (0.4%)	0	0
Propiomazine	1 (0.4%)	0	0	0	0
Triazolam	0	0	1 (0.4%)	0	0
Anxiolytics	14 (5.9%)	18 (7.4%)	39 (13.9%)	43 (13.5%)	16 (15.5%)
Lorazepam	5 (2.1%)	7 (2.9%)	11 (3.9%)	19 (6.0%)	9 (8.7%)
Alprazolam	1 (0.4%)	2 (0.8%)	10 (3.6%)	7 (2.2%)	3 (2.9%)
Diazepam	2 (0.8%)	4 (1.6%)	5 (1.8%)	7 (2.2%)	3 (2.9%)
Hydroxyzine	1 (0.4%)	3 (1.2%)	7 (2.5%)	7 (2.2%)	2 (1.9%)
Oxazepam	0	0	2 (0.7%)	6 (1.9%)	0
Clotiazepam	0	0	0	2 (0.6%)	0
Bromazepam	5 (2.1%)	1 (0.4%)	3 (1.1%)	1 (0.3%)	0
Buspirone	0	0	1 (0.4%)	1 (0.3%)	0
Phenazepam	0	0	1 (0.4%)	0	0
Tofisopam	0	1 (0.4%)	0	0	0
Antipsychotics	11 (4.6%)	9 (3.7%)	12 (4.3%)	14 (4.4%)	8 (7.8%)
Prochlorperazine	3 (1.3%)	4 (1.6%)	4 (1.4%)	6 (1.9%)	7 (6.8%)
Haloperidol	3 (1.3%)	4 (1.6%)	4 (1.4%)	3 (0.9%)	1 (1.0%)
Quetiapine	2 (0.8%)	1 (0.4%)	3 (1.1%)	2 (0.6%)	1 (1.0%)
Amisulpride	0	0	0	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Chlorpromazine	2 (0.8%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	1 (1.0%)
Levomepromazine	1 (0.4%)	0	2 (0.7%)	1 (0.3%)	0
Paliperidone	0	0	0	1 (0.3%)	0
Risperidone	2 (0.8%)	0	0	1 (0.3%)	0
Droperidol	0	1 (0.4%)	0	0	0
Olanzapine	0	2 (0.8%)	1 (0.4%)	0	0
Pipamperone	1 (0.4%)	0	0	0	0
Cough and cold preparations	37 (15.6%)	49 (20.2%)	76 (27.0%)	79 (24.8%)	21 (20.4%)
Expectorants, excl. combinations with cough suppressants	32 (13.5%)	46 (18.9%)	55 (19.6%)	61 (19.2%)	9 (8.7%)
Acetylcysteine	19 (8.0%)	24 (9.9%)	22 (7.8%)	29 (9.1%)	1 (1.0%)
Ambroxol	7 (3.0%)	14 (5.8%)	19 (6.8%)	18 (5.7%)	0
Carbocisteine	1 (0.4%)	0	8 (2.8%)	9 (2.8%)	1 (1.0%)
Guaifenesin	1 (0.4%)	4 (1.6%)	4 (1.4%)	7 (2.2%)	7 (6.8%)
Bromhexine	1 (0.4%)	3 (1.2%)	6 (2.1%)	6 (1.9%)	0
Ambroxol acefyllinate	0	0	0	2 (0.6%)	0
Erdosteine	2 (0.8%)	4 (1.6%)	2 (0.7%)	2 (0.6%)	0
Bisolvomed	1 (0.4%)	0	0	1 (0.3%)	0
Bromhexine hydrochloride w/guaifenesin	0	0	0	1 (0.3%)	0
Helicidine	0	0	1 (0.4%)	1 (0.3%)	0
Bromhexine w/ephedrine	0	1 (0.4%)	0	0	0
Bronchostop /01345801/	0	1 (0.4%)	0	0	0
Eprazinone	0	0	1 (0.4%)	0	0
Mucolytics	1 (0.4%)	1 (0.4%)	0	0	0
Myrtol	0	2 (0.8%)	0	0	0
Cough suppressants, excl. combinations with expectorants	8 (3.4%)	10 (4.1%)	30 (10.7%)	40 (12.6%)	12 (11.7%)
Codeine	4 (1.7%)	7 (2.9%)	10 (3.6%)	13 (4.1%)	1 (1.0%)
Dextromethorphan	0	0	7 (2.5%)	12 (3.8%)	2 (1.9%)
Benzonatate	1 (0.4%)	0	3 (1.1%)	5 (1.6%)	4 (3.9%)
Levodropropizine	0	1 (0.4%)	1 (0.4%)	5 (1.6%)	0
Ethylmorphine	1 (0.4%)	0	2 (0.7%)	3 (0.9%)	0
Codeine linctus	0	0	2 (0.7%)	2 (0.6%)	0
Benproperine	1 (0.4%)	2 (0.8%)	3 (1.1%)	1 (0.3%)	0
Cardiazol-paracodina	0	0	0	1 (0.3%)	0
Dextromethorphan w/paracetamol/phenylephrine	0	0	0	1 (0.3%)	0
Dimemorfan	0	0	1 (0.4%)	1 (0.3%)	0
Medicon a	0	0	0	1 (0.3%)	0
Other cough suppressants	0	0	0	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Pholcodine	0	1 (0.4%)	0	1 (0.3%)	0
Butamirate	0	1 (0.4%)	0	0	0
Clofedanol	0	0	1 (0.4%)	0	0
Cloperastine	0	0	1 (0.4%)	0	0
Dextromethorphan w/pseudoephedrine	0	0	0	0	1 (1.0%)
Euphon /00959801/	0	0	2 (0.7%)	0	0
Hydrocodone	0	0	3 (1.1%)	0	2 (1.9%)
Hydrocodone compound /01224801/	0	0	0	0	3 (2.9%)
Opium alkaloids and derivatives	1 (0.4%)	0	0	0	0
Promethazine w/codeine	0	0	0	0	1 (1.0%)
Vicks /01806101/	0	1 (0.4%)	0	0	0
Zipeprol	0	1 (0.4%)	0	0	0
Cough suppressants and expectorants, combinations	3 (1.3%)	4 (1.6%)	5 (1.8%)	17 (5.3%)	3 (2.9%)
Brown mixture /01682301/	0	0	1 (0.4%)	3 (0.9%)	0
Cocillana-etyfin /06573601/	0	1 (0.4%)	1 (0.4%)	3 (0.9%)	0
Cocillana-etyfin /00223001/	1 (0.4%)	0	0	2 (0.6%)	0
Cough s	0	0	0	2 (0.6%)	0
Meiji sekidome	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Cheracol /00693301/	0	0	0	1 (0.3%)	1 (1.0%)
Codeine phosphate w/guaifenesin/pheniramine m	0	0	0	1 (0.3%)	0
Cough syrup /00872901/	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
Thiocodin /01295801/	0	0	0	1 (0.3%)	0
Tussex cough	0	0	0	1 (0.3%)	1 (1.0%)
Bronchosedal	0	0	1 (0.4%)	0	0
Opium derivatives and expectorants	0	1 (0.4%)	1 (0.4%)	0	0
Tussin dm	1 (0.4%)	0	0	0	1 (1.0%)
Uncoded	0	0	4 (1.4%)	8 (2.5%)	0
Cough and cold preparations	0	0	3 (1.1%)	8 (2.5%)	0
Kikyosekko	0	0	1 (0.4%)	0	0
Other cold preparations	0	0	1 (0.4%)	2 (0.6%)	1 (1.0%)
Benylin dry cough /01325601/	0	0	0	1 (0.3%)	0
Propalgina	0	0	0	1 (0.3%)	0
Cheratussin	0	0	0	0	1 (1.0%)
Provax	0	0	1 (0.4%)	0	0
Drugs for constipation	37 (15.6%)	47 (19.3%)	66 (23.5%)	77 (24.2%)	30 (29.1%)
Drugs for constipation	37 (15.6%)	47 (19.3%)	66 (23.5%)	77 (24.2%)	30 (29.1%)
Lactulose	11 (4.6%)	18 (7.4%)	18 (6.4%)	20 (6.3%)	9 (8.7%)
Bisacodyl	2 (0.8%)	4 (1.6%)	5 (1.8%)	14 (4.4%)	4 (3.9%)
Docusate	1 (0.4%)	4 (1.6%)	9 (3.2%)	13 (4.1%)	14 (13.6%)

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Movicol /01749801/	10 (4.2%)	8 (3.3%)	10 (3.6%)	11 (3.5%)	1 (1.0%)
Sennoside a+b	1 (0.4%)	0	12 (4.3%)	11 (3.5%)	2 (1.9%)
Sodium picosulfate	4 (1.7%)	3 (1.2%)	3 (1.1%)	9 (2.8%)	0
Macrogol	4 (1.7%)	7 (2.9%)	9 (3.2%)	7 (2.2%)	7 (6.8%)
Coloxyl with senna	6 (2.5%)	7 (2.9%)	2 (0.7%)	3 (0.9%)	1 (1.0%)
Glycerol	1 (0.4%)	2 (0.8%)	2 (0.7%)	3 (0.9%)	0
Macrogol 4000	1 (0.4%)	0	3 (1.1%)	3 (0.9%)	5 (4.9%)
Drugs for constipation	0	0	4 (1.4%)	2 (0.6%)	0
Fleet /01605601/	0	0	0	2 (0.6%)	0
Portalak /00723101/	0	0	1 (0.4%)	2 (0.6%)	0
Fosfosoda /01544501/	0	0	1 (0.4%)	1 (0.3%)	0
Glyceol /00744501/	0	0	0	1 (0.3%)	0
Micolette /01380801/	0	0	0	1 (0.3%)	0
New lecicarbon	0	0	2 (0.7%)	1 (0.3%)	0
Paraffin, liquid	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
Peri-colace	0	0	0	1 (0.3%)	0
Polycarbophil	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Psyllium hydrophilic mucilloid	0	1 (0.4%)	0	1 (0.3%)	0
Surulac-s	0	0	0	1 (0.3%)	0
Bicoside	1 (0.4%)	1 (0.4%)	0	0	0
Compound thymol glycerin	1 (0.4%)	1 (0.4%)	0	0	0
Docusate w/senna	0	1 (0.4%)	0	0	1 (1.0%)
Docusate w/sennoside a+b	0	0	1 (0.4%)	0	0
Dulcodos	0	1 (0.4%)	1 (0.4%)	0	0
Eductyl	0	0	0	0	1 (1.0%)
Electrolytes nos w/macrogol 3350	0	0	1 (0.4%)	0	0
Enemas	0	1 (0.4%)	0	0	0
Enterospasmyl	0	1 (0.4%)	0	0	0
Golytely	0	0	1 (0.4%)	0	0
Herron sennesoft	0	0	1 (0.4%)	0	0
Lubiprostone	0	0	0	0	1 (1.0%)
Macrogol 3350	1 (0.4%)	0	1 (0.4%)	0	0
Meroken new	3 (1.3%)	5 (2.1%)	1 (0.4%)	0	0
Methylnaltrexone	1 (0.4%)	0	0	0	0
Micolette /06423601/	1 (0.4%)	0	0	0	0
Microklist	0	2 (0.8%)	0	0	0
Microlax /00285401/	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0
Movicol /08437601/	0	1 (0.4%)	0	0	0
Moviprep /06224801/	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Phosphates /00766901/	0	0	1 (0.4%)	0	0
Proctosol	0	0	1 (0.4%)	0	0
Prucalopride	0	0	1 (0.4%)	0	0
Prunacolon	1 (0.4%)	0	0	0	0
Sennoside b	0	0	1 (0.4%)	0	0
Sodium phosphate	1 (0.4%)	0	0	0	0
Sodium phosphate monobasic (anhydrate)	1 (0.4%)	0	2 (0.7%)	0	0
Sorbitol	1 (0.4%)	0	0	0	0
Drugs for obstructive airway diseases	32 (13.5%)	65 (26.7%)	49 (17.4%)	77 (24.2%)	30 (29.1%)
Adrenergics, inhalants	22 (9.3%)	54 (22.2%)	35 (12.5%)	57 (17.9%)	27 (26.2%)
Salbutamol	11 (4.6%)	34 (14.0%)	21 (7.5%)	32 (10.1%)	18 (17.5%)
Duovent	4 (1.7%)	8 (3.3%)	2 (0.7%)	8 (2.5%)	0
Budesonide w/formoterol fumarate	2 (0.8%)	2 (0.8%)	3 (1.1%)	7 (2.2%)	3 (2.9%)
Terbutaline	0	1 (0.4%)	3 (1.1%)	5 (1.6%)	6 (5.8%)
Breva	0	1 (0.4%)	0	4 (1.3%)	0
Seretide	0	3 (1.2%)	5 (1.8%)	2 (0.6%)	2 (1.9%)
Bekform	0	1 (0.4%)	0	1 (0.3%)	0
Budesonide w/formoterol	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
Combivent	0	4 (1.6%)	0	1 (0.3%)	2 (1.9%)
Epinephrine	3 (1.3%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	0
Formoterol	2 (0.8%)	2 (0.8%)	0	1 (0.3%)	0
Allergospasmin	0	1 (0.4%)	0	0	0
Fenoterol	3 (1.3%)	3 (1.2%)	0	0	0
Fluticasone w/salmeterol	0	0	1 (0.4%)	0	0
Formosone	1 (0.4%)	0	0	0	0
Indacaterol	0	1 (0.4%)	0	0	0
Ipratropium w/salbutamol	1 (0.4%)	0	0	0	0
Levosalbutamol	0	1 (0.4%)	2 (0.7%)	0	1 (1.0%)
Salmeterol	1 (0.4%)	0	0	0	0
Tulobuterol	0	1 (0.4%)	0	0	0
Other drugs for obstructive airway diseases, inhalants	15 (6.3%)	29 (11.9%)	21 (7.5%)	28 (8.8%)	7 (6.8%)
Ipratropium	11 (4.6%)	16 (6.6%)	12 (4.3%)	19 (6.0%)	5 (4.9%)
Budesonide	5 (2.1%)	6 (2.5%)	1 (0.4%)	9 (2.8%)	2 (1.9%)
Tiotropium	1 (0.4%)	3 (1.2%)	2 (0.7%)	4 (1.3%)	1 (1.0%)
Beclometasone	1 (0.4%)	6 (2.5%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
Fluticasone	0	3 (1.2%)	3 (1.1%)	2 (0.6%)	0
Aclidinium	0	0	0	1 (0.3%)	0
Mometasone	0	0	1 (0.4%)	1 (0.3%)	0
Fenspiride	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Oxitropium	0	1 (0.4%)	0	0	0
Other systemic drugs for obstructive airway diseases	5 (2.1%)	13 (5.3%)	10 (3.6%)	12 (3.8%)	4 (3.9%)
Theophylline	3 (1.3%)	3 (1.2%)	4 (1.4%)	6 (1.9%)	0
Aminophylline	4 (1.7%)	5 (2.1%)	5 (1.8%)	3 (0.9%)	0
Theobromine	0	0	1 (0.4%)	3 (0.9%)	0
Doxofylline	0	1 (0.4%)	0	0	0
Montelukast	0	3 (1.2%)	0	0	4 (3.9%)
Roflumilast	0	1 (0.4%)	0	0	0
Adrenergics for systemic use	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Bambuterol	0	0	0	1 (0.3%)	0
Fenoterol	0	1 (0.4%)	1 (0.4%)	0	0
Antidiarrheals, intestinal antiinflammatory/antiinfective agents	37 (15.6%)	46 (18.9%)	35 (12.5%)	75 (23.6%)	24 (23.3%)
Antipropulsives	25 (10.5%)	23 (9.5%)	20 (7.1%)	51 (16.0%)	14 (13.6%)
Loperamide	25 (10.5%)	20 (8.2%)	20 (7.1%)	50 (15.7%)	14 (13.6%)
Lomotil /00034001/	0	4 (1.6%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
Intestinal adsorbents	4 (1.7%)	6 (2.5%)	5 (1.8%)	15 (4.7%)	6 (5.8%)
Diosmectite	4 (1.7%)	6 (2.5%)	4 (1.4%)	11 (3.5%)	4 (3.9%)
Bismuth	0	0	1 (0.4%)	4 (1.3%)	1 (1.0%)
Carbosylane /00814601/	0	0	0	1 (0.3%)	0
Charcoal, activated	0	1 (0.4%)	0	0	1 (1.0%)
Kaopectate /00140201/	0	0	1 (0.4%)	0	0
Intestinal antiinfectives	13 (5.5%)	14 (5.8%)	11 (3.9%)	14 (4.4%)	2 (1.9%)
Nystatin	8 (3.4%)	9 (3.7%)	6 (2.1%)	8 (2.5%)	0
Miconazole	2 (0.8%)	2 (0.8%)	3 (1.1%)	7 (2.2%)	1 (1.0%)
Neomycin	0	0	0	2 (0.6%)	0
Colistin	0	0	1 (0.4%)	0	0
Intetrix	1 (0.4%)	0	0	0	0
Natamycin	0	0	1 (0.4%)	0	0
Nifuroxazide	1 (0.4%)	2 (0.8%)	0	0	1 (1.0%)
Rifaximin	1 (0.4%)	3 (1.2%)	0	0	0
Other antidiarrheals	0	3 (1.2%)	1 (0.4%)	8 (2.5%)	5 (4.9%)
Racecadotril	0	1 (0.4%)	1 (0.4%)	7 (2.2%)	5 (4.9%)
Seirogan	0	0	0	1 (0.3%)	0
Albumin tannate	0	2 (0.8%)	0	0	0
Antidiarrheal microorganisms	4 (1.7%)	9 (3.7%)	6 (2.1%)	5 (1.6%)	2 (1.9%)
Bifidobacterium lactis	0	0	0	2 (0.6%)	1 (1.0%)
Antidiarrheal microorganisms	0	3 (1.2%)	0	1 (0.3%)	0
Lactobacillus fermentum	0	0	0	1 (0.3%)	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Saccharomyces boulardii	1 (0.4%)	2 (0.8%)	3 (1.1%)	1 (0.3%)	0
Bacillus subtilis	1 (0.4%)	0	0	0	0
Bifidobacterium bifidum	0	1 (0.4%)	0	0	0
Biolac /07958501/	0	0	1 (0.4%)	0	0
Hylak forte	0	1 (0.4%)	0	0	0
Lactic acid	0	0	1 (0.4%)	0	0
Lactobacillus acidophilus	2 (0.8%)	1 (0.4%)	0	0	1 (1.0%)
Lactobacillus nos	0	1 (0.4%)	0	0	0
Lactobacillus reuteri	0	0	1 (0.4%)	0	0
Lactobacillus rhamnosus	1 (0.4%)	0	0	0	0
Lactomin	1 (0.4%)	0	0	0	0
Electrolytes with carbohydrates	1 (0.4%)	0	0	0	0
Oral rehydration salt formulations	1 (0.4%)	0	0	0	0
Intestinal antiinflammatory agents	0	1 (0.4%)	1 (0.4%)	0	0
Cromoglicic acid	0	1 (0.4%)	0	0	0
Sulfasalazine	0	0	1 (0.4%)	0	0
Uncoded	0	1 (0.4%)	0	0	0
Bifidobacterium bifidum w/lactobaci/06870601/	0	1 (0.4%)	0	0	0
Drugs for functional gastrointestinal disorders	32 (13.5%)	43 (17.7%)	36 (12.8%)	66 (20.8%)	13 (12.6%)
Propulsives	25 (10.5%)	29 (11.9%)	30 (10.7%)	58 (18.2%)	6 (5.8%)
Metoclopramide	21 (8.9%)	25 (10.3%)	22 (7.8%)	45 (14.2%)	6 (5.8%)
Domperidone	2 (0.8%)	1 (0.4%)	3 (1.1%)	8 (2.5%)	0
Alizapride	0	2 (0.8%)	5 (1.8%)	3 (0.9%)	0
Mosapride	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	0
Itopride	0	0	0	1 (0.3%)	0
Bromopride	1 (0.4%)	1 (0.4%)	0	0	0
Drugs for functional gastrointestinal disorders	6 (2.5%)	13 (5.3%)	5 (1.8%)	10 (3.1%)	8 (7.8%)
Spasfon /00765801/	0	0	1 (0.4%)	3 (0.9%)	2 (1.9%)
Trimebutine	1 (0.4%)	2 (0.8%)	2 (0.7%)	3 (0.9%)	2 (1.9%)
Glycopyrronium	0	1 (0.4%)	0	1 (0.3%)	2 (1.9%)
Grandpaze f	0	0	0	1 (0.3%)	0
Mebeverine	0	0	0	1 (0.3%)	0
Meteospasmyl /02143701/	0	0	0	1 (0.3%)	0
Otilonium	0	0	0	1 (0.3%)	0
Pinaverium	0	0	0	1 (0.3%)	0
Simeticone	1 (0.4%)	2 (0.8%)	2 (0.7%)	1 (0.3%)	2 (1.9%)
Tiropramide	0	1 (0.4%)	0	1 (0.3%)	0
Bendazol	0	1 (0.4%)	0	0	0
Dicycloverine	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Drotaverine	2 (0.8%)	5 (2.1%)	0	0	0
Meteospasmyl /01017401/	1 (0.4%)	0	0	0	0
Pepsane	0	1 (0.4%)	0	0	0
Platyphylline	0	1 (0.4%)	0	0	0
Proctolog /01026901/	1 (0.4%)	0	0	0	0
Belladonna and derivatives, plain	4 (1.7%)	4 (1.6%)	2 (0.7%)	5 (1.6%)	0
Hyoscine	2 (0.8%)	3 (1.2%)	1 (0.4%)	4 (1.3%)	0
Butylscopolamine	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
Cimetropium	1 (0.4%)	0	1 (0.4%)	0	0
Antispasmodics and anticholinergics in combination with other drugs	0	0	1 (0.4%)	0	0
Spasmalgin	0	0	1 (0.4%)	0	0
Drugs for treatment of bone diseases	48 (20.3%)	56 (23.0%)	75 (26.7%)	65 (20.4%)	22 (21.4%)
Drugs affecting bone structure and mineralization	48 (20.3%)	56 (23.0%)	75 (26.7%)	65 (20.4%)	22 (21.4%)
Zoledronic acid	29 (12.2%)	35 (14.4%)	48 (17.1%)	41 (12.9%)	17 (16.5%)
Pamidronic acid	19 (8.0%)	20 (8.2%)	26 (9.3%)	23 (7.2%)	4 (3.9%)
Alendronic acid	0	0	0	1 (0.3%)	0
Denosumab	0	0	0	1 (0.3%)	0
Clodronic acid	1 (0.4%)	5 (2.1%)	6 (2.1%)	0	1 (1.0%)
Ibandronic acid	2 (0.8%)	5 (2.1%)	1 (0.4%)	0	0
Risedronic acid	0	0	1 (0.4%)	0	0
Antianemic preparations	27 (11.4%)	26 (10.7%)	38 (13.5%)	58 (18.2%)	13 (12.6%)
Other antianemic preparations	14 (5.9%)	17 (7.0%)	28 (10.0%)	39 (12.3%)	11 (10.7%)
Erythropoietin human	9 (3.8%)	13 (5.3%)	15 (5.3%)	25 (7.9%)	4 (3.9%)
Darbepoetin alfa	3 (1.3%)	3 (1.2%)	12 (4.3%)	13 (4.1%)	6 (5.8%)
Erythropoietin	2 (0.8%)	1 (0.4%)	2 (0.7%)	6 (1.9%)	1 (1.0%)
Methoxy polyethylene glycol-epoetin beta	0	0	1 (0.4%)	0	0
Vitamin b12 and folic acid	10 (4.2%)	10 (4.1%)	11 (3.9%)	19 (6.0%)	2 (1.9%)
Folic acid	7 (3.0%)	1 (0.4%)	5 (1.8%)	10 (3.1%)	1 (1.0%)
Cyanocobalamin	2 (0.8%)	4 (1.6%)	3 (1.1%)	4 (1.3%)	1 (1.0%)
Mecobalamin	1 (0.4%)	3 (1.2%)	3 (1.1%)	3 (0.9%)	0
Vitamin b12 nos	1 (0.4%)	2 (0.8%)	3 (1.1%)	3 (0.9%)	1 (1.0%)
Cobamamide	0	0	0	1 (0.3%)	0
Iron preparations	5 (2.1%)	5 (2.1%)	4 (1.4%)	11 (3.5%)	1 (1.0%)
Iron	5 (2.1%)	4 (1.6%)	4 (1.4%)	10 (3.1%)	0
Ferritin	0	0	0	1 (0.3%)	0
Ferrous forte	0	0	0	0	1 (1.0%)
Kendural c	0	1 (0.4%)	0	0	0
Tot'hema /01747601/	0	1 (0.4%)	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Antigout preparations	45 (19.0%)	53 (21.8%)	45 (16.0%)	52 (16.4%)	11 (10.7%)
Antigout preparations	45 (19.0%)	53 (21.8%)	45 (16.0%)	52 (16.4%)	11 (10.7%)
Allopurinol	45 (19.0%)	52 (21.4%)	38 (13.5%)	50 (15.7%)	10 (9.7%)
Colchicine	0	0	7 (2.5%)	1 (0.3%)	0
Febuxostat	0	1 (0.4%)	3 (1.1%)	1 (0.3%)	0
Colchimax /00728901/	0	0	1 (0.4%)	0	0
Colchimax /01722001/	0	0	2 (0.7%)	0	0
Probenecid	0	0	0	0	1 (1.0%)
Diuretics	42 (17.7%)	66 (27.2%)	45 (16.0%)	40 (12.6%)	18 (17.5%)
High-ceiling diuretics	38 (16.0%)	57 (23.5%)	41 (14.6%)	36 (11.3%)	16 (15.5%)
Furosemide	31 (13.1%)	53 (21.8%)	40 (14.2%)	36 (11.3%)	15 (14.6%)
Torasemide	9 (3.8%)	5 (2.1%)	2 (0.7%)	4 (1.3%)	1 (1.0%)
Bumetanide	0	0	1 (0.4%)	0	0
Potassium-sparing agents	2 (0.8%)	8 (3.3%)	6 (2.1%)	6 (1.9%)	1 (1.0%)
Spironolactone	2 (0.8%)	7 (2.9%)	5 (1.8%)	4 (1.3%)	0
Amiloride	0	0	0	2 (0.6%)	1 (1.0%)
Canrenoic acid	0	2 (0.8%)	1 (0.4%)	0	0
Low-ceiling diuretics, excl. thiazides	3 (1.3%)	4 (1.6%)	0	1 (0.3%)	0
Chlortalidone	0	0	0	1 (0.3%)	0
Indapamide	1 (0.4%)	1 (0.4%)	0	0	0
Xipamide	2 (0.8%)	3 (1.2%)	0	0	0
Low-ceiling diuretics, thiazides	2 (0.8%)	4 (1.6%)	3 (1.1%)	1 (0.3%)	1 (1.0%)
Hydrochlorothiazide	2 (0.8%)	4 (1.6%)	3 (1.1%)	1 (0.3%)	1 (1.0%)
Diuretics and potassium-sparing agents in combination	2 (0.8%)	4 (1.6%)	2 (0.7%)	0	0
Amicloton	0	3 (1.2%)	0	0	0
Furesis comp	1 (0.4%)	0	0	0	0
Moduretic	1 (0.4%)	0	1 (0.4%)	0	0
Osyrol-lasix	0	1 (0.4%)	1 (0.4%)	0	0
Other diuretics	0	0	1 (0.4%)	0	0
Tolvaptan	0	0	1 (0.4%)	0	0
All other therapeutic products	14 (5.9%)	16 (6.6%)	15 (5.3%)	36 (11.3%)	13 (12.6%)
All other therapeutic products	14 (5.9%)	16 (6.6%)	15 (5.3%)	36 (11.3%)	13 (12.6%)
Oxygen	3 (1.3%)	6 (2.5%)	1 (0.4%)	17 (5.3%)	6 (5.8%)
Folinic acid	0	0	6 (2.1%)	13 (4.1%)	5 (4.9%)
All other therapeutic products	4 (1.7%)	1 (0.4%)	2 (0.7%)	7 (2.2%)	0
Mesna	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Propylparaben	0	0	0	1 (0.3%)	0
Sodium polystyrene sulfonate	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
Calcium polystyrene sulfonate	1 (0.4%)	0	2 (0.7%)	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Deferasirox	1 (0.4%)	0	0	0	0
Flumazenil	0	0	1 (0.4%)	0	0
Homeopathic preparation	1 (0.4%)	0	0	0	0
Meglumine sodium succinate	1 (0.4%)	3 (1.2%)	0	0	0
Naloxone	1 (0.4%)	0	1 (0.4%)	0	0
Rasburicase	0	4 (1.6%)	1 (0.4%)	0	2 (1.9%)
Sebidin /01397101/	2 (0.8%)	0	0	0	0
Sevelamer	0	0	0	0	1 (1.0%)
Sodium thiosulfate	0	1 (0.4%)	0	0	0
Psychoanaleptics	19 (8.0%)	23 (9.5%)	29 (10.3%)	36 (11.3%)	10 (9.7%)
Antidepressants	18 (7.6%)	16 (6.6%)	24 (8.5%)	34 (10.7%)	9 (8.7%)
Amitriptyline	3 (1.3%)	3 (1.2%)	9 (3.2%)	10 (3.1%)	1 (1.0%)
Duloxetine	6 (2.5%)	5 (2.1%)	4 (1.4%)	6 (1.9%)	1 (1.0%)
Mirtazapine	1 (0.4%)	3 (1.2%)	1 (0.4%)	5 (1.6%)	0
Escitalopram	0	2 (0.8%)	2 (0.7%)	4 (1.3%)	2 (1.9%)
Sertraline	1 (0.4%)	2 (0.8%)	3 (1.1%)	4 (1.3%)	0
Citalopram	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.6%)	1 (1.0%)
Mianserin	0	0	0	2 (0.6%)	0
Trazodone	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	3 (2.9%)
Venlafaxine	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	1 (1.0%)
Clomipramine	0	0	0	1 (0.3%)	0
Fluoxetine	2 (0.8%)	0	0	1 (0.3%)	0
Paroxetine	0	0	1 (0.4%)	1 (0.3%)	0
Tianeptine	0	0	0	1 (0.3%)	0
Doxepin	0	0	2 (0.7%)	0	0
Imipramine	1 (0.4%)	0	0	0	1 (1.0%)
Maprotiline	1 (0.4%)	0	0	0	0
Nortriptyline	0	0	2 (0.7%)	0	0
Anti-dementia drugs	2 (0.8%)	6 (2.5%)	0	1 (0.3%)	0
Ipidacrine	2 (0.8%)	5 (2.1%)	0	1 (0.3%)	0
Donepezil	0	1 (0.4%)	0	0	0
Psychostimulants, agents used for adhd and nootropics	1 (0.4%)	6 (2.5%)	6 (2.1%)	1 (0.3%)	1 (1.0%)
Methylphenidate	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Centrum /06095001/	1 (0.4%)	3 (1.2%)	0	0	0
Cytoflavin	0	1 (0.4%)	1 (0.4%)	0	0
Ethanolamine alfoscerate	0	0	1 (0.4%)	0	0
Modafinil	0	0	1 (0.4%)	0	0
Phenibut	0	1 (0.4%)	0	0	0
Piracetam	0	1 (0.4%)	2 (0.7%)	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Vinpocetine	0	1 (0.4%)	0	0	0
Psycholeptics and psychoanaleptics in combination	0	0	1 (0.4%)	0	0
Deanxit	0	0	1 (0.4%)	0	0
Antifungals for dermatological use	21 (8.9%)	21 (8.6%)	26 (9.3%)	35 (11.0%)	4 (3.9%)
Antifungals for topical use	21 (8.9%)	21 (8.6%)	25 (8.9%)	34 (10.7%)	4 (3.9%)
Fluconazole	18 (7.6%)	20 (8.2%)	19 (6.8%)	28 (8.8%)	3 (2.9%)
Clotrimazole	3 (1.3%)	1 (0.4%)	4 (1.4%)	7 (2.2%)	0
Amorolfine	0	0	0	1 (0.3%)	0
Antifungals for topical use	0	0	0	1 (0.3%)	0
Bifonazole	0	0	1 (0.4%)	1 (0.3%)	0
Canesten-hc	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Diflucortolone valerate w/isoconazole	0	0	0	1 (0.3%)	0
Isoconazole	0	0	1 (0.4%)	1 (0.3%)	0
Brentan /00745201/	0	0	1 (0.4%)	0	0
Daktacort	0	0	1 (0.4%)	0	0
Daktozin	0	0	0	0	1 (1.0%)
Antifungals for systemic use	0	0	1 (0.4%)	1 (0.3%)	0
Terbinafine	0	0	1 (0.4%)	1 (0.3%)	0
Nasal preparations	6 (2.5%)	19 (7.8%)	20 (7.1%)	33 (10.4%)	3 (2.9%)
Decongestants and other nasal preparations for topical use	4 (1.7%)	13 (5.3%)	9 (3.2%)	18 (5.7%)	3 (2.9%)
Xylometazoline	0	4 (1.6%)	2 (0.7%)	4 (1.3%)	0
Oxymetazoline	1 (0.4%)	5 (2.1%)	1 (0.4%)	2 (0.6%)	0
Tetryzoline	0	1 (0.4%)	0	2 (0.6%)	0
Beclometasone	0	0	0	1 (0.3%)	0
Budesonide	0	0	1 (0.4%)	1 (0.3%)	0
Dexa-rhinospray /00397101/	0	0	0	1 (0.3%)	0
Duonase /06209401/	0	0	0	1 (0.3%)	0
Fluticasone	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	3 (2.9%)
Mometasone	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
Naphazoline	0	0	0	1 (0.3%)	0
Olopatadine	0	0	1 (0.4%)	1 (0.3%)	0
Rhinaris /00678601/	0	0	0	1 (0.3%)	0
Tixocortol	0	0	1 (0.4%)	1 (0.3%)	0
Triamcinolone	0	0	0	1 (0.3%)	0
Triofan	0	0	0	1 (0.3%)	0
Azelastine	0	0	1 (0.4%)	0	1 (1.0%)
Ketotifen	1 (0.4%)	0	0	0	0
Levocabastine	1 (0.4%)	0	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Rinofluimucil s	0	1 (0.4%)	0	0	0
Nasal decongestants for systemic use	3 (1.3%)	8 (3.3%)	12 (4.3%)	14 (4.4%)	2 (1.9%)
Actifed /00005601/	0	0	2 (0.7%)	5 (1.6%)	0
Pseudoephedrine	2 (0.8%)	5 (2.1%)	5 (1.8%)	4 (1.3%)	1 (1.0%)
Allegra-d /01367401/	0	0	0	2 (0.6%)	0
Actifedrin /01573901/	0	0	0	1 (0.3%)	0
Cirrus	1 (0.4%)	0	0	1 (0.3%)	0
Loratadine w/pseudoephedrine	0	0	0	1 (0.3%)	0
Nussidex	0	0	0	1 (0.3%)	0
Chlorphenamine w/phenylephrine	0	0	1 (0.4%)	0	0
Narine /01202601/	0	1 (0.4%)	3 (1.1%)	0	1 (1.0%)
Rino ebastel	0	2 (0.8%)	0	0	0
Sympathomimetics	0	0	1 (0.4%)	0	0
Uncoded	0	0	0	1 (0.3%)	0
Nasal preparations	0	0	0	1 (0.3%)	0
Antiinflammatory and antirheumatic products	26 (11.0%)	22 (9.1%)	29 (10.3%)	32 (10.1%)	8 (7.8%)
Antiinflammatory and antirheumatic products, non-steroids	26 (11.0%)	22 (9.1%)	29 (10.3%)	32 (10.1%)	8 (7.8%)
Ibuprofen	7 (3.0%)	5 (2.1%)	7 (2.5%)	5 (1.6%)	4 (3.9%)
Naproxen	0	1 (0.4%)	3 (1.1%)	5 (1.6%)	2 (1.9%)
Benzydamine	1 (0.4%)	2 (0.8%)	3 (1.1%)	4 (1.3%)	0
Celecoxib	1 (0.4%)	0	4 (1.4%)	4 (1.3%)	0
Ketoprofen	6 (2.5%)	7 (2.9%)	3 (1.1%)	3 (0.9%)	0
Ketorolac	3 (1.3%)	3 (1.2%)	0	3 (0.9%)	0
Carol-f	0	0	0	2 (0.6%)	0
Dexketoprofen	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Indometacin	1 (0.4%)	1 (0.4%)	4 (1.4%)	2 (0.6%)	0
Zaltoprofen	1 (0.4%)	2 (0.8%)	3 (1.1%)	2 (0.6%)	0
Azulene	0	0	2 (0.7%)	1 (0.3%)	0
Bromfenac	0	0	0	1 (0.3%)	1 (1.0%)
Dexibuprofen	0	0	0	1 (0.3%)	0
Etodolac	0	0	0	1 (0.3%)	1 (1.0%)
Flurbiprofen	0	0	0	1 (0.3%)	0
Lornoxicam	0	1 (0.4%)	0	1 (0.3%)	0
Loxoprofen	0	0	0	1 (0.3%)	0
Meloxicam	3 (1.3%)	3 (1.2%)	0	1 (0.3%)	0
Talniflumate	0	0	0	1 (0.3%)	0
Aceclofenac	0	0	1 (0.4%)	0	0
Artrotin /03040901/	0	1 (0.4%)	0	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Dimethyl sulfoxide	1 (0.4%)	0	0	0	0
Etoricoxib	0	1 (0.4%)	1 (0.4%)	0	0
Glucosamine	0	0	1 (0.4%)	0	0
Mefenamic acid	1 (0.4%)	0	0	0	0
Nimesulide	3 (1.3%)	0	1 (0.4%)	0	0
Paracetamol forte raffo	0	0	1 (0.4%)	0	0
Parecoxib	0	0	1 (0.4%)	0	0
Propionic acid derivatives	0	1 (0.4%)	0	0	0
Tenoxicam	0	0	1 (0.4%)	0	0
Antiinflammatory/antirheumatic agents in combination	0	0	0	1 (0.3%)	0
Advil pm /05810501/	0	0	0	1 (0.3%)	0
Unspecified herbal and traditional medicine	6 (2.5%)	11 (4.5%)	26 (9.3%)	31 (9.7%)	11 (10.7%)
Uncoded	6 (2.5%)	11 (4.5%)	26 (9.3%)	31 (9.7%)	11 (10.7%)
Senna alexandrina	2 (0.8%)	1 (0.4%)	8 (2.8%)	11 (3.5%)	8 (7.8%)
Unspecified herbal	2 (0.8%)	5 (2.1%)	4 (1.4%)	4 (1.3%)	0
Kakkonto /07985901/	0	0	0	3 (0.9%)	0
Hedera helix	0	0	0	2 (0.6%)	0
Platycodon grandiflorus	0	0	1 (0.4%)	2 (0.6%)	0
Aloe vera	0	0	0	1 (0.3%)	0
Arachis hypogaea	0	0	0	1 (0.3%)	0
Bakumondoto	0	0	0	1 (0.3%)	0
Euphytose /05965601/	0	0	0	1 (0.3%)	0
Ginkgo biloba	0	0	1 (0.4%)	1 (0.3%)	0
Goshajinkigan	0	0	0	1 (0.3%)	0
Hamamelis virginiana	0	0	0	1 (0.3%)	0
Mentha x piperita	0	0	0	1 (0.3%)	0
Rhamnus purshiana	0	0	0	1 (0.3%)	0
Sterculia urens	0	0	0	1 (0.3%)	0
Althaea officinalis	0	1 (0.4%)	0	0	0
Avena sativa	0	0	0	0	1 (1.0%)
Cannabis sativa	0	0	1 (0.4%)	0	0
Convallaria majalis	1 (0.4%)	1 (0.4%)	0	0	0
Crataegus laevigata	0	0	1 (0.4%)	0	0
Cyamopsis tetragonoloba	0	0	0	0	1 (1.0%)
Cynara cardunculus	0	1 (0.4%)	0	0	0
Herbal extract nos	0	1 (0.4%)	0	0	0
Hypericum perforatum	0	0	0	0	1 (1.0%)
Juzentaihoto /07985601/	0	0	1 (0.4%)	0	0
Kakkontokasenkyushin'i /07986001/	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Linum usitatissimum	0	1 (0.4%)	0	0	0
Matricaria recutita	0	1 (0.4%)	0	0	0
Melaleuca alternifolia	0	0	1 (0.4%)	0	0
Papaver somniferum	0	1 (0.4%)	0	0	1 (1.0%)
Plantago afra	0	0	1 (0.4%)	0	0
Plantago ovata	0	0	1 (0.4%)	0	0
Prunus africana	0	0	1 (0.4%)	0	0
Shakuyakukanzoto	0	0	4 (1.4%)	0	0
Silybum marianum	0	1 (0.4%)	0	0	0
Unspecified herbal and traditional medicine	0	2 (0.8%)	0	0	0
Valeriana officinalis	1 (0.4%)	0	0	0	0
Ophthalmologicals	16 (6.8%)	30 (12.3%)	30 (10.7%)	29 (9.1%)	7 (6.8%)
Antiinflammatory agents	3 (1.3%)	11 (4.5%)	12 (4.3%)	16 (5.0%)	3 (2.9%)
Diclofenac	2 (0.8%)	9 (3.7%)	9 (3.2%)	10 (3.1%)	2 (1.9%)
Dexamethasone	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
Loteprednol	0	0	1 (0.4%)	1 (0.3%)	0
Nepafenac	0	0	1 (0.4%)	1 (0.3%)	0
Piroxicam	0	0	0	1 (0.3%)	0
Prednefrin /00330801/	0	0	0	1 (0.3%)	0
Fluorometholone	0	0	1 (0.4%)	0	0
Prednisolone	0	1 (0.4%)	0	0	1 (1.0%)
Other ophthalmologicals	4 (1.7%)	6 (2.5%)	6 (2.1%)	7 (2.2%)	2 (1.9%)
Carbomer	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (0.9%)	0
Carmellose	0	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
Systane lubricant	0	0	1 (0.4%)	2 (0.6%)	0
Azapentacen	0	0	1 (0.4%)	1 (0.3%)	0
Diquafosol	0	1 (0.4%)	0	1 (0.3%)	0
Artificial tears /90046201/	0	0	1 (0.4%)	0	0
Lacri-lube	1 (0.4%)	0	0	0	0
Other ophthalmologicals	0	1 (0.4%)	0	0	0
Tears natural ii	1 (0.4%)	1 (0.4%)	0	0	0
Tears naturale /00635701/	1 (0.4%)	0	1 (0.4%)	0	0
Tears plus	0	1 (0.4%)	0	0	0
Xantofyl	0	0	1 (0.4%)	0	0
Surgical aids	3 (1.3%)	3 (1.2%)	3 (1.1%)	6 (1.9%)	0
Hyaluronic acid	2 (0.8%)	2 (0.8%)	1 (0.4%)	4 (1.3%)	0
Hypromellose	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Viscoat /01834201/	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Antiinflammatory agents and antiinfectives in combination	3 (1.3%)	4 (1.6%)	4 (1.4%)	3 (0.9%)	0
Ciprodac-dm	0	0	0	1 (0.3%)	0
Maxitrol	0	0	0	1 (0.3%)	0
Tobradex	3 (1.3%)	1 (0.4%)	3 (1.1%)	1 (0.3%)	0
Gentason /03027301/	0	1 (0.4%)	0	0	0
Neodecadron	0	0	1 (0.4%)	0	0
Polydexa	0	1 (0.4%)	0	0	0
Zylet	0	1 (0.4%)	0	0	0
Antiglaucoma preparations and miotics	2 (0.8%)	3 (1.2%)	4 (1.4%)	2 (0.6%)	2 (1.9%)
Acetazolamide	0	0	1 (0.4%)	1 (0.3%)	0
Cosopt	1 (0.4%)	0	0	1 (0.3%)	0
Timolol	0	0	1 (0.4%)	1 (0.3%)	0
Travoprost	0	0	0	1 (0.3%)	1 (1.0%)
Azarga	0	1 (0.4%)	0	0	0
Bimatoprost	1 (0.4%)	0	2 (0.7%)	0	0
Dorzolamide	1 (0.4%)	0	0	0	0
Elazop	0	0	1 (0.4%)	0	0
Neostigmine	1 (0.4%)	2 (0.8%)	0	0	1 (1.0%)
Xalacom	0	1 (0.4%)	0	0	0
Mydriatics and cycloplegics	2 (0.8%)	3 (1.2%)	3 (1.1%)	2 (0.6%)	1 (1.0%)
Hyoscine	0	0	0	1 (0.3%)	0
Tropicamide	0	0	0	1 (0.3%)	0
Atropine	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	1 (1.0%)
Homatropine	0	0	1 (0.4%)	0	0
Mydrin p	0	1 (0.4%)	1 (0.4%)	0	0
Antiinfectives	2 (0.8%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	0
Fusidic acid	2 (0.8%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	0
Sulfacetamide	0	0	0	1 (0.3%)	0
Decongestants and antiallergics	1 (0.4%)	1 (0.4%)	0	0	0
Tetryzoline	1 (0.4%)	0	0	0	0
Vasocon-a	0	1 (0.4%)	0	0	0
Ocular vascular disorder agents	0	0	2 (0.7%)	0	0
Aflibercept	0	0	1 (0.4%)	0	0
Verteporfin	0	0	1 (0.4%)	0	0
Vitamins	19 (8.0%)	35 (14.4%)	26 (9.3%)	27 (8.5%)	13 (12.6%)
Vitamin a and d, incl. combinations of the two	5 (2.1%)	7 (2.9%)	16 (5.7%)	9 (2.8%)	11 (10.7%)
Colecalciferol	3 (1.3%)	6 (2.5%)	8 (2.8%)	5 (1.6%)	7 (6.8%)
Vitamin d nos	1 (0.4%)	1 (0.4%)	7 (2.5%)	3 (0.9%)	2 (1.9%)

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Calcitriol	0	0	0	1 (0.3%)	0
Retinol	0	0	0	1 (0.3%)	1 (1.0%)
Alfacalcidol	0	0	1 (0.4%)	0	0
Ergocalciferol	1 (0.4%)	0	0	0	1 (1.0%)
Multivitamins, plain	1 (0.4%)	5 (2.1%)	1 (0.4%)	8 (2.5%)	1 (1.0%)
Vitamins nos	1 (0.4%)	4 (1.6%)	1 (0.4%)	8 (2.5%)	1 (1.0%)
Cernevit /06027301/	0	1 (0.4%)	0	0	0
Vitamin b1, plain and in combination with vitamin b6 and b12	5 (2.1%)	12 (4.9%)	3 (1.1%)	4 (1.3%)	0
Befact /00527001/	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Milgamma na /01350701/	0	1 (0.4%)	0	1 (0.3%)	0
Thiamine	1 (0.4%)	3 (1.2%)	1 (0.4%)	1 (0.3%)	0
Trineurin /00499701/	0	0	0	1 (0.3%)	0
Neurobion /00176001/	3 (1.3%)	7 (2.9%)	1 (0.4%)	0	0
Neurogrisevit /00091901/	1 (0.4%)	0	0	0	0
Vitamin b1 in combination with vitamin b6 and	0	1 (0.4%)	0	0	0
Other plain vitamin preparations	4 (1.7%)	4 (1.6%)	4 (1.4%)	3 (0.9%)	0
Dexpanthenol	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
Pantethine	0	0	1 (0.4%)	1 (0.3%)	0
Tocopherol	0	0	2 (0.7%)	1 (0.3%)	0
Biotin	0	1 (0.4%)	0	0	0
Flavine adenine dinucleotide	0	0	1 (0.4%)	0	0
Pyridoxine	3 (1.3%)	2 (0.8%)	0	0	0
Other vitamin products, combinations	2 (0.8%)	9 (3.7%)	1 (0.4%)	3 (0.9%)	0
Vitamedin /00274301/	1 (0.4%)	0	0	2 (0.6%)	0
Vitamins, other combinations	0	0	0	1 (0.3%)	0
Alanerv	1 (0.4%)	2 (0.8%)	0	0	0
Calcium mefolinate w/pyridoxine hydrochloride	0	1 (0.4%)	0	0	0
Hepasol /00356501/	0	2 (0.8%)	0	0	0
Neurotonic	0	1 (0.4%)	0	0	0
Nucleo c.m.p. /00659201/	0	1 (0.4%)	0	0	0
Other vitamin products, combinations	0	1 (0.4%)	0	0	0
Vitamedin intravenous	0	1 (0.4%)	1 (0.4%)	0	0
Vitamins with minerals	0	1 (0.4%)	0	0	0
Vitamin b-complex, incl. combinations	1 (0.4%)	1 (0.4%)	3 (1.1%)	2 (0.6%)	0
B-komplex	0	0	0	1 (0.3%)	0
Vitamin b complex	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Minerals nos w/vitamin b nos	0	0	1 (0.4%)	0	0
Parentrovite /00041801/	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Tpn /00897001/	0	0	1 (0.4%)	0	0
Multivitamins, combinations	1 (0.4%)	0	0	1 (0.3%)	0
Ascorbic acid w/biotin/calcium chloride/calci	0	0	0	1 (0.3%)	0
Ascorbic acid w/betacarotene/biotin/08281401/	1 (0.4%)	0	0	0	0
Ascorbic acid (vitamin c), incl. combinations	2 (0.8%)	6 (2.5%)	1 (0.4%)	0	2 (1.9%)
Ascorbic acid	2 (0.8%)	6 (2.5%)	1 (0.4%)	0	2 (1.9%)
Ascorbic acid (vitamin c), combinations	0	0	0	0	1 (1.0%)
Antiemetics and antinauseants	17 (7.2%)	23 (9.5%)	12 (4.3%)	26 (8.2%)	31 (30.1%)
Antiemetics and antinauseants	17 (7.2%)	23 (9.5%)	12 (4.3%)	26 (8.2%)	31 (30.1%)
Ondansetron	11 (4.6%)	19 (7.8%)	12 (4.3%)	20 (6.3%)	31 (30.1%)
Granisetron	5 (2.1%)	4 (1.6%)	0	6 (1.9%)	1 (1.0%)
Aprepitant	0	1 (0.4%)	0	0	0
Palonosetron	0	1 (0.4%)	0	0	0
Tropisetron	1 (0.4%)	1 (0.4%)	0	0	0
Beta blocking agents	10 (4.2%)	16 (6.6%)	11 (3.9%)	26 (8.2%)	8 (7.8%)
Beta blocking agents	10 (4.2%)	16 (6.6%)	11 (3.9%)	26 (8.2%)	8 (7.8%)
Bisoprolol	4 (1.7%)	6 (2.5%)	7 (2.5%)	12 (3.8%)	1 (1.0%)
Metoprolol	3 (1.3%)	5 (2.1%)	4 (1.4%)	10 (3.1%)	3 (2.9%)
Carvedilol	3 (1.3%)	2 (0.8%)	0	2 (0.6%)	2 (1.9%)
Sotalol	0	0	0	2 (0.6%)	0
Carteolol	0	0	0	1 (0.3%)	0
Nebivolol	0	1 (0.4%)	0	1 (0.3%)	0
Atenolol	1 (0.4%)	2 (0.8%)	0	0	0
Propranolol	0	2 (0.8%)	1 (0.4%)	0	2 (1.9%)
Beta blocking agents and thiazides	0	0	0	1 (0.3%)	0
Biselect /01166101/	0	0	0	1 (0.3%)	0
Throat preparations	12 (5.1%)	3 (1.2%)	23 (8.2%)	25 (7.9%)	8 (7.8%)
Throat preparations	12 (5.1%)	3 (1.2%)	23 (8.2%)	25 (7.9%)	8 (7.8%)
Lidocaine	7 (3.0%)	2 (0.8%)	11 (3.9%)	13 (4.1%)	7 (6.8%)
Chlorhexidine	4 (1.7%)	0	10 (3.6%)	7 (2.2%)	1 (1.0%)
Povidone-iodine	1 (0.4%)	0	3 (1.1%)	4 (1.3%)	0
Antiseptics	0	0	0	1 (0.3%)	0
Colludol	0	0	0	1 (0.3%)	0
Strepsils /00200801/	0	0	0	1 (0.3%)	0
Biclotymol	0	0	1 (0.4%)	0	0
Cetylpyridinium	0	1 (0.4%)	0	0	0
Corticosteroids, dermatological preparations	8 (3.4%)	9 (3.7%)	23 (8.2%)	24 (7.5%)	4 (3.9%)
Corticosteroids, plain	6 (2.5%)	8 (3.3%)	21 (7.5%)	23 (7.2%)	4 (3.9%)
Mometasone	0	2 (0.8%)	4 (1.4%)	6 (1.9%)	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Betamethasone	1 (0.4%)	1 (0.4%)	3 (1.1%)	5 (1.6%)	1 (1.0%)
Hydrocortisone	4 (1.7%)	3 (1.2%)	4 (1.4%)	4 (1.3%)	0
Triamcinolone	1 (0.4%)	1 (0.4%)	3 (1.1%)	4 (1.3%)	2 (1.9%)
Dexamethasone	0	0	0	2 (0.6%)	0
Beclometasone	0	0	1 (0.4%)	1 (0.3%)	0
Clobetasol	0	0	0	1 (0.3%)	2 (1.9%)
Desonide	0	0	2 (0.7%)	1 (0.3%)	0
Desoximetasone	0	0	2 (0.7%)	1 (0.3%)	0
Fluorometholone	0	0	1 (0.4%)	1 (0.3%)	0
Difluprednate	0	0	1 (0.4%)	0	0
Fluticasone	1 (0.4%)	1 (0.4%)	0	0	0
Methylprednisolone	0	0	2 (0.7%)	0	0
Corticosteroids, combinations with antibiotics	1 (0.4%)	0	2 (0.7%)	4 (1.3%)	0
Mycolog	0	0	0	2 (0.6%)	0
Valisone-g	0	0	1 (0.4%)	2 (0.6%)	0
Pimafucort /00191101/	1 (0.4%)	0	0	0	0
Polycutan	0	0	1 (0.4%)	0	0
Corticosteroids, combinations with antiseptics	0	0	1 (0.4%)	1 (0.3%)	0
Lacticare hc /02298001/	0	0	1 (0.4%)	1 (0.3%)	0
Corticosteroids, other combinations	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
Corticosteroids, other combinations	0	0	1 (0.4%)	1 (0.3%)	0
Betadermic	1 (0.4%)	0	0	0	0
Uncoded	0	1 (0.4%)	0	0	0
Corticosteroids, dermatological preparations	0	1 (0.4%)	0	0	0
Vaccines	6 (2.5%)	11 (4.5%)	22 (7.8%)	24 (7.5%)	11 (10.7%)
Viral vaccines	5 (2.1%)	11 (4.5%)	20 (7.1%)	23 (7.2%)	10 (9.7%)
Influenza vaccine	5 (2.1%)	9 (3.7%)	18 (6.4%)	21 (6.6%)	10 (9.7%)
Hepatitis b vaccine	0	1 (0.4%)	0	1 (0.3%)	0
Polio vaccine	0	0	0	1 (0.3%)	0
Twinrix	0	0	0	1 (0.3%)	0
Hepatitis a vaccine	0	1 (0.4%)	1 (0.4%)	0	0
Measles mumps & rubella live attenuated (free	0	1 (0.4%)	1 (0.4%)	0	0
Yellow fever vaccine	0	0	1 (0.4%)	0	0
Bacterial vaccines	1 (0.4%)	1 (0.4%)	6 (2.1%)	2 (0.6%)	2 (1.9%)
Haemophilus influenza type b vaccine	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Pneumococcal vaccine	0	0	5 (1.8%)	1 (0.3%)	2 (1.9%)
Pneumococcal vaccines	0	0	0	1 (0.3%)	0
Vaccin ipad d.t.c.	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
Ditemer	0	0	1 (0.4%)	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Tetanus vaccine	1 (0.4%)	0	0	0	0
Typhoid vaccine	0	1 (0.4%)	0	0	0
Bacterial and viral vaccines, combined	0	1 (0.4%)	0	0	0
Quadracel	0	1 (0.4%)	0	0	0
Drugs used in diabetes	13 (5.5%)	25 (10.3%)	23 (8.2%)	21 (6.6%)	10 (9.7%)
Insulins and analogues	9 (3.8%)	17 (7.0%)	15 (5.3%)	17 (5.3%)	4 (3.9%)
Insulin human	4 (1.7%)	5 (2.1%)	8 (2.8%)	7 (2.2%)	0
Insulin glargine	2 (0.8%)	1 (0.4%)	6 (2.1%)	5 (1.6%)	0
Insulin aspart	1 (0.4%)	4 (1.6%)	3 (1.1%)	3 (0.9%)	1 (1.0%)
Insulin	3 (1.3%)	0	1 (0.4%)	2 (0.6%)	0
Humalog mix	0	0	0	1 (0.3%)	0
Insulin glulisine	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
Insulin lispro	0	4 (1.6%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
Novomix	2 (0.8%)	3 (1.2%)	1 (0.4%)	1 (0.3%)	0
Human mixtard	0	0	1 (0.4%)	0	0
Insulin bovine	0	1 (0.4%)	1 (0.4%)	0	2 (1.9%)
Insulin detemir	0	2 (0.8%)	2 (0.7%)	0	0
Insulin porcine	0	1 (0.4%)	0	0	0
Blood glucose lowering drugs, excl. insulins	9 (3.8%)	14 (5.8%)	13 (4.6%)	11 (3.5%)	8 (7.8%)
Metformin	4 (1.7%)	8 (3.3%)	7 (2.5%)	4 (1.3%)	4 (3.9%)
Sitagliptin	0	0	1 (0.4%)	3 (0.9%)	1 (1.0%)
Gliclazide	2 (0.8%)	2 (0.8%)	2 (0.7%)	2 (0.6%)	0
Alogliptin	0	0	1 (0.4%)	1 (0.3%)	0
Diapride forte	0	0	0	1 (0.3%)	0
Glimepiride	1 (0.4%)	2 (0.8%)	3 (1.1%)	1 (0.3%)	1 (1.0%)
Mitiglinide	0	0	0	1 (0.3%)	0
Repaglinide	0	0	0	1 (0.3%)	1 (1.0%)
Vildagliptin	0	0	0	1 (0.3%)	0
Acarbose	1 (0.4%)	0	0	0	0
Eucreas	0	0	2 (0.7%)	0	0
Glipizide	0	0	1 (0.4%)	0	1 (1.0%)
Jentadueto	0	0	1 (0.4%)	0	0
Linagliptin	2 (0.8%)	2 (0.8%)	0	0	0
Lixisenatide	0	0	1 (0.4%)	0	0
Pioglitazone	0	0	1 (0.4%)	0	0
Saxagliptin	0	0	0	0	1 (1.0%)
Sil-norboral /01503701/	0	1 (0.4%)	0	0	0
Cardiac therapy	19 (8.0%)	36 (14.8%)	18 (6.4%)	20 (6.3%)	9 (8.7%)
Antiarrhythmics, class i and iii	2 (0.8%)	6 (2.5%)	3 (1.1%)	10 (3.1%)	4 (3.9%)

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Amiodarone	2 (0.8%)	6 (2.5%)	3 (1.1%)	8 (2.5%)	2 (1.9%)
Flecainide	0	0	0	2 (0.6%)	1 (1.0%)
Propafenone	0	0	0	1 (0.3%)	1 (1.0%)
Dofetilide	0	0	0	0	1 (1.0%)
Cardiac stimulants excl. cardiac glycosides	4 (1.7%)	7 (2.9%)	6 (2.1%)	8 (2.5%)	3 (2.9%)
Norepinephrine	3 (1.3%)	1 (0.4%)	3 (1.1%)	4 (1.3%)	0
Bucladesine	0	0	0	1 (0.3%)	0
Dobutamine	0	0	0	1 (0.3%)	0
Dopamine	2 (0.8%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
Levosimendan	0	0	0	1 (0.3%)	0
Midodrine	0	0	0	1 (0.3%)	0
Phenylephrine	1 (0.4%)	3 (1.2%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
Ephedrine	0	0	0	0	1 (1.0%)
Isoprenaline	0	0	0	0	1 (1.0%)
Metaraminol	1 (0.4%)	2 (0.8%)	0	0	0
Vasodilators used in cardiac diseases	4 (1.7%)	8 (3.3%)	9 (3.2%)	6 (1.9%)	2 (1.9%)
Glyceryl trinitrate	2 (0.8%)	7 (2.9%)	5 (1.8%)	6 (1.9%)	1 (1.0%)
Isosorbide mononitrate	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
Isosorbide dinitrate	2 (0.8%)	1 (0.4%)	3 (1.1%)	0	0
Nicorandil	0	0	1 (0.4%)	0	0
Nitric oxide	0	0	1 (0.4%)	0	0
Cardiac glycosides	1 (0.4%)	1 (0.4%)	4 (1.4%)	2 (0.6%)	0
Digoxin	1 (0.4%)	1 (0.4%)	4 (1.4%)	2 (0.6%)	0
Other cardiac preparations	13 (5.5%)	20 (8.2%)	1 (0.4%)	2 (0.6%)	0
Adenosine	0	2 (0.8%)	0	1 (0.3%)	0
Trophicard	12 (5.1%)	16 (6.6%)	0	1 (0.3%)	0
Meldonium	1 (0.4%)	4 (1.6%)	0	0	0
Thiotriazoline	2 (0.8%)	7 (2.9%)	0	0	0
Trimetazidine	1 (0.4%)	4 (1.6%)	1 (0.4%)	0	0
Immune sera and immunoglobulins	13 (5.5%)	15 (6.2%)	16 (5.7%)	20 (6.3%)	9 (8.7%)
Immunoglobulins	13 (5.5%)	15 (6.2%)	16 (5.7%)	20 (6.3%)	9 (8.7%)
Immunoglobulin human normal	10 (4.2%)	13 (5.3%)	11 (3.9%)	19 (6.0%)	3 (2.9%)
Immunoglobulins nos	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	4 (3.9%)
Immunoglobulin g human	2 (0.8%)	0	0	0	0
Immunoglobulins	0	1 (0.4%)	5 (1.8%)	0	1 (1.0%)
Immunoglobulins, normal human	0	1 (0.4%)	0	0	2 (1.9%)
Agents acting on the renin-angiotensin system	13 (5.5%)	18 (7.4%)	8 (2.8%)	19 (6.0%)	5 (4.9%)
Ace inhibitors, plain	8 (3.4%)	8 (3.3%)	5 (1.8%)	12 (3.8%)	4 (3.9%)
Ramipril	2 (0.8%)	3 (1.2%)	3 (1.1%)	4 (1.3%)	1 (1.0%)

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Captopril	1 (0.4%)	2 (0.8%)	0	3 (0.9%)	0
Enalapril	4 (1.7%)	2 (0.8%)	1 (0.4%)	2 (0.6%)	0
Perindopril	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Lisinopril	1 (0.4%)	0	0	1 (0.3%)	3 (2.9%)
Angiotensin ii antagonists, plain	2 (0.8%)	10 (4.1%)	2 (0.7%)	5 (1.6%)	2 (1.9%)
Candesartan	0	3 (1.2%)	0	2 (0.6%)	0
Losartan	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	2 (1.9%)
Telmisartan	0	1 (0.4%)	0	1 (0.3%)	0
Azilsartan	0	0	1 (0.4%)	0	0
Irbesartan	1 (0.4%)	2 (0.8%)	0	0	0
Olmesartan	0	1 (0.4%)	0	0	0
Valsartan	1 (0.4%)	2 (0.8%)	0	0	0
Ace inhibitors, combinations	2 (0.8%)	2 (0.8%)	0	1 (0.3%)	0
Udramil	0	0	0	1 (0.3%)	0
Capozide	1 (0.4%)	0	0	0	0
Coveram	1 (0.4%)	0	0	0	0
Salutec	0	1 (0.4%)	0	0	0
Zestoretic	0	1 (0.4%)	0	0	0
Angiotensin ii antagonists, combinations	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
Hyzaar	0	0	0	1 (0.3%)	0
Benicar hct	0	0	1 (0.4%)	0	0
Pritorplus	1 (0.4%)	0	0	0	0
Gynecological antiinfectives and antiseptics	8 (3.4%)	10 (4.1%)	15 (5.3%)	19 (6.0%)	6 (5.8%)
Antiinfectives and antiseptics, excl. combinations with corticosteroids	8 (3.4%)	10 (4.1%)	15 (5.3%)	19 (6.0%)	6 (5.8%)
Metronidazole	7 (3.0%)	9 (3.7%)	10 (3.6%)	16 (5.0%)	5 (4.9%)
Ciclopirox	0	0	1 (0.4%)	1 (0.3%)	0
Sertaconazole	0	0	0	1 (0.3%)	0
Tinidazole	0	0	0	1 (0.3%)	0
Econazole	0	0	3 (1.1%)	0	1 (1.0%)
Lactobacillus gasseri	1 (0.4%)	0	0	0	0
Mycomnes	0	1 (0.4%)	0	0	0
Ornidazole	0	0	1 (0.4%)	0	0
Antiepileptics	20 (8.4%)	31 (12.8%)	13 (4.6%)	17 (5.3%)	8 (7.8%)
Antiepileptics	20 (8.4%)	31 (12.8%)	13 (4.6%)	17 (5.3%)	8 (7.8%)
Gabapentin	17 (7.2%)	24 (9.9%)	11 (3.9%)	10 (3.1%)	7 (6.8%)
Clonazepam	2 (0.8%)	5 (2.1%)	2 (0.7%)	5 (1.6%)	0
Levetiracetam	0	0	0	2 (0.6%)	1 (1.0%)
Carbamazepine	0	2 (0.8%)	0	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Lacosamide	0	0	0	1 (0.3%)	0
Lamotrigine	0	0	0	1 (0.3%)	0
Phenytoin	0	0	0	1 (0.3%)	0
Benzodiazepine derivatives	1 (0.4%)	0	0	0	0
Ergenyl chrono	1 (0.4%)	0	0	0	0
Primidone	0	0	1 (0.4%)	0	0
Valproic acid	0	1 (0.4%)	0	0	0
Antimycotics for systemic use	7 (3.0%)	7 (2.9%)	8 (2.8%)	17 (5.3%)	4 (3.9%)
Antimycotics for systemic use	7 (3.0%)	7 (2.9%)	8 (2.8%)	17 (5.3%)	4 (3.9%)
Amphotericin b	4 (1.7%)	5 (2.1%)	3 (1.1%)	5 (1.6%)	1 (1.0%)
Voriconazole	1 (0.4%)	2 (0.8%)	3 (1.1%)	5 (1.6%)	2 (1.9%)
Caspofungin	1 (0.4%)	1 (0.4%)	2 (0.7%)	3 (0.9%)	0
Ketoconazole	0	0	0	3 (0.9%)	1 (1.0%)
Micafungin	1 (0.4%)	0	0	2 (0.6%)	1 (1.0%)
Anidulafungin	1 (0.4%)	0	0	0	0
Fluconazole	0	0	1 (0.4%)	0	0
Posaconazole	1 (0.4%)	0	2 (0.7%)	0	0
Calcium channel blockers	11 (4.6%)	15 (6.2%)	7 (2.5%)	17 (5.3%)	4 (3.9%)
Selective calcium channel blockers with mainly vascular effects	10 (4.2%)	15 (6.2%)	7 (2.5%)	15 (4.7%)	3 (2.9%)
Amlodipine	9 (3.8%)	8 (3.3%)	5 (1.8%)	7 (2.2%)	3 (2.9%)
Lercanidipine	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Nicardipine	0	0	0	2 (0.6%)	0
Nifedipine	1 (0.4%)	5 (2.1%)	1 (0.4%)	2 (0.6%)	0
Barnidipine	0	0	0	1 (0.3%)	0
Benidipine	0	0	0	1 (0.3%)	0
Cilnidipine	0	0	0	1 (0.3%)	0
Nitrendipine	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
Selective calcium channel blockers with direct cardiac effects	2 (0.8%)	0	0	2 (0.6%)	1 (1.0%)
Diltiazem	1 (0.4%)	0	0	1 (0.3%)	1 (1.0%)
Verapamil	1 (0.4%)	0	0	1 (0.3%)	0
Non-selective calcium channel blockers	1 (0.4%)	0	0	0	0
Perhexiline	1 (0.4%)	0	0	0	0
Lipid modifying agents	7 (3.0%)	10 (4.1%)	19 (6.8%)	17 (5.3%)	6 (5.8%)
Lipid modifying agents, plain	7 (3.0%)	10 (4.1%)	18 (6.4%)	17 (5.3%)	6 (5.8%)
Atorvastatin	3 (1.3%)	1 (0.4%)	6 (2.1%)	8 (2.5%)	1 (1.0%)
Simvastatin	1 (0.4%)	3 (1.2%)	4 (1.4%)	3 (0.9%)	0
Colestipol	0	0	1 (0.4%)	2 (0.6%)	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Colestyramine	0	0	3 (1.1%)	2 (0.6%)	1 (1.0%)
Colesevelam	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Fish oil	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
Rosuvastatin	0	0	1 (0.4%)	1 (0.3%)	0
Bezafibrate	0	0	1 (0.4%)	0	0
Docosahexaenoic acid	0	0	0	0	1 (1.0%)
Fluvastatin	0	0	1 (0.4%)	0	0
Phospholipids	3 (1.3%)	4 (1.6%)	0	0	0
Pitavastatin	0	1 (0.4%)	1 (0.4%)	0	0
Pravastatin	0	1 (0.4%)	1 (0.4%)	0	0
Lipid modifying agents, combinations	0	0	1 (0.4%)	0	0
Inegy	0	0	1 (0.4%)	0	0
General nutrients	4 (1.7%)	12 (4.9%)	12 (4.3%)	16 (5.0%)	4 (3.9%)
Other nutrients	4 (1.7%)	9 (3.7%)	10 (3.6%)	13 (4.1%)	1 (1.0%)
Glucose	3 (1.3%)	6 (2.5%)	9 (3.2%)	9 (2.8%)	1 (1.0%)
Amino acids nos w/electrolytes nos/glucose/th	0	0	0	3 (0.9%)	0
Amino acids nos w/carbohydrates nos/07403601/	0	0	0	1 (0.3%)	0
Other combinations of nutrients	1 (0.4%)	0	0	1 (0.3%)	0
Ascorbic acid w/biotin/calcium/carb/08371201/	0	1 (0.4%)	0	0	0
Caffeine w/carbohydrates nos/cholin/08302001/	0	0	1 (0.4%)	0	0
Ketosteril	0	2 (0.8%)	0	0	0
Uncoded	0	3 (1.2%)	2 (0.7%)	4 (1.3%)	0
General nutrients	0	2 (0.8%)	0	2 (0.6%)	0
Nutrients nos	0	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
Protein supplements	0	0	0	1 (0.3%)	3 (2.9%)
Carbohydrates nos w/lipids nos/mine/07460201/	0	0	0	1 (0.3%)	3 (2.9%)
Antiprotozoals	1 (0.4%)	4 (1.6%)	8 (2.8%)	14 (4.4%)	5 (4.9%)
Agents against leishmaniasis and trypanosomiasis	1 (0.4%)	3 (1.2%)	6 (2.1%)	10 (3.1%)	2 (1.9%)
Pentamidine	1 (0.4%)	3 (1.2%)	6 (2.1%)	10 (3.1%)	2 (1.9%)
Agents against amoebiasis and other protozoal diseases	0	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
Atovaquone	0	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
Antimalarials	0	0	2 (0.7%)	2 (0.6%)	1 (1.0%)
Quinine	0	0	2 (0.7%)	2 (0.6%)	1 (1.0%)
Emollients and protectives	3 (1.3%)	6 (2.5%)	10 (3.6%)	14 (4.4%)	3 (2.9%)
Emollients and protectives	3 (1.3%)	6 (2.5%)	10 (3.6%)	14 (4.4%)	3 (2.9%)
Dimeticone	2 (0.8%)	1 (0.4%)	2 (0.7%)	4 (1.3%)	0
Other emollients and protectives	0	0	1 (0.4%)	2 (0.6%)	0
Aqueous /00662801/	0	0	0	1 (0.3%)	0
Dexeryl /01579901/	0	0	0	1 (0.3%)	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Emollients and protectives	0	1 (0.4%)	0	1 (0.3%)	0
Paraffin soft	0	0	0	1 (0.3%)	0
Petrolatum	0	0	0	1 (0.3%)	0
Salicylic acid	0	0	0	1 (0.3%)	1 (1.0%)
Vitapantol	0	0	1 (0.4%)	1 (0.3%)	0
White soft paraffin	0	0	0	1 (0.3%)	0
Ammonium lactate	0	0	0	0	1 (1.0%)
Cream e45	0	0	2 (0.7%)	0	0
Eucerin /01160201/	0	1 (0.4%)	0	0	0
Fenuril	0	0	1 (0.4%)	0	0
Paraffin	0	0	1 (0.4%)	0	0
Propylene glycol	0	0	1 (0.4%)	0	0
Sorbolene	0	2 (0.8%)	0	0	0
Sprilon	0	0	1 (0.4%)	0	0
Urea	1 (0.4%)	2 (0.8%)	2 (0.7%)	0	0
Zinc	0	0	0	0	1 (1.0%)
Urologicals	7 (3.0%)	1 (0.4%)	11 (3.9%)	14 (4.4%)	5 (4.9%)
Drugs used in benign prostatic hypertrophy	7 (3.0%)	1 (0.4%)	4 (1.4%)	9 (2.8%)	4 (3.9%)
Tamsulosin	6 (2.5%)	0	4 (1.4%)	6 (1.9%)	4 (3.9%)
Alfuzosin	0	0	0	2 (0.6%)	0
Finasteride	0	0	0	2 (0.6%)	0
Dutasteride	2 (0.8%)	0	0	0	0
Silodosin	1 (0.4%)	0	0	0	0
Terazosin	1 (0.4%)	1 (0.4%)	0	0	0
Urologicals	0	0	8 (2.8%)	5 (1.6%)	1 (1.0%)
Reducto	0	0	3 (1.1%)	2 (0.6%)	0
Mirabegron	0	0	2 (0.7%)	1 (0.3%)	0
Rowatinex /00499401/	0	0	0	1 (0.3%)	0
Sildenafil	0	0	1 (0.4%)	1 (0.3%)	0
Fesoterodine	0	0	1 (0.4%)	0	0
Phenazopyridine	0	0	1 (0.4%)	0	1 (1.0%)
Udenafil	0	0	1 (0.4%)	0	0
Anesthetics	6 (2.5%)	15 (6.2%)	9 (3.2%)	10 (3.1%)	5 (4.9%)
Anesthetics, general	4 (1.7%)	6 (2.5%)	5 (1.8%)	5 (1.6%)	3 (2.9%)
Propofol	4 (1.7%)	3 (1.2%)	5 (1.8%)	3 (0.9%)	2 (1.9%)
Alfentanil	0	0	0	1 (0.3%)	0
Remifentanil	0	0	0	1 (0.3%)	0
Etomidate	0	0	0	0	2 (1.9%)
Ketamine	0	4 (1.6%)	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Nitrous oxide	0	1 (0.4%)	0	0	0
Sufentanil	0	1 (0.4%)	0	0	0
Anesthetics, local	2 (0.8%)	10 (4.1%)	6 (2.1%)	5 (1.6%)	2 (1.9%)
Xylocaine-epinephrine	0	0	0	2 (0.6%)	0
Bupivacaine	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Lidocaine	1 (0.4%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	0
Ottocain	0	0	0	1 (0.3%)	0
Oxetacaine	0	0	2 (0.7%)	1 (0.3%)	0
Cepacol anesthetic	0	1 (0.4%)	1 (0.4%)	0	0
Emla /00675501/	0	1 (0.4%)	0	0	1 (1.0%)
Lidocaine/phenylephrine	0	1 (0.4%)	0	0	0
Marcaine with epinephrine /00879801/	1 (0.4%)	0	0	0	0
Mepivacaine	0	2 (0.8%)	0	0	0
Procaine	0	1 (0.4%)	0	0	0
Sulfocamphocain	0	1 (0.4%)	0	0	0
Antibiotics and chemotherapeutics for dermatological use	2 (0.8%)	1 (0.4%)	15 (5.3%)	10 (3.1%)	4 (3.9%)
Antibiotics for topical use	2 (0.8%)	1 (0.4%)	12 (4.3%)	8 (2.5%)	2 (1.9%)
Mupirocin	2 (0.8%)	0	7 (2.5%)	3 (0.9%)	1 (1.0%)
Naseptin	0	0	1 (0.4%)	2 (0.6%)	0
Neotracin /00038301/	0	0	0	2 (0.6%)	0
Terramycin ophthalmic	0	0	0	1 (0.3%)	0
Doxycycline	0	0	1 (0.4%)	0	0
Neosporin /00130801/	0	0	1 (0.4%)	0	1 (1.0%)
Oxytetracycline	0	1 (0.4%)	0	0	0
Spersin /00125501/	0	0	1 (0.4%)	0	0
Tetracycline	0	0	1 (0.4%)	0	0
Chemotherapeutics for topical use	0	0	3 (1.1%)	2 (0.6%)	2 (1.9%)
Sulfadiazine	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Sulfathiazole	0	0	0	1 (0.3%)	0
Imiquimod	0	0	0	0	1 (1.0%)
Ingenol	0	0	1 (0.4%)	0	0
Lysozyme	0	0	1 (0.4%)	0	0
Antihemorrhagics	7 (3.0%)	20 (8.2%)	11 (3.9%)	9 (2.8%)	3 (2.9%)
Vitamin k and other hemostatics	5 (2.1%)	12 (4.9%)	8 (2.8%)	7 (2.2%)	3 (2.9%)
Phytomenadione	0	1 (0.4%)	3 (1.1%)	4 (1.3%)	2 (1.9%)
Etamsilate	3 (1.3%)	9 (3.7%)	1 (0.4%)	2 (0.6%)	0
Vitamin k nos	2 (0.8%)	3 (1.2%)	3 (1.1%)	2 (0.6%)	0
Prothrombinex	1 (0.4%)	0	0	1 (0.3%)	0
Carbazochrome	0	0	1 (0.4%)	0	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Eltrombopag	0	0	0	0	1 (1.0%)
Factor viii (antihaemophilic factor)	0	0	1 (0.4%)	0	0
Antifibrinolytics	2 (0.8%)	13 (5.3%)	6 (2.1%)	3 (0.9%)	1 (1.0%)
Tranexamic acid	2 (0.8%)	13 (5.3%)	5 (1.8%)	3 (0.9%)	0
Aminocaproic acid	0	0	0	1 (0.3%)	1 (1.0%)
Amino acids	0	0	1 (0.4%)	0	0
Muscle relaxants	4 (1.7%)	10 (4.1%)	16 (5.7%)	9 (2.8%)	8 (7.8%)
Muscle relaxants, centrally acting agents	3 (1.3%)	7 (2.9%)	14 (5.0%)	8 (2.5%)	5 (4.9%)
Baclofen	1 (0.4%)	2 (0.8%)	7 (2.5%)	5 (1.6%)	1 (1.0%)
Cyclobenzaprine	0	2 (0.8%)	0	3 (0.9%)	3 (2.9%)
Methocarbamol	0	0	0	1 (0.3%)	0
Norgesic /00070401/	0	0	0	1 (0.3%)	0
Tizanidine	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Chlormezanone	0	0	1 (0.4%)	0	0
Chlorzoxazone	0	0	3 (1.1%)	0	0
Dorflex	1 (0.4%)	0	0	0	0
Eperisone	0	1 (0.4%)	2 (0.7%)	0	0
Mephenesin	0	0	0	0	1 (1.0%)
Thiocolchicoside	0	0	1 (0.4%)	0	0
Tolperisone	1 (0.4%)	1 (0.4%)	0	0	0
Muscle relaxants, peripherally acting agents	1 (0.4%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	3 (2.9%)
Cisatracurium	0	1 (0.4%)	0	1 (0.3%)	0
Atracurium	0	0	2 (0.7%)	0	0
Rocuronium	1 (0.4%)	2 (0.8%)	0	0	1 (1.0%)
Suxamethonium	0	1 (0.4%)	0	0	2 (1.9%)
Other drugs for disorders of the musculo-skeletal system	3 (1.3%)	4 (1.6%)	2 (0.7%)	8 (2.5%)	2 (1.9%)
Other drugs for disorders of the musculo-skeletal system	3 (1.3%)	4 (1.6%)	2 (0.7%)	8 (2.5%)	2 (1.9%)
Quinine	0	1 (0.4%)	0	5 (1.6%)	0
Hydroquinine	0	0	1 (0.4%)	2 (0.6%)	0
Quinamm /00172101/	0	0	0	1 (0.3%)	0
Serrapeptase	1 (0.4%)	0	0	1 (0.3%)	0
Cytidine	0	1 (0.4%)	0	0	0
Hexaquine	0	0	1 (0.4%)	0	2 (1.9%)
Keltican n	2 (0.8%)	2 (0.8%)	0	0	0
Nucleo cmp forte /06294601/	0	1 (0.4%)	0	0	0
Other drugs for disorders of the musculo-skel	0	1 (0.4%)	0	0	0
Sex hormones and modulators of the genital system	4 (1.7%)	4 (1.6%)	7 (2.5%)	8 (2.5%)	2 (1.9%)
Hormonal contraceptives for systemic use	4 (1.7%)	4 (1.6%)	6 (2.1%)	7 (2.2%)	1 (1.0%)

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Megestrol	4 (1.7%)	4 (1.6%)	6 (2.1%)	6 (1.9%)	1 (1.0%)
Femodene	0	0	0	1 (0.3%)	0
Androgens	0	0	0	1 (0.3%)	1 (1.0%)
Testosterone	0	0	0	1 (0.3%)	1 (1.0%)
Estrogens	0	0	1 (0.4%)	0	0
Estriol	0	0	1 (0.4%)	0	0
Vasoprotectives	3 (1.3%)	9 (3.7%)	5 (1.8%)	8 (2.5%)	2 (1.9%)
Agents for treatment of hemorrhoids and anal fissures for topical use	2 (0.8%)	2 (0.8%)	4 (1.4%)	7 (2.2%)	2 (1.9%)
Anamantle hc /02344701/	0	0	0	1 (0.3%)	0
Corticosteroid nos	0	0	1 (0.4%)	1 (0.3%)	0
Doloproct /00951901/	0	0	0	1 (0.3%)	0
Ego soov it	0	0	0	1 (0.3%)	0
Fluocinonide	0	0	0	1 (0.3%)	0
Hemcort h.c.	0	0	0	1 (0.3%)	0
Other agents for treatment of hemorrhoids and	0	0	0	1 (0.3%)	0
Xyloproct plus	0	0	0	1 (0.3%)	0
Anusol /01604901/	0	0	0	0	1 (1.0%)
Corticosteroids	0	0	0	0	1 (1.0%)
Levan h	0	1 (0.4%)	1 (0.4%)	0	0
Pramocaine	0	1 (0.4%)	1 (0.4%)	0	0
Proctolyn	1 (0.4%)	0	0	0	0
Rectinol	0	0	1 (0.4%)	0	0
Scheriproct /01814801/	1 (0.4%)	0	0	0	0
Capillary stabilizing agents	1 (0.4%)	7 (2.9%)	1 (0.4%)	1 (0.3%)	0
Diosmin	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Ascorutin	0	4 (1.6%)	0	0	0
Escin	1 (0.4%)	2 (0.8%)	0	0	0
Other alimentary tract and metabolism products	6 (2.5%)	24 (9.9%)	5 (1.8%)	7 (2.2%)	3 (2.9%)
Other alimentary tract and metabolism products	6 (2.5%)	23 (9.5%)	5 (1.8%)	6 (1.9%)	3 (2.9%)
Phosphorus	1 (0.4%)	0	0	3 (0.9%)	0
Clostridium butyricum	0	0	0	2 (0.6%)	0
Probiotics nos	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
Ademetionine	1 (0.4%)	5 (2.1%)	2 (0.7%)	0	0
Glycine	0	1 (0.4%)	0	0	0
Levocarnitine	0	0	0	0	1 (1.0%)
Thioctic acid	4 (1.7%)	20 (8.2%)	1 (0.4%)	0	0
Ubidecarenone	0	0	1 (0.4%)	0	0
Uncoded	0	1 (0.4%)	0	1 (0.3%)	0

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	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Other alimentary tract and metabolism product	0	0	0	1 (0.3%)	0
Fibre, dietary	0	1 (0.4%)	0	0	0
Antihypertensives	2 (0.8%)	5 (2.1%)	2 (0.7%)	5 (1.6%)	2 (1.9%)
Antiadrenergic agents, peripherally acting	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
Doxazosin	0	0	1 (0.4%)	1 (0.3%)	0
Urapidil	0	1 (0.4%)	0	1 (0.3%)	0
Antiadrenergic agents, centrally acting	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
Clonidine	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
Moxonidine	1 (0.4%)	0	0	0	0
Arteriolar smooth muscle, agents acting on	0	2 (0.8%)	0	1 (0.3%)	1 (1.0%)
Nitroprusside	0	0	0	1 (0.3%)	0
Hydralazine	0	2 (0.8%)	0	0	1 (1.0%)
Other antihypertensives	0	0	0	1 (0.3%)	0
Tadalafil	0	0	0	1 (0.3%)	0
Uncoded	1 (0.4%)	0	0	0	0
Antihypertensives	1 (0.4%)	0	0	0	0
Digestives, incl. enzymes	1 (0.4%)	7 (2.9%)	4 (1.4%)	5 (1.6%)	0
Digestives, incl. enzymes	1 (0.4%)	7 (2.9%)	4 (1.4%)	5 (1.6%)	0
Pangest f	0	0	0	2 (0.6%)	0
Beszyme	0	0	1 (0.4%)	1 (0.3%)	0
Enzyme preparations	0	0	0	1 (0.3%)	0
Pancreatin	0	6 (2.5%)	1 (0.4%)	1 (0.3%)	0
Citrarginine	0	1 (0.4%)	0	0	0
Citric acid	0	0	1 (0.4%)	0	0
Mezym /00506801/	0	1 (0.4%)	0	0	0
Pancreas extract	0	1 (0.4%)	0	0	0
Pankreosil	1 (0.4%)	0	0	0	0
Voltmie	0	0	1 (0.4%)	0	0
Other hematological agents	0	0	3 (1.1%)	5 (1.6%)	0
Other hematological agents	0	0	3 (1.1%)	5 (1.6%)	0
Varidase	0	0	2 (0.7%)	3 (0.9%)	0
Bromelains	0	0	1 (0.4%)	1 (0.3%)	0
Pronase	0	0	0	1 (0.3%)	0
Stomatological preparations	3 (1.3%)	3 (1.2%)	4 (1.4%)	5 (1.6%)	3 (2.9%)
Stomatological preparations	3 (1.3%)	3 (1.2%)	4 (1.4%)	5 (1.6%)	3 (2.9%)
Frubienzym	0	0	0	1 (0.3%)	0
Hexetidine	0	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
Magic mouthwash	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
Periodil /02665801/	0	0	0	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Stomatologicals, mouth preparations	0	0	0	1 (0.3%)	0
Difflam mouth	0	0	1 (0.4%)	0	0
Difflam-c	3 (1.3%)	1 (0.4%)	0	0	0
Eludril /02860401/	0	0	0	0	1 (1.0%)
Bile and liver therapy	5 (2.1%)	6 (2.5%)	2 (0.7%)	4 (1.3%)	0
Bile therapy	1 (0.4%)	3 (1.2%)	1 (0.4%)	3 (0.9%)	0
Ursodeoxycholic acid	1 (0.4%)	3 (1.2%)	1 (0.4%)	3 (0.9%)	0
Liver therapy, lipotropics	4 (1.7%)	4 (1.6%)	1 (0.4%)	1 (0.3%)	0
Phosphogliv /06724301/	0	0	1 (0.4%)	1 (0.3%)	0
Arginine glutamate	2 (0.8%)	4 (1.6%)	0	0	0
Glutargin /01615901/	1 (0.4%)	0	0	0	0
Liver therapy	0	2 (0.8%)	0	0	0
Ornithine	0	1 (0.4%)	0	0	0
Silibinin	1 (0.4%)	0	0	0	0
Anti-acne preparations	0	1 (0.4%)	0	3 (0.9%)	0
Anti-acne preparations for topical use	0	1 (0.4%)	0	3 (0.9%)	0
Clindamycin	0	0	0	1 (0.3%)	0
Dapsone	0	1 (0.4%)	0	1 (0.3%)	0
Tretinoin	0	0	0	1 (0.3%)	0
Anti-parkinson drugs	1 (0.4%)	0	0	3 (0.9%)	1 (1.0%)
Dopaminergic agents	1 (0.4%)	0	0	3 (0.9%)	1 (1.0%)
Pramipexole	1 (0.4%)	0	0	2 (0.6%)	0
Stalevo /01631201/	0	0	0	1 (0.3%)	0
Amantadine	0	0	0	0	1 (1.0%)
Antineoplastic agents	0	0	4 (1.4%)	3 (0.9%)	0
Antimetabolites	0	0	2 (0.7%)	2 (0.6%)	0
Azacitidine	0	0	0	1 (0.3%)	0
Fluorouracil	0	0	2 (0.7%)	1 (0.3%)	0
Cytotoxic antibiotics and related substances	0	0	1 (0.4%)	1 (0.3%)	0
Doxorubicin	0	0	1 (0.4%)	1 (0.3%)	0
Other antineoplastic agents	0	0	1 (0.4%)	0	0
Calcium folinate w/fluorouracil/iri/08195201/	0	0	1 (0.4%)	0	0
Calcium homeostasis	0	0	1 (0.4%)	3 (0.9%)	4 (3.9%)
Anti-parathyroid agents	0	0	1 (0.4%)	3 (0.9%)	4 (3.9%)
Calcitonin	0	0	1 (0.4%)	3 (0.9%)	4 (3.9%)
Cinacalcet	0	0	0	0	1 (1.0%)
Other nervous system drugs	4 (1.7%)	7 (2.9%)	6 (2.1%)	3 (0.9%)	2 (1.9%)
Antivertigo preparations	0	3 (1.2%)	4 (1.4%)	1 (0.3%)	0
Acetylleucine	0	0	0	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Antivert /07534501/	0	0	1 (0.4%)	0	0
Betahistine	0	2 (0.8%)	1 (0.4%)	0	0
Flunarizine	0	1 (0.4%)	2 (0.7%)	0	0
Other nervous system drugs	0	0	1 (0.4%)	1 (0.3%)	0
Edaravone	0	0	0	1 (0.3%)	0
Fampridine	0	0	1 (0.4%)	0	0
Parasympathomimetics	2 (0.8%)	2 (0.8%)	0	1 (0.3%)	1 (1.0%)
Bethanechol	0	0	0	1 (0.3%)	0
Choline alfoscerate	1 (0.4%)	1 (0.4%)	0	0	0
Neostigmine	1 (0.4%)	1 (0.4%)	0	0	1 (1.0%)
Drugs used in addictive disorders	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	1 (1.0%)
Methadone	0	2 (0.8%)	1 (0.4%)	0	1 (1.0%)
Naloxone	1 (0.4%)	0	0	0	0
Nicotine	1 (0.4%)	0	0	0	0
Peripheral vasodilators	2 (0.8%)	6 (2.5%)	4 (1.4%)	3 (0.9%)	0
Peripheral vasodilators	2 (0.8%)	6 (2.5%)	4 (1.4%)	3 (0.9%)	0
Histamine	0	0	0	1 (0.3%)	0
Methylethylpiridinol	2 (0.8%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
Nicergoline	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Pentoxifylline	0	4 (1.6%)	1 (0.4%)	0	0
Xantinol nicotinate	0	1 (0.4%)	0	0	0
Topical products for joint and muscular pain	0	0	4 (1.4%)	3 (0.9%)	0
Topical products for joint and muscular pain	0	0	4 (1.4%)	3 (0.9%)	0
Etofenamate	0	0	0	1 (0.3%)	0
Felbinac	0	0	0	1 (0.3%)	0
Salicylic acid	0	0	0	1 (0.3%)	0
Capsaicin	0	0	3 (1.1%)	0	0
Menthol w/methyl salicylate	0	0	1 (0.4%)	0	0
Antiseptics and disinfectants	1 (0.4%)	8 (3.3%)	5 (1.8%)	2 (0.6%)	0
Antiseptics and disinfectants	1 (0.4%)	8 (3.3%)	5 (1.8%)	2 (0.6%)	0
Dequalinium	0	0	2 (0.7%)	1 (0.3%)	0
Phenylmercuric borate	0	0	0	1 (0.3%)	0
Alkonium	0	1 (0.4%)	0	0	0
Benzethonium	0	0	1 (0.4%)	0	0
Boric acid	1 (0.4%)	2 (0.8%)	0	0	0
Chloroxine	0	2 (0.8%)	0	0	0
Decamethoxin	0	3 (1.2%)	0	0	0
Dermalex	0	0	1 (0.4%)	0	0
Hexamidine	0	0	1 (0.4%)	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Hydrogen peroxide	0	1 (0.4%)	0	0	0
Iodine	0	1 (0.4%)	0	0	0
Nitrofural	0	1 (0.4%)	0	0	0
Savlon hospital	0	0	1 (0.4%)	0	0
Contrast media	0	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
Magnetic resonance imaging contrast media	0	0	1 (0.4%)	1 (0.3%)	0
Gadobutrol	0	0	0	1 (0.3%)	0
Gadobenic acid	0	0	1 (0.4%)	0	0
X-ray contrast media, iodinated	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Gastrografin	0	0	0	1 (0.3%)	0
Iohexol	0	0	1 (0.4%)	0	0
Iomeprol	0	1 (0.4%)	0	0	0
Corticosteroids for systemic use	4 (1.7%)	1 (0.4%)	0	2 (0.6%)	0
Corticosteroids for systemic use, plain	4 (1.7%)	0	0	1 (0.3%)	0
Corticosteroids for systemic use, plain	0	0	0	1 (0.3%)	0
Fludrocortisone	4 (1.7%)	0	0	0	0
Uncoded	0	1 (0.4%)	0	1 (0.3%)	0
Corticosteroids for systemic use	0	0	0	1 (0.3%)	0
Corticosteroids	0	1 (0.4%)	0	0	0
Preparations for treatment of wounds and ulcers	0	0	2 (0.7%)	2 (0.6%)	0
Cicatrizants	0	0	0	1 (0.3%)	0
Vita merfen	0	0	0	1 (0.3%)	0
Uncoded	0	0	1 (0.4%)	1 (0.3%)	0
Cb /01734801/	0	0	1 (0.4%)	1 (0.3%)	0
Enzymes	0	0	1 (0.4%)	0	0
Collagenase	0	0	1 (0.4%)	0	0
Thyroid therapy	0	4 (1.6%)	6 (2.1%)	2 (0.6%)	0
Thyroid preparations	0	3 (1.2%)	5 (1.8%)	2 (0.6%)	0
Levothyroxine	0	3 (1.2%)	5 (1.8%)	2 (0.6%)	0
Antithyroid preparations	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
Carbimazole	0	1 (0.4%)	0	1 (0.3%)	0
Sodium perchlorate	0	1 (0.4%)	0	1 (0.3%)	0
Thiamazole	0	0	1 (0.4%)	0	0
All other non-therapeutic products	0	1 (0.4%)	0	1 (0.3%)	0
All other non-therapeutic products	0	1 (0.4%)	0	1 (0.3%)	0
All other non-therapeutic products	0	0	0	1 (0.3%)	0
Blood, calf, deprot., lmw portion	0	1 (0.4%)	0	0	0
Antimycobacterials	0	0	2 (0.7%)	1 (0.3%)	0
Drugs for treatment of tuberculosis	0	0	2 (0.7%)	1 (0.3%)	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Rifampicin	0	0	1 (0.4%)	1 (0.3%)	0
Rifinah	0	0	1 (0.4%)	0	0
Medicated dressings	0	0	0	1 (0.3%)	0
Medicated dressings	0	0	0	1 (0.3%)	0
Medicated dressings with antiinfectives	0	0	0	1 (0.3%)	0
Tonics	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
Tonics	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
Curcumin	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
Dietary supplement	0	0	0	0	1 (1.0%)
Anthelmintics	0	1 (0.4%)	0	0	0
Antinematodal agents	0	1 (0.4%)	0	0	0
Ivermectin	0	1 (0.4%)	0	0	0
Endocrine therapy	1 (0.4%)	1 (0.4%)	0	0	0
Hormone antagonists and related agents	1 (0.4%)	1 (0.4%)	0	0	0
Tamoxifen	1 (0.4%)	0	0	0	0
Toremifene	0	1 (0.4%)	0	0	0
Immunosuppressants	0	0	1 (0.4%)	0	0
Immunosuppressants	0	0	1 (0.4%)	0	0
Tacrolimus	0	0	1 (0.4%)	0	0
Ophthalmological and otological preparations	0	1 (0.4%)	0	0	0
Corticosteroids and antiinfectives in combination	0	1 (0.4%)	0	0	0
Netildex	0	1 (0.4%)	0	0	0
Other dermatological preparations	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	1 (1.0%)
Other dermatological preparations	0	0	2 (0.7%)	0	0
Guaiazulene	0	0	2 (0.7%)	0	0
Uncoded	1 (0.4%)	1 (0.4%)	0	0	1 (1.0%)
Other dermatological preparations	1 (0.4%)	1 (0.4%)	0	0	1 (1.0%)
Otologicals	0	2 (0.8%)	2 (0.7%)	0	0
Corticosteroids	0	0	1 (0.4%)	0	0
Dexamethasone	0	0	1 (0.4%)	0	0
Corticosteroids and antiinfectives in combination	0	1 (0.4%)	1 (0.4%)	0	0
Auricularum	0	0	1 (0.4%)	0	0
Cortison chemicetina	0	1 (0.4%)	0	0	0
Other otologicals	0	1 (0.4%)	0	0	0
Sea water	0	1 (0.4%)	0	0	0
Pituitary and hypothalamic hormones and analogues	1 (0.4%)	0	3 (1.1%)	0	0
Anterior pituitary lobe hormones and analogues	1 (0.4%)	0	1 (0.4%)	0	0
Corticotropin	0	0	1 (0.4%)	0	0
Tetracosactide	1 (0.4%)	0	0	0	0

TSICM01A: Summary of Concomitant Medications with Onset During Study Treatment by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Hypothalamic hormones	0	0	1 (0.4%)	0	0
Octreotide	0	0	1 (0.4%)	0	0
Posterior pituitary lobe hormones	0	0	1 (0.4%)	0	0
Vasopressin	0	0	1 (0.4%)	0	0
Therapeutic radiopharmaceuticals	0	1 (0.4%)	0	0	0
Other therapeutic radiopharmaceuticals	0	1 (0.4%)	0	0	0
Iodine (131 i)	0	1 (0.4%)	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: Corticosteroids for systemic use are excluded.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSICM01A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSICM01A.SAS] 01JUN2016, 10:46

表 2.7.4-付録-22 Summary of Concomitant Medication; All-treated Analysis Set (Study 54767414MMY1005)

TSICM01: Summary of Concomitant Medication; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Total number of subjects with 1 or more concomitant medications	8 (100.0%)
Therapeutic class/pharmacologic class/preferred term	
Drugs for acid related disorders	8 (100.0%)
Drugs for peptic ulcer and gastro-oesophageal reflux disease (gord)	8 (100.0%)
Lansoprazole	4 (50.0%)
Rabeprazole sodium	2 (25.0%)
Rebamipide	2 (25.0%)
Famotidine	1 (12.5%)
Omeprazole	1 (12.5%)
Proton pump inhibitors	1 (12.5%)
Rabeprazole	1 (12.5%)
Sodium alginate	1 (12.5%)
Sulpiride	1 (12.5%)
Antacids	5 (62.5%)
Magnesium oxide	5 (62.5%)
Analgesics	7 (87.5%)
Other analgesics and antipyretics	7 (87.5%)
Paracetamol	5 (62.5%)
Acetylsalicylic acid	2 (25.0%)
Pregabalin	2 (25.0%)
Pa	1 (12.5%)
Opioids	3 (37.5%)
Oxycodone hydrochloride	2 (25.0%)
Tramadol hydrochloride	1 (12.5%)
Antivirals for systemic use	7 (87.5%)
Direct acting antivirals	7 (87.5%)
Aciclovir	6 (75.0%)
Oseltamivir phosphate	1 (12.5%)
Valaciclovir hydrochloride	1 (12.5%)
Antibacterials for systemic use	6 (75.0%)
Sulfonamides and trimethoprim	5 (62.5%)
Sulfamethoxazole	3 (37.5%)
Bactrim	2 (25.0%)
Other beta-lactam antibacterials	3 (37.5%)
Cefdinir	2 (25.0%)
Cefozopran hydrochloride	1 (12.5%)
Flomoxef sodium	1 (12.5%)
Beta-lactam antibacterials, penicillins	2 (25.0%)
Amoxicillin trihydrate	1 (12.5%)
Pip/tazo	1 (12.5%)
Quinolone antibacterials	1 (12.5%)
Ciprofloxacin hydrochloride	1 (12.5%)
Psycholeptics	5 (62.5%)
Hypnotics and sedatives	5 (62.5%)
Brotizolam	3 (37.5%)
Zopiclone	2 (25.0%)
Ramelteon	1 (12.5%)
Rilmazafone hydrochloride	1 (12.5%)
Antipsychotics	1 (12.5%)
Haloperidol	1 (12.5%)
Antiinflammatory and antirheumatic products	4 (50.0%)
Antiinflammatory and antirheumatic products, non-steroids	4 (50.0%)
Loxoprofen sodium	2 (25.0%)
Azulene	1 (12.5%)
Hachiazule /00523101/	1 (12.5%)
Pranoprofen	1 (12.5%)
Corticosteroids for systemic use	4 (50.0%)
Corticosteroids for systemic use, plain	4 (50.0%)

TSICM01: Summary of Concomitant Medication; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Hydrocortisone sodium succinate	2 (25.0%)
Hydrocortisone butyrate	1 (12.5%)
Methylprednisolone sodium succinate	1 (12.5%)
Prednisolone	1 (12.5%)
Lipid modifying agents	4 (50.0%)
Lipid modifying agents, plain	4 (50.0%)
Atorvastatin	1 (12.5%)
Atorvastatin calcium	1 (12.5%)
Eicosapentaenoic acid ethyl ester	1 (12.5%)
Pitavastatin calcium	1 (12.5%)
Simvastatin	1 (12.5%)
Vitamins	4 (50.0%)
Other plain vitamin preparations	2 (25.0%)
Pantethine	2 (25.0%)
Tocopheryl acetate	1 (12.5%)
Vitamin a and d, incl. combinations of the two	1 (12.5%)
Alfacalcidol	1 (12.5%)
Vitamin b-complex, incl. combinations	1 (12.5%)
Amino acids nos w/enzymes nos/minerals nos/ni	1 (12.5%)
Agents acting on the renin-angiotensin system	3 (37.5%)
Angiotensin ii antagonists, plain	3 (37.5%)
Valsartan	2 (25.0%)
Telmisartan	1 (12.5%)
Calcium channel blockers	3 (37.5%)
Selective calcium channel blockers with mainly vascular effects	3 (37.5%)
Amlodipine	1 (12.5%)
Amlodipine besilate	1 (12.5%)
Cilnidipine	1 (12.5%)
Drugs for constipation	3 (37.5%)
Drugs for constipation	3 (37.5%)
Sennoside a+b calcium	2 (25.0%)
Drugs for constipation	1 (12.5%)
Glycerol	1 (12.5%)
Lubiprostone	1 (12.5%)
Sennoside a+b	1 (12.5%)
Sodium picosulfate	1 (12.5%)
Mineral supplements	3 (37.5%)
Potassium	2 (25.0%)
Potassium chloride	2 (25.0%)
Calcium	1 (12.5%)
Aspartate calcium	1 (12.5%)
Unspecified herbal and traditional medicine	3 (37.5%)
Uncoded	3 (37.5%)
Shakuyakukanzoto	3 (37.5%)
Antidiarrheals, intestinal antiinflammatory/antiinfective agents	2 (25.0%)
Antidiarrheal microorganisms	1 (12.5%)
Bifidobacterium bifidum	1 (12.5%)
Antipropulsives	1 (12.5%)
Loperamide hydrochloride	1 (12.5%)
Antifungals for dermatological use	2 (25.0%)
Antifungals for topical use	2 (25.0%)
Fluconazole	2 (25.0%)
Antihistamines for systemic use	2 (25.0%)
Antihistamines for systemic use	2 (25.0%)
Chlorphenamine maleate	1 (12.5%)
Fexofenadine hydrochloride	1 (12.5%)
Olopatadine hydrochloride	1 (12.5%)
Antipsoriatics	2 (25.0%)
Antipsoriatics for topical use	2 (25.0%)
Calcipotriol	1 (12.5%)
Daivobet	1 (12.5%)
Blood substitutes and perfusion solutions	2 (25.0%)
I.v. solutions	1 (12.5%)
Ringer-lactate	1 (12.5%)

TSICM01: Summary of Concomitant Medication; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Uncoded	1 (12.5%)
Carbohydrates nos w/potassium chloride/sodium	1 (12.5%)
Diuretics	2 (25.0%)
High-ceiling diuretics	1 (12.5%)
Furosemide	1 (12.5%)
Low-ceiling diuretics, thiazides	1 (12.5%)
Trichlormethiazide	1 (12.5%)
Drugs for treatment of bone diseases	2 (25.0%)
Drugs affecting bone structure and mineralization	2 (25.0%)
Alendronate sodium	1 (12.5%)
Zoledronic acid	1 (12.5%)
Drugs used in diabetes	2 (25.0%)
Blood glucose lowering drugs, excl. insulins	2 (25.0%)
Alogliptin benzoate	1 (12.5%)
Dapagliflozin propanediol monohydrate	1 (12.5%)
Glimepiride	1 (12.5%)
Sitagliptin phosphate monohydrate	1 (12.5%)
Insulins and analogues	2 (25.0%)
Insulin human	2 (25.0%)
Insulin aspart	1 (12.5%)
Ophthalmologicals	2 (25.0%)
Surgical aids	2 (25.0%)
Hyaluronate sodium	2 (25.0%)
All other therapeutic products	1 (12.5%)
All other therapeutic products	1 (12.5%)
Calcium polystyrene sulfonate	1 (12.5%)
Antianemic preparations	1 (12.5%)
Vitamin b12 and folic acid	1 (12.5%)
Mecobalamin	1 (12.5%)
Antigout preparations	1 (12.5%)
Antigout preparations	1 (12.5%)
Allopurinol	1 (12.5%)
Antihypertensives	1 (12.5%)
Antiadrenergic agents, peripherally acting	1 (12.5%)
Doxazosin	1 (12.5%)
Antithrombotic agents	1 (12.5%)
Antithrombotic agents	1 (12.5%)
Heparinoid	1 (12.5%)
Cardiac therapy	1 (12.5%)
Other cardiac preparations	1 (12.5%)
Limaprost alfadex	1 (12.5%)
Corticosteroids, dermatological preparations	1 (12.5%)
Corticosteroids, plain	1 (12.5%)
Clobetasol propionate	1 (12.5%)
Cough and cold preparations	1 (12.5%)
Cough suppressants, excl. combinations with expectorants	1 (12.5%)
Tipepidine hibenzate	1 (12.5%)
Expectorants, excl. combinations with cough suppressants	1 (12.5%)
Carbocisteine	1 (12.5%)
Uncoded	1 (12.5%)
Cough and cold preparations	1 (12.5%)
Drugs for functional gastrointestinal disorders	1 (12.5%)
Propulsives	1 (12.5%)
Metoclopramide hydrochloride	1 (12.5%)
Drugs for obstructive airway diseases	1 (12.5%)
Adrenergics, inhalants	1 (12.5%)
Breo ellipta	1 (12.5%)
Salbutamol sulfate	1 (12.5%)
Immune sera and immunoglobulins	1 (12.5%)
Immunoglobulins	1 (12.5%)
Immunoglobulin human normal	1 (12.5%)
Other alimentary tract and metabolism products	1 (12.5%)
Other alimentary tract and metabolism products	1 (12.5%)
Clostridium butyricum	1 (12.5%)
Urologicals	1 (12.5%)

TSICM01: Summary of Concomitant Medication; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Urologicals	1 (12.5%)
Flavoxate hydrochloride	1 (12.5%)
Vasoprotectives	1 (12.5%)
Agents for treatment of hemorrhoids and anal fissures for topical use	1 (12.5%)
Borraza-g	1 (12.5%)
Neriproct	1 (12.5%)

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSICM01.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSICM01.SAS] 28SEP2016, 04:30

表 2.7.4-付録-23 Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: intent-to-treat	15	44	283	21	52	286	36	96	569
Total number of subjects with 1 or more concomitant medications	15 (100.0%)	44 (100.0%)	281 (99.3%)	20 (95.2%)	51 (98.1%)	283 (99.0%)	35 (97.2%)	95 (99.0%)	564 (99.1%)
Therapeutic class/pharmacologic class/drug									
Analgesics	15 (100.0%)	44 (100.0%)	263 (92.9%)	20 (95.2%)	50 (96.2%)	265 (92.7%)	35 (97.2%)	94 (97.9%)	528 (92.8%)
Other analgesics and antipyretics	15 (100.0%)	44 (100.0%)	252 (89.0%)	20 (95.2%)	49 (94.2%)	255 (89.2%)	35 (97.2%)	93 (96.9%)	507 (89.1%)
Acetylsalicylic acid	13 (86.7%)	38 (86.4%)	213 (75.3%)	18 (85.7%)	47 (90.4%)	218 (76.2%)	31 (86.1%)	85 (88.5%)	431 (75.7%)
Paracetamol	8 (53.3%)	29 (65.9%)	126 (44.5%)	12 (57.1%)	30 (57.7%)	140 (49.0%)	20 (55.6%)	59 (61.5%)	266 (46.7%)
Pregabalin	1 (6.7%)	7 (15.9%)	26 (9.2%)	2 (9.5%)	7 (13.5%)	25 (8.7%)	3 (8.3%)	14 (14.6%)	51 (9.0%)
Metamizole	0	0	14 (4.9%)	0	0	15 (5.2%)	0	0	29 (5.1%)
Nefopam	0	0	4 (1.4%)	0	0	3 (1.0%)	0	0	7 (1.2%)
Pa	1 (6.7%)	1 (2.3%)	1 (0.4%)	5 (23.8%)	5 (9.6%)	5 (1.7%)	6 (16.7%)	6 (6.3%)	6 (1.1%)
Lenoltec with codeine no 1	0	0	1 (0.4%)	0	0	4 (1.4%)	0	0	5 (0.9%)
Propacetamol	0	1 (2.3%)	1 (0.4%)	0	3 (5.8%)	3 (1.0%)	0	4 (4.2%)	4 (0.7%)
Solpadeine /00154101/	0	0	1 (0.4%)	0	0	3 (1.0%)	0	0	4 (0.7%)
Carbasalate	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Medinite	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Tylenol sinus medication	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Anilides	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Benylin 4 flu /01328001/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Cotylenol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Dolo mobilat /00544301/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dozol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Flupirtine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Magnyl /02350501/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
New lulu a	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Robaxisal compuesto	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Salicylic acid	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Thomapyrin n	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Topiramate	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Vicks formula 44m /01056501/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Vicks nyquil cold and flu multi-symptom	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Opioids	5 (33.3%)	31 (70.5%)	124 (43.8%)	6 (28.6%)	31 (59.6%)	122 (42.7%)	11 (30.6%)	62 (64.6%)	246 (43.2%)
Oxycodone	3 (20.0%)	12 (27.3%)	38 (13.4%)	4 (19.0%)	8 (15.4%)	42 (14.7%)	7 (19.4%)	20 (20.8%)	80 (14.1%)
Tramadol	1 (6.7%)	13 (29.5%)	38 (13.4%)	1 (4.8%)	12 (23.1%)	36 (12.6%)	2 (5.6%)	25 (26.0%)	74 (13.0%)
Morphine	0	6 (13.6%)	36 (12.7%)	0	6 (11.5%)	31 (10.8%)	0	12 (12.5%)	67 (11.8%)
Fentanyl	1 (6.7%)	5 (11.4%)	26 (9.2%)	1 (4.8%)	3 (5.8%)	27 (9.4%)	2 (5.6%)	8 (8.3%)	53 (9.3%)
Ultracet	1 (6.7%)	18 (40.9%)	23 (8.1%)	1 (4.8%)	13 (25.0%)	17 (5.9%)	2 (5.6%)	31 (32.3%)	40 (7.0%)
Panadeine co	0	0	15 (5.3%)	0	0	11 (3.8%)	0	0	26 (4.6%)
Targin	0	5 (11.4%)	8 (2.8%)	0	1 (1.9%)	9 (3.1%)	0	6 (6.3%)	17 (3.0%)
Pethidine	0	8 (18.2%)	9 (3.2%)	0	7 (13.5%)	7 (2.4%)	0	15 (15.6%)	16 (2.8%)
Hydromorphone	0	0	7 (2.5%)	0	3 (5.8%)	8 (2.8%)	0	3 (3.1%)	15 (2.6%)
Oxycocet	0	0	6 (2.1%)	0	0	6 (2.1%)	0	0	12 (2.1%)
Vicodin	0	0	4 (1.4%)	0	0	3 (1.0%)	0	0	7 (1.2%)
Dihydrocodeine	0	0	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Lamaline /01708901/	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Myprodol	0	2 (4.5%)	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	3 (3.1%)	3 (0.5%)
Procet /01554201/	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Valoron n /00628301/	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Buprenorphine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ketobemidone	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Nalbuphine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Paracetamol w/tramadol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Pentazocine	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Piritramide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antimigraine preparations	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Sumatriptan	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antibacterials for systemic use	13 (86.7%)	36 (81.8%)	235 (83.0%)	18 (85.7%)	41 (78.8%)	248 (86.7%)	31 (86.1%)	77 (80.2%)	483 (84.9%)
Beta-lactam antibacterials, penicillins	1 (6.7%)	15 (34.1%)	124 (43.8%)	4 (19.0%)	19 (36.5%)	143 (50.0%)	5 (13.9%)	34 (35.4%)	267 (46.9%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Amoxicillin	0	2 (4.5%)	52 (18.4%)	1 (4.8%)	5 (9.6%)	51 (17.8%)	1 (2.8%)	7 (7.3%)	103 (18.1%)
Augmentin /00756801/	0	3 (6.8%)	40 (14.1%)	1 (4.8%)	5 (9.6%)	49 (17.1%)	1 (2.8%)	8 (8.3%)	89 (15.6%)
Pip/tazo	0	5 (11.4%)	31 (11.0%)	2 (9.5%)	2 (3.8%)	42 (14.7%)	2 (5.6%)	7 (7.3%)	73 (12.8%)
Spektramox	0	2 (4.5%)	15 (5.3%)	0	3 (5.8%)	22 (7.7%)	0	5 (5.2%)	37 (6.5%)
Phenoxymethylpenicillin	0	0	19 (6.7%)	0	0	10 (3.5%)	0	0	29 (5.1%)
Amoxi-clavulanico	0	0	8 (2.8%)	0	1 (1.9%)	14 (4.9%)	0	1 (1.0%)	22 (3.9%)
Flucloxacillin	0	0	3 (1.1%)	0	0	10 (3.5%)	0	0	13 (2.3%)
Benzylpenicillin	0	1 (2.3%)	4 (1.4%)	0	0	5 (1.7%)	0	1 (1.0%)	9 (1.6%)
Amoxicillin w/clavulanate potassium	0	0	2 (0.7%)	0	1 (1.9%)	6 (2.1%)	0	1 (1.0%)	8 (1.4%)
Sultamicillin	1 (6.7%)	3 (6.8%)	3 (1.1%)	0	4 (7.7%)	5 (1.7%)	1 (2.8%)	7 (7.3%)	8 (1.4%)
Amoxicilina + clavulanico	0	0	3 (1.1%)	0	0	3 (1.0%)	0	0	6 (1.1%)
Piperacillin w/tazobactam /01606301/	0	1 (2.3%)	2 (0.7%)	0	1 (1.9%)	4 (1.4%)	0	2 (2.1%)	6 (1.1%)
Cloxacillin	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Piperacillin	0	1 (2.3%)	1 (0.4%)	0	2 (3.8%)	3 (1.0%)	0	3 (3.1%)	4 (0.7%)
Unacid /00917901/	0	0	0	1 (4.8%)	2 (3.8%)	3 (1.0%)	1 (2.8%)	2 (2.1%)	3 (0.5%)
Ampicillin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Dicloxacillin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Augmentin sr	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Clavulanic acid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Duocid /00892601/	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Pivampicillin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Pivmecillinam	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tazobactam	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Temocillin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Sulfonamides and trimethoprim	6 (40.0%)	17 (38.6%)	113 (39.9%)	14 (66.7%)	23 (44.2%)	122 (42.7%)	20 (55.6%)	40 (41.7%)	235 (41.3%)
Bactrim	6 (40.0%)	16 (36.4%)	106 (37.5%)	14 (66.7%)	23 (44.2%)	107 (37.4%)	20 (55.6%)	39 (40.6%)	213 (37.4%)
Co-trimoxazole	0	0	8 (2.8%)	0	0	16 (5.6%)	0	0	24 (4.2%)
Trimethoprim	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Sulfamethoxazole	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Quinolone antibacterials	8 (53.3%)	20 (45.5%)	95 (33.6%)	8 (38.1%)	19 (36.5%)	121 (42.3%)	16 (44.4%)	39 (40.6%)	216 (38.0%)
Levofloxacin	8 (53.3%)	16 (36.4%)	55 (19.4%)	6 (28.6%)	12 (23.1%)	48 (16.8%)	14 (38.9%)	28 (29.2%)	103 (18.1%)
Ciprofloxacin	0	1 (2.3%)	33 (11.7%)	0	6 (11.5%)	58 (20.3%)	0	7 (7.3%)	91 (16.0%)
Moxifloxacin	0	3 (6.8%)	11 (3.9%)	0	3 (5.8%)	24 (8.4%)	0	6 (6.3%)	35 (6.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Ofloxacin	0	0	5 (1.8%)	0	2 (3.8%)	7 (2.4%)	0	2 (2.1%)	12 (2.1%)
Norfloxacin	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Fluoroquinolones	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Garenoxacin	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Gatifloxacin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Pefloxacin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Pipemidic acid	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Tosufloxacin	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Other beta-lactam antibacterials	5 (33.3%)	19 (43.2%)	82 (29.0%)	7 (33.3%)	22 (42.3%)	100 (35.0%)	12 (33.3%)	41 (42.7%)	182 (32.0%)
Ceftriaxone	0	4 (9.1%)	22 (7.8%)	1 (4.8%)	4 (7.7%)	32 (11.2%)	1 (2.8%)	8 (8.3%)	54 (9.5%)
Cefuroxime	0	0	19 (6.7%)	0	2 (3.8%)	22 (7.7%)	0	2 (2.1%)	41 (7.2%)
Meropenem	2 (13.3%)	2 (4.5%)	13 (4.6%)	0	1 (1.9%)	20 (7.0%)	2 (5.6%)	3 (3.1%)	33 (5.8%)
Cefalexin	0	3 (6.8%)	14 (4.9%)	1 (4.8%)	1 (1.9%)	9 (3.1%)	1 (2.8%)	4 (4.2%)	23 (4.0%)
Cefazolin	1 (6.7%)	4 (9.1%)	7 (2.5%)	2 (9.5%)	3 (5.8%)	5 (1.7%)	3 (8.3%)	7 (7.3%)	12 (2.1%)
Cefepime	0	3 (6.8%)	4 (1.4%)	2 (9.5%)	3 (5.8%)	6 (2.1%)	2 (5.6%)	6 (6.3%)	10 (1.8%)
Cefditoren	0	4 (9.1%)	4 (1.4%)	0	2 (3.8%)	4 (1.4%)	0	6 (6.3%)	8 (1.4%)
Cefpodoxime	0	0	1 (0.4%)	0	4 (7.7%)	7 (2.4%)	0	4 (4.2%)	8 (1.4%)
Cefaclor	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	3 (5.8%)	3 (1.0%)	1 (2.8%)	4 (4.2%)	5 (0.9%)
Cefixime	0	0	2 (0.7%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	5 (0.9%)
Cefotaxime	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Cefadroxil	0	0	2 (0.7%)	0	1 (1.9%)	2 (0.7%)	0	1 (1.0%)	4 (0.7%)
Imipenem	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Cefcapene	0	1 (2.3%)	1 (0.4%)	2 (9.5%)	2 (3.8%)	2 (0.7%)	2 (5.6%)	3 (3.1%)	3 (0.5%)
Cefdinir	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	2 (5.6%)	2 (2.1%)	3 (0.5%)
Ceftazidime	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Ceftibuten	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Flomoxef	0	2 (4.5%)	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	3 (3.1%)	3 (0.5%)
Primaxin	0	0	3 (1.1%)	0	0	0	0	0	3 (0.5%)
Cefmetazole	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Cefotiam	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Cefozopran	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Cefradine	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Doripenem	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Ertapenem	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Aztreonam	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Cefalotin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Cefoperazone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ceftaroline fosamil	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Macrolides, lincosamides and streptogramins	2 (13.3%)	4 (9.1%)	56 (19.8%)	2 (9.5%)	8 (15.4%)	83 (29.0%)	4 (11.1%)	12 (12.5%)	139 (24.4%)
Azithromycin	0	0	29 (10.2%)	1 (4.8%)	5 (9.6%)	48 (16.8%)	1 (2.8%)	5 (5.2%)	77 (13.5%)
Clarithromycin	2 (13.3%)	2 (4.5%)	15 (5.3%)	1 (4.8%)	1 (1.9%)	21 (7.3%)	3 (8.3%)	3 (3.1%)	36 (6.3%)
Roxithromycin	0	2 (4.5%)	7 (2.5%)	0	2 (3.8%)	13 (4.5%)	0	4 (4.2%)	20 (3.5%)
Clindamycin	0	0	3 (1.1%)	0	0	8 (2.8%)	0	0	11 (1.9%)
Pristinamycin	0	0	3 (1.1%)	0	0	3 (1.0%)	0	0	6 (1.1%)
Erythromycin	0	0	2 (0.7%)	0	0	3 (1.0%)	0	0	5 (0.9%)
Spiramycin	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Josamycin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tetracyclines	0	3 (6.8%)	22 (7.8%)	0	2 (3.8%)	26 (9.1%)	0	5 (5.2%)	48 (8.4%)
Doxycycline	0	2 (4.5%)	21 (7.4%)	0	1 (1.9%)	24 (8.4%)	0	3 (3.1%)	45 (7.9%)
Tetracycline	0	1 (2.3%)	2 (0.7%)	0	1 (1.9%)	2 (0.7%)	0	2 (2.1%)	4 (0.7%)
Minocycline	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Oxytetracycline	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other antibacterials	0	1 (2.3%)	16 (5.7%)	0	2 (3.8%)	13 (4.5%)	0	3 (3.1%)	29 (5.1%)
Vancomycin	0	0	6 (2.1%)	0	1 (1.9%)	5 (1.7%)	0	1 (1.0%)	11 (1.9%)
Nitrofurantoin	0	0	4 (1.4%)	0	0	3 (1.0%)	0	0	7 (1.2%)
Teicoplanin	0	1 (2.3%)	3 (1.1%)	0	1 (1.9%)	3 (1.0%)	0	2 (2.1%)	6 (1.1%)
Linezolid	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Fosfomycin	0	0	3 (1.1%)	0	0	0	0	0	3 (0.5%)
Daptomycin	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Methenamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Aminoglycoside antibacterials	0	3 (6.8%)	15 (5.3%)	0	0	13 (4.5%)	0	3 (3.1%)	28 (4.9%)
Amikacin	0	1 (2.3%)	6 (2.1%)	0	0	8 (2.8%)	0	1 (1.0%)	14 (2.5%)
Gentamicin	0	1 (2.3%)	6 (2.1%)	0	0	4 (1.4%)	0	1 (1.0%)	10 (1.8%)
Tobramycin	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Isepamicin	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Combinations of antibacterials	0	0	4 (1.4%)	0	1 (1.9%)	6 (2.1%)	0	1 (1.0%)	10 (1.8%)
Cefoperazone w/sulbactam	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Sulperazon	0	0	1 (0.4%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	4 (0.7%)
Norflox-tz	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Amphenicols	0	0	6 (2.1%)	0	0	3 (1.0%)	0	0	9 (1.6%)
Chloramphenicol	0	0	5 (1.8%)	0	0	3 (1.0%)	0	0	8 (1.4%)
Thiamphenicol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Uncoded	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Antibiotics	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Drugs for acid related disorders	15 (100.0%)	40 (90.9%)	196 (69.3%)	18 (85.7%)	45 (86.5%)	214 (74.8%)	33 (91.7%)	85 (88.5%)	410 (72.1%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Drugs for peptic ulcer and gastro-oesophageal reflux disease (gord)	13 (86.7%)	28 (63.6%)	183 (64.7%)	16 (76.2%)	36 (69.2%)	202 (70.6%)	29 (80.6%)	64 (66.7%)	385 (67.7%)
Omeprazole	2 (13.3%)	2 (4.5%)	101 (35.7%)	0	0	83 (29.0%)	2 (5.6%)	2 (2.1%)	184 (32.3%)
Pantoprazole	0	0	27 (9.5%)	0	1 (1.9%)	38 (13.3%)	0	1 (1.0%)	65 (11.4%)
Esomeprazole	3 (20.0%)	6 (13.6%)	25 (8.8%)	3 (14.3%)	8 (15.4%)	30 (10.5%)	6 (16.7%)	14 (14.6%)	55 (9.7%)
Ranitidine	1 (6.7%)	4 (9.1%)	17 (6.0%)	1 (4.8%)	4 (7.7%)	22 (7.7%)	2 (5.6%)	8 (8.3%)	39 (6.9%)
Lansoprazole	3 (20.0%)	4 (9.1%)	13 (4.6%)	5 (23.8%)	7 (13.5%)	21 (7.3%)	8 (22.2%)	11 (11.5%)	34 (6.0%)
Famotidine	2 (13.3%)	9 (20.5%)	10 (3.5%)	3 (14.3%)	12 (23.1%)	20 (7.0%)	5 (13.9%)	21 (21.9%)	30 (5.3%)
Rabeprazole	3 (20.0%)	4 (9.1%)	8 (2.8%)	3 (14.3%)	5 (9.6%)	10 (3.5%)	6 (16.7%)	9 (9.4%)	18 (3.2%)
Sucralfate	0	1 (2.3%)	1 (0.4%)	1 (4.8%)	4 (7.7%)	5 (1.7%)	1 (2.8%)	5 (5.2%)	6 (1.1%)
Rebamipide	1 (6.7%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	3 (5.8%)	3 (1.0%)	2 (5.6%)	5 (5.2%)	5 (0.9%)
Gualenic acid	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Teprenone	0	3 (6.8%)	3 (1.1%)	0	0	0	0	3 (3.1%)	3 (0.5%)
Lafutidine	0	0	0	1 (4.8%)	2 (3.8%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Other drugs for peptic ulcer and gastro-oesop	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Proton pump inhibitors	0	0	0	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Irsogladine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Nizatidine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Polaprezinc	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Sulpiride	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antacids	9 (60.0%)	30 (68.2%)	44 (15.5%)	14 (66.7%)	31 (59.6%)	68 (23.8%)	23 (63.9%)	61 (63.5%)	112 (19.7%)
Magnesium oxide	9 (60.0%)	22 (50.0%)	23 (8.1%)	14 (66.7%)	27 (51.9%)	31 (10.8%)	23 (63.9%)	49 (51.0%)	54 (9.5%)
Calcium carbonate	0	4 (9.1%)	14 (4.9%)	0	1 (1.9%)	15 (5.2%)	0	5 (5.2%)	29 (5.1%)
Magnesium hydroxide	0	3 (6.8%)	5 (1.8%)	0	2 (3.8%)	9 (3.1%)	0	5 (5.2%)	14 (2.5%)
Magnesium carbonate	0	0	1 (0.4%)	0	0	6 (2.1%)	0	0	7 (1.2%)
Almagate	0	4 (9.1%)	4 (1.4%)	0	2 (3.8%)	2 (0.7%)	0	6 (6.3%)	6 (1.1%)
Aludrox /00082501/	0	0	1 (0.4%)	0	0	4 (1.4%)	0	0	5 (0.9%)
Diovol /00018101/	0	0	0	0	1 (1.9%)	2 (0.7%)	0	1 (1.0%)	2 (0.4%)
Gaviscon /01405501/	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Topaal /00894301/	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Topal	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Antacids with antiflatulents	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Hydrotalcite	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Magnesia komp n	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Mylanta /00036701/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Rani-q /01722401/	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Simeco /00416501/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antivirals for systemic use	9 (60.0%)	25 (56.8%)	155 (54.8%)	15 (71.4%)	34 (65.4%)	200 (69.9%)	24 (66.7%)	59 (61.5%)	355 (62.4%)
Direct acting antivirals	9 (60.0%)	25 (56.8%)	155 (54.8%)	15 (71.4%)	34 (65.4%)	200 (69.9%)	24 (66.7%)	59 (61.5%)	355 (62.4%)
Aciclovir	7 (46.7%)	15 (34.1%)	89 (31.4%)	11 (52.4%)	22 (42.3%)	127 (44.4%)	18 (50.0%)	37 (38.5%)	216 (38.0%)
Valaciclovir	2 (13.3%)	9 (20.5%)	60 (21.2%)	4 (19.0%)	9 (17.3%)	63 (22.0%)	6 (16.7%)	18 (18.8%)	123 (21.6%)
Oseltamivir	0	3 (6.8%)	18 (6.4%)	0	2 (3.8%)	28 (9.8%)	0	5 (5.2%)	46 (8.1%)
Zanamivir	0	1 (2.3%)	2 (0.7%)	0	1 (1.9%)	4 (1.4%)	0	2 (2.1%)	6 (1.1%)
Famciclovir	0	2 (4.5%)	2 (0.7%)	0	2 (3.8%)	3 (1.0%)	0	4 (4.2%)	5 (0.9%)
Entecavir	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Ganciclovir	0	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Imidazolyl ethanamide pentandioic acid	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Lamivudine	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Ribavirin	0	0	0	0	1 (1.9%)	2 (0.7%)	0	1 (1.0%)	2 (0.4%)
Peramivir	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Valganciclovir	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Vidarabine	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Drugs for treatment of bone diseases	4 (26.7%)	16 (36.4%)	139 (49.1%)	4 (19.0%)	20 (38.5%)	138 (48.3%)	8 (22.2%)	36 (37.5%)	277 (48.7%)
Drugs affecting bone structure and mineralization	4 (26.7%)	16 (36.4%)	139 (49.1%)	4 (19.0%)	20 (38.5%)	138 (48.3%)	8 (22.2%)	36 (37.5%)	277 (48.7%)
Zoledronic acid	3 (20.0%)	9 (20.5%)	82 (29.0%)	3 (14.3%)	11 (21.2%)	84 (29.4%)	6 (16.7%)	20 (20.8%)	166 (29.2%)
Pamidronic acid	0	7 (15.9%)	55 (19.4%)	0	8 (15.4%)	55 (19.2%)	0	15 (15.6%)	110 (19.3%)
Clodronic acid	0	0	10 (3.5%)	0	0	3 (1.0%)	0	0	13 (2.3%)
Alendronic acid	1 (6.7%)	1 (2.3%)	3 (1.1%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Bisphosphonates	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Ibandronic acid	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Denosumab	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Etidronic acid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Risedronic acid	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Antithrombotic agents	2 (13.3%)	5 (11.4%)	113 (39.9%)	8 (38.1%)	10 (19.2%)	125 (43.7%)	10 (27.8%)	15 (15.6%)	238 (41.8%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Antithrombotic agents	2 (13.3%)	5 (11.4%)	113 (39.9%)	8 (38.1%)	10 (19.2%)	125 (43.7%)	10 (27.8%)	15 (15.6%)	238 (41.8%)
Enoxaparin	0	0	53 (18.7%)	0	0	56 (19.6%)	0	0	109 (19.2%)
Dalteparin	0	0	16 (5.7%)	1 (4.8%)	1 (1.9%)	19 (6.6%)	1 (2.8%)	1 (1.0%)	35 (6.2%)
Tinzaparin	0	0	16 (5.7%)	0	0	17 (5.9%)	0	0	33 (5.8%)
Warfarin	0	0	13 (4.6%)	2 (9.5%)	2 (3.8%)	16 (5.6%)	2 (5.6%)	2 (2.1%)	29 (5.1%)
Heparin	0	2 (4.5%)	12 (4.2%)	1 (4.8%)	3 (5.8%)	9 (3.1%)	1 (2.8%)	5 (5.2%)	21 (3.7%)
Rivaroxaban	0	0	10 (3.5%)	1 (4.8%)	1 (1.9%)	5 (1.7%)	1 (2.8%)	1 (1.0%)	15 (2.6%)
Clopidogrel	0	1 (2.3%)	4 (1.4%)	0	0	9 (3.1%)	0	1 (1.0%)	13 (2.3%)
Heparinoid	2 (13.3%)	3 (6.8%)	3 (1.1%)	5 (23.8%)	5 (9.6%)	6 (2.1%)	7 (19.4%)	8 (8.3%)	9 (1.6%)
Nadroparin	0	0	3 (1.1%)	0	0	5 (1.7%)	0	0	8 (1.4%)
Fondaparinux	0	0	3 (1.1%)	0	0	4 (1.4%)	0	0	7 (1.2%)
Bemiparin	0	0	3 (1.1%)	0	0	3 (1.0%)	0	0	6 (1.1%)
Fluindione	0	0	4 (1.4%)	0	0	1 (0.3%)	0	0	5 (0.9%)
Apixaban	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Acenocoumarol	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Cilostazol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Edoxaban	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Phenprocoumon	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Prasugrel	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ticagrelor	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Tirofiban	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Psycholeptics	8 (53.3%)	25 (56.8%)	103 (36.4%)	10 (47.6%)	24 (46.2%)	114 (39.9%)	18 (50.0%)	49 (51.0%)	217 (38.1%)
Hypnotics and sedatives	7 (46.7%)	17 (38.6%)	63 (22.3%)	8 (38.1%)	17 (32.7%)	69 (24.1%)	15 (41.7%)	34 (35.4%)	132 (23.2%)
Zopiclone	1 (6.7%)	3 (6.8%)	17 (6.0%)	0	1 (1.9%)	26 (9.1%)	1 (2.8%)	4 (4.2%)	43 (7.6%)
Zolpidem	0	7 (15.9%)	19 (6.7%)	2 (9.5%)	8 (15.4%)	15 (5.2%)	2 (5.6%)	15 (15.6%)	34 (6.0%)
Midazolam	0	1 (2.3%)	10 (3.5%)	0	0	13 (4.5%)	0	1 (1.0%)	23 (4.0%)
Brotizolam	4 (26.7%)	4 (9.1%)	7 (2.5%)	5 (23.8%)	5 (9.6%)	9 (3.1%)	9 (25.0%)	9 (9.4%)	16 (2.8%)
Temazepam	0	0	7 (2.5%)	0	0	4 (1.4%)	0	0	11 (1.9%)
Lormetazepam	0	0	4 (1.4%)	0	0	3 (1.0%)	0	0	7 (1.2%)
Estazolam	0	2 (4.5%)	2 (0.7%)	0	3 (5.8%)	3 (1.0%)	0	5 (5.2%)	5 (0.9%)
Melatonin	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Triazolam	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Flunitrazepam	0	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Alteril	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Eszopiclone	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Nitrazepam	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Propiomazine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ramelteon	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Rilmazafone	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Serenade /00857801/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Anxiolytics	3 (20.0%)	15 (34.1%)	59 (20.8%)	3 (14.3%)	12 (23.1%)	56 (19.6%)	6 (16.7%)	27 (28.1%)	115 (20.2%)
Lorazepam	0	5 (11.4%)	25 (8.8%)	0	3 (5.8%)	26 (9.1%)	0	8 (8.3%)	51 (9.0%)
Alprazolam	0	4 (9.1%)	13 (4.6%)	0	3 (5.8%)	10 (3.5%)	0	7 (7.3%)	23 (4.0%)
Hydroxyzine	2 (13.3%)	5 (11.4%)	8 (2.8%)	0	3 (5.8%)	6 (2.1%)	2 (5.6%)	8 (8.3%)	14 (2.5%)
Diazepam	0	0	6 (2.1%)	1 (4.8%)	1 (1.9%)	7 (2.4%)	1 (2.8%)	1 (1.0%)	13 (2.3%)
Oxazepam	0	0	2 (0.7%)	0	0	8 (2.8%)	0	0	10 (1.8%)
Bromazepam	0	0	4 (1.4%)	0	0	1 (0.3%)	0	0	5 (0.9%)
Buspirone	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Clotiazepam	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	2 (5.6%)	2 (2.1%)	3 (0.5%)
Ethyl loflazepate	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Etizolam	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Phenazepam	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antipsychotics	3 (20.0%)	5 (11.4%)	17 (6.0%)	3 (14.3%)	6 (11.5%)	20 (7.0%)	6 (16.7%)	11 (11.5%)	37 (6.5%)
Prochlorperazine	1 (6.7%)	1 (2.3%)	5 (1.8%)	1 (4.8%)	3 (5.8%)	10 (3.5%)	2 (5.6%)	4 (4.2%)	15 (2.6%)
Haloperidol	0	2 (4.5%)	5 (1.8%)	0	0	3 (1.0%)	0	2 (2.1%)	8 (1.4%)
Quetiapine	0	1 (2.3%)	4 (1.4%)	0	1 (1.9%)	3 (1.0%)	0	2 (2.1%)	7 (1.2%)
Olanzapine	1 (6.7%)	1 (2.3%)	3 (1.1%)	2 (9.5%)	2 (3.8%)	3 (1.0%)	3 (8.3%)	3 (3.1%)	6 (1.1%)
Chlorpromazine	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Levomepromazine	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Risperidone	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Amisulpride	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Paliperidone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Immunostimulants	3 (20.0%)	15 (34.1%)	81 (28.6%)	9 (42.9%)	27 (51.9%)	131 (45.8%)	12 (33.3%)	42 (43.8%)	212 (37.3%)
Immunostimulants	3 (20.0%)	15 (34.1%)	81 (28.6%)	9 (42.9%)	27 (51.9%)	131 (45.8%)	12 (33.3%)	42 (43.8%)	212 (37.3%)
Filgrastim	3 (20.0%)	14 (31.8%)	66 (23.3%)	8 (38.1%)	22 (42.3%)	98 (34.3%)	11 (30.6%)	36 (37.5%)	164 (28.8%)
Lenograstim	0	1 (2.3%)	9 (3.2%)	2 (9.5%)	5 (9.6%)	17 (5.9%)	2 (5.6%)	6 (6.3%)	26 (4.6%)
Granulocyte colony stimulating factor	0	0	6 (2.1%)	0	2 (3.8%)	19 (6.6%)	0	2 (2.1%)	25 (4.4%)
Pegfilgrastim	0	0	2 (0.7%)	0	0	6 (2.1%)	0	0	8 (1.4%)
Lipegfilgrastim	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Tilorone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Mineral supplements	0	10 (22.7%)	94 (33.2%)	1 (4.8%)	15 (28.8%)	115 (40.2%)	1 (2.8%)	25 (26.0%)	209 (36.7%)
Calcium	0	6 (13.6%)	54 (19.1%)	1 (4.8%)	10 (19.2%)	59 (20.6%)	1 (2.8%)	16 (16.7%)	113 (19.9%)
Lekovit ca	0	5 (11.4%)	23 (8.1%)	0	7 (13.5%)	33 (11.5%)	0	12 (12.5%)	56 (9.8%)
Calcium	0	1 (2.3%)	21 (7.4%)	0	0	14 (4.9%)	0	1 (1.0%)	35 (6.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Calcium gluconate	0	0	3 (1.1%)	0	2 (3.8%)	6 (2.1%)	0	2 (2.1%)	9 (1.6%)
Calcium w/vitamin d nos	0	0	4 (1.4%)	0	0	2 (0.7%)	0	0	6 (1.1%)
Calcium d3 /01483701/	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Calcium carbonate w/vitamin d nos	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Calcium sandoz forte d	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Homeopatics nos	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Calcet /00637401/	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Calcifort /01767901/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Calcium citrate w/colecalciferol	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Calcium w/magnesium	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Super cal600-mg300	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Potassium	0	5 (11.4%)	41 (14.5%)	0	6 (11.5%)	54 (18.9%)	0	11 (11.5%)	95 (16.7%)
Potassium	0	5 (11.4%)	41 (14.5%)	0	5 (9.6%)	51 (17.8%)	0	10 (10.4%)	92 (16.2%)
Neutra-phos-k /00599901/	0	0	1 (0.4%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	4 (0.7%)
Kalinor-acid	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Potassium citrate	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Potassium phosphate monobasic	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Potassium-sandoz	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other mineral supplements	0	3 (6.8%)	36 (12.7%)	0	2 (3.8%)	32 (11.2%)	0	5 (5.2%)	68 (12.0%)
Magnesium	0	1 (2.3%)	23 (8.1%)	0	1 (1.9%)	14 (4.9%)	0	2 (2.1%)	37 (6.5%)
Magnesium sulfate	0	2 (4.5%)	11 (3.9%)	0	1 (1.9%)	8 (2.8%)	0	3 (3.1%)	19 (3.3%)
Magnesium citrate	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Dynamag	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Promagnor	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Chromium	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Copper	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
K-phos neutral	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Magnesium chelate	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other mineral products	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Phosphate-sandoz	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Sodium fluoride	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Uncoded	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Fosetamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Mineral supplements	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antihistamines for systemic use	7 (46.7%)	28 (63.6%)	71 (25.1%)	8 (38.1%)	31 (59.6%)	126 (44.1%)	15 (41.7%)	59 (61.5%)	197 (34.6%)
Antihistamines for systemic use	7 (46.7%)	28 (63.6%)	71 (25.1%)	8 (38.1%)	31 (59.6%)	126 (44.1%)	15 (41.7%)	59 (61.5%)	197 (34.6%)
Diphenhydramine	2 (13.3%)	6 (13.6%)	15 (5.3%)	1 (4.8%)	4 (7.7%)	32 (11.2%)	3 (8.3%)	10 (10.4%)	47 (8.3%)
Chlorphenamine	0	8 (18.2%)	9 (3.2%)	0	9 (17.3%)	22 (7.7%)	0	17 (17.7%)	31 (5.4%)
Fexofenadine	3 (20.0%)	8 (18.2%)	10 (3.5%)	2 (9.5%)	9 (17.3%)	19 (6.6%)	5 (13.9%)	17 (17.7%)	29 (5.1%)
Cetirizine	0	2 (4.5%)	14 (4.9%)	1 (4.8%)	2 (3.8%)	10 (3.5%)	1 (2.8%)	4 (4.2%)	24 (4.2%)
Dexchlorpheniramine	1 (6.7%)	1 (2.3%)	3 (1.1%)	1 (4.8%)	1 (1.9%)	14 (4.9%)	2 (5.6%)	2 (2.1%)	17 (3.0%)
Clemastine	0	0	0	0	0	14 (4.9%)	0	0	14 (2.5%)
Levocetirizine	2 (13.3%)	8 (18.2%)	8 (2.8%)	0	6 (11.5%)	6 (2.1%)	2 (5.6%)	14 (14.6%)	14 (2.5%)
Desloratadine	0	1 (2.3%)	5 (1.8%)	0	0	6 (2.1%)	0	1 (1.0%)	11 (1.9%)
Loratadine	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	9 (3.1%)	1 (2.8%)	1 (1.0%)	10 (1.8%)
Cyclizine	0	0	4 (1.4%)	0	0	4 (1.4%)	0	0	8 (1.4%)
Dimetindene	0	0	3 (1.1%)	0	0	4 (1.4%)	0	0	7 (1.2%)
Promethazine	0	0	0	0	0	7 (2.4%)	0	0	7 (1.2%)
Dimenhydrinate	0	0	4 (1.4%)	0	0	2 (0.7%)	0	0	6 (1.1%)
Ebastine	0	0	1 (0.4%)	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	3 (0.5%)
Olopatadine	0	1 (2.3%)	1 (0.4%)	2 (9.5%)	2 (3.8%)	2 (0.7%)	2 (5.6%)	3 (3.1%)	3 (0.5%)
Piprinhydrinate	0	0	0	0	3 (5.8%)	3 (1.0%)	0	3 (3.1%)	3 (0.5%)
Bepotastine	0	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Cyproheptadine	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Mequitazine	1 (6.7%)	2 (4.5%)	2 (0.7%)	0	0	0	1 (2.8%)	2 (2.1%)	2 (0.4%)
Alimemazine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Astemizole	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Difenidol	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Doxylamine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Epinastine	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Ketotifen	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Oxomemazine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Pheniramine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Triprolidine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Corticosteroids for systemic use	3 (20.0%)	15 (34.1%)	58 (20.5%)	6 (28.6%)	21 (40.4%)	115 (40.2%)	9 (25.0%)	36 (37.5%)	173 (30.4%)
Corticosteroids for systemic use, plain	3 (20.0%)	15 (34.1%)	58 (20.5%)	6 (28.6%)	21 (40.4%)	115 (40.2%)	9 (25.0%)	36 (37.5%)	173 (30.4%)
Hydrocortisone	1 (6.7%)	6 (13.6%)	16 (5.7%)	3 (14.3%)	14 (26.9%)	62 (21.7%)	4 (11.1%)	20 (20.8%)	78 (13.7%)
Dexamethasone	0	1 (2.3%)	21 (7.4%)	1 (4.8%)	2 (3.8%)	18 (6.3%)	1 (2.8%)	3 (3.1%)	39 (6.9%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Methylprednisolone	1 (6.7%)	2 (4.5%)	9 (3.2%)	2 (9.5%)	4 (7.7%)	25 (8.7%)	3 (8.3%)	6 (6.3%)	34 (6.0%)
Prednisolone	1 (6.7%)	9 (20.5%)	14 (4.9%)	1 (4.8%)	4 (7.7%)	19 (6.6%)	2 (5.6%)	13 (13.5%)	33 (5.8%)
Prednisone	0	0	13 (4.6%)	0	0	13 (4.5%)	0	0	26 (4.6%)
Betamethasone	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Budesonide	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Cortisone	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Di-hydrocortisone	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Corticosteroids for systemic use, plain	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Diprospan /00582101/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Prednisolon streuli /06304501/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Uncoded	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Corticosteroids for systemic use	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Drugs for constipation	11 (73.3%)	21 (47.7%)	83 (29.3%)	12 (57.1%)	26 (50.0%)	90 (31.5%)	23 (63.9%)	47 (49.0%)	173 (30.4%)
Drugs for constipation	11 (73.3%)	21 (47.7%)	83 (29.3%)	12 (57.1%)	26 (50.0%)	90 (31.5%)	23 (63.9%)	47 (49.0%)	173 (30.4%)
Lactulose	0	4 (9.1%)	20 (7.1%)	1 (4.8%)	7 (13.5%)	22 (7.7%)	1 (2.8%)	11 (11.5%)	42 (7.4%)
Movicol /01749801/	0	1 (2.3%)	18 (6.4%)	0	0	15 (5.2%)	0	1 (1.0%)	33 (5.8%)
Sennoside a+b	9 (60.0%)	12 (27.3%)	13 (4.6%)	6 (28.6%)	14 (26.9%)	16 (5.6%)	15 (41.7%)	26 (27.1%)	29 (5.1%)
Macrogol	0	0	16 (5.7%)	0	0	12 (4.2%)	0	0	28 (4.9%)
Docusate	0	1 (2.3%)	9 (3.2%)	0	0	17 (5.9%)	0	1 (1.0%)	26 (4.6%)
Bisacodyl	0	4 (9.1%)	6 (2.1%)	2 (9.5%)	7 (13.5%)	14 (4.9%)	2 (5.6%)	11 (11.5%)	20 (3.5%)
Sodium picosulfate	4 (26.7%)	4 (9.1%)	8 (2.8%)	6 (28.6%)	6 (11.5%)	9 (3.1%)	10 (27.8%)	10 (10.4%)	17 (3.0%)
Coloxyl with senna	0	0	3 (1.1%)	0	0	4 (1.4%)	0	0	7 (1.2%)
Drugs for constipation	0	3 (6.8%)	5 (1.8%)	0	0	2 (0.7%)	0	3 (3.1%)	7 (1.2%)
Glycerol	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	3 (1.0%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Polycarbophil	1 (6.7%)	2 (4.5%)	3 (1.1%)	0	2 (3.8%)	2 (0.7%)	1 (2.8%)	4 (4.2%)	5 (0.9%)
Portalak /00723101/	0	0	1 (0.4%)	0	0	4 (1.4%)	0	0	5 (0.9%)
Macrogol 4000	0	0	3 (1.1%)	0	0	1 (0.3%)	0	0	4 (0.7%)
Meroken new	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
New lecicarbon	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Paraffin, liquid	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Fleet /01605601/	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Fosfosoda /01544501/	0	0	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Sodium phosphate monobasic (anhydrate)	0	1 (2.3%)	2 (0.7%)	0	0	0	0	1 (1.0%)	2 (0.4%)
Contact laxatives	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Docusate w/sennoside a+b	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Dulcodos	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Electrolytes nos w/macrogol 3350	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Glyceol /00744501/	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Golytely	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Herron sennesoft	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Lubiprostone	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Macrogol 3350	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Micolette /01380801/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Microklist	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Microlax /00285401/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Moviprep /06224801/	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Osmotically acting laxatives	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Peri-colace	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Phosphates /00766901/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Proctosol	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Prucalopride	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Psyllium hydrophilic mucilloid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Sennoside b	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Senokot-s	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Surulac-s	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Cough and cold preparations	9 (60.0%)	30 (68.2%)	81 (28.6%)	6 (28.6%)	32 (61.5%)	79 (27.6%)	15 (41.7%)	62 (64.6%)	160 (28.1%)
Expectorants, excl. combinations with cough suppressants	7 (46.7%)	28 (63.6%)	59 (20.8%)	6 (28.6%)	32 (61.5%)	63 (22.0%)	13 (36.1%)	60 (62.5%)	122 (21.4%)
Acetylcysteine	0	11 (25.0%)	23 (8.1%)	0	10 (19.2%)	30 (10.5%)	0	21 (21.9%)	53 (9.3%)
Ambroxol	2 (13.3%)	14 (31.8%)	21 (7.4%)	0	15 (28.8%)	17 (5.9%)	2 (5.6%)	29 (30.2%)	38 (6.7%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Carbocisteine	4 (26.7%)	5 (11.4%)	9 (3.2%)	6 (28.6%)	9 (17.3%)	10 (3.5%)	10 (27.8%)	14 (14.6%)	19 (3.3%)
Bromhexine	1 (6.7%)	2 (4.5%)	6 (2.1%)	0	3 (5.8%)	6 (2.1%)	1 (2.8%)	5 (5.2%)	12 (2.1%)
Guaifenesin	0	0	4 (1.4%)	0	3 (5.8%)	7 (2.4%)	0	3 (3.1%)	11 (1.9%)
Erdosteine	0	1 (2.3%)	2 (0.7%)	0	2 (3.8%)	2 (0.7%)	0	3 (3.1%)	4 (0.7%)
Ambroxol acefyllinate	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Helicidine	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Bisolvomed	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Bromhexine hydrochloride w/guaifenesin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Bromhexine w/ephedrine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Eprazinone	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Sobrerol	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Cough suppressants, excl. combinations with expectorants	5 (33.3%)	14 (31.8%)	34 (12.0%)	4 (19.0%)	22 (42.3%)	39 (13.6%)	9 (25.0%)	36 (37.5%)	73 (12.8%)
Codeine	1 (6.7%)	3 (6.8%)	12 (4.2%)	0	7 (13.5%)	13 (4.5%)	1 (2.8%)	10 (10.4%)	25 (4.4%)
Dextromethorphan	2 (13.3%)	6 (13.6%)	8 (2.8%)	3 (14.3%)	10 (19.2%)	12 (4.2%)	5 (13.9%)	16 (16.7%)	20 (3.5%)
Benzonatate	0	3 (6.8%)	4 (1.4%)	0	1 (1.9%)	4 (1.4%)	0	4 (4.2%)	8 (1.4%)
Levodropropizine	0	2 (4.5%)	2 (0.7%)	0	5 (9.6%)	5 (1.7%)	0	7 (7.3%)	7 (1.2%)
Ethylmorphine	0	0	2 (0.7%)	0	0	3 (1.0%)	0	0	5 (0.9%)
Benproperine	0	3 (6.8%)	3 (1.1%)	0	1 (1.9%)	1 (0.3%)	0	4 (4.2%)	4 (0.7%)
Codeine linctus	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Hydrocodone	0	0	3 (1.1%)	0	0	1 (0.3%)	0	0	4 (0.7%)
Dimemorfan	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Euphon /00959801/	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Clofedanol	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Cloperastine	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Dextromethorphan w/paracetamol/phenylephrine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Medicon a	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Other cough suppressants	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Pholcodine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Cough suppressants and expectorants, combinations	0	4 (9.1%)	7 (2.5%)	0	9 (17.3%)	19 (6.6%)	0	13 (13.5%)	26 (4.6%)
Cocillana-etyfin /06573601/	0	0	1 (0.4%)	0	0	4 (1.4%)	0	0	5 (0.9%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Brown mixture /01682301/	0	1 (2.3%)	1 (0.4%)	0	3 (5.8%)	3 (1.0%)	0	4 (4.2%)	4 (0.7%)
Meiji sekidome	0	2 (4.5%)	2 (0.7%)	0	2 (3.8%)	2 (0.7%)	0	4 (4.2%)	4 (0.7%)
Cocillana-etyfin /00223001/	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Cough s	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Cough syrup /00872901/	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Bronchosedal	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Cheracol /00693301/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Codeine phosphate w/guaifenesin/pheniramine m	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Duro-tuss expectorant	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Opium derivatives and expectorants	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Thiocodin /01295801/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tussex cough	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Uncoded	1 (6.7%)	4 (9.1%)	4 (1.4%)	0	8 (15.4%)	8 (2.8%)	1 (2.8%)	12 (12.5%)	12 (2.1%)
Cough and cold preparations	0	3 (6.8%)	3 (1.1%)	0	8 (15.4%)	8 (2.8%)	0	11 (11.5%)	11 (1.9%)
Kikyosekko	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Other cold preparations	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Benylin dry cough /01325601/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Propalgina	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Provax	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Agents acting on the renin-angiotensin system	2 (13.3%)	4 (9.1%)	80 (28.3%)	3 (14.3%)	4 (7.7%)	71 (24.8%)	5 (13.9%)	8 (8.3%)	151 (26.5%)
Ace inhibitors, plain	0	0	47 (16.6%)	1 (4.8%)	1 (1.9%)	37 (12.9%)	1 (2.8%)	1 (1.0%)	84 (14.8%)
Enalapril	0	0	20 (7.1%)	1 (4.8%)	1 (1.9%)	12 (4.2%)	1 (2.8%)	1 (1.0%)	32 (5.6%)
Ramipril	0	0	17 (6.0%)	0	0	10 (3.5%)	0	0	27 (4.7%)
Perindopril	0	0	5 (1.8%)	0	0	6 (2.1%)	0	0	11 (1.9%)
Lisinopril	0	0	4 (1.4%)	0	0	6 (2.1%)	0	0	10 (1.8%)
Captopril	0	0	2 (0.7%)	0	0	3 (1.0%)	0	0	5 (0.9%)
Benazepril	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Angiotensin ii antagonists, plain	2 (13.3%)	4 (9.1%)	19 (6.7%)	2 (9.5%)	2 (3.8%)	22 (7.7%)	4 (11.1%)	6 (6.3%)	41 (7.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Losartan	0	1 (2.3%)	4 (1.4%)	0	0	8 (2.8%)	0	1 (1.0%)	12 (2.1%)
Valsartan	0	0	4 (1.4%)	1 (4.8%)	1 (1.9%)	5 (1.7%)	1 (2.8%)	1 (1.0%)	9 (1.6%)
Olmesartan	1 (6.7%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	4 (1.4%)	2 (5.6%)	3 (3.1%)	6 (1.1%)
Candesartan	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Irbesartan	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Telmisartan	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Azilsartan	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Angiotensin ii antagonists, combinations	1 (6.7%)	1 (2.3%)	9 (3.2%)	0	1 (1.9%)	9 (3.1%)	1 (2.8%)	2 (2.1%)	18 (3.2%)
Benicar hct	0	0	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Hyzaar	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Candesartan w/hydrochlorothiazide	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Co-diovan	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Diovan amlo	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Amlodipine w/olmesartan	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Angiotensin ii antagonists, combinations	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Blopress plus	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Emestar plus	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Karvea hct	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Pritorplus	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ace inhibitors, combinations	0	0	8 (2.8%)	0	0	3 (1.0%)	0	0	11 (1.9%)
Bi predonium	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Vaseretic	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Coveram	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dynorm plus	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Elidiur	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Enalapril w/lercanidipine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Indapamide w/perindopril	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Perindopril arg/amlodipine fisher	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Zestoretic	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other agents acting on the renin-angiotensin system	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Aliskiren	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Blood substitutes and perfusion solutions	1 (6.7%)	9 (20.5%)	56 (19.8%)	5 (23.8%)	18 (34.6%)	83 (29.0%)	6 (16.7%)	27 (28.1%)	139 (24.4%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Irrigating solutions	1 (6.7%)	6 (13.6%)	46 (16.3%)	1 (4.8%)	11 (21.2%)	59 (20.6%)	2 (5.6%)	17 (17.7%)	105 (18.5%)
Sodium chloride	1 (6.7%)	5 (11.4%)	37 (13.1%)	0	8 (15.4%)	51 (17.8%)	1 (2.8%)	13 (13.5%)	88 (15.5%)
Sodium bicarbonate	0	2 (4.5%)	11 (3.9%)	1 (4.8%)	5 (9.6%)	12 (4.2%)	1 (2.8%)	7 (7.3%)	23 (4.0%)
Colyte /00751601/	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Ringer /01179901/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Sodium citrate	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
I.v. solutions	0	7 (15.9%)	15 (5.3%)	2 (9.5%)	9 (17.3%)	20 (7.0%)	2 (5.6%)	16 (16.7%)	35 (6.2%)
Smoflipid	0	2 (4.5%)	2 (0.7%)	0	3 (5.8%)	3 (1.0%)	0	5 (5.2%)	5 (0.9%)
Dextrose and sodium chloride injection	0	2 (4.5%)	3 (1.1%)	0	0	0	0	2 (2.1%)	3 (0.5%)
Electrolytes nos w/glucose	0	2 (4.5%)	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	3 (3.1%)	3 (0.5%)
Flebobag ring lact	0	0	3 (1.1%)	0	0	0	0	0	3 (0.5%)
I.v. solutions	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Lactec /00490001/	0	0	0	2 (9.5%)	2 (3.8%)	3 (1.0%)	2 (5.6%)	2 (2.1%)	3 (0.5%)
Ringer-lactate	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Solutions for parenteral nutrition	0	2 (4.5%)	3 (1.1%)	0	0	0	0	2 (2.1%)	3 (0.5%)
Amino acids nos w/electrolytes nos/glucose	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Dextrose w/potassium chloride	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
El-4	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Electrolytes nos	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Solutions affecting the electrolyte balance	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Amino acids nos w/electrolytes nos//07977301/	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Aminofluid	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Freamine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Jonosteril /00351401/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Mannitol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Olimel n5e	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Osmotan	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Phosphate /01684601/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Potassium phosphate dibasic w/sodium	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Smofkabiven perifer	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Sodium lactate	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Solita-t1	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Solutions producing osmotic diuresis	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
I.v. solution additives	0	2 (4.5%)	7 (2.5%)	0	1 (1.9%)	11 (3.8%)	0	3 (3.1%)	18 (3.2%)
Sodium phosphate	0	2 (4.5%)	6 (2.1%)	0	1 (1.9%)	6 (2.1%)	0	3 (3.1%)	12 (2.1%)
Phosphoric acid	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Electrolyte solutions /90010101/	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Lysine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Blood and related products	0	3 (6.8%)	5 (1.8%)	0	1 (1.9%)	3 (1.0%)	0	4 (4.2%)	8 (1.4%)
Albumin human	0	2 (4.5%)	3 (1.1%)	0	0	1 (0.3%)	0	2 (2.1%)	4 (0.7%)
Dextran sulfate	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Erythrocytes	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Gelatin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Hetastarch	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Infukoll hes	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Plasma	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Uncoded	0	0	0	4 (19.0%)	4 (7.7%)	4 (1.4%)	4 (11.1%)	4 (4.2%)	4 (0.7%)
Carbohydrates nos w/potassium chloride/sodium	0	0	0	3 (14.3%)	3 (5.8%)	3 (1.0%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Solacet f	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Hemodialytics and hemofiltrates	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Ringer-acetat	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Drugs for obstructive airway diseases	3 (20.0%)	10 (22.7%)	61 (21.6%)	1 (4.8%)	8 (15.4%)	76 (26.6%)	4 (11.1%)	18 (18.8%)	137 (24.1%)
Adrenergics, inhalants	3 (20.0%)	6 (13.6%)	41 (14.5%)	1 (4.8%)	1 (1.9%)	57 (19.9%)	4 (11.1%)	7 (7.3%)	98 (17.2%)
Salbutamol	1 (6.7%)	2 (4.5%)	22 (7.8%)	1 (4.8%)	1 (1.9%)	32 (11.2%)	2 (5.6%)	3 (3.1%)	54 (9.5%)
Seretide	1 (6.7%)	2 (4.5%)	7 (2.5%)	0	0	7 (2.4%)	1 (2.8%)	2 (2.1%)	14 (2.5%)
Budesonide w/formoterol fumarate	0	0	3 (1.1%)	0	0	8 (2.8%)	0	0	11 (1.9%)
Duovent	0	0	3 (1.1%)	0	0	8 (2.8%)	0	0	11 (1.9%)
Terbutaline	1 (6.7%)	1 (2.3%)	3 (1.1%)	0	0	5 (1.7%)	1 (2.8%)	1 (1.0%)	8 (1.4%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Breva	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Budesonide w/formoterol	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Epinephrine	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Fluticasone propionate w/salmeterol	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Formoterol	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Levosalbutamol	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Bekform	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Combivent	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Fluticasone w/salmeterol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Indacaterol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other drugs for obstructive airway diseases, inhalants	2 (13.3%)	4 (9.1%)	31 (11.0%)	0	1 (1.9%)	26 (9.1%)	2 (5.6%)	5 (5.2%)	57 (10.0%)
Ipratropium	0	0	13 (4.6%)	0	1 (1.9%)	20 (7.0%)	0	1 (1.0%)	33 (5.8%)
Budesonide	0	0	4 (1.4%)	0	0	9 (3.1%)	0	0	13 (2.3%)
Tiotropium	1 (6.7%)	2 (4.5%)	5 (1.8%)	0	0	4 (1.4%)	1 (2.8%)	2 (2.1%)	9 (1.6%)
Fluticasone	1 (6.7%)	1 (2.3%)	3 (1.1%)	0	0	2 (0.7%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Mometasone	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Beclometasone	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Fenspiride	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Aclidinium	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ciclesonide	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Other systemic drugs for obstructive airway diseases	0	5 (11.4%)	12 (4.2%)	0	4 (7.7%)	13 (4.5%)	0	9 (9.4%)	25 (4.4%)
Theophylline	0	4 (9.1%)	6 (2.1%)	0	1 (1.9%)	7 (2.4%)	0	5 (5.2%)	13 (2.3%)
Aminophylline	0	0	5 (1.8%)	0	0	3 (1.0%)	0	0	8 (1.4%)
Theobromine	0	1 (2.3%)	1 (0.4%)	0	3 (5.8%)	3 (1.0%)	0	4 (4.2%)	4 (0.7%)
Montelukast	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Adrenergics for systemic use	0	1 (2.3%)	1 (0.4%)	0	2 (3.8%)	2 (0.7%)	0	3 (3.1%)	3 (0.5%)
Fenoterol	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Bambuterol	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Vitamins	5 (33.3%)	13 (29.5%)	63 (22.3%)	7 (33.3%)	16 (30.8%)	67 (23.4%)	12 (33.3%)	29 (30.2%)	130 (22.8%)
Vitamin a and d, incl. combinations of the two	3 (20.0%)	3 (6.8%)	39 (13.8%)	1 (4.8%)	1 (1.9%)	29 (10.1%)	4 (11.1%)	4 (4.2%)	68 (12.0%)
Colecalciferol	0	0	16 (5.7%)	0	0	17 (5.9%)	0	0	33 (5.8%)
Vitamin d nos	0	0	17 (6.0%)	0	0	8 (2.8%)	0	0	25 (4.4%)
Alfacalcidol	3 (20.0%)	3 (6.8%)	6 (2.1%)	0	0	2 (0.7%)	3 (8.3%)	3 (3.1%)	8 (1.4%)
Calcitriol	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Ergocalciferol	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Retinol	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Multivitamins, plain	0	1 (2.3%)	5 (1.8%)	0	7 (13.5%)	20 (7.0%)	0	8 (8.3%)	25 (4.4%)
Vitamins nos	0	1 (2.3%)	5 (1.8%)	0	7 (13.5%)	20 (7.0%)	0	8 (8.3%)	25 (4.4%)
Other plain vitamin preparations	2 (13.3%)	5 (11.4%)	8 (2.8%)	4 (19.0%)	4 (7.7%)	10 (3.5%)	6 (16.7%)	9 (9.4%)	18 (3.2%)
Pyridoxine	0	2 (4.5%)	3 (1.1%)	0	0	4 (1.4%)	0	2 (2.1%)	7 (1.2%)
Tocopherol	0	1 (2.3%)	3 (1.1%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	5 (0.9%)
Pantethine	1 (6.7%)	1 (2.3%)	1 (0.4%)	3 (14.3%)	3 (5.8%)	3 (1.0%)	4 (11.1%)	4 (4.2%)	4 (0.7%)
Biotin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dexpanthenol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Flavine adenine dinucleotide	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Vitamin b-complex, incl. combinations	0	5 (11.4%)	8 (2.8%)	0	3 (5.8%)	8 (2.8%)	0	8 (8.3%)	16 (2.8%)
Cebetabs	0	4 (9.1%)	4 (1.4%)	0	2 (3.8%)	2 (0.7%)	0	6 (6.3%)	6 (1.1%)
Vitamin b complex	0	0	2 (0.7%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	5 (0.9%)
B-komplex	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Bevital	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Minerals nos w/vitamin b nos	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Parentrovite /00041801/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Tpn /00897001/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Yeast	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Vitamin b1, plain and in combination with vitamin b6 and b12	0	1 (2.3%)	8 (2.8%)	0	0	5 (1.7%)	0	1 (1.0%)	13 (2.3%)
Befact /00527001/	0	0	4 (1.4%)	0	0	1 (0.3%)	0	0	5 (0.9%)
Thiamine	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Neurobion /00176001/	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Milgamma na /01350701/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Neurogrisevit /00091901/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Trineurin /00499701/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Ascorbic acid (vitamin c), incl. combinations	0	1 (2.3%)	5 (1.8%)	0	0	2 (0.7%)	0	1 (1.0%)	7 (1.2%)
Ascorbic acid	0	1 (2.3%)	5 (1.8%)	0	0	2 (0.7%)	0	1 (1.0%)	7 (1.2%)
Multivitamins, combinations	0	1 (2.3%)	3 (1.1%)	0	0	3 (1.0%)	0	1 (1.0%)	6 (1.1%)
Minerals nos w/vitamins nos	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Ascorbic acid w/biotin/calcium chloride/calci	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ascorbic acid w/calcium/minerals nos/retinol/	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Multivitamins	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other vitamin products, combinations	1 (6.7%)	1 (2.3%)	1 (0.4%)	2 (9.5%)	2 (3.8%)	5 (1.7%)	3 (8.3%)	3 (3.1%)	6 (1.1%)
Vitamedin /00274301/	0	0	0	2 (9.5%)	2 (3.8%)	2 (0.7%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Vitamins, other combinations	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Sanatogen multivitamins	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Vitamedin intravenous	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Antigout preparations	4 (26.7%)	4 (9.1%)	62 (21.9%)	2 (9.5%)	3 (5.8%)	65 (22.7%)	6 (16.7%)	7 (7.3%)	127 (22.3%)
Antigout preparations	4 (26.7%)	4 (9.1%)	62 (21.9%)	2 (9.5%)	3 (5.8%)	65 (22.7%)	6 (16.7%)	7 (7.3%)	127 (22.3%)
Allopurinol	0	0	53 (18.7%)	1 (4.8%)	2 (3.8%)	64 (22.4%)	1 (2.8%)	2 (2.1%)	117 (20.6%)
Colchicine	0	0	7 (2.5%)	0	0	0	0	0	7 (1.2%)
Febuxostat	4 (26.7%)	4 (9.1%)	5 (1.8%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	5 (13.9%)	5 (5.2%)	7 (1.2%)
Colchimax /01722001/	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Colchimax /00728901/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Lipid modifying agents	1 (6.7%)	6 (13.6%)	66 (23.3%)	3 (14.3%)	4 (7.7%)	57 (19.9%)	4 (11.1%)	10 (10.4%)	123 (21.6%)
Lipid modifying agents, plain	1 (6.7%)	5 (11.4%)	64 (22.6%)	3 (14.3%)	4 (7.7%)	56 (19.6%)	4 (11.1%)	9 (9.4%)	120 (21.1%)
Atorvastatin	0	2 (4.5%)	18 (6.4%)	1 (4.8%)	1 (1.9%)	22 (7.7%)	1 (2.8%)	3 (3.1%)	40 (7.0%)
Simvastatin	0	0	21 (7.4%)	0	1 (1.9%)	14 (4.9%)	0	1 (1.0%)	35 (6.2%)
Rosuvastatin	0	2 (4.5%)	11 (3.9%)	2 (9.5%)	2 (3.8%)	9 (3.1%)	2 (5.6%)	4 (4.2%)	20 (3.5%)
Pravastatin	0	0	6 (2.1%)	0	0	2 (0.7%)	0	0	8 (1.4%)
Colestyramine	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Fish oil	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Fenofibrate	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Bezafibrate	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	3 (0.5%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Colestipol	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Ezetimibe	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Fluvastatin	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Colesevelam	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Gemfibrozil	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Omega-3 fatty acids	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Lovastatin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Pitavastatin	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Lipid modifying agents, combinations	0	1 (2.3%)	3 (1.1%)	0	0	1 (0.3%)	0	1 (1.0%)	4 (0.7%)
Inegy	0	1 (2.3%)	3 (1.1%)	0	0	1 (0.3%)	0	1 (1.0%)	4 (0.7%)
Antianemic preparations	4 (26.7%)	11 (25.0%)	54 (19.1%)	3 (14.3%)	9 (17.3%)	63 (22.0%)	7 (19.4%)	20 (20.8%)	117 (20.6%)
Other antianemic preparations	1 (6.7%)	3 (6.8%)	28 (9.9%)	0	0	33 (11.5%)	1 (2.8%)	3 (3.1%)	61 (10.7%)
Erythropoietin human	0	0	15 (5.3%)	0	0	22 (7.7%)	0	0	37 (6.5%)
Darbepoetin alfa	1 (6.7%)	3 (6.8%)	12 (4.2%)	0	0	11 (3.8%)	1 (2.8%)	3 (3.1%)	23 (4.0%)
Erythropoietin	0	0	2 (0.7%)	0	0	7 (2.4%)	0	0	9 (1.6%)
Methoxy polyethylene glycol-epoetin beta	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Vitamin b12 and folic acid	3 (20.0%)	9 (20.5%)	27 (9.5%)	3 (14.3%)	9 (17.3%)	33 (11.5%)	6 (16.7%)	18 (18.8%)	60 (10.5%)
Folic acid	0	4 (9.1%)	13 (4.6%)	0	3 (5.8%)	19 (6.6%)	0	7 (7.3%)	32 (5.6%)
Vitamin b12 nos	0	0	7 (2.5%)	0	1 (1.9%)	8 (2.8%)	0	1 (1.0%)	15 (2.6%)
Cyanocobalamin	0	0	7 (2.5%)	2 (9.5%)	2 (3.8%)	7 (2.4%)	2 (5.6%)	2 (2.1%)	14 (2.5%)
Mecobalamin	3 (20.0%)	6 (13.6%)	6 (2.1%)	1 (4.8%)	4 (7.7%)	4 (1.4%)	4 (11.1%)	10 (10.4%)	10 (1.8%)
Cobamamide	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Hepagrisevit forte-n /01079901/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Hydroxocobalamin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Iron preparations	0	0	4 (1.4%)	0	0	9 (3.1%)	0	0	13 (2.3%)
Iron	0	0	4 (1.4%)	0	0	8 (2.8%)	0	0	12 (2.1%)
Ferritin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Beta blocking agents	0	1 (2.3%)	50 (17.7%)	2 (9.5%)	2 (3.8%)	66 (23.1%)	2 (5.6%)	3 (3.1%)	116 (20.4%)
Beta blocking agents	0	1 (2.3%)	48 (17.0%)	2 (9.5%)	2 (3.8%)	64 (22.4%)	2 (5.6%)	3 (3.1%)	112 (19.7%)
Bisoprolol	0	0	22 (7.8%)	1 (4.8%)	1 (1.9%)	23 (8.0%)	1 (2.8%)	1 (1.0%)	45 (7.9%)
Metoprolol	0	0	16 (5.7%)	0	0	23 (8.0%)	0	0	39 (6.9%)
Atenolol	0	0	4 (1.4%)	0	0	4 (1.4%)	0	0	8 (1.4%)
Nebivolol	0	0	4 (1.4%)	0	0	4 (1.4%)	0	0	8 (1.4%)
Carvedilol	0	0	0	0	0	6 (2.1%)	0	0	6 (1.1%)
Propranolol	0	1 (2.3%)	3 (1.1%)	0	0	1 (0.3%)	0	1 (1.0%)	4 (0.7%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Carteolol	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Sotalol	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Beta blocking agents and other antihypertensives	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Modiloc	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Nif-ten	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Beta blocking agents and thiazides	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Biselect /01166101/	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Beta blocking agents and other diuretics	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tenoretic	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antidiarrheals, intestinal antiinflammatory/antiinfective agents	2 (13.3%)	6 (13.6%)	43 (15.2%)	5 (23.8%)	15 (28.8%)	69 (24.1%)	7 (19.4%)	21 (21.9%)	112 (19.7%)
Antipropulsives	1 (6.7%)	4 (9.1%)	24 (8.5%)	1 (4.8%)	9 (17.3%)	45 (15.7%)	2 (5.6%)	13 (13.5%)	69 (12.1%)
Loperamide	1 (6.7%)	4 (9.1%)	23 (8.1%)	1 (4.8%)	9 (17.3%)	44 (15.4%)	2 (5.6%)	13 (13.5%)	67 (11.8%)
Lomotil /00034001/	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Intestinal antiinfectives	0	1 (2.3%)	12 (4.2%)	1 (4.8%)	2 (3.8%)	13 (4.5%)	1 (2.8%)	3 (3.1%)	25 (4.4%)
Nystatin	0	1 (2.3%)	7 (2.5%)	0	0	8 (2.8%)	0	1 (1.0%)	15 (2.6%)
Miconazole	0	0	3 (1.1%)	0	0	6 (2.1%)	0	0	9 (1.6%)
Neomycin	0	0	0	1 (4.8%)	2 (3.8%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Colistin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Natamycin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Intestinal adsorbents	0	1 (2.3%)	6 (2.1%)	0	5 (9.6%)	14 (4.9%)	0	6 (6.3%)	20 (3.5%)
Diosmectite	0	1 (2.3%)	4 (1.4%)	0	5 (9.6%)	10 (3.5%)	0	6 (6.3%)	14 (2.5%)
Bismuth	0	0	1 (0.4%)	0	0	4 (1.4%)	0	0	5 (0.9%)
Carbosylane /00814601/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Intestinal adsorbents	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Kaopectate /00140201/	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Antidiarrheal microorganisms	1 (6.7%)	2 (4.5%)	7 (2.5%)	4 (19.0%)	4 (7.7%)	5 (1.7%)	5 (13.9%)	6 (6.3%)	12 (2.1%)
Saccharomyces boulardii	0	0	4 (1.4%)	0	0	1 (0.3%)	0	0	5 (0.9%)
Bifidobacterium lactis	0	0	0	3 (14.3%)	3 (5.8%)	3 (1.0%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Bio-three	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Biolac /07958501/	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Lactic acid	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Lactobacillus reuteri	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other antidiarrheals	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	7 (2.4%)	1 (2.8%)	1 (1.0%)	8 (1.4%)
Racecadotril	0	0	1 (0.4%)	0	0	6 (2.1%)	0	0	7 (1.2%)
Seirogan	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Intestinal antiinflammatory agents	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Sulfasalazine	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Cromoglicic acid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Diuretics	1 (6.7%)	7 (15.9%)	57 (20.1%)	1 (4.8%)	2 (3.8%)	52 (18.2%)	2 (5.6%)	9 (9.4%)	109 (19.2%)
High-ceiling diuretics	1 (6.7%)	7 (15.9%)	47 (16.6%)	1 (4.8%)	2 (3.8%)	40 (14.0%)	2 (5.6%)	9 (9.4%)	87 (15.3%)
Furosemide	1 (6.7%)	7 (15.9%)	45 (15.9%)	1 (4.8%)	2 (3.8%)	40 (14.0%)	2 (5.6%)	9 (9.4%)	85 (14.9%)
Torasemide	0	0	3 (1.1%)	0	0	4 (1.4%)	0	0	7 (1.2%)
Bumetanide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Potassium-sparing agents	0	0	6 (2.1%)	0	0	11 (3.8%)	0	0	17 (3.0%)
Spironolactone	0	0	5 (1.8%)	0	0	9 (3.1%)	0	0	14 (2.5%)
Amiloride	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Canrenoic acid	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Low-ceiling diuretics, thiazides	0	0	8 (2.8%)	0	0	3 (1.0%)	0	0	11 (1.9%)
Hydrochlorothiazide	0	0	8 (2.8%)	0	0	2 (0.7%)	0	0	10 (1.8%)
Salures-k	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Diuretics and potassium-sparing agents in combination	0	1 (2.3%)	5 (1.8%)	0	0	1 (0.3%)	0	1 (1.0%)	6 (1.1%)
Moduretic	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Aldactazine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Dyazide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Frumil	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Osyrol-lasix	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Low-ceiling diuretics, excl. thiazides	0	0	0	0	0	6 (2.1%)	0	0	6 (1.1%)
Indapamide	0	0	0	0	0	4 (1.4%)	0	0	4 (0.7%)
Chlortalidone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Xipamide	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other diuretics	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Tolvaptan	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Drugs for functional gastrointestinal disorders	3 (20.0%)	13 (29.5%)	42 (14.8%)	6 (28.6%)	17 (32.7%)	65 (22.7%)	9 (25.0%)	30 (31.3%)	107 (18.8%)
Propulsives	3 (20.0%)	11 (25.0%)	35 (12.4%)	5 (23.8%)	14 (26.9%)	56 (19.6%)	8 (22.2%)	25 (26.0%)	91 (16.0%)
Metoclopramide	2 (13.3%)	7 (15.9%)	25 (8.8%)	5 (23.8%)	12 (23.1%)	44 (15.4%)	7 (19.4%)	19 (19.8%)	69 (12.1%)
Domperidone	0	1 (2.3%)	5 (1.8%)	0	1 (1.9%)	9 (3.1%)	0	2 (2.1%)	14 (2.5%)
Alizapride	0	0	5 (1.8%)	0	0	3 (1.0%)	0	0	8 (1.4%)
Mosapride	1 (6.7%)	4 (9.1%)	4 (1.4%)	0	2 (3.8%)	2 (0.7%)	1 (2.8%)	6 (6.3%)	6 (1.1%)
Itopride	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Drugs for functional gastrointestinal disorders	0	4 (9.1%)	7 (2.5%)	2 (9.5%)	4 (7.7%)	11 (3.8%)	2 (5.6%)	8 (8.3%)	18 (3.2%)
Trimebutine	0	1 (2.3%)	2 (0.7%)	2 (9.5%)	2 (3.8%)	4 (1.4%)	2 (5.6%)	3 (3.1%)	6 (1.1%)
Simeticone	0	2 (4.5%)	3 (1.1%)	0	0	1 (0.3%)	0	2 (2.1%)	4 (0.7%)
Spasfon /00765801/	0	0	1 (0.4%)	0	0	3 (1.0%)	0	0	4 (0.7%)
Otilonium	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Pinaverium	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Dicycloverine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Glycopyrronium	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Grandpaze f	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Mebeverine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Meteospasmyl /02143701/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tiropramide	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Belladonna and derivatives, plain	0	1 (2.3%)	2 (0.7%)	0	1 (1.9%)	5 (1.7%)	0	2 (2.1%)	7 (1.2%)
Hyoscine	0	0	1 (0.4%)	0	1 (1.9%)	4 (1.4%)	0	1 (1.0%)	5 (0.9%)
Butylscopolamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Cimetropium	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Antispasmodics and anticholinergics in combination with other drugs	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Spasmalgin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Psychoanaleptics	2 (13.3%)	9 (20.5%)	47 (16.6%)	0	5 (9.6%)	57 (19.9%)	2 (5.6%)	14 (14.6%)	104 (18.3%)
Antidepressants	2 (13.3%)	8 (18.2%)	44 (15.5%)	0	5 (9.6%)	54 (18.9%)	2 (5.6%)	13 (13.5%)	98 (17.2%)
Amitriptyline	1 (6.7%)	4 (9.1%)	13 (4.6%)	0	3 (5.8%)	12 (4.2%)	1 (2.8%)	7 (7.3%)	25 (4.4%)
Escitalopram	0	0	6 (2.1%)	0	0	9 (3.1%)	0	0	15 (2.6%)
Duloxetine	0	3 (6.8%)	6 (2.1%)	0	0	8 (2.8%)	0	3 (3.1%)	14 (2.5%)
Mirtazapine	0	1 (2.3%)	6 (2.1%)	0	1 (1.9%)	6 (2.1%)	0	2 (2.1%)	12 (2.1%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Sertraline	0	0	5 (1.8%)	0	0	5 (1.7%)	0	0	10 (1.8%)
Citalopram	0	0	4 (1.4%)	0	0	5 (1.7%)	0	0	9 (1.6%)
Venlafaxine	0	0	1 (0.4%)	0	0	5 (1.7%)	0	0	6 (1.1%)
Fluoxetine	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Paroxetine	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Trazodone	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	2 (0.7%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Bupropion	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Clomipramine	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Doxepin	0	1 (2.3%)	2 (0.7%)	0	0	0	0	1 (1.0%)	2 (0.4%)
Mianserin	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Nortriptyline	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Desvenlafaxine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Fluvoxamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Imipramine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Tianeptine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Trimipramine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Psychostimulants, agents used for adhd and nootropics	0	1 (2.3%)	7 (2.5%)	0	0	1 (0.3%)	0	1 (1.0%)	8 (1.4%)
Methylphenidate	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Piracetam	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Acetylcarnitine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Cytoflavin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Ethanolamine alfoscerate	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Modafinil	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Psycholeptics and psychoanaleptics in combination	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Deanxit	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Etrafon-d	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Anti-dementia drugs	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ipidacrine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antiinflammatory and antirheumatic products	6 (40.0%)	17 (38.6%)	41 (14.5%)	7 (33.3%)	20 (38.5%)	45 (15.7%)	13 (36.1%)	37 (38.5%)	86 (15.1%)
Antiinflammatory and antirheumatic products, non-steroids	6 (40.0%)	17 (38.6%)	41 (14.5%)	7 (33.3%)	20 (38.5%)	45 (15.7%)	13 (36.1%)	37 (38.5%)	86 (15.1%)
Ibuprofen	0	2 (4.5%)	11 (3.9%)	0	1 (1.9%)	8 (2.8%)	0	3 (3.1%)	19 (3.3%)
Celecoxib	1 (6.7%)	3 (6.8%)	5 (1.8%)	0	3 (5.8%)	5 (1.7%)	1 (2.8%)	6 (6.3%)	10 (1.8%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Ketoprofen	2 (13.3%)	2 (4.5%)	4 (1.4%)	4 (19.0%)	5 (9.6%)	6 (2.1%)	6 (16.7%)	7 (7.3%)	10 (1.8%)
Benzydamine	0	2 (4.5%)	3 (1.1%)	0	5 (9.6%)	6 (2.1%)	0	7 (7.3%)	9 (1.6%)
Naproxen	0	2 (4.5%)	3 (1.1%)	0	2 (3.8%)	6 (2.1%)	0	4 (4.2%)	9 (1.6%)
Indometacin	1 (6.7%)	2 (4.5%)	4 (1.4%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	2 (5.6%)	3 (3.1%)	6 (1.1%)
Zaltoprofen	0	4 (9.1%)	4 (1.4%)	0	2 (3.8%)	2 (0.7%)	0	6 (6.3%)	6 (1.1%)
Dexketoprofen	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Loxoprofen	1 (6.7%)	2 (4.5%)	2 (0.7%)	2 (9.5%)	2 (3.8%)	2 (0.7%)	3 (8.3%)	4 (4.2%)	4 (0.7%)
Azulene	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Flurbiprofen	0	0	0	2 (9.5%)	3 (5.8%)	3 (1.0%)	2 (5.6%)	3 (3.1%)	3 (0.5%)
Glucosamine	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Ketorolac	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Aceclofenac	0	0	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Bromfenac	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Carol-f	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Diclofenac	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Theraflex	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Chondroitin sulfate w/glucosamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dexibuprofen	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Etodolac	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Etoricoxib	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Lornoxicam	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Meloxicam	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Nimesulide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Paracetamol forte raffo	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Parecoxib	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Pranoprofen	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Talniflumate	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Tenoxicam	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Antiinflammatory/antirheumatic agents in combination	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Advil pm /05810501/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Calcium channel blockers	2 (13.3%)	8 (18.2%)	37 (13.1%)	8 (38.1%)	10 (19.2%)	48 (16.8%)	10 (27.8%)	18 (18.8%)	85 (14.9%)
Selective calcium channel blockers with mainly vascular effects	2 (13.3%)	8 (18.2%)	34 (12.0%)	7 (33.3%)	9 (17.3%)	46 (16.1%)	9 (25.0%)	17 (17.7%)	80 (14.1%)
Amlodipine	1 (6.7%)	6 (13.6%)	26 (9.2%)	4 (19.0%)	6 (11.5%)	32 (11.2%)	5 (13.9%)	12 (12.5%)	58 (10.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Lercanidipine	0	0	2 (0.7%)	0	0	7 (2.4%)	0	0	9 (1.6%)
Nifedipine	0	1 (2.3%)	4 (1.4%)	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	2 (2.1%)	7 (1.2%)
Felodipine	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Benidipine	0	0	0	2 (9.5%)	2 (3.8%)	2 (0.7%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Cilnidipine	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Nicardipine	0	0	0	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Barnidipine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Nitrendipine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Selective calcium channel blockers with direct cardiac effects	0	1 (2.3%)	4 (1.4%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	6 (1.1%)
Diltiazem	0	1 (2.3%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	4 (0.7%)
Verapamil	0	1 (2.3%)	3 (1.1%)	0	0	0	0	1 (1.0%)	3 (0.5%)
Drugs used in diabetes	2 (13.3%)	7 (15.9%)	46 (16.3%)	4 (19.0%)	7 (13.5%)	36 (12.6%)	6 (16.7%)	14 (14.6%)	82 (14.4%)
Blood glucose lowering drugs, excl. insulins	2 (13.3%)	6 (13.6%)	33 (11.7%)	3 (14.3%)	5 (9.6%)	27 (9.4%)	5 (13.9%)	11 (11.5%)	60 (10.5%)
Metformin	1 (6.7%)	4 (9.1%)	27 (9.5%)	1 (4.8%)	2 (3.8%)	19 (6.6%)	2 (5.6%)	6 (6.3%)	46 (8.1%)
Glimepiride	0	1 (2.3%)	8 (2.8%)	0	0	3 (1.0%)	0	1 (1.0%)	11 (1.9%)
Sitagliptin	1 (6.7%)	1 (2.3%)	3 (1.1%)	2 (9.5%)	3 (5.8%)	7 (2.4%)	3 (8.3%)	4 (4.2%)	10 (1.8%)
Gliclazide	0	0	3 (1.1%)	0	0	3 (1.0%)	0	0	6 (1.1%)
Repaglinide	0	0	3 (1.1%)	0	0	3 (1.0%)	0	0	6 (1.1%)
Eucreas	0	1 (2.3%)	4 (1.4%)	0	0	1 (0.3%)	0	1 (1.0%)	5 (0.9%)
Vildagliptin	1 (6.7%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	3 (3.1%)	3 (0.5%)
Alogliptin	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Ristfor	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Diapride forte	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Glibenclamide	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Glipizide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Gliquidone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Jentadueto	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Liraglutide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Lixisenatide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Mitiglinide	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Pioglitazone	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Saxagliptin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Voglibose	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Insulins and analogues	1 (6.7%)	2 (4.5%)	24 (8.5%)	2 (9.5%)	4 (7.7%)	20 (7.0%)	3 (8.3%)	6 (6.3%)	44 (7.7%)
Insulin glargine	0	0	12 (4.2%)	1 (4.8%)	2 (3.8%)	7 (2.4%)	1 (2.8%)	2 (2.1%)	19 (3.3%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Insulin human	0	1 (2.3%)	10 (3.5%)	1 (4.8%)	3 (5.8%)	8 (2.8%)	1 (2.8%)	4 (4.2%)	18 (3.2%)
Insulin aspart	0	0	4 (1.4%)	0	0	5 (1.7%)	0	0	9 (1.6%)
Insulin lispro	0	0	4 (1.4%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	6 (1.1%)
Insulin	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Insulin detemir	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Insulin glulisine	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Novomix	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Humalog mix	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Human mixtard	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Insulin bovine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Insulin porcine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Unspecified herbal and traditional medicine	9 (60.0%)	15 (34.1%)	37 (13.1%)	9 (42.9%)	14 (26.9%)	41 (14.3%)	18 (50.0%)	29 (30.2%)	78 (13.7%)
Uncoded	9 (60.0%)	15 (34.1%)	37 (13.1%)	9 (42.9%)	14 (26.9%)	41 (14.3%)	18 (50.0%)	29 (30.2%)	78 (13.7%)
Senna alexandrina	2 (13.3%)	2 (4.5%)	13 (4.6%)	2 (9.5%)	2 (3.8%)	15 (5.2%)	4 (11.1%)	4 (4.2%)	28 (4.9%)
Unspecified herbal	1 (6.7%)	4 (9.1%)	6 (2.1%)	1 (4.8%)	2 (3.8%)	4 (1.4%)	2 (5.6%)	6 (6.3%)	10 (1.8%)
Shakuyakukanzoto	5 (33.3%)	5 (11.4%)	5 (1.8%)	0	0	0	5 (13.9%)	5 (5.2%)	5 (0.9%)
Cannabis sativa	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Kakkonto /07985901/	0	0	0	3 (14.3%)	3 (5.8%)	3 (1.0%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Platycodon grandiflorus	0	1 (2.3%)	1 (0.4%)	0	2 (3.8%)	2 (0.7%)	0	3 (3.1%)	3 (0.5%)
Ginkgo biloba	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Hedera helix	0	0	0	0	1 (1.9%)	2 (0.7%)	0	1 (1.0%)	2 (0.4%)
Plantago ovata	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Sterculia urens	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Aloe vera	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Alosenn /00476901/	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Arachis hypogaea	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Bakumondoto	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Crataegus laevigata	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Curcuma longa	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Euphytose /05965601/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Goshajinkigan	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Hamamelis virginiana	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Herbal extract nos	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Juzentaihoto /07985601/	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Kakkontokasenkyushin'i /07986001/	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Lespedeza capitata	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Linum usitatissimum	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Melaleuca alternifolia	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Mentha x piperita	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Monascus purpureus	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Orengedokuto	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Plantago afra	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Prunus africana	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Rhamnus purshiana	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Serenoa repens	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Ulmus rubra	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Vaccinium macrocarpon	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Ophthalmologicals	2 (13.3%)	7 (15.9%)	36 (12.7%)	3 (14.3%)	12 (23.1%)	41 (14.3%)	5 (13.9%)	19 (19.8%)	77 (13.5%)
Antiinflammatory agents	0	1 (2.3%)	14 (4.9%)	0	3 (5.8%)	18 (6.3%)	0	4 (4.2%)	32 (5.6%)
Diclofenac	0	1 (2.3%)	10 (3.5%)	0	3 (5.8%)	12 (4.2%)	0	4 (4.2%)	22 (3.9%)
Dexamethasone	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Nepafenac	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Loteprednol	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Fluorometholone	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Piroxicam	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Prednefrin /00330801/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other ophthalmologicals	1 (6.7%)	2 (4.5%)	7 (2.5%)	1 (4.8%)	5 (9.6%)	11 (3.8%)	2 (5.6%)	7 (7.3%)	18 (3.2%)
Carbomer	0	0	1 (0.4%)	0	1 (1.9%)	5 (1.7%)	0	1 (1.0%)	6 (1.1%)
Systane lubricant	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Artificial tears /90046201/	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	0	1 (2.8%)	1 (1.0%)	2 (0.4%)
Azapentacen	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Carmellose	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Diquafosol	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Hyaluronidase	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Pirenoxine	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Tears naturale /00635701/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Xantofyl	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antiglaucoma preparations and miotics	1 (6.7%)	1 (2.3%)	7 (2.5%)	0	1 (1.9%)	9 (3.1%)	1 (2.8%)	2 (2.1%)	16 (2.8%)
Latanoprost	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	3 (1.0%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Timolol	0	0	1 (0.4%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	4 (0.7%)
Bimatoprost	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Cosopt	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Acetazolamide	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Xalacom	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Betaxolol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Brinzolamide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Dorzolamide w/timolol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Elazop	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Travoprost	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Surgical aids	1 (6.7%)	4 (9.1%)	5 (1.8%)	2 (9.5%)	4 (7.7%)	7 (2.4%)	3 (8.3%)	8 (8.3%)	12 (2.1%)
Hyaluronic acid	1 (6.7%)	3 (6.8%)	3 (1.1%)	2 (9.5%)	3 (5.8%)	5 (1.7%)	3 (8.3%)	6 (6.3%)	8 (1.4%)
Hypromellose	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	2 (0.7%)	0	2 (2.1%)	3 (0.5%)
Viscoat /01834201/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antiinflammatory agents and antiinfectives in combination	0	0	4 (1.4%)	0	0	4 (1.4%)	0	0	8 (1.4%)
Tobradex	0	0	3 (1.1%)	0	0	1 (0.3%)	0	0	4 (0.7%)
Ciprodac-dm	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dexamytrex /01106201/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Maxitrol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Neodecadron	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antiinfectives	0	0	4 (1.4%)	0	0	1 (0.3%)	0	0	5 (0.9%)
Fusidic acid	0	0	3 (1.1%)	0	0	1 (0.3%)	0	0	4 (0.7%)
Sulfacetamide	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Mydriatics and cycloplegics	0	1 (2.3%)	3 (1.1%)	0	1 (1.9%)	2 (0.7%)	0	2 (2.1%)	5 (0.9%)
Atropine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Homatropine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Hyoscine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Mydrin p	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Tropicamide	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ocular vascular disorder agents	0	0	3 (1.1%)	0	0	0	0	0	3 (0.5%)
Aflibercept	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Ranibizumab	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Verteporfin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antifungals for dermatological use	1 (6.7%)	5 (11.4%)	32 (11.3%)	4 (19.0%)	10 (19.2%)	43 (15.0%)	5 (13.9%)	15 (15.6%)	75 (13.2%)
Antifungals for topical use	1 (6.7%)	5 (11.4%)	30 (10.6%)	4 (19.0%)	10 (19.2%)	42 (14.7%)	5 (13.9%)	15 (15.6%)	72 (12.7%)
Fluconazole	0	3 (6.8%)	22 (7.8%)	3 (14.3%)	7 (13.5%)	34 (11.9%)	3 (8.3%)	10 (10.4%)	56 (9.8%)
Clotrimazole	0	0	5 (1.8%)	0	0	6 (2.1%)	0	0	11 (1.9%)
Bifonazole	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Canesten-hc	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Isoconazole	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Amorolfine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Antifungals for topical use	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Brentan /00745201/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Butenafine	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Daktacort	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Diflucortolone valerate w/isoconazole	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Efinaconazole	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Sulconazole	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Antifungals for systemic use	0	0	2 (0.7%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Terbinafine	0	0	2 (0.7%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Antiepileptics	2 (13.3%)	11 (25.0%)	31 (11.0%)	1 (4.8%)	8 (15.4%)	31 (10.8%)	3 (8.3%)	19 (19.8%)	62 (10.9%)
Antiepileptics	2 (13.3%)	11 (25.0%)	31 (11.0%)	1 (4.8%)	8 (15.4%)	31 (10.8%)	3 (8.3%)	19 (19.8%)	62 (10.9%)
Gabapentin	0	9 (20.5%)	25 (8.8%)	0	6 (11.5%)	21 (7.3%)	0	15 (15.6%)	46 (8.1%)
Clonazepam	1 (6.7%)	1 (2.3%)	3 (1.1%)	0	1 (1.9%)	6 (2.1%)	1 (2.8%)	2 (2.1%)	9 (1.6%)
Levetiracetam	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Carbamazepine	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Valproic acid	1 (6.7%)	2 (4.5%)	2 (0.7%)	0	0	0	1 (2.8%)	2 (2.1%)	2 (0.4%)
Ergenyl chrono	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Lacosamide	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Lamotrigine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Phenytoin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Primidone	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Urologicals	2 (13.3%)	7 (15.9%)	30 (10.6%)	1 (4.8%)	5 (9.6%)	32 (11.2%)	3 (8.3%)	12 (12.5%)	62 (10.9%)
Drugs used in benign prostatic hypertrophy	1 (6.7%)	5 (11.4%)	20 (7.1%)	1 (4.8%)	5 (9.6%)	26 (9.1%)	2 (5.6%)	10 (10.4%)	46 (8.1%)
Tamsulosin	0	4 (9.1%)	15 (5.3%)	1 (4.8%)	3 (5.8%)	16 (5.6%)	1 (2.8%)	7 (7.3%)	31 (5.4%)
Alfuzosin	0	0	3 (1.1%)	0	1 (1.9%)	4 (1.4%)	0	1 (1.0%)	7 (1.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Finasteride	0	0	2 (0.7%)	0	1 (1.9%)	4 (1.4%)	0	1 (1.0%)	6 (1.1%)
Dutasteride	0	0	3 (1.1%)	0	0	1 (0.3%)	0	0	4 (0.7%)
Dutas-t	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Silodosin	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	2 (0.4%)
Urologicals	1 (6.7%)	3 (6.8%)	14 (4.9%)	0	0	8 (2.8%)	1 (2.8%)	3 (3.1%)	22 (3.9%)
Reducto	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Sildenafil	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Fesoterodine	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Mirabegron	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Solifenacin	0	0	3 (1.1%)	0	0	0	0	0	3 (0.5%)
Tolterodine	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Oxybutynin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Phenazopyridine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Rowatinex /00499401/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Udenafil	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Vardenafil	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Nasal preparations	1 (6.7%)	12 (27.3%)	23 (8.1%)	0	12 (23.1%)	33 (11.5%)	1 (2.8%)	24 (25.0%)	56 (9.8%)
Nasal decongestants for systemic use	1 (6.7%)	11 (25.0%)	14 (4.9%)	0	10 (19.2%)	16 (5.6%)	1 (2.8%)	21 (21.9%)	30 (5.3%)
Pseudoephedrine	0	5 (11.4%)	6 (2.1%)	0	2 (3.8%)	4 (1.4%)	0	7 (7.3%)	10 (1.8%)
Actifed /00005601/	0	3 (6.8%)	3 (1.1%)	0	5 (9.6%)	5 (1.7%)	0	8 (8.3%)	8 (1.4%)
Narine /01202601/	0	3 (6.8%)	4 (1.4%)	0	0	2 (0.7%)	0	3 (3.1%)	6 (1.1%)
Allegra-d /01367401/	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Actifedrin /01573901/	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Chlorphenamine w/phenylephrine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Loratadine w/pseudoephedrine	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Nussidex	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Phenylpropanolamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Sympathomimetics	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Decongestants and other nasal preparations for topical use	0	3 (6.8%)	11 (3.9%)	0	2 (3.8%)	18 (6.3%)	0	5 (5.2%)	29 (5.1%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Xylometazoline	0	0	2 (0.7%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	5 (0.9%)
Oxymetazoline	0	0	1 (0.4%)	0	0	3 (1.0%)	0	0	4 (0.7%)
Olopatadine	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	2 (0.7%)	0	2 (2.1%)	3 (0.5%)
Budesonide	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Fluticasone	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Mometasone	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Tetryzoline	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Azelastine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Beclometasone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dexa-rhinospray /00397101/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Duonase /06209401/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Endal	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Naphazoline	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Rhinaris /00678601/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tixocortol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Tramazoline	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Triamcinolone	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Triofan	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
All other therapeutic products	1 (6.7%)	2 (4.5%)	19 (6.7%)	2 (9.5%)	4 (7.7%)	36 (12.6%)	3 (8.3%)	6 (6.3%)	55 (9.7%)
All other therapeutic products	1 (6.7%)	2 (4.5%)	19 (6.7%)	2 (9.5%)	4 (7.7%)	36 (12.6%)	3 (8.3%)	6 (6.3%)	55 (9.7%)
Folinic acid	0	0	10 (3.5%)	0	0	12 (4.2%)	0	0	22 (3.9%)
Oxygen	0	0	1 (0.4%)	2 (9.5%)	3 (5.8%)	17 (5.9%)	2 (5.6%)	3 (3.1%)	18 (3.2%)
All other therapeutic products	0	0	2 (0.7%)	0	1 (1.9%)	7 (2.4%)	0	1 (1.0%)	9 (1.6%)
Calcium polystyrene sulfonate	0	1 (2.3%)	2 (0.7%)	0	0	0	0	1 (1.0%)	2 (0.4%)
Mesna	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Sodium polystyrene sulfonate	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Flumazenil	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Herbal extract nos w/nicotinic acid/riboflavi	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Naloxone	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Propylparaben	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Rasburicase	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Corticosteroids, dermatological preparations	3 (20.0%)	9 (20.5%)	27 (9.5%)	8 (38.1%)	14 (26.9%)	28 (9.8%)	11 (30.6%)	23 (24.0%)	55 (9.7%)
Corticosteroids, plain	3 (20.0%)	9 (20.5%)	26 (9.2%)	8 (38.1%)	14 (26.9%)	27 (9.4%)	11 (30.6%)	23 (24.0%)	53 (9.3%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Mometasone	0	0	4 (1.4%)	2 (9.5%)	3 (5.8%)	7 (2.4%)	2 (5.6%)	3 (3.1%)	11 (1.9%)
Betamethasone	1 (6.7%)	1 (2.3%)	4 (1.4%)	2 (9.5%)	2 (3.8%)	5 (1.7%)	3 (8.3%)	3 (3.1%)	9 (1.6%)
Hydrocortisone	0	1 (2.3%)	5 (1.8%)	0	0	4 (1.4%)	0	1 (1.0%)	9 (1.6%)
Triamcinolone	0	0	4 (1.4%)	0	2 (3.8%)	5 (1.7%)	0	2 (2.1%)	9 (1.6%)
Clobetasol	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	2 (0.7%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Desonide	0	2 (4.5%)	2 (0.7%)	0	0	1 (0.3%)	0	2 (2.1%)	3 (0.5%)
Desoximetasone	0	2 (4.5%)	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	3 (3.1%)	3 (0.5%)
Dexamethasone	0	0	0	1 (4.8%)	3 (5.8%)	3 (1.0%)	1 (2.8%)	3 (3.1%)	3 (0.5%)
Fluorometholone	0	1 (2.3%)	1 (0.4%)	1 (4.8%)	2 (3.8%)	2 (0.7%)	1 (2.8%)	3 (3.1%)	3 (0.5%)
Beclometasone	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Difluprednate	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Methylprednisolone	0	1 (2.3%)	2 (0.7%)	0	0	0	0	1 (1.0%)	2 (0.4%)
Alclometasone	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Prednisolone	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Corticosteroids, combinations with antibiotics	2 (13.3%)	2 (4.5%)	3 (1.1%)	3 (14.3%)	3 (5.8%)	5 (1.7%)	5 (13.9%)	5 (5.2%)	8 (1.4%)
Valisone-g	2 (13.3%)	2 (4.5%)	2 (0.7%)	3 (14.3%)	3 (5.8%)	3 (1.0%)	5 (13.9%)	5 (5.2%)	5 (0.9%)
Mycolog	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Polycutan	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Corticosteroids, combinations with antiseptics	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Lacticare hc /02298001/	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Corticosteroids, other combinations	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Corticosteroids, other combinations	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Throat preparations	4 (26.7%)	14 (31.8%)	29 (10.2%)	6 (28.6%)	11 (21.2%)	26 (9.1%)	10 (27.8%)	25 (26.0%)	55 (9.7%)
Throat preparations	4 (26.7%)	14 (31.8%)	29 (10.2%)	6 (28.6%)	11 (21.2%)	26 (9.1%)	10 (27.8%)	25 (26.0%)	55 (9.7%)
Lidocaine	3 (20.0%)	11 (25.0%)	16 (5.7%)	4 (19.0%)	7 (13.5%)	15 (5.2%)	7 (19.4%)	18 (18.8%)	31 (5.4%)
Chlorhexidine	0	5 (11.4%)	12 (4.2%)	0	2 (3.8%)	7 (2.4%)	0	7 (7.3%)	19 (3.3%)
Povidone-iodine	2 (13.3%)	2 (4.5%)	5 (1.8%)	3 (14.3%)	3 (5.8%)	3 (1.0%)	5 (13.9%)	5 (5.2%)	8 (1.4%)
Antiseptics	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Biclotymol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Colludol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Strepsils /00200801/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Cardiac therapy	0	4 (9.1%)	26 (9.2%)	2 (9.5%)	3 (5.8%)	26 (9.1%)	2 (5.6%)	7 (7.3%)	52 (9.1%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Vasodilators used in cardiac diseases	0	1 (2.3%)	10 (3.5%)	1 (4.8%)	1 (1.9%)	9 (3.1%)	1 (2.8%)	2 (2.1%)	19 (3.3%)
Glyceryl trinitrate	0	0	6 (2.1%)	1 (4.8%)	1 (1.9%)	7 (2.4%)	1 (2.8%)	1 (1.0%)	13 (2.3%)
Isosorbide dinitrate	0	1 (2.3%)	3 (1.1%)	0	0	0	0	1 (1.0%)	3 (0.5%)
Isosorbide mononitrate	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Molsidomine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Nicorandil	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Nitric oxide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Antiarrhythmics, class i and iii	0	0	5 (1.8%)	0	0	12 (4.2%)	0	0	17 (3.0%)
Amiodarone	0	0	4 (1.4%)	0	0	9 (3.1%)	0	0	13 (2.3%)
Flecainide	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Propafenone	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Cardiac stimulants excl. cardiac glycosides	0	1 (2.3%)	6 (2.1%)	1 (4.8%)	2 (3.8%)	8 (2.8%)	1 (2.8%)	3 (3.1%)	14 (2.5%)
Norepinephrine	0	0	3 (1.1%)	0	1 (1.9%)	4 (1.4%)	0	1 (1.0%)	7 (1.2%)
Dopamine	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Phenylephrine	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Bucladesine	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Dobutamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Levosimendan	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Midodrine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Cardiac glycosides	0	0	5 (1.8%)	0	0	5 (1.7%)	0	0	10 (1.8%)
Digoxin	0	0	5 (1.8%)	0	0	5 (1.7%)	0	0	10 (1.8%)
Other cardiac preparations	0	2 (4.5%)	5 (1.8%)	0	0	1 (0.3%)	0	2 (2.1%)	6 (1.1%)
Limaprost	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Trimetazidine	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Adenosine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Trophicard	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Vaccines	4 (26.7%)	7 (15.9%)	23 (8.1%)	3 (14.3%)	7 (13.5%)	26 (9.1%)	7 (19.4%)	14 (14.6%)	49 (8.6%)
Viral vaccines	4 (26.7%)	6 (13.6%)	21 (7.4%)	3 (14.3%)	7 (13.5%)	25 (8.7%)	7 (19.4%)	13 (13.5%)	46 (8.1%)
Influenza vaccine	4 (26.7%)	6 (13.6%)	19 (6.7%)	3 (14.3%)	7 (13.5%)	24 (8.4%)	7 (19.4%)	13 (13.5%)	43 (7.6%)
Hepatitis a vaccine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Hepatitis b vaccine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Measles mumps & rubella live attenuated (free	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Yellow fever vaccine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Bacterial vaccines	0	1 (2.3%)	6 (2.1%)	0	0	1 (0.3%)	0	1 (1.0%)	7 (1.2%)
Pneumococcal vaccine	0	1 (2.3%)	5 (1.8%)	0	0	1 (0.3%)	0	1 (1.0%)	6 (1.1%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Ditemer	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Haemophilus influenza type b vaccine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Vaccin ipad d.t.c.	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Immune sera and immunoglobulins	2 (13.3%)	3 (6.8%)	21 (7.4%)	3 (14.3%)	4 (7.7%)	23 (8.0%)	5 (13.9%)	7 (7.3%)	44 (7.7%)
Immunoglobulins	2 (13.3%)	3 (6.8%)	21 (7.4%)	3 (14.3%)	4 (7.7%)	23 (8.0%)	5 (13.9%)	7 (7.3%)	44 (7.7%)
Immunoglobulin human normal	2 (13.3%)	3 (6.8%)	16 (5.7%)	3 (14.3%)	3 (5.8%)	21 (7.3%)	5 (13.9%)	6 (6.3%)	37 (6.5%)
Immunoglobulins	0	0	5 (1.8%)	0	0	1 (0.3%)	0	0	6 (1.1%)
Immunoglobulin g human	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Thyroid therapy	0	0	24 (8.5%)	0	0	17 (5.9%)	0	0	41 (7.2%)
Thyroid preparations	0	0	22 (7.8%)	0	0	17 (5.9%)	0	0	39 (6.9%)
Levothyroxine	0	0	22 (7.8%)	0	0	17 (5.9%)	0	0	39 (6.9%)
Antithyroid preparations	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Thiamazole	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Carbimazole	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Sodium perchlorate	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antiemetics and antinauseants	0	0	12 (4.2%)	0	2 (3.8%)	28 (9.8%)	0	2 (2.1%)	40 (7.0%)
Antiemetics and antinauseants	0	0	12 (4.2%)	0	2 (3.8%)	28 (9.8%)	0	2 (2.1%)	40 (7.0%)
Ondansetron	0	0	12 (4.2%)	0	1 (1.9%)	23 (8.0%)	0	1 (1.0%)	35 (6.2%)
Granisetron	0	0	0	0	1 (1.9%)	5 (1.7%)	0	1 (1.0%)	5 (0.9%)
Gynecological antiinfectives and antiseptics	0	0	16 (5.7%)	0	3 (5.8%)	17 (5.9%)	0	3 (3.1%)	33 (5.8%)
Antiinfectives and antiseptics, excl. combinations with corticosteroids	0	0	16 (5.7%)	0	3 (5.8%)	17 (5.9%)	0	3 (3.1%)	33 (5.8%)
Metronidazole	0	0	11 (3.9%)	0	1 (1.9%)	13 (4.5%)	0	1 (1.0%)	24 (4.2%)
Ciclopirox	0	0	1 (0.4%)	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	3 (0.5%)
Econazole	0	0	3 (1.1%)	0	0	0	0	0	3 (0.5%)
Ornidazole	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Sertaconazole	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tinidazole	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
General nutrients	0	2 (4.5%)	13 (4.6%)	5 (23.8%)	6 (11.5%)	17 (5.9%)	5 (13.9%)	8 (8.3%)	30 (5.3%)
Other nutrients	0	2 (4.5%)	10 (3.5%)	4 (19.0%)	5 (9.6%)	13 (4.5%)	4 (11.1%)	7 (7.3%)	23 (4.0%)
Glucose	0	2 (4.5%)	9 (3.2%)	1 (4.8%)	1 (1.9%)	9 (3.1%)	1 (2.8%)	3 (3.1%)	18 (3.2%)
Amino acids nos w/electrolytes nos/glucose/th	0	0	0	3 (14.3%)	3 (5.8%)	3 (1.0%)	3 (8.3%)	3 (3.1%)	3 (0.5%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Amino acids nos w/carbohydrates nos/07403601/	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Caffeine w/carbohydrates nos/cholin/08302001/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other combinations of nutrients	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Uncoded	0	0	3 (1.1%)	2 (9.5%)	2 (3.8%)	6 (2.1%)	2 (5.6%)	2 (2.1%)	9 (1.6%)
Nutrients nos	0	0	2 (0.7%)	2 (9.5%)	2 (3.8%)	3 (1.0%)	2 (5.6%)	2 (2.1%)	5 (0.9%)
General nutrients	0	0	1 (0.4%)	0	0	3 (1.0%)	0	0	4 (0.7%)
Protein supplements	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Carbohydrates nos w/lipids nos/mine/07460201/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antimycotics for systemic use	0	1 (2.3%)	9 (3.2%)	4 (19.0%)	4 (7.7%)	19 (6.6%)	4 (11.1%)	5 (5.2%)	28 (4.9%)
Antimycotics for systemic use	0	1 (2.3%)	9 (3.2%)	4 (19.0%)	4 (7.7%)	19 (6.6%)	4 (11.1%)	5 (5.2%)	28 (4.9%)
Amphotericin b	0	0	3 (1.1%)	1 (4.8%)	1 (1.9%)	6 (2.1%)	1 (2.8%)	1 (1.0%)	9 (1.6%)
Voriconazole	0	0	3 (1.1%)	1 (4.8%)	1 (1.9%)	5 (1.7%)	1 (2.8%)	1 (1.0%)	8 (1.4%)
Caspofungin	0	0	2 (0.7%)	0	0	3 (1.0%)	0	0	5 (0.9%)
Ketoconazole	0	0	0	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Itraconazole	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Micafungin	0	0	0	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Posaconazole	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Fluconazole	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Emollients and protectives	2 (13.3%)	2 (4.5%)	12 (4.2%)	4 (19.0%)	8 (15.4%)	16 (5.6%)	6 (16.7%)	10 (10.4%)	28 (4.9%)
Emollients and protectives	2 (13.3%)	2 (4.5%)	12 (4.2%)	4 (19.0%)	8 (15.4%)	16 (5.6%)	6 (16.7%)	10 (10.4%)	28 (4.9%)
Dimeticone	2 (13.3%)	2 (4.5%)	2 (0.7%)	3 (14.3%)	4 (7.7%)	5 (1.7%)	5 (13.9%)	6 (6.3%)	7 (1.2%)
Urea	0	0	4 (1.4%)	0	0	0	0	0	4 (0.7%)
Other emollients and protectives	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Cream e45	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Paraffin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Salicylic acid	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Vitapantol	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Aqueous /00662801/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Dexeryl /01579901/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Emollients and protectives	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

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	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Fenuril	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Paraffin soft	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Petrolatum	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Propylene glycol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Sprilon	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
White soft paraffin	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Muscle relaxants	2 (13.3%)	11 (25.0%)	18 (6.4%)	0	0	10 (3.5%)	2 (5.6%)	11 (11.5%)	28 (4.9%)
Muscle relaxants, centrally acting agents	2 (13.3%)	11 (25.0%)	16 (5.7%)	0	0	9 (3.1%)	2 (5.6%)	11 (11.5%)	25 (4.4%)
Baclofen	1 (6.7%)	6 (13.6%)	7 (2.5%)	0	0	6 (2.1%)	1 (2.8%)	6 (6.3%)	13 (2.3%)
Chlorzoxazone	0	3 (6.8%)	4 (1.4%)	0	0	0	0	3 (3.1%)	4 (0.7%)
Cyclobenzaprine	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Tizanidine	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	3 (0.5%)
Eperisone	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Afloqualone	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Chlormezanone	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Methocarbamol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Norgesic /00070401/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Thiocolchicoside	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Muscle relaxants, peripherally acting agents	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Atracurium	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Cisatracurium	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antibiotics and chemotherapeutics for dermatological use	0	8 (18.2%)	15 (5.3%)	0	5 (9.6%)	11 (3.8%)	0	13 (13.5%)	26 (4.6%)
Antibiotics for topical use	0	7 (15.9%)	12 (4.2%)	0	4 (7.7%)	8 (2.8%)	0	11 (11.5%)	20 (3.5%)
Mupirocin	0	5 (11.4%)	7 (2.5%)	0	3 (5.8%)	4 (1.4%)	0	8 (8.3%)	11 (1.9%)
Naseptin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Neotracin /00038301/	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Doxycycline	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Neosporin /00130801/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Spersin /00125501/	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Terramycin ophthalmic	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Tetracycline	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Chemotherapeutics for topical use	0	1 (2.3%)	3 (1.1%)	0	1 (1.9%)	3 (1.0%)	0	2 (2.1%)	6 (1.1%)
Lysozyme	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Sulfadiazine	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Ingenol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Sulfathiazole	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antihemorrhagics	2 (13.3%)	5 (11.4%)	12 (4.2%)	1 (4.8%)	2 (3.8%)	13 (4.5%)	3 (8.3%)	7 (7.3%)	25 (4.4%)
Vitamin k and other hemostatics	1 (6.7%)	2 (4.5%)	8 (2.8%)	0	0	8 (2.8%)	1 (2.8%)	2 (2.1%)	16 (2.8%)
Phytomenadione	0	1 (2.3%)	3 (1.1%)	0	0	4 (1.4%)	0	1 (1.0%)	7 (1.2%)
Vitamin k nos	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Etamsilate	0	0	1 (0.4%)	0	0	2 (0.7%)	0	0	3 (0.5%)
Carbazochrome	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Factor viii (antihaemophilic factor)	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Prothrombinex	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antifibrinolytics	1 (6.7%)	4 (9.1%)	7 (2.5%)	1 (4.8%)	2 (3.8%)	6 (2.1%)	2 (5.6%)	6 (6.3%)	13 (2.3%)
Tranexamic acid	1 (6.7%)	2 (4.5%)	5 (1.8%)	1 (4.8%)	2 (3.8%)	6 (2.1%)	2 (5.6%)	4 (4.2%)	11 (1.9%)
Amino acids	0	2 (4.5%)	2 (0.7%)	0	0	0	0	2 (2.1%)	2 (0.4%)
Aminocaproic acid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Sex hormones and modulators of the genital system	0	8 (18.2%)	13 (4.6%)	0	6 (11.5%)	12 (4.2%)	0	14 (14.6%)	25 (4.4%)
Hormonal contraceptives for systemic use	0	7 (15.9%)	7 (2.5%)	0	6 (11.5%)	8 (2.8%)	0	13 (13.5%)	15 (2.6%)
Megestrol	0	7 (15.9%)	7 (2.5%)	0	6 (11.5%)	7 (2.4%)	0	13 (13.5%)	14 (2.5%)
Femodene	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Androgens	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Testosterone	0	0	3 (1.1%)	0	0	2 (0.7%)	0	0	5 (0.9%)
Estrogens	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Estriol	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Progestogens and estrogens in combination	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Femseven /06804201/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Oestranorm	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Progestogens	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Progesterone	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Anesthetics	0	2 (4.5%)	11 (3.9%)	2 (9.5%)	4 (7.7%)	12 (4.2%)	2 (5.6%)	6 (6.3%)	23 (4.0%)
Anesthetics, general	0	0	6 (2.1%)	0	0	7 (2.4%)	0	0	13 (2.3%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Propofol	0	0	6 (2.1%)	0	0	5 (1.7%)	0	0	11 (1.9%)
Alfentanil	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Remifentanil	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Anesthetics, local	0	2 (4.5%)	7 (2.5%)	2 (9.5%)	4 (7.7%)	5 (1.7%)	2 (5.6%)	6 (6.3%)	12 (2.1%)
Lidocaine	0	0	3 (1.1%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Oxetacaine	0	2 (4.5%)	2 (0.7%)	0	1 (1.9%)	1 (0.3%)	0	3 (3.1%)	3 (0.5%)
Bupivacaine	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Xylocaine-epinephrine	0	0	0	2 (9.5%)	2 (3.8%)	2 (0.7%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Cepacol anesthetic	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Ottocain	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Antiprotozoals	1 (6.7%)	1 (2.3%)	8 (2.8%)	1 (4.8%)	1 (1.9%)	14 (4.9%)	2 (5.6%)	2 (2.1%)	22 (3.9%)
Agents against leishmaniasis and trypanosomiasis	1 (6.7%)	1 (2.3%)	6 (2.1%)	1 (4.8%)	1 (1.9%)	10 (3.5%)	2 (5.6%)	2 (2.1%)	16 (2.8%)
Pentamidine	1 (6.7%)	1 (2.3%)	6 (2.1%)	1 (4.8%)	1 (1.9%)	10 (3.5%)	2 (5.6%)	2 (2.1%)	16 (2.8%)
Antimalarials	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Quinine	0	0	2 (0.7%)	0	0	2 (0.7%)	0	0	4 (0.7%)
Agents against amoebiasis and other protozoal diseases	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Atovaquone	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Other alimentary tract and metabolism products	1 (6.7%)	3 (6.8%)	8 (2.8%)	2 (9.5%)	2 (3.8%)	9 (3.1%)	3 (8.3%)	5 (5.2%)	17 (3.0%)
Other alimentary tract and metabolism products	1 (6.7%)	3 (6.8%)	8 (2.8%)	2 (9.5%)	2 (3.8%)	8 (2.8%)	3 (8.3%)	5 (5.2%)	16 (2.8%)
Clostridium butyricum	1 (6.7%)	1 (2.3%)	1 (0.4%)	2 (9.5%)	2 (3.8%)	2 (0.7%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Phosphorus	0	0	0	0	0	3 (1.0%)	0	0	3 (0.5%)
Thioctic acid	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Ubidecarenone	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.3%)	0	1 (1.0%)	3 (0.5%)
Ademetionine	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Probiotics nos	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Uncoded	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other alimentary tract and metabolism product	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antihypertensives	1 (6.7%)	1 (2.3%)	9 (3.2%)	0	1 (1.9%)	7 (2.4%)	1 (2.8%)	2 (2.1%)	16 (2.8%)
Antiadrenergic agents, peripherally acting	1 (6.7%)	1 (2.3%)	6 (2.1%)	0	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	8 (1.4%)
Doxazosin	1 (6.7%)	1 (2.3%)	6 (2.1%)	0	0	0	1 (2.8%)	1 (1.0%)	6 (1.1%)
Naftopidil	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Urapidil	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Antiadrenergic agents, centrally acting	0	0	1 (0.4%)	0	0	3 (1.0%)	0	0	4 (0.7%)
Clonidine	0	0	1 (0.4%)	0	0	3 (1.0%)	0	0	4 (0.7%)
Arteriolar smooth muscle, agents acting on	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Hydralazine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Nitroprusside	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other antihypertensives	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Tadalafil	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Other nervous system drugs	1 (6.7%)	2 (4.5%)	10 (3.5%)	1 (4.8%)	2 (3.8%)	4 (1.4%)	2 (5.6%)	4 (4.2%)	14 (2.5%)
Antivertigo preparations	1 (6.7%)	2 (4.5%)	7 (2.5%)	0	0	1 (0.3%)	1 (2.8%)	2 (2.1%)	8 (1.4%)
Betahistine	1 (6.7%)	1 (2.3%)	4 (1.4%)	0	0	0	1 (2.8%)	1 (1.0%)	4 (0.7%)
Flunarizine	0	1 (2.3%)	2 (0.7%)	0	0	0	0	1 (1.0%)	2 (0.4%)
Acetylleucine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antivert /07534501/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Drugs used in addictive disorders	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Methadone	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Other nervous system drugs	0	0	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Edaravone	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Fampridine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Parasympathomimetics	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Bethanechol	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Vasoprotectives	0	1 (2.3%)	6 (2.1%)	0	1 (1.9%)	8 (2.8%)	0	2 (2.1%)	14 (2.5%)
Agents for treatment of hemorrhoids and anal fissures for topical use	0	1 (2.3%)	5 (1.8%)	0	1 (1.9%)	7 (2.4%)	0	2 (2.1%)	12 (2.1%)
Corticosteroid nos	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Anamantle hc /02344701/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Doloproct /00951901/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Ego soov it	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Fluocinonide	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Hemcort h.c.	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Levan h	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Other agents for treatment of hemorrhoids and	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Pramocaine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Rectinol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Scheriproct /01814801/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Xyloproct plus	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Capillary stabilizing agents	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Diosmin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Peripheral vasodilators	0	2 (4.5%)	7 (2.5%)	0	2 (3.8%)	6 (2.1%)	0	4 (4.2%)	13 (2.3%)
Peripheral vasodilators	0	2 (4.5%)	7 (2.5%)	0	2 (3.8%)	6 (2.1%)	0	4 (4.2%)	13 (2.3%)
Nicergoline	0	1 (2.3%)	3 (1.1%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	4 (0.7%)
Pentoxifylline	0	1 (2.3%)	2 (0.7%)	0	1 (1.9%)	2 (0.7%)	0	2 (2.1%)	4 (0.7%)
Methylethylpiridinol	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Histamine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Nicotinic acid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Digestives, incl. enzymes	1 (6.7%)	2 (4.5%)	7 (2.5%)	0	4 (7.7%)	5 (1.7%)	1 (2.8%)	6 (6.3%)	12 (2.1%)
Digestives, incl. enzymes	1 (6.7%)	2 (4.5%)	7 (2.5%)	0	4 (7.7%)	5 (1.7%)	1 (2.8%)	6 (6.3%)	12 (2.1%)
Pancreatin	0	0	4 (1.4%)	0	0	1 (0.3%)	0	0	5 (0.9%)
Beszyme	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Pangest f	0	0	0	0	2 (3.8%)	2 (0.7%)	0	2 (2.1%)	2 (0.4%)
Citric acid	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Enzyme preparations	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Voltmie	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Stomatological preparations	1 (6.7%)	1 (2.3%)	6 (2.1%)	1 (4.8%)	1 (1.9%)	6 (2.1%)	2 (5.6%)	2 (2.1%)	12 (2.1%)
Stomatological preparations	1 (6.7%)	1 (2.3%)	6 (2.1%)	1 (4.8%)	1 (1.9%)	6 (2.1%)	2 (5.6%)	2 (2.1%)	12 (2.1%)
Hexetidine	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Gualenic acid	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	2 (5.6%)	2 (2.1%)	2 (0.4%)
Magic mouthwash	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Periodil /02665801/	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Difflam mouth	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Frubienzym	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Saliveht	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Stomatologicals, mouth preparations	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Other drugs for disorders of the musculo-skeletal system	0	0	2 (0.7%)	0	1 (1.9%)	7 (2.4%)	0	1 (1.0%)	9 (1.6%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Other drugs for disorders of the musculo-skeletal system	0	0	2 (0.7%)	0	1 (1.9%)	7 (2.4%)	0	1 (1.0%)	9 (1.6%)
Quinine	0	0	0	0	0	5 (1.7%)	0	0	5 (0.9%)
Hydroquinine	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Hexaquine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Quinamm /00172101/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Serrapeptase	0	0	0	0	1 (1.9%)	1 (0.3%)	0	1 (1.0%)	1 (0.2%)
Antiseptics and disinfectants	2 (13.3%)	2 (4.5%)	5 (1.8%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	3 (8.3%)	3 (3.1%)	7 (1.2%)
Antiseptics and disinfectants	2 (13.3%)	2 (4.5%)	5 (1.8%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	3 (8.3%)	3 (3.1%)	7 (1.2%)
Dequalinium	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Benzethonium	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0	1 (2.8%)	1 (1.0%)	1 (0.2%)
Dermalex	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Hexamidine	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Phenylmercuric borate	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Savlon hospital	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other hematological agents	0	3 (6.8%)	3 (1.1%)	1 (4.8%)	4 (7.7%)	4 (1.4%)	1 (2.8%)	7 (7.3%)	7 (1.2%)
Other hematological agents	0	3 (6.8%)	3 (1.1%)	1 (4.8%)	4 (7.7%)	4 (1.4%)	1 (2.8%)	7 (7.3%)	7 (1.2%)
Varidase	0	2 (4.5%)	2 (0.7%)	0	3 (5.8%)	3 (1.0%)	0	5 (5.2%)	5 (0.9%)
Bromelains	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Pronase	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Topical products for joint and muscular pain	0	1 (2.3%)	4 (1.4%)	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	2 (2.1%)	7 (1.2%)
Topical products for joint and muscular pain	0	1 (2.3%)	4 (1.4%)	1 (4.8%)	1 (1.9%)	3 (1.0%)	1 (2.8%)	2 (2.1%)	7 (1.2%)
Capsaicin	0	1 (2.3%)	3 (1.1%)	0	0	0	0	1 (1.0%)	3 (0.5%)
Etofenamate	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Felbinac	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Menthol w/methyl salicylate	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Salicylic acid	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Anti-parkinson drugs	0	0	0	1 (4.8%)	1 (1.9%)	6 (2.1%)	1 (2.8%)	1 (1.0%)	6 (1.1%)
Dopaminergic agents	0	0	0	1 (4.8%)	1 (1.9%)	6 (2.1%)	1 (2.8%)	1 (1.0%)	6 (1.1%)
Pramipexole	0	0	0	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	1 (1.0%)	2 (0.4%)
Ropinirole	0	0	0	0	0	2 (0.7%)	0	0	2 (0.4%)
Amantadine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Madopar	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Sinemet	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Stalevo /01631201/	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antineoplastic agents	0	0	4 (1.4%)	0	0	2 (0.7%)	0	0	6 (1.1%)
Antimetabolites	0	0	2 (0.7%)	0	0	1 (0.3%)	0	0	3 (0.5%)
Fluorouracil	0	0	2 (0.7%)	0	0	0	0	0	2 (0.4%)
Azacitidine	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Cytotoxic antibiotics and related substances	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Doxorubicin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Other antineoplastic agents	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Bevacizumab	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Calcium folinate w/fluorouracil/iri/08195201/	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Anti-acne preparations	0	0	0	1 (4.8%)	1 (1.9%)	5 (1.7%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Anti-acne preparations for topical use	0	0	0	1 (4.8%)	1 (1.9%)	5 (1.7%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Dapsone	0	0	0	1 (4.8%)	1 (1.9%)	4 (1.4%)	1 (2.8%)	1 (1.0%)	4 (0.7%)
Tretinoin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antimycobacterials	0	1 (2.3%)	3 (1.1%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	5 (0.9%)
Drugs for treatment of tuberculosis	0	1 (2.3%)	3 (1.1%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	5 (0.9%)
Rifampicin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Cycloserine	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Isoniazid	0	0	0	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	1 (1.0%)	1 (0.2%)
Pyrazinamide	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Rifinah	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Bile and liver therapy	0	1 (2.3%)	3 (1.1%)	1 (4.8%)	1 (1.9%)	2 (0.7%)	1 (2.8%)	2 (2.1%)	5 (0.9%)
Bile therapy	0	1 (2.3%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	3 (0.5%)
Ursodeoxycholic acid	0	1 (2.3%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	1 (2.8%)	2 (2.1%)	3 (0.5%)
Liver therapy, lipotropics	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Phosphogliv /06724301/	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Calcium homeostasis	0	0	2 (0.7%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	5 (0.9%)
Anti-parathyroid agents	0	0	2 (0.7%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	5 (0.9%)
Calcitonin	0	0	1 (0.4%)	0	1 (1.9%)	3 (1.0%)	0	1 (1.0%)	4 (0.7%)
Cinacalcet	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Endocrine therapy	0	1 (2.3%)	3 (1.1%)	0	0	2 (0.7%)	0	1 (1.0%)	5 (0.9%)
Hormones and related agents	0	1 (2.3%)	3 (1.1%)	0	0	2 (0.7%)	0	1 (1.0%)	5 (0.9%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Estradiol	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Estrogens conjugated	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Triptorelin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Contrast media	0	1 (2.3%)	2 (0.7%)	0	0	2 (0.7%)	0	1 (1.0%)	4 (0.7%)
Magnetic resonance imaging contrast media	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (1.0%)	2 (0.4%)
Gadobenic acid	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Gadobutrol	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
X-ray contrast media, iodinated	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Gastrografin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Iohexol	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Preparations for treatment of wounds and ulcers	0	1 (2.3%)	2 (0.7%)	0	1 (1.9%)	2 (0.7%)	0	2 (2.1%)	4 (0.7%)
Uncoded	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Cb /01734801/	0	1 (2.3%)	1 (0.4%)	0	1 (1.9%)	1 (0.3%)	0	2 (2.1%)	2 (0.4%)
Cicatrizants	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Vita merfen	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Enzymes	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Collagenase	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Other dermatological preparations	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Other dermatological preparations	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Guaiazulene	2 (13.3%)	2 (4.5%)	2 (0.7%)	1 (4.8%)	1 (1.9%)	1 (0.3%)	3 (8.3%)	3 (3.1%)	3 (0.5%)
Pituitary and hypothalamic hormones and analogues	0	1 (2.3%)	3 (1.1%)	0	0	0	0	1 (1.0%)	3 (0.5%)
Anterior pituitary lobe hormones and analogues	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Corticotropin	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Hypothalamic hormones	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Octreotide	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Posterior pituitary lobe hormones	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Vasopressin	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Immunosuppressants	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Immunosuppressants	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Leflunomide	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Tacrolimus	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

TSICM01_3003: Summary of Concomitant Medications by Therapeutic Class, Pharmacologic Class, and Drug; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Otologicals	0	1 (2.3%)	2 (0.7%)	0	0	0	0	1 (1.0%)	2 (0.4%)
Corticosteroids	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Dexamethasone	0	1 (2.3%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (0.2%)
Corticosteroids and antiinfectives in combination	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Auricularum	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)
Tonics	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Tonics	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Curcumin	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	2 (0.4%)
Antipsoriatics	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Antipsoriatics for systemic use	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Acitretin	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Medicated dressings	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Medicated dressings	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)
Medicated dressings with antiinfectives	0	0	0	0	0	1 (0.3%)	0	0	1 (0.2%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Percentages calculated with the number of subjects in each treatment group as denominator.

[TSICM01_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSICM01_3003.SAS] 02JUL2016, 00:00

表 2.7.4-付録-24 Selected Concomitant Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSICM01: Selected Concomitant Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Total number of subjects received the selected concomitant medications	22 (95.7%)	54 (98.2%)	155 (99.4%)	3 (100.0%)	234 (98.7%)
Therapeutic class/Pharmacologic class/Preferred term					
Analgesics	17 (73.9%)	43 (78.2%)	136 (87.2%)	2 (66.7%)	198 (83.5%)
Other analgesics and antipyretics	16 (69.6%)	34 (61.8%)	113 (72.4%)	1 (33.3%)	164 (69.2%)
Paracetamol	12 (52.2%)	22 (40.0%)	62 (39.7%)	1 (33.3%)	97 (40.9%)
Acetylsalicylic acid	7 (30.4%)	10 (18.2%)	54 (34.6%)	0	71 (30.0%)
Pregabalin	3 (13.0%)	5 (9.1%)	16 (10.3%)	0	24 (10.1%)
Carbasalate	0	6 (10.9%)	3 (1.9%)	0	9 (3.8%)
Dozol	0	0	2 (1.3%)	0	2 (0.8%)
Metamizole	0	0	2 (1.3%)	0	2 (0.8%)
Albyl-enterosolubile	1 (4.3%)	1 (1.8%)	1 (0.6%)	0	3 (1.3%)
Lenoltec with codeine no 1	0	0	1 (0.6%)	0	1 (0.4%)
Magnyl /02350501/	0	0	1 (0.6%)	0	1 (0.4%)
Phenflu g	0	0	1 (0.6%)	0	1 (0.4%)
Robaxisal compuesto	0	0	1 (0.6%)	0	1 (0.4%)
Tylenol sinus medication	0	0	1 (0.6%)	0	1 (0.4%)
Vicks formula 44m /01056501/	0	0	1 (0.6%)	0	1 (0.4%)
Opioids	11 (47.8%)	29 (52.7%)	97 (62.2%)	1 (33.3%)	138 (58.2%)
Oxycodone	5 (21.7%)	16 (29.1%)	44 (28.2%)	1 (33.3%)	66 (27.8%)
Morphine	5 (21.7%)	7 (12.7%)	23 (14.7%)	0	35 (14.8%)
Fentanyl	2 (8.7%)	10 (18.2%)	17 (10.9%)	0	29 (12.2%)
Hydromorphone	0	1 (1.8%)	17 (10.9%)	0	18 (7.6%)
Tramadol	3 (13.0%)	4 (7.3%)	15 (9.6%)	0	22 (9.3%)
Vicodin	0	3 (5.5%)	8 (5.1%)	0	11 (4.6%)
Oxycocet	0	1 (1.8%)	7 (4.5%)	0	8 (3.4%)
Panadeine co	0	3 (5.5%)	5 (3.2%)	0	8 (3.4%)
Pethidine	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
Procet /01554201/	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
Ketogin	0	0	2 (1.3%)	0	2 (0.8%)
Oxycodone hydrochloride	0	2 (3.6%)	1 (0.6%)	0	3 (1.3%)
Oxycodone/apap /01601701/	0	0	1 (0.6%)	0	1 (0.4%)
Tylox /00446701/	0	0	1 (0.6%)	0	1 (0.4%)
Ultracet	0	0	1 (0.6%)	0	1 (0.4%)
Ketobemidone	1 (4.3%)	0	0	0	1 (0.4%)
Morphine sulfate	0	1 (1.8%)	0	0	1 (0.4%)
Antimigraine preparations	0	0	2 (1.3%)	0	2 (0.8%)
Rizatriptan	0	0	1 (0.6%)	0	1 (0.4%)

TSICM01: Selected Concomitant Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Sumatriptan	0	0	1 (0.6%)	0	1 (0.4%)
Antibacterials for systemic use	9 (39.1%)	42 (76.4%)	115 (73.7%)	2 (66.7%)	168 (70.9%)
Quinolone antibacterials	4 (17.4%)	14 (25.5%)	57 (36.5%)	2 (66.7%)	77 (32.5%)
Levofloxacin	0	6 (10.9%)	32 (20.5%)	0	38 (16.0%)
Ciprofloxacin	3 (13.0%)	8 (14.5%)	27 (17.3%)	2 (66.7%)	40 (16.9%)
Ciprofloxacin hydrochloride	0	0	1 (0.6%)	0	1 (0.4%)
Garenoxacin mesilate	0	0	1 (0.6%)	0	1 (0.4%)
Moxifloxacin	1 (4.3%)	3 (5.5%)	1 (0.6%)	0	5 (2.1%)
Norfloxacin	0	0	1 (0.6%)	0	1 (0.4%)
Sulfonamides and trimethoprim	4 (17.4%)	20 (36.4%)	49 (31.4%)	0	73 (30.8%)
Bactrim	3 (13.0%)	20 (36.4%)	47 (30.1%)	0	70 (29.5%)
Sulfamethoxazole	0	0	2 (1.3%)	0	2 (0.8%)
Co-trimoxazole	2 (8.7%)	0	1 (0.6%)	0	3 (1.3%)
Beta-lactam antibacterials, penicillins	5 (21.7%)	10 (18.2%)	38 (24.4%)	2 (66.7%)	55 (23.2%)
Amoxicillin	3 (13.0%)	2 (3.6%)	10 (6.4%)	0	15 (6.3%)
Augmentin /00756801/	0	2 (3.6%)	9 (5.8%)	0	11 (4.6%)
Pip/tazo	0	0	9 (5.8%)	1 (33.3%)	10 (4.2%)
Spektramox	1 (4.3%)	4 (7.3%)	7 (4.5%)	1 (33.3%)	13 (5.5%)
Piperacillin w/tazobactam /01606301/	0	0	3 (1.9%)	0	3 (1.3%)
Amoxi-clavulanico	0	0	1 (0.6%)	0	1 (0.4%)
Benzylpenicillin	0	0	1 (0.6%)	0	1 (0.4%)
Flucloxacillin	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
Penicillin nos	0	0	1 (0.6%)	0	1 (0.4%)
Pheneticillin	0	0	1 (0.6%)	0	1 (0.4%)
Piperacillin	0	0	1 (0.6%)	0	1 (0.4%)
Tazobactam	0	0	1 (0.6%)	0	1 (0.4%)
Phenoxymethylpenicillin	0	1 (1.8%)	0	0	1 (0.4%)
Pivmecillinam	1 (4.3%)	2 (3.6%)	0	1 (33.3%)	4 (1.7%)
Macrolides, lincosamides and streptogramins	3 (13.0%)	10 (18.2%)	26 (16.7%)	0	39 (16.5%)
Azithromycin	3 (13.0%)	9 (16.4%)	24 (15.4%)	0	36 (15.2%)
Clarithromycin	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
Clindamycin	0	0	2 (1.3%)	0	2 (0.8%)
Erythromycin	0	0	1 (0.6%)	0	1 (0.4%)
Other beta-lactam antibacterials	0	8 (14.5%)	20 (12.8%)	1 (33.3%)	29 (12.2%)
Ceftriaxone	0	3 (5.5%)	7 (4.5%)	0	10 (4.2%)
Aztreonam	0	0	3 (1.9%)	0	3 (1.3%)
Meropenem	0	3 (5.5%)	3 (1.9%)	0	6 (2.5%)
Cefalexin	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
Cefepime	0	0	2 (1.3%)	0	2 (0.8%)
Cefuroxime	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
Cefadroxil	0	0	1 (0.6%)	0	1 (0.4%)

TSICM01: Selected Concomitant Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Cefazolin	0	0	1 (0.6%)	0	1 (0.4%)
Cefepime hydrochloride	0	0	1 (0.6%)	0	1 (0.4%)
Cefpodoxime	0	0	1 (0.6%)	0	1 (0.4%)
Ceftazidime	0	2 (3.6%)	1 (0.6%)	0	3 (1.3%)
Ceftriaxone sodium	0	0	1 (0.6%)	0	1 (0.4%)
Ertapenem	0	0	0	1 (33.3%)	1 (0.4%)
Other antibacterials	0	4 (7.3%)	13 (8.3%)	0	17 (7.2%)
Vancomycin	0	3 (5.5%)	9 (5.8%)	0	12 (5.1%)
Daptomycin	0	0	2 (1.3%)	0	2 (0.8%)
Nitrofurantoin	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
Linezolid	0	0	1 (0.6%)	0	1 (0.4%)
Teicoplanin	0	0	1 (0.6%)	0	1 (0.4%)
Aminoglycoside antibacterials	0	0	4 (2.6%)	0	4 (1.7%)
Amikacin	0	0	2 (1.3%)	0	2 (0.8%)
Gentamicin	0	0	2 (1.3%)	0	2 (0.8%)
Tobramycin	0	0	1 (0.6%)	0	1 (0.4%)
Tetracyclines	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
Doxycycline	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
Minocycline	0	0	1 (0.6%)	0	1 (0.4%)
Tigecycline	0	0	1 (0.6%)	0	1 (0.4%)
Antivirals for systemic use	7 (30.4%)	38 (69.1%)	114 (73.1%)	0	159 (67.1%)
Direct acting antivirals	7 (30.4%)	38 (69.1%)	114 (73.1%)	0	159 (67.1%)
Aciclovir	5 (21.7%)	26 (47.3%)	66 (42.3%)	0	97 (40.9%)
Valaciclovir	2 (8.7%)	9 (16.4%)	52 (33.3%)	0	63 (26.6%)
Oseltamivir	0	2 (3.6%)	6 (3.8%)	0	8 (3.4%)
Ganciclovir	0	0	2 (1.3%)	0	2 (0.8%)
Brivudine	0	0	1 (0.6%)	0	1 (0.4%)
Ribavirin	0	0	1 (0.6%)	0	1 (0.4%)
Tenofovir	0	0	1 (0.6%)	0	1 (0.4%)
Valaciclovir hydrochloride	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
Valganciclovir	0	0	1 (0.6%)	0	1 (0.4%)
Antianemic preparations	4 (17.4%)	21 (38.2%)	38 (24.4%)	0	63 (26.6%)
Vitamin b12 and folic acid	2 (8.7%)	15 (27.3%)	25 (16.0%)	0	42 (17.7%)
Folic acid	1 (4.3%)	5 (9.1%)	12 (7.7%)	0	18 (7.6%)
Cyanocobalamin	1 (4.3%)	3 (5.5%)	7 (4.5%)	0	11 (4.6%)
Vitamin b12 nos	0	1 (1.8%)	6 (3.8%)	0	7 (3.0%)
Hepagrisevit forte-n /01079901/	0	4 (7.3%)	2 (1.3%)	0	6 (2.5%)
Hydroxocobalamin	0	2 (3.6%)	1 (0.6%)	0	3 (1.3%)
Mecobalamin	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
Juice plus	0	1 (1.8%)	0	0	1 (0.4%)
Other antianemic preparations	2 (8.7%)	6 (10.9%)	17 (10.9%)	0	25 (10.5%)

TSICM01: Selected Concomitant Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Darbepoetin alfa	2 (8.7%)	5 (9.1%)	9 (5.8%)	0	16 (6.8%)
Erythropoietin human	0	1 (1.8%)	7 (4.5%)	0	8 (3.4%)
Erythropoietin	0	0	1 (0.6%)	0	1 (0.4%)
Iron preparations	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
Iron	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
Polysaccharide-iron complex	0	0	1 (0.6%)	0	1 (0.4%)
Corticosteroids for systemic use	1 (4.3%)	10 (18.2%)	37 (23.7%)	0	48 (20.3%)
Corticosteroids for systemic use, plain	1 (4.3%)	10 (18.2%)	37 (23.7%)	0	48 (20.3%)
Hydrocortisone	0	3 (5.5%)	19 (12.2%)	0	22 (9.3%)
Methylprednisolone	0	5 (9.1%)	10 (6.4%)	0	15 (6.3%)
Prednisone	0	2 (3.6%)	9 (5.8%)	0	11 (4.6%)
Dexamethasone	1 (4.3%)	0	4 (2.6%)	0	5 (2.1%)
Hydrocortisone sodium succinate	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
Prednisolone	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
Betamethasone valerate	0	1 (1.8%)	0	0	1 (0.4%)
Immunostimulants	2 (8.7%)	1 (1.8%)	19 (12.2%)	0	22 (9.3%)
Immunostimulants	2 (8.7%)	1 (1.8%)	19 (12.2%)	0	22 (9.3%)
Filgrastim	2 (8.7%)	0	16 (10.3%)	0	18 (7.6%)
Pegfilgrastim	0	0	3 (1.9%)	0	3 (1.3%)
Granulocyte colony stimulating factor	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
Blood substitutes and perfusion solutions	4 (17.4%)	5 (9.1%)	6 (3.8%)	1 (33.3%)	16 (6.8%)
Blood and related products	4 (17.4%)	5 (9.1%)	6 (3.8%)	1 (33.3%)	16 (6.8%)
Red blood cells	4 (17.4%)	1 (1.8%)	3 (1.9%)	1 (33.3%)	9 (3.8%)
Albumin human	0	0	1 (0.6%)	0	1 (0.4%)
Erythrocytes	0	0	1 (0.6%)	0	1 (0.4%)
Platelets	0	3 (5.5%)	1 (0.6%)	0	4 (1.7%)
Blood, whole	0	1 (1.8%)	0	0	1 (0.4%)

表 2.7.4-付録-25 Summary of Concomitant Medication (excluding post-infusion medications); All Treated Analysis Population (Study 54767414MMY1002)

TSICM02: Summary of Concomitant Medication (excluding post-infusion medications); All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Number of subjects with any concomitant medications	4 (100.0%)	5 (100.0%)	9 (100.0%)
ADRENERGICS, INHALANTS	0	1 (20.0%)	1 (11.1%)
SALBUTAMOL SULFATE	0	1 (20.0%)	1 (11.1%)
AGENTS AGAINST LEISHMANIASIS AND TRYPANOSOMIASIS	0	1 (20.0%)	1 (11.1%)
PENTAMIDINE ISETHIONATE	0	1 (20.0%)	1 (11.1%)
ALL OTHER THERAPEUTIC PRODUCTS	0	2 (40.0%)	2 (22.2%)
OXYGEN	0	1 (20.0%)	1 (11.1%)
RASBURICASE	0	1 (20.0%)	1 (11.1%)
SODIUM POLYSTYRENE SULFONATE	0	1 (20.0%)	1 (11.1%)
ANTACIDS	0	2 (40.0%)	2 (22.2%)
MAGNESIUM OXIDE	0	2 (40.0%)	2 (22.2%)
ANTIFUNGALS FOR TOPICAL USE	1 (25.0%)	0	1 (11.1%)
FLUCONAZOLE	1 (25.0%)	0	1 (11.1%)
ANTIGOUT PREPARATIONS	1 (25.0%)	3 (60.0%)	4 (44.4%)
FEBUXOSTAT	1 (25.0%)	3 (60.0%)	4 (44.4%)
ANTIHISTAMINES FOR SYSTEMIC USE	2 (50.0%)	0	2 (22.2%)
DEXCHLORPHENIRAMINE MALEATE	1 (25.0%)	0	1 (11.1%)
FEXOFENADINE HYDROCHLORIDE	1 (25.0%)	0	1 (11.1%)
OLOPATADINE HYDROCHLORIDE	1 (25.0%)	0	1 (11.1%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	1 (25.0%)	2 (40.0%)	3 (33.3%)
AZULENE SODIUM SULFONATE	0	1 (20.0%)	1 (11.1%)
INDOMETACIN	0	1 (20.0%)	1 (11.1%)
LOXOPROFEN SODIUM	1 (25.0%)	0	1 (11.1%)
ANTIMYCOTICS FOR SYSTEMIC USE	0	1 (20.0%)	1 (11.1%)
AMPHOTERICIN B, LIPOSOME	0	1 (20.0%)	1 (11.1%)
VORICONAZOLE	0	1 (20.0%)	1 (11.1%)
ANTIPSYCHOTICS	1 (25.0%)	0	1 (11.1%)
PROCHLORPERAZINE	1 (25.0%)	0	1 (11.1%)
ATC Level 3 Not Coded	1 (25.0%)	1 (20.0%)	2 (22.2%)
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	0	1 (20.0%)	1 (11.1%)
KAKKONTO /07985901/	1 (25.0%)	0	1 (11.1%)
BLOOD AND RELATED PRODUCTS	0	1 (20.0%)	1 (11.1%)
ALBUMIN HUMAN	0	1 (20.0%)	1 (11.1%)
CARDIAC STIMULANTS EXCL. CARDIAC GLYCOSIDES	0	1 (20.0%)	1 (11.1%)
NOREPINEPHRINE	0	1 (20.0%)	1 (11.1%)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	2 (50.0%)	3 (60.0%)	5 (55.6%)
BETAMETHASONE VALERATE	1 (25.0%)	0	1 (11.1%)
HYDROCORTISONE	0	1 (20.0%)	1 (11.1%)
HYDROCORTISONE SODIUM SUCCINATE	1 (25.0%)	1 (20.0%)	2 (22.2%)
PREDNISOLONE	1 (25.0%)	1 (20.0%)	2 (22.2%)
CORTICOSTEROIDS, PLAIN	1 (25.0%)	0	1 (11.1%)
DIFLUPREDNATE	1 (25.0%)	0	1 (11.1%)
DIRECT ACTING ANTIVIRALS	3 (75.0%)	3 (60.0%)	6 (66.7%)
ACICLOVIR	1 (25.0%)	0	1 (11.1%)
VALACICLOVIR	1 (25.0%)	2 (40.0%)	3 (33.3%)
VALACICLOVIR HYDROCHLORIDE	1 (25.0%)	1 (20.0%)	2 (22.2%)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	0	1 (20.0%)	1 (11.1%)
ZOLEDRONIC ACID	0	1 (20.0%)	1 (11.1%)
DRUGS FOR CONSTIPATION	1 (25.0%)	1 (20.0%)	2 (22.2%)
NEW LECICARBON	0	1 (20.0%)	1 (11.1%)
SENNOSIDE A+B	1 (25.0%)	1 (20.0%)	2 (22.2%)
SENNOSIDE A+B CALCIUM	0	1 (20.0%)	1 (11.1%)
SODIUM PICOSULFATE	1 (25.0%)	1 (20.0%)	2 (22.2%)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE	0	1 (20.0%)	1 (11.1%)

TSICM02: Summary of Concomitant Medication (excluding post-infusion medications); All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
OMEPRAZOLE	0	1 (20.0%)	1 (11.1%)
HIGH-CEILING DIURETICS	0	1 (20.0%)	1 (11.1%)
FUROSEMIDE	0	1 (20.0%)	1 (11.1%)
I.V. SOLUTIONS	1 (25.0%)	1 (20.0%)	2 (22.2%)
AMINO ACIDS NOS W/COPPER/ELECTROLYTES NOS/GLU	0	1 (20.0%)	1 (11.1%)
SOLITA-T1	1 (25.0%)	0	1 (11.1%)
IMMUNOGLOBULINS	1 (25.0%)	0	1 (11.1%)
IMMUNOGLOBULIN HUMAN NORMAL	1 (25.0%)	0	1 (11.1%)
IMMUNOSTIMULANTS	0	1 (20.0%)	1 (11.1%)
FILGRASTIM	0	1 (20.0%)	1 (11.1%)
INSULINS AND ANALOGUES	0	1 (20.0%)	1 (11.1%)
INSULIN HUMAN	0	1 (20.0%)	1 (11.1%)
LIPID MODIFYING AGENTS, PLAIN	0	1 (20.0%)	1 (11.1%)
ATORVASTATIN	0	1 (20.0%)	1 (11.1%)
OPIOIDS	1 (25.0%)	0	1 (11.1%)
MORPHINE SULFATE	1 (25.0%)	0	1 (11.1%)
OXYCODONE HYDROCHLORIDE	1 (25.0%)	0	1 (11.1%)
OTHER ANALGESICS AND ANTIPYRETICS	1 (25.0%)	5 (100.0%)	6 (66.7%)
PA	0	1 (20.0%)	1 (11.1%)
PARACETAMOL	1 (25.0%)	5 (100.0%)	6 (66.7%)
OTHER ANTIBACTERIALS	0	1 (20.0%)	1 (11.1%)
VANCOMYCIN	0	1 (20.0%)	1 (11.1%)
OTHER BETA-LACTAM ANTIBACTERIALS	0	3 (60.0%)	3 (33.3%)
CEFEPIME HYDROCHLORIDE	0	1 (20.0%)	1 (11.1%)
CEFTRIAXONE SODIUM	0	1 (20.0%)	1 (11.1%)
MEROPENEM	0	1 (20.0%)	1 (11.1%)
QUINOLONE ANTIBACTERIALS	0	3 (60.0%)	3 (33.3%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (20.0%)	1 (11.1%)
GARENOXACIN MESILATE	0	1 (20.0%)	1 (11.1%)
LEVOFLOXACIN	0	1 (20.0%)	1 (11.1%)
SULFONAMIDES AND TRIMETHOPRIM	3 (75.0%)	3 (60.0%)	6 (66.7%)
BACTRIM	3 (75.0%)	3 (60.0%)	6 (66.7%)
VIRAL VACCINES	0	2 (40.0%)	2 (22.2%)
INFLUENZA VACCINE	0	2 (40.0%)	2 (22.2%)

Note: Medication is categorized using Anatomical Therapeutic Chemical class and drug preferred term

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表 2.7.4-付録-26 Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with TEAE	226 (95.4%)	240 (98.8%)	274 (97.5%)	313 (98.4%)	103 (100.0%)
MedDRA system organ class / Preferred term					
感染症および寄生虫症	126 (53.2%)	164 (67.5%)	204 (72.6%)	265 (83.3%)	72 (69.9%)
上気道感染	43 (18.1%)	60 (24.7%)	58 (20.6%)	98 (30.8%)	26 (25.2%)
鼻咽頭炎	9 (3.8%)	17 (7.0%)	43 (15.3%)	76 (23.9%)	8 (7.8%)
気管支炎	13 (5.5%)	28 (11.5%)	34 (12.1%)	46 (14.5%)	10 (9.7%)
肺炎	28 (11.8%)	29 (11.9%)	37 (13.2%)	41 (12.9%)	11 (10.7%)
気道感染	3 (1.3%)	0	22 (7.8%)	33 (10.4%)	0
インフルエンザ	7 (3.0%)	8 (3.3%)	13 (4.6%)	23 (7.2%)	5 (4.9%)
鼻炎	2 (0.8%)	7 (2.9%)	3 (1.1%)	20 (6.3%)	5 (4.9%)
副鼻腔炎	3 (1.3%)	10 (4.1%)	10 (3.6%)	19 (6.0%)	13 (12.6%)
下気道感染	3 (1.3%)	3 (1.2%)	9 (3.2%)	17 (5.3%)	0
尿路感染	6 (2.5%)	12 (4.9%)	11 (3.9%)	17 (5.3%)	7 (6.8%)
胃腸炎	4 (1.7%)	5 (2.1%)	4 (1.4%)	13 (4.1%)	3 (2.9%)
結膜炎	7 (3.0%)	21 (8.6%)	3 (1.1%)	12 (3.8%)	2 (1.9%)
帯状疱疹	7 (3.0%)	13 (5.3%)	5 (1.8%)	9 (2.8%)	2 (1.9%)
口腔ヘルペス	2 (0.8%)	6 (2.5%)	2 (0.7%)	8 (2.5%)	1 (1.0%)
咽頭炎	1 (0.4%)	5 (2.1%)	7 (2.5%)	8 (2.5%)	1 (1.0%)
感染	3 (1.3%)	1 (0.4%)	5 (1.8%)	7 (2.2%)	0
ウイルス感染	1 (0.4%)	0	7 (2.5%)	7 (2.2%)	0
蜂巣炎	1 (0.4%)	2 (0.8%)	3 (1.1%)	6 (1.9%)	2 (1.9%)
口腔カンジダ症	5 (2.1%)	4 (1.6%)	4 (1.4%)	6 (1.9%)	0
口腔真菌感染	2 (0.8%)	2 (0.8%)	5 (1.8%)	5 (1.6%)	0
皮膚感染	2 (0.8%)	1 (0.4%)	5 (1.8%)	5 (1.6%)	0
膀胱炎	0	3 (1.2%)	7 (2.5%)	4 (1.3%)	0
耳感染	0	0	3 (1.1%)	4 (1.3%)	1 (1.0%)
真菌感染	0	1 (0.4%)	1 (0.4%)	4 (1.3%)	0
ヘルペスウイルス感染	0	0	0	4 (1.3%)	0
肺感染	2 (0.8%)	1 (0.4%)	2 (0.7%)	4 (1.3%)	2 (1.9%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
インフルエンザ性肺炎	0	0	0	4 (1.3%)	0
気管支肺炎	2 (0.8%)	3 (1.2%)	1 (0.4%)	3 (0.9%)	0
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (0.9%)	0
消化管感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (0.9%)	0
歯周炎	0	0	1 (0.4%)	3 (0.9%)	0
ＲＳウイルス感染	0	1 (0.4%)	0	3 (0.9%)	3 (2.9%)
敗血症性ショック	1 (0.4%)	0	2 (0.7%)	3 (0.9%)	0
歯膿瘍	1 (0.4%)	0	6 (2.1%)	3 (0.9%)	1 (1.0%)
歯感染	0	1 (0.4%)	2 (0.7%)	3 (0.9%)	3 (2.9%)
ウイルス性上気道感染	0	2 (0.8%)	2 (0.7%)	3 (0.9%)	0
外陰部腟カンジダ症	0	0	0	3 (0.9%)	0
急性副鼻腔炎	1 (0.4%)	0	0	2 (0.6%)	0
虫垂炎	0	0	1 (0.4%)	2 (0.6%)	0
細気管支炎	0	0	1 (0.4%)	2 (0.6%)	0
カンピロバクター胃腸炎	0	1 (0.4%)	0	2 (0.6%)	0
丹毒	0	2 (0.8%)	2 (0.7%)	2 (0.6%)	0
大腸菌性尿路感染	0	0	0	2 (0.6%)	0
眼感染	4 (1.7%)	0	2 (0.7%)	2 (0.6%)	0
毛包炎	0	2 (0.8%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
皮膚真菌感染	0	0	1 (0.4%)	2 (0.6%)	0
せつ	1 (0.4%)	2 (0.8%)	0	2 (0.6%)	1 (1.0%)
歯肉炎	0	1 (0.4%)	4 (1.4%)	2 (0.6%)	0
Ｈ１Ｎ１インフルエンザ	0	0	1 (0.4%)	2 (0.6%)	0
大葉性肺炎	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	0
好中球減少性敗血症	0	0	0	2 (0.6%)	0
口腔感染	0	0	0	2 (0.6%)	0
中耳炎	1 (0.4%)	3 (1.2%)	1 (0.4%)	2 (0.6%)	0
パラインフルエンザウイルス感染	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	2 (1.9%)
耳下腺炎	0	0	0	2 (0.6%)	1 (1.0%)
レンサ球菌性咽頭炎	0	0	1 (0.4%)	2 (0.6%)	0
細菌性肺炎	0	0	1 (0.4%)	2 (0.6%)	0
ウイルス性気道感染	3 (1.3%)	6 (2.5%)	0	2 (0.6%)	0
敗血症	3 (1.3%)	2 (0.8%)	6 (2.1%)	2 (0.6%)	4 (3.9%)
皮下組織膿瘍	0	1 (0.4%)	0	2 (0.6%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
足部白癬	0	2 (0.8%)	3 (1.1%)	2 (0.6%)	0
細菌性上気道感染	0	0	0	2 (0.6%)	0
急性扁桃炎	0	0	0	1 (0.3%)	1 (1.0%)
無症候性細菌尿	0	0	0	1 (0.3%)	0
バチルス感染	0	0	0	1 (0.3%)	0
細菌感染	1 (0.4%)	0	0	1 (0.3%)	0
カンジダ性亀頭炎	0	0	0	1 (0.3%)	0
細菌性気管支炎	0	0	0	1 (0.3%)	0
カンピロバクター感染	0	0	0	1 (0.3%)	0
カンジダ感染	3 (1.3%)	2 (0.8%)	2 (0.7%)	1 (0.3%)	0
カテーテル留置部位膿瘍	0	0	0	1 (0.3%)	0
カテーテル留置部位感染	0	0	0	1 (0.3%)	0
慢性副鼻腔炎	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
ウイルス性結膜炎	0	0	1 (0.4%)	1 (0.3%)	0
コロナウイルス感染	0	0	0	1 (0.3%)	1 (1.0%)
サイトメガロウイルス感染	0	0	0	1 (0.3%)	0
ウイルス性腸炎	0	0	0	1 (0.3%)	0
喉頭蓋炎	0	0	0	1 (0.3%)	0
大腸菌性菌血症	0	0	0	1 (0.3%)	0
硬膜外膿瘍	0	0	0	1 (0.3%)	0
感染性舌炎	0	0	0	1 (0.3%)	0
感染性脊椎炎	0	0	0	1 (0.3%)	0
注入部位蜂巣炎	0	0	0	1 (0.3%)	0
ウイルス性喉頭炎	0	0	0	1 (0.3%)	0
リステリア性敗血症	0	0	0	1 (0.3%)	0
限局性感染	1 (0.4%)	0	5 (1.8%)	1 (0.3%)	0
ウイルス性下気道感染	0	0	1 (0.4%)	1 (0.3%)	0
粘膜感染	2 (0.8%)	0	3 (1.1%)	1 (0.3%)	0
鼻膿瘍	0	0	0	1 (0.3%)	0
中咽頭カンジダ症	0	0	0	1 (0.3%)	0
外耳炎	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
急性中耳炎	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
耳管炎	0	0	0	1 (0.3%)	0
眼窩周囲蜂巣炎	0	0	0	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
ヘモフィルス性肺炎	0	0	0	1 (0.3%)	0
クレブシエラ菌性肺炎	0	0	0	1 (0.3%)	0
レジオネラ菌性肺炎	0	0	1 (0.4%)	1 (0.3%)	0
レンサ球菌性肺炎	0	0	0	1 (0.3%)	0
ウイルス性肺炎	0	0	0	1 (0.3%)	0
前立腺感染	0	0	0	1 (0.3%)	0
シュードモナス感染	0	0	0	1 (0.3%)	0
腎盂腎炎	0	1 (0.4%)	0	1 (0.3%)	0
膿疱性皮疹	0	0	0	1 (0.3%)	0
呼吸器モニリア症	0	0	0	1 (0.3%)	0
サルモネラ性菌血症	0	0	0	1 (0.3%)	0
軟部組織感染	0	0	0	1 (0.3%)	0
扁桃炎	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
気管炎	0	0	1 (0.4%)	1 (0.3%)	0
尿道炎	0	0	0	1 (0.3%)	0
子宮膿瘍	0	0	0	1 (0.3%)	0
腟感染	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
ウイルス性鼻炎	0	0	0	1 (0.3%)	0
内臓リーシュマニア症	0	0	0	1 (0.3%)	0
外陰腟真菌感染	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
創傷感染	0	0	3 (1.1%)	1 (0.3%)	0
四肢膿瘍	0	0	1 (0.4%)	0	0
頚部膿瘍	0	1 (0.4%)	0	0	0
アデノウイルス感染	0	0	1 (0.4%)	0	0
肛門膿瘍	0	0	1 (0.4%)	0	0
体部白癬	1 (0.4%)	0	0	0	0
脳膿瘍	1 (0.4%)	0	0	0	0
ウイルス性気管支炎	0	0	2 (0.7%)	0	0
海綿静脈洞血栓症	1 (0.4%)	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (1.0%)
クロストリジウム・ディフィシレ感染	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	1 (1.0%)
細菌性結膜炎	0	1 (0.4%)	1 (0.4%)	0	0
細菌性膀胱炎	1 (0.4%)	0	0	0	0
大腸菌性膀胱炎	1 (0.4%)	0	0	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
医療機器関連感染	1 (0.4%)	2 (0.8%)	0	0	0
憩室炎	0	1 (0.4%)	0	0	2 (1.9%)
赤痢	0	1 (0.4%)	0	0	0
蓄膿	0	0	1 (0.4%)	0	0
心内膜炎	1 (0.4%)	0	0	0	0
感染性腸炎	0	0	0	0	1 (1.0%)
感染性小腸結腸炎	0	0	2 (0.7%)	0	0
精巣上体炎	1 (0.4%)	0	0	0	0
伝染性紅斑	0	1 (0.4%)	0	0	0
大腸菌性敗血症	1 (0.4%)	0	0	0	0
真菌性眼感染	0	0	1 (0.4%)	0	0
眼瞼感染	0	1 (0.4%)	0	0	0
熱性感染症	0	0	1 (0.4%)	0	0
真菌性食道炎	0	1 (0.4%)	0	0	0
壊疽	1 (0.4%)	0	0	0	0
サルモネラ菌性胃腸炎	0	1 (0.4%)	0	0	0
陰部ヘルペス	0	1 (0.4%)	0	0	2 (1.9%)
陰部単純ヘルペス	0	0	1 (0.4%)	0	0
真菌性性器感染	0	0	1 (0.4%)	0	0
ヘモフィルス感染	0	1 (0.4%)	1 (0.4%)	0	0
単純ヘルペス	1 (0.4%)	0	1 (0.4%)	0	0
麦粒腫	3 (1.3%)	4 (1.6%)	2 (0.7%)	0	0
咬傷感染	0	0	1 (0.4%)	0	0
感染性筋炎	0	0	1 (0.4%)	0	0
真菌性角膜炎	0	0	1 (0.4%)	0	0
喉頭炎	0	1 (0.4%)	1 (0.4%)	0	2 (1.9%)
乳腺炎	0	0	0	0	1 (1.0%)
メタニューモウイルス感染	0	2 (0.8%)	0	0	0
爪床感染	1 (0.4%)	0	0	0	0
爪感染	1 (0.4%)	0	0	0	0
鼻ヘルペス	0	0	1 (0.4%)	0	0
壊死性筋膜炎	0	0	1 (0.4%)	0	0
ノカルジア症	1 (0.4%)	0	0	0	0
食道カンジダ症	0	1 (0.4%)	0	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
眼部単純ヘルペス	1 (0.4%)	0	0	0	0
口腔ウイルス感染	0	0	1 (0.4%)	0	0
骨髄炎	0	0	2 (0.7%)	0	0
爪囲炎	1 (0.4%)	0	1 (0.4%)	0	0
腹膜炎	0	1 (0.4%)	0	0	0
百日咳	0	1 (0.4%)	1 (0.4%)	0	0
ニューモシスチス・イロベチイ肺炎	0	1 (0.4%)	0	0	0
サイトメガロウイルス性肺炎	0	2 (0.8%)	0	0	0
肺炎球菌性肺炎	0	1 (0.4%)	0	0	0
進行性多巣性白質脳症	0	0	0	0	1 (1.0%)
シュードモナス性敗血症	0	0	0	0	1 (1.0%)
肺敗血症	0	2 (0.8%)	0	0	0
肺結核	0	0	1 (0.4%)	0	0
歯髄炎	0	0	1 (0.4%)	0	0
穿刺部位感染	1 (0.4%)	0	0	0	0
急性腎盂腎炎	0	0	1 (0.4%)	0	0
慢性腎盂腎炎	1 (0.4%)	0	0	0	0
ライノウイルス感染	1 (0.4%)	1 (0.4%)	0	0	0
唾液腺炎	0	1 (0.4%)	0	0	1 (1.0%)
皮膚カンジダ	0	0	3 (1.1%)	0	0
脊髄感染	0	0	0	0	1 (1.0%)
ブドウ球菌性菌血症	1 (0.4%)	0	0	0	0
ブドウ球菌感染	0	0	1 (0.4%)	0	0
ブドウ球菌性咽頭炎	0	1 (0.4%)	0	0	0
ブドウ球菌皮膚感染	0	0	1 (0.4%)	0	0
ステノトロフォモナス感染	1 (0.4%)	0	0	0	0
股部白癬	1 (0.4%)	0	0	0	0
白癬感染	1 (0.4%)	0	0	0	0
癜風	0	0	0	0	1 (1.0%)
真菌性舌感染	0	1 (0.4%)	0	0	0
気管気管支炎	1 (0.4%)	1 (0.4%)	0	0	0
尿路性敗血症	0	0	1 (0.4%)	0	0
水痘	0	0	1 (0.4%)	0	0
水痘帯状疱疹ウイルス感染	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
ウイルス性咽頭炎	1 (0.4%)	0	0	0	0
ウイルス性ぶどう膜炎	1 (0.4%)	0	0	0	0
外陰部腟炎	0	0	1 (0.4%)	0	0
胃腸障害	110 (46.4%)	143 (58.8%)	164 (58.4%)	242 (76.1%)	81 (78.6%)
下痢	53 (22.4%)	77 (31.7%)	69 (24.6%)	136 (42.8%)	39 (37.9%)
便秘	37 (15.6%)	48 (19.8%)	71 (25.3%)	90 (28.3%)	34 (33.0%)
悪心	26 (11.0%)	34 (14.0%)	40 (14.2%)	77 (24.2%)	31 (30.1%)
嘔吐	9 (3.8%)	26 (10.7%)	15 (5.3%)	51 (16.0%)	22 (21.4%)
上腹部痛	7 (3.0%)	14 (5.8%)	10 (3.6%)	24 (7.5%)	4 (3.9%)
腹痛	11 (4.6%)	9 (3.7%)	11 (3.9%)	21 (6.6%)	10 (9.7%)
消化不良	13 (5.5%)	5 (2.1%)	6 (2.1%)	19 (6.0%)	2 (1.9%)
口内炎	2 (0.8%)	3 (1.2%)	6 (2.1%)	17 (5.3%)	3 (2.9%)
歯痛	2 (0.8%)	1 (0.4%)	5 (1.8%)	10 (3.1%)	4 (3.9%)
腹部不快感	4 (1.7%)	6 (2.5%)	3 (1.1%)	8 (2.5%)	0
腹部膨満	8 (3.4%)	9 (3.7%)	5 (1.8%)	8 (2.5%)	2 (1.9%)
口内乾燥	2 (0.8%)	3 (1.2%)	6 (2.1%)	8 (2.5%)	0
胃食道逆流性疾患	2 (0.8%)	6 (2.5%)	6 (2.1%)	7 (2.2%)	6 (5.8%)
痔核	2 (0.8%)	0	3 (1.1%)	7 (2.2%)	3 (2.9%)
口腔内潰瘍形成	1 (0.4%)	1 (0.4%)	4 (1.4%)	7 (2.2%)	0
嚥下障害	1 (0.4%)	3 (1.2%)	1 (0.4%)	6 (1.9%)	1 (1.0%)
放屁	3 (1.3%)	2 (0.8%)	0	5 (1.6%)	4 (3.9%)
胃腸障害	1 (0.4%)	0	0	5 (1.6%)	0
舌痛	1 (0.4%)	0	4 (1.4%)	4 (1.3%)	0
直腸出血	0	0	1 (0.4%)	4 (1.3%)	2 (1.9%)
口の感覚鈍麻	0	1 (0.4%)	0	3 (0.9%)	2 (1.9%)
嚥下痛	0	0	1 (0.4%)	3 (0.9%)	0
口腔内痛	2 (0.8%)	0	4 (1.4%)	3 (0.9%)	0
口の錯感覚	0	0	2 (0.7%)	3 (0.9%)	0
アフタ性口内炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.6%)	0
便通不規則	0	0	0	2 (0.6%)	0
大腸炎	0	0	1 (0.4%)	2 (0.6%)	0
憩室穿孔	0	1 (0.4%)	0	2 (0.6%)	0
胃炎	2 (0.8%)	4 (1.6%)	1 (0.4%)	2 (0.6%)	0
裂孔ヘルニア	0	0	1 (0.4%)	2 (0.6%)	1 (1.0%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
腹部腫瘤	0	0	0	1 (0.3%)	0
下腹部痛	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
腹壁血腫	0	0	0	1 (0.3%)	0
裂肛	0	0	0	1 (0.3%)	0
肛門出血	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
胆汁酸吸収不良	0	0	0	1 (0.3%)	0
口唇炎	0	1 (0.4%)	0	1 (0.3%)	0
歯不快感	0	0	0	1 (0.3%)	0
横隔膜ヘルニア	0	0	0	1 (0.3%)	0
腸憩室	0	0	0	1 (0.3%)	0
心窩部不快感	0	0	0	1 (0.3%)	2 (1.9%)
おくび	0	0	1 (0.4%)	1 (0.3%)	0
変色便	0	0	0	1 (0.3%)	1 (1.0%)
胃拡張	0	0	0	1 (0.3%)	0
胃出血	0	0	0	1 (0.3%)	0
出血性胃腸管血管異形成	0	0	0	1 (0.3%)	0
胃腸毒性	0	0	0	1 (0.3%)	0
吐血	0	0	1 (0.4%)	1 (0.3%)	0
血便排泄	0	0	0	1 (0.3%)	0
鼠径ヘルニア	1 (0.4%)	0	3 (1.1%)	1 (0.3%)	1 (1.0%)
口唇びらん	0	0	0	1 (0.3%)	0
口唇そう痒症	0	0	0	1 (0.3%)	0
口唇腫脹	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
弛緩歯	0	1 (0.4%)	0	1 (0.3%)	0
非感染性歯肉炎	0	0	0	1 (0.3%)	0
口腔障害	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
口腔粘膜水疱形成	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
肛門周囲痛	0	0	0	1 (0.3%)	1 (1.0%)
直腸ポリープ	0	0	0	1 (0.3%)	0
直腸しぶり	0	0	0	1 (0.3%)	0
唾液腺結石	0	0	0	1 (0.3%)	0
歯の知覚過敏	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
顎下腺腫大	0	0	0	1 (0.3%)	0
地図状舌	0	0	1 (0.4%)	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
腹部ヘルニア	0	1 (0.4%)	0	0	0
腹部硬直	0	0	0	0	1 (1.0%)
腹壁障害	0	1 (0.4%)	0	0	0
痔瘻	0	0	1 (0.4%)	0	0
肛門の炎症	0	1 (0.4%)	0	0	0
肛門そう痒症	1 (0.4%)	0	0	0	0
腹水	1 (0.4%)	0	0	0	0
バレット食道	0	0	1 (0.4%)	0	0
呼気臭	0	0	1 (0.4%)	0	0
口唇のひび割れ	0	0	1 (0.4%)	0	0
潰瘍性大腸炎	0	0	1 (0.4%)	0	0
齲歯	0	1 (0.4%)	5 (1.8%)	0	0
憩室	0	0	0	0	2 (1.9%)
十二指腸潰瘍	0	1 (0.4%)	0	0	0
十二指腸炎	0	1 (0.4%)	0	0	0
細菌叢異常症	0	1 (0.4%)	0	0	0
便失禁	0	0	1 (0.4%)	0	1 (1.0%)
糞塊	1 (0.4%)	0	1 (0.4%)	0	0
白色便	0	1 (0.4%)	0	0	0
胃障害	0	0	2 (0.7%)	0	0
胃潰瘍	1 (0.4%)	0	0	0	0
びらん性胃炎	0	1 (0.4%)	0	0	0
胃十二指腸炎	0	1 (0.4%)	0	0	0
消化管運動障害	0	0	1 (0.4%)	0	0
消化器痛	0	1 (0.4%)	1 (0.4%)	0	0
歯肉出血	0	0	1 (0.4%)	0	0
歯肉痛	0	1 (0.4%)	0	0	2 (1.9%)
歯肉腫脹	1 (0.4%)	0	0	0	0
歯肉潰瘍	0	0	1 (0.4%)	0	0
痔出血	0	1 (0.4%)	0	0	0
イレウス	1 (0.4%)	0	0	0	0
嵌頓臍ヘルニア	1 (0.4%)	0	0	0	0
腸閉塞	0	1 (0.4%)	1 (0.4%)	0	0
腸管穿孔	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
過敏性腸症候群	0	0	2 (0.7%)	0	0
大腸ポリープ	0	0	1 (0.4%)	0	0
口唇水疱	0	0	0	0	1 (1.0%)
下部消化管出血	0	0	1 (0.4%)	0	0
マロリー・ワイス症候群	1 (0.4%)	0	0	0	0
メレナ	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	0
口腔内出血	0	0	1 (0.4%)	0	1 (1.0%)
食道痛	1 (0.4%)	0	1 (0.4%)	0	0
食道炎	0	0	1 (0.4%)	0	1 (1.0%)
口腔内不快感	1 (0.4%)	1 (0.4%)	0	0	0
口腔粘膜血腫	0	1 (0.4%)	0	0	0
排便痛	0	0	0	0	1 (1.0%)
口蓋浮腫	0	1 (0.4%)	0	0	0
膵嚢胞	0	0	0	0	1 (1.0%)
膵炎	1 (0.4%)	0	1 (0.4%)	0	0
急性膵炎	0	1 (0.4%)	0	0	0
慢性膵炎	0	2 (0.8%)	0	0	0
歯周の炎症	0	0	1 (0.4%)	0	0
小腸閉塞	0	1 (0.4%)	0	0	3 (2.9%)
ストレス潰瘍	0	0	1 (0.4%)	0	0
舌変色	0	1 (0.4%)	0	0	0
舌浮腫	0	1 (0.4%)	0	0	0
舌そう痒症	0	1 (0.4%)	0	0	0
舌潰瘍	1 (0.4%)	0	1 (0.4%)	0	0
歯の脱落	0	0	1 (0.4%)	0	0
上部消化管出血	0	1 (0.4%)	0	0	0
血液およびリンパ系障害	135 (57.0%)	163 (67.1%)	184 (65.5%)	231 (72.6%)	91 (88.3%)
好中球減少症	22 (9.3%)	43 (17.7%)	121 (43.1%)	197 (61.9%)	81 (78.6%)
貧血	74 (31.2%)	64 (26.3%)	98 (34.9%)	97 (30.5%)	54 (52.4%)
血小板減少症	104 (43.9%)	143 (58.8%)	77 (27.4%)	86 (27.0%)	42 (40.8%)
白血球減少症	11 (4.6%)	19 (7.8%)	17 (6.0%)	28 (8.8%)	38 (36.9%)
リンパ球減少症	9 (3.8%)	32 (13.2%)	15 (5.3%)	21 (6.6%)	22 (21.4%)
発熱性好中球減少症	1 (0.4%)	4 (1.6%)	7 (2.5%)	17 (5.3%)	7 (6.8%)
白血球増加症	3 (1.3%)	0	2 (0.7%)	2 (0.6%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
リンパ節症	0	0	2 (0.7%)	2 (0.6%)	1 (1.0%)
凝血異常	0	0	0	1 (0.3%)	0
好酸球増加症	0	0	0	1 (0.3%)	0
内出血発生の増加傾向	0	0	0	1 (0.3%)	0
リンパ球増加症	0	0	0	1 (0.3%)	0
好中球増加症	0	0	0	1 (0.3%)	0
血液障害	1 (0.4%)	2 (0.8%)	0	0	0
骨髄機能不全	0	0	1 (0.4%)	0	0
骨髄浮腫	0	0	1 (0.4%)	0	0
播種性血管内凝固	0	0	1 (0.4%)	0	0
溶血	0	0	0	0	1 (1.0%)
出血性素因	0	0	1 (0.4%)	0	0
出血性障害	0	0	1 (0.4%)	0	0
過粘稠度症候群	0	0	1 (0.4%)	0	1 (1.0%)
鉄欠乏性貧血	0	1 (0.4%)	0	0	0
無胆汁色素尿性黄疸	0	0	1 (0.4%)	0	0
小球性貧血	0	0	1 (0.4%)	0	0
傍気管リンパ節腫脹	1 (0.4%)	0	0	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0
脾臓障害	0	0	1 (0.4%)	0	0
血小板増加症	0	1 (0.4%)	0	0	0
血栓性血小板減少性紫斑病	0	0	1 (0.4%)	0	0
一般・全身障害および投与部位の状態	123 (51.9%)	131 (53.9%)	156 (55.5%)	226 (71.1%)	82 (79.6%)
疲労	58 (24.5%)	52 (21.4%)	78 (27.8%)	112 (35.2%)	51 (49.5%)
発熱	27 (11.4%)	38 (15.6%)	31 (11.0%)	67 (21.1%)	26 (25.2%)
末梢性浮腫	19 (8.0%)	40 (16.5%)	37 (13.2%)	54 (17.0%)	16 (15.5%)
無力症	37 (15.6%)	21 (8.6%)	36 (12.8%)	50 (15.7%)	15 (14.6%)
インフルエンザ様疾患	7 (3.0%)	6 (2.5%)	12 (4.3%)	20 (6.3%)	5 (4.9%)
悪寒	3 (1.3%)	11 (4.5%)	9 (3.2%)	18 (5.7%)	21 (20.4%)
非心臓性胸痛	1 (0.4%)	1 (0.4%)	5 (1.8%)	11 (3.5%)	15 (14.6%)
倦怠感	2 (0.8%)	6 (2.5%)	4 (1.4%)	10 (3.1%)	2 (1.9%)
末梢腫脹	2 (0.8%)	3 (1.2%)	6 (2.1%)	9 (2.8%)	2 (1.9%)
胸部不快感	2 (0.8%)	3 (1.2%)	1 (0.4%)	7 (2.2%)	2 (1.9%)
胸痛	1 (0.4%)	6 (2.5%)	8 (2.8%)	6 (1.9%)	2 (1.9%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
冷感	0	0	1 (0.4%)	6 (1.9%)	1 (1.0%)
全身健康状態低下	6 (2.5%)	2 (0.8%)	3 (1.1%)	5 (1.6%)	2 (1.9%)
浮腫	9 (3.8%)	14 (5.8%)	3 (1.1%)	5 (1.6%)	4 (3.9%)
疼痛	5 (2.1%)	9 (3.7%)	4 (1.4%)	4 (1.3%)	11 (10.7%)
顔面浮腫	0	4 (1.6%)	3 (1.1%)	3 (0.9%)	1 (1.0%)
歩行障害	0	4 (1.6%)	3 (1.1%)	3 (0.9%)	3 (2.9%)
医薬品副作用	0	0	0	2 (0.6%)	0
嚢胞	0	0	1 (0.4%)	2 (0.6%)	0
薬物不耐性	0	0	0	2 (0.6%)	0
熱感	0	0	0	2 (0.6%)	1 (1.0%)
びくびく感	0	0	0	2 (0.6%)	2 (1.9%)
腋窩痛	0	0	2 (0.7%)	1 (0.3%)	0
カテーテル留置部位関連反応	0	0	0	1 (0.3%)	0
運動耐性低下	0	0	0	1 (0.3%)	0
溢出	0	0	0	1 (0.3%)	0
顔面痛	0	0	0	1 (0.3%)	1 (1.0%)
脂肪組織増加	0	0	0	1 (0.3%)	0
空腹	0	0	0	1 (0.3%)	0
高熱	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	2 (1.9%)
治癒不良	0	0	0	1 (0.3%)	0
炎症	0	0	0	1 (0.3%)	0
注入部位血管外漏出	0	3 (1.2%)	0	1 (0.3%)	0
注入部位静脈炎	0	0	0	1 (0.3%)	0
注入部位発疹	0	0	0	1 (0.3%)	0
注射部位内出血	1 (0.4%)	0	0	1 (0.3%)	0
注射部位紅斑	7 (3.0%)	6 (2.5%)	0	1 (0.3%)	0
注射部位知覚異常	0	0	0	1 (0.3%)	0
限局性浮腫	1 (0.4%)	0	0	1 (0.3%)	1 (1.0%)
粘膜の炎症	0	0	0	1 (0.3%)	0
多臓器不全	0	0	0	1 (0.3%)	0
小結節	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
分泌物分泌	0	0	0	1 (0.3%)	0
苦悶感	0	0	1 (0.4%)	1 (0.3%)	0
全身性炎症反応症候群	0	0	0	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
突出痛	0	0	0	0	1 (1.0%)
カテーテル留置部位疼痛	0	1 (0.4%)	0	0	1 (1.0%)
状態悪化	3 (1.3%)	0	0	0	0
捻髪音	0	0	1 (0.4%)	0	0
泣き	0	0	0	0	1 (1.0%)
不快感	0	0	1 (0.4%)	0	0
異常感	0	0	2 (0.7%)	0	0
全身性浮腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
低体温	0	0	0	0	1 (1.0%)
注入部位紅斑	1 (0.4%)	1 (0.4%)	0	0	0
注入部位そう痒感	0	1 (0.4%)	0	0	0
注射部位漏出	0	0	0	0	1 (1.0%)
注射部位炎症	1 (0.4%)	0	0	0	0
注射部位刺激感	0	1 (0.4%)	0	0	0
注射部位浮腫	1 (0.4%)	0	0	0	0
注射部位疼痛	0	1 (0.4%)	0	0	0
注射部位発疹	1 (0.4%)	2 (0.8%)	0	0	0
注射部位反応	2 (0.8%)	4 (1.6%)	0	0	0
注射部位腫脹	0	0	0	0	1 (1.0%)
局所腫脹	0	0	2 (0.7%)	0	1 (1.0%)
腫瘤	0	0	0	0	1 (1.0%)
粘膜乾燥	0	0	1 (0.4%)	0	0
粘膜浮腫	0	1 (0.4%)	0	0	0
異物感	0	1 (0.4%)	0	0	1 (1.0%)
圧痛	0	0	1 (0.4%)	0	0
口渇	0	0	1 (0.4%)	0	0
医療機器関連の血栓症	1 (0.4%)	0	0	0	0
呼吸器、胸郭および縦隔障害	77 (32.5%)	130 (53.5%)	114 (40.6%)	196 (61.6%)	80 (77.7%)
咳嗽	30 (12.7%)	58 (23.9%)	35 (12.5%)	99 (31.1%)	37 (35.9%)
呼吸困難	21 (8.9%)	45 (18.5%)	32 (11.4%)	56 (17.6%)	31 (30.1%)
アレルギー性鼻炎	2 (0.8%)	4 (1.6%)	3 (1.1%)	18 (5.7%)	2 (1.9%)
発声障害	6 (2.5%)	2 (0.8%)	7 (2.5%)	17 (5.3%)	5 (4.9%)
鼻閉	3 (1.3%)	12 (4.9%)	4 (1.4%)	16 (5.0%)	16 (15.5%)
湿性咳嗽	3 (1.3%)	9 (3.7%)	8 (2.8%)	16 (5.0%)	12 (11.7%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
気管支痙攣	1 (0.4%)	23 (9.5%)	1 (0.4%)	15 (4.7%)	0
労作性呼吸困難	6 (2.5%)	10 (4.1%)	5 (1.8%)	14 (4.4%)	4 (3.9%)
口腔咽頭痛	9 (3.8%)	8 (3.3%)	10 (3.6%)	14 (4.4%)	7 (6.8%)
鼻漏	1 (0.4%)	7 (2.9%)	6 (2.1%)	11 (3.5%)	3 (2.9%)
鼻出血	12 (5.1%)	12 (4.9%)	12 (4.3%)	10 (3.1%)	5 (4.9%)
咽喉刺激感	1 (0.4%)	12 (4.9%)	0	10 (3.1%)	9 (8.7%)
肺塞栓症	2 (0.8%)	2 (0.8%)	11 (3.9%)	9 (2.8%)	1 (1.0%)
喘鳴	0	5 (2.1%)	0	9 (2.8%)	9 (8.7%)
しゃっくり	5 (2.1%)	2 (0.8%)	9 (3.2%)	8 (2.5%)	3 (2.9%)
喉頭浮腫	0	2 (0.8%)	0	7 (2.2%)	2 (1.9%)
低酸素症	0	0	1 (0.4%)	6 (1.9%)	5 (4.9%)
肺水腫	2 (0.8%)	0	2 (0.7%)	5 (1.6%)	0
胸水	2 (0.8%)	2 (0.8%)	2 (0.7%)	4 (1.3%)	3 (2.9%)
副鼻腔うっ血	2 (0.8%)	1 (0.4%)	3 (1.1%)	4 (1.3%)	3 (2.9%)
くしゃみ	0	1 (0.4%)	0	3 (0.9%)	5 (4.9%)
アレルギー性呼吸器症状	0	0	0	2 (0.6%)	0
慢性閉塞性肺疾患	2 (0.8%)	3 (1.2%)	3 (1.1%)	2 (0.6%)	2 (1.9%)
肺障害	0	0	2 (0.7%)	2 (0.6%)	1 (1.0%)
鼻閉塞	0	1 (0.4%)	0	2 (0.6%)	0
誤嚥性肺炎	0	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
肺臓炎	0	0	0	2 (0.6%)	1 (1.0%)
呼吸不全	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
急性肺水腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
アレルギー性咽頭炎	0	0	0	1 (0.3%)	0
窒息	0	1 (0.4%)	0	1 (0.3%)	0
気管支拡張症	0	0	0	1 (0.3%)	0
喀血	1 (0.4%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	2 (1.9%)
胸水症	0	1 (0.4%)	0	1 (0.3%)	0
喉頭不快感	0	0	0	1 (0.3%)	0
喉頭痛	0	0	0	1 (0.3%)	0
喉頭狭窄	0	0	0	1 (0.3%)	0
喉頭刺激感	0	0	0	1 (0.3%)	1 (1.0%)
鼻部不快感	0	0	0	1 (0.3%)	0
鼻乾燥	0	0	2 (0.7%)	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
器質化肺炎	0	1 (0.4%)	0	1 (0.3%)	0
咽頭紅斑	0	0	1 (0.4%)	1 (0.3%)	0
胸膜痛	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
呼気延長	0	0	0	1 (0.3%)	0
肺石灰化	0	0	0	1 (0.3%)	0
肺うっ血	0	0	0	1 (0.3%)	0
肺高血圧症	0	0	0	1 (0.3%)	0
肺腫瘤	0	0	0	1 (0.3%)	0
気道うっ血	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	4 (3.9%)
副鼻腔障害	0	0	0	1 (0.3%)	0
上気道性喘鳴	0	0	0	1 (0.3%)	0
窒息感	0	0	0	1 (0.3%)	0
頻呼吸	0	1 (0.4%)	0	1 (0.3%)	2 (1.9%)
咽喉絞扼感	0	4 (1.6%)	0	1 (0.3%)	1 (1.0%)
急性呼吸不全	0	0	1 (0.4%)	0	0
アレルギー性咳嗽	0	2 (0.8%)	0	0	1 (1.0%)
喘息	0	3 (1.2%)	0	0	1 (1.0%)
無気肺	1 (0.4%)	0	1 (0.4%)	0	0
気管支反応性亢進	0	0	1 (0.4%)	0	1 (1.0%)
気管支閉塞	0	1 (0.4%)	0	0	0
慢性気管支炎	1 (0.4%)	1 (0.4%)	0	0	0
気管支肺症	0	0	0	0	1 (1.0%)
カタル	0	2 (0.8%)	5 (1.8%)	0	0
発作性夜間呼吸困難	0	0	0	0	1 (1.0%)
過換気	0	1 (0.4%)	0	0	0
低換気	1 (0.4%)	0	0	0	0
上気道分泌増加	1 (0.4%)	0	0	0	0
間質性肺疾患	1 (0.4%)	0	1 (0.4%)	0	2 (1.9%)
喉頭の炎症	0	0	1 (0.4%)	0	0
肺硬化	1 (0.4%)	0	0	0	0
口腔咽頭不快感	0	1 (0.4%)	1 (0.4%)	0	0
口腔咽頭腫脹	0	1 (0.4%)	0	0	0
副鼻腔不快感	0	0	0	0	3 (2.9%)
副鼻腔分泌過多	0	0	0	0	1 (1.0%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
咽頭浮腫	0	1 (0.4%)	0	0	0
胸膜炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
気胸	0	0	1 (0.4%)	0	0
肺胞出血	1 (0.4%)	0	0	0	0
肺動脈血栓症	0	1 (0.4%)	0	0	0
肺出血	0	1 (0.4%)	0	0	0
ラ音	1 (0.4%)	0	0	0	0
呼吸窮迫	0	1 (0.4%)	0	0	0
鼻痛	0	0	1 (0.4%)	0	0
萎縮性鼻炎	0	1 (0.4%)	0	0	0
低音性連続性ラ音	0	1 (0.4%)	0	0	0
睡眠時無呼吸症候群	0	1 (0.4%)	0	0	0
上気道の炎症	0	0	2 (0.7%)	0	0
上気道咳症候群	0	1 (0.4%)	0	0	3 (2.9%)
筋骨格系および結合組織障害	87 (36.7%)	111 (45.7%)	154 (54.8%)	187 (58.8%)	74 (71.8%)
筋痙縮	5 (2.1%)	19 (7.8%)	52 (18.5%)	90 (28.3%)	27 (26.2%)
背部痛	24 (10.1%)	33 (13.6%)	48 (17.1%)	57 (17.9%)	26 (25.2%)
関節痛	11 (4.6%)	23 (9.5%)	21 (7.5%)	26 (8.2%)	23 (22.3%)
四肢痛	16 (6.8%)	22 (9.1%)	30 (10.7%)	26 (8.2%)	15 (14.6%)
骨痛	14 (5.9%)	14 (5.8%)	12 (4.3%)	24 (7.5%)	13 (12.6%)
筋力低下	6 (2.5%)	4 (1.6%)	22 (7.8%)	23 (7.2%)	8 (7.8%)
筋骨格痛	3 (1.3%)	11 (4.5%)	16 (5.7%)	20 (6.3%)	9 (8.7%)
筋肉痛	4 (1.7%)	11 (4.5%)	9 (3.2%)	19 (6.0%)	9 (8.7%)
筋骨格系胸痛	5 (2.1%)	16 (6.6%)	17 (6.0%)	16 (5.0%)	13 (12.6%)
頚部痛	1 (0.4%)	5 (2.1%)	11 (3.9%)	7 (2.2%)	3 (2.9%)
顎痛	0	3 (1.2%)	4 (1.4%)	6 (1.9%)	1 (1.0%)
脊椎痛	5 (2.1%)	6 (2.5%)	6 (2.1%)	6 (1.9%)	3 (2.9%)
側腹部痛	0	2 (0.8%)	1 (0.4%)	5 (1.6%)	2 (1.9%)
顎骨壊死	1 (0.4%)	1 (0.4%)	4 (1.4%)	5 (1.6%)	1 (1.0%)
肌径部痛	0	1 (0.4%)	1 (0.4%)	3 (0.9%)	2 (1.9%)
骨壊死	1 (0.4%)	0	0	3 (0.9%)	1 (1.0%)
関節炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
出血性関節症	0	1 (0.4%)	0	2 (0.6%)	0
椎間板突出	1 (0.4%)	0	0	2 (0.6%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
筋肉疲労	0	1 (0.4%)	0	2 (0.6%)	0
筋骨格硬直	0	0	3 (1.1%)	2 (0.6%)	0
ミオパチー	3 (1.3%)	7 (2.9%)	3 (1.1%)	2 (0.6%)	0
筋萎縮症	0	0	0	1 (0.3%)	0
滑液包炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
デュプイトラン拘縮	0	0	0	1 (0.3%)	0
痛風性関節炎	0	0	0	1 (0.3%)	0
椎間板圧迫	0	0	0	1 (0.3%)	0
関節硬直	0	1 (0.4%)	0	1 (0.3%)	0
関節腫脹	1 (0.4%)	2 (0.8%)	6 (2.1%)	1 (0.3%)	3 (2.9%)
四肢不快感	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
中足骨痛	0	0	0	1 (0.3%)	0
運動性低下	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
筋骨格不快感	0	0	1 (0.4%)	1 (0.3%)	0
筋炎	0	0	0	1 (0.3%)	0
骨炎	0	0	0	1 (0.3%)	0
変形性関節症	0	3 (1.2%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
仙腸骨炎	0	0	0	1 (0.3%)	0
脊椎障害	0	0	0	1 (0.3%)	0
変形性脊椎症	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
顎関節症候群	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
腱石灰化	0	0	0	1 (0.3%)	0
腱痛	0	2 (0.8%)	0	1 (0.3%)	0
骨脱灰	0	0	1 (0.4%)	0	0
骨障害	0	0	0	0	1 (1.0%)
骨形成亢進	0	1 (0.4%)	0	0	0
骨病変	0	1 (0.4%)	0	0	0
軟骨石灰化症	0	0	1 (0.4%)	0	0
尾骨痛	1 (0.4%)	0	1 (0.4%)	0	0
結晶性関節障害	0	0	1 (0.4%)	0	0
腱付着部症	1 (0.4%)	0	0	0	0
足変形	0	0	1 (0.4%)	0	0
顎障害	1 (0.4%)	0	1 (0.4%)	0	0
関節滲出液	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
関節弛緩	0	0	0	0	1 (1.0%)
関節可動域低下	0	0	0	0	1 (1.0%)
下肢腫瘤	0	1 (0.4%)	0	0	0
筋拘縮	0	0	0	0	2 (1.9%)
筋緊張	0	1 (0.4%)	1 (0.4%)	0	1 (1.0%)
筋攣縮	2 (0.8%)	0	0	0	0
骨減少症	0	1 (0.4%)	0	0	1 (1.0%)
骨粗鬆症	0	1 (0.4%)	1 (0.4%)	0	0
病的骨折	0	2 (0.8%)	2 (0.7%)	0	0
足底筋膜炎	0	0	1 (0.4%)	0	0
多発性関節炎	1 (0.4%)	0	0	0	0
脊柱管狭窄症	1 (0.4%)	0	3 (1.1%)	0	0
滑液嚢腫	0	1 (0.4%)	1 (0.4%)	0	0
腱障害	0	1 (0.4%)	0	0	0
腱炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	0
斜頸	0	0	0	0	1 (1.0%)
開口障害	0	0	1 (0.4%)	0	0
椎間孔狭窄	0	0	0	0	1 (1.0%)
神経系障害	131 (55.3%)	153 (63.0%)	124 (44.1%)	160 (50.3%)	62 (60.2%)
頭痛	14 (5.9%)	25 (10.3%)	19 (6.8%)	43 (13.5%)	17 (16.5%)
末梢性感覚ニューロパチー	89 (37.6%)	115 (47.3%)	19 (6.8%)	31 (9.7%)	8 (7.8%)
振戦	8 (3.4%)	3 (1.2%)	24 (8.5%)	28 (8.8%)	20 (19.4%)
浮動性めまい	24 (10.1%)	24 (9.9%)	24 (8.5%)	24 (7.5%)	22 (21.4%)
味覚異常	10 (4.2%)	9 (3.7%)	15 (5.3%)	23 (7.2%)	4 (3.9%)
錯感覚	14 (5.9%)	11 (4.5%)	10 (3.6%)	17 (5.3%)	7 (6.8%)
感覚鈍麻	4 (1.7%)	3 (1.2%)	5 (1.8%)	14 (4.4%)	4 (3.9%)
末梢性ニューロパチー	0	1 (0.4%)	15 (5.3%)	12 (3.8%)	7 (6.8%)
失神	6 (2.5%)	1 (0.4%)	2 (0.7%)	11 (3.5%)	3 (2.9%)
嗜眠	2 (0.8%)	6 (2.5%)	4 (1.4%)	6 (1.9%)	0
味覚消失	1 (0.4%)	0	1 (0.4%)	5 (1.6%)	0
失神寸前の状態	1 (0.4%)	3 (1.2%)	0	5 (1.6%)	2 (1.9%)
認知障害	2 (0.8%)	0	2 (0.7%)	4 (1.3%)	1 (1.0%)
神経痛	26 (11.0%)	33 (13.6%)	3 (1.1%)	4 (1.3%)	1 (1.0%)
平衡障害	3 (1.3%)	1 (0.4%)	2 (0.7%)	3 (0.9%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
注意力障害	1 (0.4%)	4 (1.6%)	1 (0.4%)	3 (0.9%)	1 (1.0%)
脳血管発作	1 (0.4%)	0	0	2 (0.6%)	1 (1.0%)
異常感覚	1 (0.4%)	2 (0.8%)	1 (0.4%)	2 (0.6%)	0
知覚過敏	0	0	0	2 (0.6%)	1 (1.0%)
記憶障害	1 (0.4%)	3 (1.2%)	8 (2.8%)	2 (0.6%)	3 (2.9%)
痙攣発作	0	0	0	2 (0.6%)	1 (1.0%)
視野欠損	0	0	0	2 (0.6%)	0
健忘	3 (1.3%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
無嗅覚	1 (0.4%)	0	0	1 (0.3%)	0
失声症	0	0	0	1 (0.3%)	0
灼熱感	0	1 (0.4%)	0	1 (0.3%)	0
小脳性運動失調	0	0	0	1 (0.3%)	0
脳梗塞	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
体位性めまい	0	0	1 (0.4%)	1 (0.3%)	0
構語障害	0	0	0	1 (0.3%)	1 (1.0%)
てんかん	0	0	0	1 (0.3%)	0
過眠症	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
運動低下	0	0	0	1 (0.3%)	0
レルミット徴候	0	0	0	1 (0.3%)	0
筋痙直	0	0	0	1 (0.3%)	0
神経系障害	0	0	1 (0.4%)	1 (0.3%)	0
眼振	0	0	0	1 (0.3%)	0
嗅覚錯誤	1 (0.4%)	0	0	1 (0.3%)	0
腓骨神経麻痺	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
ヘルペス後神経痛	2 (0.8%)	2 (0.8%)	2 (0.7%)	1 (0.3%)	0
精神運動亢進	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
下肢静止不能症候群	2 (0.8%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
坐骨神経痛	3 (1.3%)	0	3 (1.1%)	1 (0.3%)	1 (1.0%)
感覚障害	0	0	0	1 (0.3%)	0
副鼻腔炎に伴う頭痛	0	1 (0.4%)	0	1 (0.3%)	0
傾眠	3 (1.3%)	2 (0.8%)	4 (1.4%)	1 (0.3%)	2 (1.9%)
脊髄浮腫	0	0	0	1 (0.3%)	0
一過性脳虚血発作	0	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
三叉神経障害	0	0	0	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
アカシジア	0	0	2 (0.7%)	0	0
異痛症	0	0	0	0	1 (1.0%)
失語症	0	0	1 (0.4%)	0	0
運動失調	2 (0.8%)	0	0	0	2 (1.9%)
アテトーゼ	0	0	1 (0.4%)	0	0
自律神経ニューロパチー	1 (0.4%)	0	0	0	0
粘膜の灼熱感	1 (0.4%)	0	0	0	0
頚動脈硬化症	0	0	1 (0.4%)	0	0
手根管症候群	1 (0.4%)	0	0	0	0
脳出血	0	0	1 (0.4%)	0	0
脳虚血	1 (0.4%)	0	0	0	0
頚腕症候群	0	0	0	0	1 (1.0%)
認知症	1 (0.4%)	0	1 (0.4%)	0	0
労作性めまい	0	0	1 (0.4%)	0	0
統合運動障害	0	0	1 (0.4%)	0	0
塞栓性脳卒中	0	1 (0.4%)	0	0	0
脳症	1 (0.4%)	0	0	0	0
顔面不全麻痺	0	0	0	0	1 (1.0%)
蟻走感	0	0	1 (0.4%)	0	0
頭部不快感	0	1 (0.4%)	0	0	0
不全片麻痺	0	0	1 (0.4%)	0	1 (1.0%)
味覚減退	0	1 (0.4%)	2 (0.7%)	0	0
筋緊張低下	1 (0.4%)	0	0	0	0
企図振戦	0	1 (0.4%)	0	0	0
肋間神経痛	0	0	1 (0.4%)	0	0
虚血性脳卒中	0	2 (0.8%)	1 (0.4%)	0	0
意識消失	0	0	1 (0.4%)	0	1 (1.0%)
精神的機能障害	0	1 (0.4%)	0	0	0
代謝性脳症	0	1 (0.4%)	0	0	0
片頭痛	0	0	2 (0.7%)	0	0
不全単麻痺	1 (0.4%)	0	0	0	0
不随意性筋収縮	0	0	1 (0.4%)	0	0
不全対麻痺	0	1 (0.4%)	0	0	0
末梢性運動ニューロパチー	5 (2.1%)	8 (3.3%)	0	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
末梢性感覚運動ニューロパチー	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	0
根症候群	0	1 (0.4%)	0	0	0
感覚運動障害	0	0	1 (0.4%)	0	0
感覚消失	1 (0.4%)	0	0	0	0
会話障害	0	0	0	0	1 (1.0%)
脊髄圧迫	0	0	2 (0.7%)	0	1 (1.0%)
くも膜下出血	1 (0.4%)	0	0	0	0
上位運動ニューロンの病変	0	0	1 (0.4%)	0	0
第７脳神経麻痺	0	1 (0.4%)	2 (0.7%)	0	0
第６脳神経麻痺	0	2 (0.8%)	0	0	1 (1.0%)
血管性脳症	0	2 (0.8%)	1 (0.4%)	0	0
代謝および栄養障害	66 (27.8%)	93 (38.3%)	95 (33.8%)	127 (39.9%)	49 (47.6%)
食欲減退	12 (5.1%)	22 (9.1%)	29 (10.3%)	34 (10.7%)	11 (10.7%)
低カリウム血症	11 (4.6%)	22 (9.1%)	22 (7.8%)	33 (10.4%)	16 (15.5%)
高血糖	18 (7.6%)	21 (8.6%)	19 (6.8%)	27 (8.5%)	13 (12.6%)
低カルシウム血症	11 (4.6%)	10 (4.1%)	11 (3.9%)	20 (6.3%)	5 (4.9%)
低リン酸血症	7 (3.0%)	13 (5.3%)	11 (3.9%)	16 (5.0%)	6 (5.8%)
脱水	3 (1.3%)	3 (1.2%)	2 (0.7%)	10 (3.1%)	4 (3.9%)
低マグネシウム血症	2 (0.8%)	4 (1.6%)	12 (4.3%)	9 (2.8%)	9 (8.7%)
低ナトリウム血症	6 (2.5%)	9 (3.7%)	2 (0.7%)	8 (2.5%)	8 (7.8%)
高尿酸血症	6 (2.5%)	4 (1.6%)	8 (2.8%)	7 (2.2%)	3 (2.9%)
高カルシウム血症	6 (2.5%)	7 (2.9%)	5 (1.8%)	5 (1.6%)	8 (7.8%)
高カリウム血症	2 (0.8%)	3 (1.2%)	2 (0.7%)	3 (0.9%)	2 (1.9%)
糖尿病	2 (0.8%)	7 (2.9%)	0	2 (0.6%)	1 (1.0%)
痛風	0	0	8 (2.8%)	2 (0.6%)	0
高コレステロール血症	0	0	1 (0.4%)	2 (0.6%)	2 (1.9%)
高脂血症	0	0	2 (0.7%)	2 (0.6%)	0
低アルブミン血症	2 (0.8%)	8 (3.3%)	5 (1.8%)	2 (0.6%)	6 (5.8%)
ビタミンＢ１２欠乏	0	1 (0.4%)	3 (1.1%)	2 (0.6%)	0
アシドーシス	0	1 (0.4%)	0	1 (0.3%)	0
悪液質	0	0	0	1 (0.3%)	0
電解質失調	0	0	0	1 (0.3%)	0
酵素異常	0	0	0	1 (0.3%)	0
体液平衡失調	0	0	1 (0.4%)	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
水分過負荷	0	2 (0.8%)	0	1 (0.3%)	0
体液貯留	3 (1.3%)	2 (0.8%)	0	1 (0.3%)	0
葉酸欠乏	0	0	0	1 (0.3%)	0
食物不耐性	0	0	0	1 (0.3%)	0
ヘモクロマトーシス	0	0	0	1 (0.3%)	0
高ナトリウム血症	3 (1.3%)	4 (1.6%)	1 (0.4%)	1 (0.3%)	0
高トリグリセリド血症	0	0	0	1 (0.3%)	1 (1.0%)
低血糖症	2 (0.8%)	0	2 (0.7%)	1 (0.3%)	3 (2.9%)
鉄欠乏	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
１型糖尿病	0	0	0	1 (0.3%)	0
ビタミンＤ欠乏	1 (0.4%)	0	2 (0.7%)	1 (0.3%)	1 (1.0%)
コントロール不良の糖尿病	0	1 (0.4%)	0	0	0
糖尿病性ケトアシドーシス	1 (0.4%)	0	0	0	0
脂質異常症	1 (0.4%)	1 (0.4%)	0	0	0
高アミラーゼ血症	0	2 (0.8%)	0	0	0
高クレアチニン血症	0	0	0	0	1 (1.0%)
高リン酸塩血症	0	1 (0.4%)	1 (0.4%)	0	0
過小食	0	2 (0.8%)	0	0	0
血液量減少症	0	1 (0.4%)	0	0	0
食欲亢進	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (1.0%)
栄養障害	0	0	2 (0.7%)	0	2 (1.9%)
代謝性アシドーシス	1 (0.4%)	1 (0.4%)	0	0	0
多飲症	0	0	1 (0.4%)	0	0
テタニー	0	0	1 (0.4%)	0	0
腫瘍崩壊症候群	0	1 (0.4%)	0	0	0
２型糖尿病	0	1 (0.4%)	1 (0.4%)	0	0
皮膚および皮下組織障害	32 (13.5%)	49 (20.2%)	83 (29.5%)	125 (39.3%)	39 (37.9%)
発疹	7 (3.0%)	13 (5.3%)	29 (10.3%)	38 (11.9%)	3 (2.9%)
そう痒症	3 (1.3%)	5 (2.1%)	29 (10.3%)	29 (9.1%)	10 (9.7%)
多汗症	3 (1.3%)	7 (2.9%)	8 (2.8%)	24 (7.5%)	7 (6.8%)
皮膚乾燥	2 (0.8%)	0	7 (2.5%)	10 (3.1%)	3 (2.9%)
蕁麻疹	0	3 (1.2%)	6 (2.1%)	8 (2.5%)	1 (1.0%)
紅斑	3 (1.3%)	5 (2.1%)	7 (2.5%)	7 (2.2%)	2 (1.9%)
斑状丘疹状皮疹	1 (0.4%)	4 (1.6%)	3 (1.1%)	5 (1.6%)	3 (2.9%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
斑状出血	0	0	1 (0.4%)	4 (1.3%)	4 (3.9%)
寝汗	2 (0.8%)	4 (1.6%)	5 (1.8%)	4 (1.3%)	1 (1.0%)
全身性皮疹	1 (0.4%)	0	5 (1.8%)	4 (1.3%)	5 (4.9%)
皮膚病変	3 (1.3%)	0	3 (1.1%)	4 (1.3%)	2 (1.9%)
皮膚潰瘍	0	3 (1.2%)	1 (0.4%)	4 (1.3%)	0
脱毛症	2 (0.8%)	2 (0.8%)	0	3 (0.9%)	0
水疱	0	1 (0.4%)	0	3 (0.9%)	0
褥瘡性潰瘍	2 (0.8%)	1 (0.4%)	1 (0.4%)	3 (0.9%)	1 (1.0%)
斑状皮疹	0	0	1 (0.4%)	3 (0.9%)	0
顔面腫脹	0	1 (0.4%)	3 (1.1%)	3 (0.9%)	0
皮膚炎	1 (0.4%)	0	2 (0.7%)	2 (0.6%)	0
ざ瘡様皮膚炎	0	0	0	2 (0.6%)	1 (1.0%)
湿疹	0	2 (0.8%)	1 (0.4%)	2 (0.6%)	0
点状出血	2 (0.8%)	0	0	2 (0.6%)	1 (1.0%)
酒さ	0	0	0	2 (0.6%)	0
皮膚色素過剰	0	1 (0.4%)	0	2 (0.6%)	1 (1.0%)
皮膚腫脹	0	0	0	2 (0.6%)	0
日光角化症	0	0	2 (0.7%)	1 (0.3%)	0
冷汗	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
皮膚嚢腫	0	1 (0.4%)	0	1 (0.3%)	0
アレルギー性皮膚炎	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
薬疹	0	0	0	1 (0.3%)	1 (1.0%)
多形紅斑	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
紅色症	0	0	0	1 (0.3%)	0
全身紅斑	0	0	0	1 (0.3%)	0
毛髪成長異常	0	0	0	1 (0.3%)	0
手皮膚炎	0	0	0	1 (0.3%)	0
男性型多毛症	0	0	1 (0.4%)	1 (0.3%)	0
過角化	0	0	1 (0.4%)	1 (0.3%)	0
嵌入爪	1 (0.4%)	0	0	1 (0.3%)	0
爪甲脱落症	0	0	0	1 (0.3%)	0
皮膚疼痛	0	0	0	1 (0.3%)	0
アレルギー性そう痒症	0	0	0	1 (0.3%)	0
全身性そう痒症	1 (0.4%)	0	0	1 (0.3%)	3 (2.9%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
丘疹性皮疹	0	0	0	1 (0.3%)	0
そう痒性皮疹	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
皮膚変色	0	0	0	1 (0.3%)	0
皮膚脆弱性	0	0	0	1 (0.3%)	0
血管炎性皮疹	0	0	0	1 (0.3%)	0
黄色腫	0	0	0	1 (0.3%)	0
血性水疱	0	1 (0.4%)	0	0	0
接触性皮膚炎	0	0	1 (0.4%)	0	0
過剰肉芽組織	1 (0.4%)	0	0	0	0
毛質異常	0	0	0	0	1 (1.0%)
多毛症	0	0	1 (0.4%)	0	1 (1.0%)
乏汗症	0	0	1 (0.4%)	0	0
皮膚粘膜発疹	0	1 (0.4%)	0	0	0
爪線状隆起	1 (0.4%)	0	0	0	0
爪破損	0	0	0	0	1 (1.0%)
手掌・足底発赤知覚不全症候群	0	2 (0.8%)	0	0	0
丘疹	1 (0.4%)	0	0	0	0
陰茎潰瘍形成	0	0	0	0	1 (1.0%)
光線過敏性反応	0	1 (0.4%)	0	0	0
粃糠疹	0	0	0	0	1 (1.0%)
ばら色粃糠疹	0	0	0	0	1 (1.0%)
壊疽性膿皮症	0	0	1 (0.4%)	0	0
紅斑性皮疹	0	1 (0.4%)	0	0	1 (1.0%)
小水疱性皮疹	0	0	1 (0.4%)	0	0
痂皮	0	1 (0.4%)	0	0	0
皮膚灼熱感	0	0	1 (0.4%)	0	0
皮膚障害	1 (0.4%)	0	2 (0.7%)	0	0
皮膚剥脱	0	1 (0.4%)	0	0	1 (1.0%)
皮膚亀裂	0	1 (0.4%)	1 (0.4%)	0	0
皮膚出血	1 (0.4%)	0	0	0	0
皮膚腫瘤	1 (0.4%)	0	0	0	0
皮膚反応	1 (0.4%)	1 (0.4%)	0	0	0
うっ滞性皮膚炎	0	0	1 (0.4%)	0	0
毛細血管拡張症	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
乾皮症	0	0	1 (0.4%)	0	0
精神障害	53 (22.4%)	67 (27.6%)	93 (33.1%)	106 (33.3%)	47 (45.6%)
不眠症	35 (14.8%)	41 (16.9%)	55 (19.6%)	60 (18.9%)	24 (23.3%)
うつ病	5 (2.1%)	8 (3.3%)	5 (1.8%)	19 (6.0%)	4 (3.9%)
不安	6 (2.5%)	3 (1.2%)	12 (4.3%)	18 (5.7%)	13 (12.6%)
激越	5 (2.1%)	4 (1.6%)	9 (3.2%)	8 (2.5%)	3 (2.9%)
落ち着きのなさ	7 (3.0%)	8 (3.3%)	5 (1.8%)	8 (2.5%)	1 (1.0%)
気分変化	0	1 (0.4%)	5 (1.8%)	7 (2.2%)	0
易刺激性	4 (1.7%)	3 (1.2%)	5 (1.8%)	6 (1.9%)	4 (3.9%)
抑うつ気分	0	1 (0.4%)	2 (0.7%)	4 (1.3%)	0
睡眠障害	2 (0.8%)	4 (1.6%)	4 (1.4%)	4 (1.3%)	2 (1.9%)
気分動揺	0	2 (0.8%)	1 (0.4%)	3 (0.9%)	1 (1.0%)
錯乱状態	3 (1.3%)	3 (1.2%)	7 (2.5%)	2 (0.6%)	7 (6.8%)
精神障害	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	0
適応障害	0	0	0	1 (0.3%)	0
感情障害	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
攻撃性	0	0	0	1 (0.3%)	0
精神緩慢	0	0	0	1 (0.3%)	1 (1.0%)
譫妄	3 (1.3%)	1 (0.4%)	5 (1.8%)	1 (0.3%)	1 (1.0%)
抑うつ症状	0	0	2 (0.7%)	1 (0.3%)	0
幻覚	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
精神症状	0	0	0	1 (0.3%)	0
涙ぐむ	0	0	0	1 (0.3%)	0
感情不安定	0	0	0	0	2 (1.9%)
まとまりのない会話	0	0	1 (0.4%)	0	0
失見当識	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
転導性	2 (0.8%)	1 (0.4%)	0	0	0
気分変調性障害	0	0	1 (0.4%)	0	1 (1.0%)
感情的苦悩	1 (0.4%)	0	0	0	0
多幸気分	1 (0.4%)	0	0	0	0
リビドー減退	0	1 (0.4%)	0	0	0
言葉もれ	0	0	1 (0.4%)	0	0
リビドー消失	0	0	1 (0.4%)	0	0
精神状態変化	0	0	0	0	3 (2.9%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
神経過敏	1 (0.4%)	0	5 (1.8%)	0	0
パニック障害	0	1 (0.4%)	0	0	0
妄想症	1 (0.4%)	0	0	0	1 (1.0%)
精神的機能代償不全	0	1 (0.4%)	0	0	0
精神病性障害	0	0	1 (0.4%)	0	0
睡眠時驚愕	0	0	1 (0.4%)	0	0
ストレス	0	0	1 (0.4%)	0	0
物質誘発性精神病性障害	1 (0.4%)	0	0	0	0
自殺念慮	0	0	0	0	1 (1.0%)
思考異常	0	0	1 (0.4%)	0	0
血管障害	32 (13.5%)	52 (21.4%)	46 (16.4%)	94 (29.6%)	25 (24.3%)
高血圧	8 (3.4%)	21 (8.6%)	7 (2.5%)	30 (9.4%)	8 (7.8%)
低血圧	10 (4.2%)	12 (4.9%)	6 (2.1%)	22 (6.9%)	2 (1.9%)
潮紅	3 (1.3%)	5 (2.1%)	5 (1.8%)	10 (3.1%)	6 (5.8%)
深部静脈血栓症	1 (0.4%)	3 (1.2%)	11 (3.9%)	5 (1.6%)	1 (1.0%)
血腫	3 (1.3%)	5 (2.1%)	5 (1.8%)	5 (1.6%)	1 (1.0%)
静脈炎	0	1 (0.4%)	1 (0.4%)	5 (1.6%)	0
ほてり	1 (0.4%)	3 (1.2%)	2 (0.7%)	4 (1.3%)	4 (3.9%)
起立性低血圧	4 (1.7%)	3 (1.2%)	2 (0.7%)	4 (1.3%)	0
塞栓症	0	0	0	3 (0.9%)	0
血栓性静脈炎	0	1 (0.4%)	0	3 (0.9%)	0
表在性血栓性静脈炎	2 (0.8%)	0	6 (2.1%)	3 (0.9%)	2 (1.9%)
末梢冷感	0	0	0	2 (0.6%)	0
血栓症	1 (0.4%)	2 (0.8%)	2 (0.7%)	2 (0.6%)	0
静脈血栓症	0	0	0	2 (0.6%)	0
大動脈拡張	0	0	0	1 (0.3%)	0
出血性梗塞	0	0	0	1 (0.3%)	0
リンパ浮腫	0	0	0	1 (0.3%)	0
末梢動脈狭窄	0	0	0	1 (0.3%)	0
表在性静脈炎	0	0	0	1 (0.3%)	0
大動脈瘤	0	0	1 (0.4%)	0	0
大動脈解離	0	0	0	0	1 (1.0%)
動脈硬化症	0	0	2 (0.7%)	0	0
循環虚脱	2 (0.8%)	0	0	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
静脈塞栓症	1 (0.4%)	0	0	0	1 (1.0%)
充血	0	1 (0.4%)	0	0	0
高血圧クリーゼ	1 (0.4%)	1 (0.4%)	0	0	0
腹腔内血腫	0	1 (0.4%)	0	0	0
虚血	0	0	1 (0.4%)	0	0
蒼白	0	0	1 (0.4%)	0	0
末梢動脈瘤	0	1 (0.4%)	0	0	0
末梢動脈血栓症	0	0	0	0	1 (1.0%)
末梢静脈疾患	0	1 (0.4%)	0	0	0
静脈硬化症	0	1 (0.4%)	0	0	0
血栓後症候群	0	0	1 (0.4%)	0	0
レイノー現象	0	0	1 (0.4%)	0	0
血管拡張	0	1 (0.4%)	0	0	0
静脈閉塞	0	0	1 (0.4%)	0	0
四肢静脈血栓症	1 (0.4%)	0	1 (0.4%)	0	1 (1.0%)
臨床検査	23 (9.7%)	49 (20.2%)	48 (17.1%)	77 (24.2%)	28 (27.2%)
体重減少	3 (1.3%)	13 (5.3%)	9 (3.2%)	18 (5.7%)	9 (8.7%)
アラニンアミノトランスフェラーゼ増加	10 (4.2%)	17 (7.0%)	10 (3.6%)	17 (5.3%)	6 (5.8%)
アスパラギン酸アミノトランスフェラーゼ増加	5 (2.1%)	12 (4.9%)	9 (3.2%)	12 (3.8%)	5 (4.9%)
血中クレアチニン増加	4 (1.7%)	5 (2.1%)	11 (3.9%)	10 (3.1%)	5 (4.9%)
血中アルカリホスファターゼ増加	4 (1.7%)	4 (1.6%)	5 (1.8%)	9 (2.8%)	6 (5.8%)
γ－グルタミルトランスフェラーゼ増加	4 (1.7%)	7 (2.9%)	7 (2.5%)	7 (2.2%)	0
心電図ＱＴ延長	0	0	1 (0.4%)	6 (1.9%)	0
血圧上昇	0	0	0	4 (1.3%)	2 (1.9%)
Ｃ－反応性蛋白増加	1 (0.4%)	1 (0.4%)	2 (0.7%)	3 (0.9%)	0
腎クレアチニン・クリアランス減少	0	0	2 (0.7%)	3 (0.9%)	0
免疫グロブリン減少	0	0	0	3 (0.9%)	0
体重増加	2 (0.8%)	6 (2.5%)	4 (1.4%)	3 (0.9%)	4 (3.9%)
血中乳酸脱水素酵素増加	1 (0.4%)	3 (1.2%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
国際標準比増加	0	1 (0.4%)	0	2 (0.6%)	1 (1.0%)
アラニンアミノトランスフェラーゼ異常	0	0	0	1 (0.3%)	0
アスパラギン酸アミノトランスフェラーゼ異常	0	0	0	1 (0.3%)	0
抱合ビリルビン増加	0	0	0	1 (0.3%)	0
血中クレアチンホスホキナーゼ増加	0	0	0	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
血中鉄減少	0	0	0	1 (0.3%)	0
血中乳酸脱水素酵素減少	0	0	0	1 (0.3%)	0
血圧低下	0	0	0	1 (0.3%)	0
心雑音	0	0	0	1 (0.3%)	0
心拍数増加	0	0	0	1 (0.3%)	0
A型インフルエンザウイルス検査陽性	0	0	0	1 (0.3%)	0
好中球中毒性顆粒存在	0	0	0	1 (0.3%)	0
酸素飽和度低下	0	0	0	1 (0.3%)	0
前立腺特異性抗原増加	0	0	0	1 (0.3%)	0
肺動脈圧上昇	0	0	0	1 (0.3%)	0
網状赤血球数増加	0	0	0	1 (0.3%)	0
血清フェリチン減少	0	0	0	1 (0.3%)	0
トロポニン増加	0	0	0	1 (0.3%)	0
活性化部分トロンボプラスチン時間延長	0	1 (0.4%)	0	0	0
抗凝固薬濃度治療量以下	0	0	1 (0.4%)	0	0
血中カルシウム増加	0	0	0	0	1 (1.0%)
血中葉酸減少	0	0	1 (0.4%)	0	0
血中ホモシステイン増加	1 (0.4%)	0	0	0	0
血中リン減少	0	1 (0.4%)	0	0	2 (1.9%)
体温上昇	0	0	1 (0.4%)	0	0
呼吸音異常	0	1 (0.4%)	0	0	0
診断法	0	0	1 (0.4%)	0	0
心電図QT間隔異常	0	1 (0.4%)	0	0	0
フィブリンDダイマー増加	0	0	1 (0.4%)	0	0
γ－グルタミルトランスフェラーゼ	0	1 (0.4%)	0	0	0
糸球体濾過率減少	0	1 (0.4%)	2 (0.7%)	0	0
グリコヘモグロビン増加	0	1 (0.4%)	0	0	0
握力低下	0	0	0	0	1 (1.0%)
ヘリコバクター検査陽性	0	0	1 (0.4%)	0	0
深吸気量減少	0	1 (0.4%)	0	0	0
リパーゼ増加	0	1 (0.4%)	0	0	0
総蛋白増加	1 (0.4%)	0	0	0	0
サルモネラ検査陽性	0	0	0	0	1 (1.0%)
静脈雑音	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
眼障害	27 (11.4%)	42 (17.3%)	35 (12.5%)	64 (20.1%)	18 (17.5%)
霧視	9 (3.8%)	5 (2.1%)	14 (5.0%)	21 (6.6%)	7 (6.8%)
白内障	0	3 (1.2%)	8 (2.8%)	19 (6.0%)	1 (1.0%)
流涙増加	1 (0.4%)	11 (4.5%)	1 (0.4%)	9 (2.8%)	2 (1.9%)
眼刺激	1 (0.4%)	2 (0.8%)	1 (0.4%)	7 (2.2%)	2 (1.9%)
眼乾燥	6 (2.5%)	5 (2.1%)	3 (1.1%)	5 (1.6%)	0
結膜出血	0	3 (1.2%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
眼出血	0	1 (0.4%)	0	2 (0.6%)	1 (1.0%)
眼部腫脹	0	0	0	2 (0.6%)	1 (1.0%)
眼充血	0	2 (0.8%)	0	2 (0.6%)	0
屈折障害	0	0	0	2 (0.6%)	0
視力低下	1 (0.4%)	2 (0.8%)	1 (0.4%)	2 (0.6%)	0
視力障害	2 (0.8%)	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
眼精疲労	0	1 (0.4%)	0	1 (0.3%)	0
眼瞼炎	3 (1.3%)	0	0	1 (0.3%)	0
眼のアレルギー	0	0	0	1 (0.3%)	0
眼脂	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
眼の障害	0	2 (0.8%)	0	1 (0.3%)	0
眼の炎症	0	0	0	1 (0.3%)	0
眼球浮腫	0	0	0	1 (0.3%)	0
眼痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
眼瞼浮腫	0	1 (0.4%)	0	1 (0.3%)	0
緑内障	0	0	0	1 (0.3%)	0
眼窩周囲浮腫	0	0	1 (0.4%)	1 (0.3%)	0
後嚢破裂	0	0	0	1 (0.3%)	0
硝子体浮遊物	0	0	0	1 (0.3%)	0
眼瞼痙攣	1 (0.4%)	0	0	0	0
失明	0	0	1 (0.4%)	0	0
霰粒腫	2 (0.8%)	0	0	0	1 (1.0%)
結膜刺激	0	0	1 (0.4%)	0	0
結膜浮腫	0	3 (1.2%)	0	0	0
嚢胞様黄斑浮腫	0	1 (0.4%)	0	0	0
複視	1 (0.4%)	3 (1.2%)	0	0	3 (2.9%)
眼瞼紅斑	0	1 (0.4%)	0	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
眼そう痒症	2 (0.8%)	1 (0.4%)	0	0	2 (1.9%)
眼瞼下垂	0	0	1 (0.4%)	0	0
眼瞼発疹	0	0	1 (0.4%)	0	0
虹彩炎	0	1 (0.4%)	0	0	0
水晶体混濁	0	0	1 (0.4%)	0	0
黄斑変性	0	0	1 (0.4%)	0	0
眼部不快感	1 (0.4%)	0	0	0	0
網膜剥離	1 (0.4%)	0	0	0	0
網膜静脈血栓症	0	0	1 (0.4%)	0	0
網膜症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
潰瘍性角膜炎	1 (0.4%)	0	0	0	0
硝子体剥離	0	0	1 (0.4%)	0	1 (1.0%)
硝子体出血	0	0	1 (0.4%)	0	0
腎および尿路障害	28 (11.8%)	21 (8.6%)	45 (16.0%)	56 (17.6%)	20 (19.4%)
腎機能障害	8 (3.4%)	5 (2.1%)	13 (4.6%)	22 (6.9%)	3 (2.9%)
頻尿	1 (0.4%)	1 (0.4%)	3 (1.1%)	7 (2.2%)	1 (1.0%)
急性腎不全	4 (1.7%)	4 (1.6%)	15 (5.3%)	4 (1.3%)	5 (4.9%)
血尿	1 (0.4%)	2 (0.8%)	1 (0.4%)	4 (1.3%)	3 (2.9%)
夜間頻尿	1 (0.4%)	2 (0.8%)	1 (0.4%)	4 (1.3%)	1 (1.0%)
高窒素血症	0	0	1 (0.4%)	3 (0.9%)	0
慢性腎臓病	2 (0.8%)	2 (0.8%)	4 (1.4%)	3 (0.9%)	0
排尿困難	1 (0.4%)	0	4 (1.4%)	2 (0.6%)	4 (3.9%)
腎結石症	0	0	0	2 (0.6%)	0
膀胱結石	0	0	0	1 (0.3%)	0
失禁	0	1 (0.4%)	0	1 (0.3%)	2 (1.9%)
尿意切迫	0	1 (0.4%)	0	1 (0.3%)	0
腎仙痛	1 (0.4%)	0	0	1 (0.3%)	1 (1.0%)
腎嚢胞	0	0	0	1 (0.3%)	0
腎障害	0	0	0	1 (0.3%)	0
腎不全	2 (0.8%)	0	5 (1.8%)	1 (0.3%)	1 (1.0%)
腎出血	0	0	0	1 (0.3%)	0
有痛性排尿困難	0	0	0	1 (0.3%)	0
尿道出血	0	0	0	1 (0.3%)	0
尿失禁	0	0	2 (0.7%)	1 (0.3%)	1 (1.0%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
尿路閉塞	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
ベンスジョーンズ蛋白尿	0	0	1 (0.4%)	0	0
膀胱閉塞	1 (0.4%)	0	0	0	0
尿路結石	1 (0.4%)	0	0	0	0
着色尿	0	0	0	0	1 (1.0%)
非感染性膀胱炎	0	0	0	0	1 (1.0%)
ケトン尿	0	0	1 (0.4%)	0	0
下部尿路症状	0	0	1 (0.4%)	0	0
排尿異常	0	0	1 (0.4%)	0	0
骨髄腫円柱腎症	1 (0.4%)	1 (0.4%)	0	0	0
中毒性ネフロパシー	2 (0.8%)	0	0	0	0
多尿	0	1 (0.4%)	1 (0.4%)	0	1 (1.0%)
腎腫瘤	0	0	1 (0.4%)	0	0
腎臓痛	0	1 (0.4%)	0	0	0
腎尿細管壊死	1 (0.4%)	0	0	0	0
尿閉	4 (1.7%)	3 (1.2%)	5 (1.8%)	0	1 (1.0%)
傷害、中毒および処置合併症	21 (8.9%)	31 (12.8%)	45 (16.0%)	48 (15.1%)	26 (25.2%)
挫傷	3 (1.3%)	3 (1.2%)	6 (2.1%)	11 (3.5%)	4 (3.9%)
転倒	5 (2.1%)	6 (2.5%)	8 (2.8%)	11 (3.5%)	10 (9.7%)
靭帯捻挫	0	0	0	4 (1.3%)	0
脊椎圧迫骨折	0	1 (0.4%)	2 (0.7%)	4 (1.3%)	2 (1.9%)
裂傷	1 (0.4%)	1 (0.4%)	2 (0.7%)	3 (0.9%)	0
足骨折	0	1 (0.4%)	0	2 (0.6%)	0
関節損傷	2 (0.8%)	0	0	2 (0.6%)	0
肋骨骨折	2 (0.8%)	2 (0.8%)	4 (1.4%)	2 (0.6%)	0
熱傷	0	0	0	2 (0.6%)	0
背部損傷	0	0	1 (0.4%)	1 (0.3%)	0
脳ヘルニア	0	0	0	1 (0.3%)	0
鎖骨骨折	0	0	2 (0.7%)	1 (0.3%)	0
圧迫骨折	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
眼挫傷	0	0	1 (0.4%)	1 (0.3%)	0
手骨折	0	0	0	1 (0.3%)	0
股関節部骨折	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
注入に伴う反応	0	0	2 (0.7%)	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
肉離れ	0	0	0	1 (0.3%)	0
頚部損傷	0	0	0	1 (0.3%)	0
眼窩周囲挫傷	0	1 (0.4%)	0	1 (0.3%)	0
腓骨神経損傷	0	0	0	1 (0.3%)	0
橈骨骨折	0	0	1 (0.4%)	1 (0.3%)	0
皮膚擦過傷	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
脊椎骨折	0	1 (0.4%)	0	1 (0.3%)	0
胸骨損傷	0	0	0	1 (0.3%)	0
各種物質毒性	0	0	1 (0.4%)	1 (0.3%)	0
上肢骨折	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
創合併症	0	0	1 (0.4%)	1 (0.3%)	0
創傷出血	0	0	0	1 (0.3%)	0
手首関節骨折	0	0	0	1 (0.3%)	0
アレルギー性輸血反応	0	1 (0.4%)	0	0	0
肛門損傷	1 (0.4%)	0	0	0	0
足関節部骨折	0	1 (0.4%)	0	0	1 (1.0%)
節足動物咬傷	0	1 (0.4%)	2 (0.7%)	0	0
節足動物刺傷	1 (0.4%)	0	0	0	0
骨挫傷	0	0	0	0	1 (1.0%)
毒性物質曝露	0	0	0	0	1 (1.0%)
顔面損傷	0	0	1 (0.4%)	0	0
顔面骨骨折	0	0	1 (0.4%)	0	1 (1.0%)
大腿骨頚部骨折	0	0	1 (0.4%)	0	0
大腿骨骨折	0	2 (0.8%)	0	0	2 (1.9%)
上腕骨骨折	0	3 (1.2%)	1 (0.4%)	0	1 (1.0%)
関節脱臼	0	0	2 (0.7%)	0	0
四肢損傷	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0
腰椎骨折	0	1 (0.4%)	0	0	0
筋断裂	0	1 (0.4%)	0	0	0
過量投与	0	0	1 (0.4%)	0	0
膝蓋骨骨折	1 (0.4%)	0	0	0	0
骨盤骨折	0	0	1 (0.4%)	0	1 (1.0%)
眼窩周囲血腫	1 (0.4%)	0	0	0	0
処置後合併症	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
処置後出血	0	1 (0.4%)	0	0	0
外傷後疼痛	0	0	1 (0.4%)	0	0
処置による疼痛	0	1 (0.4%)	2 (0.7%)	0	1 (1.0%)
恥骨骨折	0	1 (0.4%)	0	0	0
橈骨神経損傷	0	1 (0.4%)	0	0	0
放射線性肺臓炎	0	0	0	0	1 (1.0%)
肩甲骨骨折	0	2 (0.8%)	0	0	0
瘢痕	0	0	1 (0.4%)	0	0
引っかき傷	0	0	1 (0.4%)	0	0
皮膚創傷	0	0	1 (0.4%)	0	0
胸骨骨折	0	0	0	0	1 (1.0%)
ストレス骨折	0	0	0	0	1 (1.0%)
皮下血腫	0	1 (0.4%)	0	0	1 (1.0%)
硬膜下血腫	1 (0.4%)	0	1 (0.4%)	0	0
腱断裂	0	0	1 (0.4%)	0	0
胸椎骨折	1 (0.4%)	0	0	0	0
脛骨骨折	0	0	1 (0.4%)	0	0
歯の完全脱臼	1 (0.4%)	0	0	0	0
歯牙破折	0	1 (0.4%)	1 (0.4%)	0	0
輸血関連呼吸困難	0	0	1 (0.4%)	0	0
外傷性血腫	0	0	1 (0.4%)	0	1 (1.0%)
創傷	0	2 (0.8%)	4 (1.4%)	0	0
心臓障害	15 (6.3%)	33 (13.6%)	25 (8.9%)	45 (14.2%)	24 (23.3%)
心房細動	4 (1.7%)	11 (4.5%)	7 (2.5%)	10 (3.1%)	7 (6.8%)
頻脈	0	1 (0.4%)	2 (0.7%)	10 (3.1%)	5 (4.9%)
狭心症	1 (0.4%)	2 (0.8%)	1 (0.4%)	7 (2.2%)	3 (2.9%)
動悸	2 (0.8%)	5 (2.1%)	3 (1.1%)	4 (1.3%)	2 (1.9%)
洞性頻脈	1 (0.4%)	6 (2.5%)	0	4 (1.3%)	4 (3.9%)
徐脈	1 (0.4%)	1 (0.4%)	2 (0.7%)	3 (0.9%)	1 (1.0%)
左室機能不全	0	0	0	3 (0.9%)	0
心房粗動	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
急性冠動脈症候群	0	1 (0.4%)	0	1 (0.3%)	0
不整脈	0	0	0	1 (0.3%)	0
第一度房室ブロック	0	0	0	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
心アミロイドーシス	0	0	0	1 (0.3%)	0
うっ血性心不全	2 (0.8%)	3 (1.2%)	0	1 (0.3%)	2 (1.9%)
心肥大	0	0	0	1 (0.3%)	0
心肺不全	0	0	0	1 (0.3%)	0
伝導障害	0	0	0	1 (0.3%)	0
拡張機能障害	0	0	0	1 (0.3%)	0
期外収縮	1 (0.4%)	0	0	1 (0.3%)	0
僧帽弁閉鎖不全症	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
心筋梗塞	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	0
心筋虚血	0	0	1 (0.4%)	1 (0.3%)	0
洞性不整脈	0	0	0	1 (0.3%)	0
上室性頻脈	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
心室性期外収縮	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	0
急性心筋梗塞	0	2 (0.8%)	3 (1.1%)	0	0
上室性不整脈	0	1 (0.4%)	0	0	0
左脚ブロック	0	1 (0.4%)	0	0	0
心停止	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
心不全	3 (1.3%)	4 (1.6%)	0	0	0
心粗動	0	0	0	0	1 (1.0%)
心原性ショック	1 (0.4%)	1 (0.4%)	0	0	0
冠動脈疾患	0	0	1 (0.4%)	0	0
冠動脈狭窄	1 (0.4%)	0	0	0	0
心嚢液貯留	0	0	2 (0.7%)	0	0
心膜炎	0	0	1 (0.4%)	0	0
肺動脈弁閉鎖不全症	0	1 (0.4%)	0	0	0
洞性徐脈	0	0	0	0	2 (1.9%)
上室性期外収縮	0	0	0	0	1 (1.0%)
三尖弁閉鎖不全症	0	1 (0.4%)	0	0	1 (1.0%)
心室性不整脈	0	1 (0.4%)	0	0	0
耳および迷路障害	4 (1.7%)	21 (8.6%)	12 (4.3%)	20 (6.3%)	8 (7.8%)
耳鳴	2 (0.8%)	6 (2.5%)	1 (0.4%)	10 (3.1%)	4 (3.9%)
回転性めまい	2 (0.8%)	9 (3.7%)	6 (2.1%)	4 (1.3%)	0
難聴	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
聴力低下	0	0	0	2 (0.6%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
片耳難聴	0	0	0	1 (0.3%)	0
耳不快感	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
耳出血	0	0	0	1 (0.3%)	0
耳痛	0	4 (1.6%)	2 (0.7%)	1 (0.3%)	1 (1.0%)
耳垢栓塞	0	1 (0.4%)	0	0	0
両耳難聴	0	1 (0.4%)	0	0	0
耳そう痒症	0	1 (0.4%)	0	0	2 (1.9%)
乳突洞滲出液	0	1 (0.4%)	0	0	0
中耳の炎症	0	1 (0.4%)	1 (0.4%)	0	0
頭位性回転性めまい	0	0	1 (0.4%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	8 (3.3%)	18 (6.4%)	19 (6.0%)	4 (3.9%)
扁平上皮癌	0	0	3 (1.1%)	3 (0.9%)	0
アクロコルドン	0	0	0	2 (0.6%)	0
基底細胞癌	0	0	2 (0.7%)	2 (0.6%)	0
脂肪腫	0	0	0	2 (0.6%)	2 (1.9%)
急性単球性白血病	0	0	0	1 (0.3%)	0
腺癌	0	0	0	1 (0.3%)	0
胃腺癌	0	0	0	1 (0.3%)	0
乳房の良性新生物	0	0	0	1 (0.3%)	0
甲状腺の良性新生物	0	0	0	1 (0.3%)	0
ボーエン病	0	0	0	1 (0.3%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.3%)	0
ケラトアカントーマ	0	0	0	1 (0.3%)	0
形質細胞性白血病	0	0	2 (0.7%)	1 (0.3%)	0
脂漏性角化症	0	0	0	1 (0.3%)	0
結腸腺癌	0	1 (0.4%)	0	0	0
肛門性器疣贅	0	0	0	0	1 (1.0%)
肛門直腸の良性新生物	0	0	1 (0.4%)	0	0
肺の良性新生物	0	0	1 (0.4%)	0	0
良性新生物	0	0	1 (0.4%)	0	0
膀胱の良性新生物	0	0	1 (0.4%)	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
乳癌	0	1 (0.4%)	0	0	0
再発乳癌	1 (0.4%)	0	0	0	0
胃腸管腺腫	0	1 (0.4%)	0	0	0
皮膚血管腫	0	0	1 (0.4%)	0	0
脂肪肉腫	0	1 (0.4%)	0	0	0
肺腺癌	0	0	1 (0.4%)	0	0
メラノサイト性母斑	0	0	0	0	1 (1.0%)
形質細胞腫	0	1 (0.4%)	1 (0.4%)	0	0
前立腺癌	0	0	1 (0.4%)	0	0
直腸腺癌	0	0	1 (0.4%)	0	0
シュワン細胞腫	0	0	1 (0.4%)	0	0
皮膚乳頭腫	0	1 (0.4%)	0	0	0
皮膚有棘細胞癌	0	1 (0.4%)	0	0	0
移行上皮癌	0	1 (0.4%)	0	0	0
子宮平滑筋腫	0	1 (0.4%)	0	0	0
免疫系障害	3 (1.3%)	1 (0.4%)	3 (1.1%)	13 (4.1%)	5 (4.9%)
低ｙグロブリン血症	1 (0.4%)	1 (0.4%)	0	5 (1.6%)	2 (1.9%)
季節性アレルギー	2 (0.8%)	0	1 (0.4%)	4 (1.3%)	2 (1.9%)
薬物過敏症	0	0	1 (0.4%)	1 (0.3%)	0
免疫系障害	0	0	0	1 (0.3%)	0
免疫抑制	0	0	0	1 (0.3%)	0
続発性免疫不全症	0	0	0	1 (0.3%)	0
サイトカイン放出症候群	0	0	0	0	1 (1.0%)
食物アレルギー	0	0	1 (0.4%)	0	0
生殖系および乳房障害	7 (3.0%)	14 (5.8%)	17 (6.0%)	12 (3.8%)	4 (3.9%)
勃起不全	0	1 (0.4%)	2 (0.7%)	3 (0.9%)	0
骨盤痛	2 (0.8%)	4 (1.6%)	6 (2.1%)	3 (0.9%)	2 (1.9%)
乳房嚢胞	0	0	0	1 (0.3%)	0
乳房腫脹	0	0	0	1 (0.3%)	0
骨盤血腫	0	0	0	1 (0.3%)	0
前立腺炎	0	0	2 (0.7%)	1 (0.3%)	0
前立腺腫大	0	0	0	1 (0.3%)	0
精巣痛	0	3 (1.2%)	0	1 (0.3%)	0
腟出血	0	0	2 (0.7%)	1 (0.3%)	0

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
腟逆流	0	0	0	1 (0.3%)	0
腺筋症	0	1 (0.4%)	0	0	0
萎縮性外陰腟炎	0	0	1 (0.4%)	0	0
亀頭包皮炎	1 (0.4%)	2 (0.8%)	0	0	0
良性前立腺肥大症	2 (0.8%)	1 (0.4%)	2 (0.7%)	0	0
乳房圧痛	0	1 (0.4%)	0	0	0
性器水疱	0	0	1 (0.4%)	0	0
生殖器痛	1 (0.4%)	0	0	0	0
性器錯感覚	0	0	0	0	1 (1.0%)
月経障害	0	1 (0.4%)	0	0	0
不規則月経	0	1 (0.4%)	0	0	0
不正子宮出血	0	0	0	0	1 (1.0%)
陰嚢痛	0	1 (0.4%)	0	0	0
精巣腫瘤	0	0	1 (0.4%)	0	0
子宮出血	1 (0.4%)	0	0	0	0
外陰腟痛	0	0	1 (0.4%)	0	0
肝胆道系障害	5 (2.1%)	9 (3.7%)	7 (2.5%)	11 (3.5%)	6 (5.8%)
高ビリルビン血症	2 (0.8%)	5 (2.1%)	2 (0.7%)	4 (1.3%)	5 (4.9%)
肝機能異常	0	0	0	2 (0.6%)	0
肝細胞損傷	0	0	0	2 (0.6%)	0
胆石症	0	0	0	1 (0.3%)	1 (1.0%)
脂肪肝	0	0	1 (0.4%)	1 (0.3%)	0
肝障害	0	0	3 (1.1%)	1 (0.3%)	0
胆管結石	0	0	1 (0.4%)	0	0
胆嚢炎	0	3 (1.2%)	0	0	0
慢性胆嚢炎	0	1 (0.4%)	0	0	0
胆汁うっ滞	1 (0.4%)	0	0	0	0
胆嚢障害	0	1 (0.4%)	0	0	0
肝アミロイドーシス	1 (0.4%)	0	0	0	0
肝腫瘤	0	0	1 (0.4%)	0	0
虚血性肝炎	1 (0.4%)	0	0	0	0
門脈域の炎症	1 (0.4%)	0	0	0	0
内分泌障害	5 (2.1%)	12 (4.9%)	10 (3.6%)	5 (1.6%)	3 (2.9%)
クッシング様症状	3 (1.3%)	7 (2.9%)	4 (1.4%)	1 (0.3%)	2 (1.9%)

TSFAE02A: Number of Subjects with 1 or more treatment-emergent adverse events by MedDRA system organ class and preferred term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
高コルチコイド症	0	0	0	1 (0.3%)	0
副甲状腺機能亢進症	0	0	1 (0.4%)	1 (0.3%)	0
甲状腺機能亢進症	0	1 (0.4%)	0	1 (0.3%)	0
ステロイド離脱症候群	0	0	2 (0.7%)	1 (0.3%)	0
副腎機能不全	2 (0.8%)	1 (0.4%)	0	0	0
クッシング症候群	0	2 (0.8%)	1 (0.4%)	0	0
甲状腺腫	0	1 (0.4%)	0	0	0
甲状腺機能低下症	0	0	1 (0.4%)	0	1 (1.0%)
下垂体依存性クッシング症候群	0	0	1 (0.4%)	0	0
先天性、家族性および遺伝性障害	0	0	0	2 (0.6%)	2 (1.9%)
角膜ジストロフィー	0	0	0	1 (0.3%)	0
包茎	0	0	0	1 (0.3%)	0
肥大型心筋症	0	0	0	0	1 (1.0%)
汗孔角化症	0	0	0	0	1 (1.0%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE02A.SAS] 01JUN2016, 10:35

表 2.7.4-付録-27 Number of Subjects with Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE02: Number of Subjects with Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: Safety	8
Total number of subjects with TEAE	8 (100.0%)
MedDRA system organ class/Preferred term	
血液およびリンパ系障害	8 (100.0%)
血小板減少症	7 (87.5%)
リンパ球減少症	5 (62.5%)
貧血	3 (37.5%)
白血球減少症	3 (37.5%)
好中球減少症	3 (37.5%)
一般・全身障害および投与部位の状態	5 (62.5%)
疲労	3 (37.5%)
悪寒	2 (25.0%)
歩行障害	1 (12.5%)
末梢性浮腫	1 (12.5%)
発熱	1 (12.5%)
感染症および寄生虫症	5 (62.5%)
鼻咽頭炎	2 (25.0%)
気管支炎	1 (12.5%)
帯状疱疹	1 (12.5%)
インフルエンザ	1 (12.5%)
代謝および栄養障害	5 (62.5%)
高血糖	3 (37.5%)
脱水	2 (25.0%)
低カリウム血症	2 (25.0%)
低リン酸血症	1 (12.5%)
神経系障害	5 (62.5%)
異常感覚	3 (37.5%)
頭痛	1 (12.5%)
神経痛	1 (12.5%)
末梢性感覚ニューロパチー	1 (12.5%)
ヘルペス後神経痛	1 (12.5%)
胃腸障害	4 (50.0%)
便秘	2 (25.0%)
下痢	2 (25.0%)
胃炎	2 (25.0%)
腹部膨満	1 (12.5%)
上腹部痛	1 (12.5%)
消化不良	1 (12.5%)
悪心	1 (12.5%)
胃肉芽腫	1 (12.5%)
嘔吐	1 (12.5%)
臨床検査	4 (50.0%)
血中乳酸脱水素酵素増加	3 (37.5%)
体重減少	3 (37.5%)
アラニンアミノトランスフェラーゼ増加	1 (12.5%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (12.5%)
血圧上昇	1 (12.5%)
血中尿素増加	1 (12.5%)
Ｃ－反応性蛋白増加	1 (12.5%)
細胞マーカー増加	1 (12.5%)
フィブリン分解産物増加	1 (12.5%)
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)

TSFAE02: Number of Subjects with Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
サーファクタントプロテイン増加	1 (12.5%)
呼吸器、胸郭および縦隔障害	4 (50.0%)
低酸素症	2 (25.0%)
喘鳴	2 (25.0%)
発声障害	1 (12.5%)
口腔咽頭不快感	1 (12.5%)
口腔咽頭痛	1 (12.5%)
皮膚および皮下組織障害	4 (50.0%)
皮膚嚢腫	1 (12.5%)
皮膚炎	1 (12.5%)
紅斑	1 (12.5%)
皮下出血	1 (12.5%)
全身性皮疹	1 (12.5%)
眼障害	2 (25.0%)
眼精疲労	1 (12.5%)
霧視	1 (12.5%)
筋骨格系および結合組織障害	2 (25.0%)
筋力低下	1 (12.5%)
ミオパチー	1 (12.5%)
精神障害	2 (25.0%)
短時間睡眠	1 (12.5%)
不眠症	1 (12.5%)
耳および迷路障害	1 (12.5%)
片耳難聴	1 (12.5%)
肝胆道系障害	1 (12.5%)
薬物性肝障害	1 (12.5%)
傷害、中毒および処置合併症	1 (12.5%)
凍瘡	1 (12.5%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)
前立腺癌	1 (12.5%)
血管障害	1 (12.5%)
高血圧	1 (12.5%)
低血圧	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE02.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE02.SAS] 28SEP2016, 04:13

表 2.7.4-付録-28 Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283
Total number of subjects with TEAE	15 (100.0%)	44 (100.0%)	274 (97.5%)	20 (100.0%)	51 (100.0%)	278 (98.2%)
MedDRA system organ class/Preferred term						
感染症および寄生虫症	13 (86.7%)	38 (86.4%)	204 (72.6%)	17 (85.0%)	44 (86.3%)	238 (84.1%)
上気道感染	3 (20.0%)	18 (40.9%)	58 (20.6%)	3 (15.0%)	22 (43.1%)	90 (31.8%)
鼻咽頭炎	4 (26.7%)	9 (20.5%)	43 (15.3%)	9 (45.0%)	17 (33.3%)	68 (24.0%)
肺炎	3 (20.0%)	6 (13.6%)	37 (13.2%)	2 (10.0%)	5 (9.8%)	40 (14.1%)
気管支炎	1 (6.7%)	2 (4.5%)	34 (12.1%)	1 (5.0%)	3 (5.9%)	38 (13.4%)
気道感染	0	0	22 (7.8%)	0	0	31 (11.0%)
インフルエンザ	0	1 (2.3%)	13 (4.6%)	0	0	21 (7.4%)
副鼻腔炎	0	2 (4.5%)	10 (3.6%)	0	4 (7.8%)	18 (6.4%)
下気道感染	0	0	9 (3.2%)	0	0	17 (6.0%)
鼻炎	0	0	3 (1.1%)	0	2 (3.9%)	15 (5.3%)
尿路感染	0	1 (2.3%)	11 (3.9%)	1 (5.0%)	2 (3.9%)	15 (5.3%)
結膜炎	0	0	3 (1.1%)	0	1 (2.0%)	11 (3.9%)
胃腸炎	0	0	4 (1.4%)	0	0	10 (3.5%)
帯状疱疹	1 (6.7%)	4 (9.1%)	5 (1.8%)	0	4 (7.8%)	6 (2.1%)
口腔カンジダ症	0	0	4 (1.4%)	0	0	6 (2.1%)
口腔ヘルペス	0	0	2 (0.7%)	0	0	6 (2.1%)
蜂巣炎	0	1 (2.3%)	3 (1.1%)	0	1 (2.0%)	5 (1.8%)
口腔真菌感染	0	0	5 (1.8%)	0	0	5 (1.8%)
皮膚感染	0	0	5 (1.8%)	1 (5.0%)	1 (2.0%)	5 (1.8%)
ウイルス感染	0	0	7 (2.5%)	0	0	5 (1.8%)
膀胱炎	1 (6.7%)	1 (2.3%)	7 (2.5%)	1 (5.0%)	2 (3.9%)	4 (1.4%)
耳感染	0	0	3 (1.1%)	0	0	4 (1.4%)
真菌感染	0	0	1 (0.4%)	0	0	4 (1.4%)
ヘルペスウイルス感染	0	0	0	0	1 (2.0%)	4 (1.4%)
感染	0	0	5 (1.8%)	0	0	4 (1.4%)
咽頭炎	1 (6.7%)	1 (2.3%)	7 (2.5%)	1 (5.0%)	1 (2.0%)	4 (1.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
インフルエンザ性肺炎	0	0	0	0	0	4 (1.4%)
気管支肺炎	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	3 (1.1%)
肺感染	0	0	2 (0.7%)	0	1 (2.0%)	3 (1.1%)
歯周炎	0	0	1 (0.4%)	1 (5.0%)	3 (5.9%)	3 (1.1%)
ＲＳウイルス感染	0	0	0	0	0	3 (1.1%)
敗血症性ショック	0	0	2 (0.7%)	0	0	3 (1.1%)
外陰部腟カンジダ症	0	0	0	0	0	3 (1.1%)
急性副鼻腔炎	0	0	0	0	0	2 (0.7%)
虫垂炎	0	0	1 (0.4%)	0	0	2 (0.7%)
細気管支炎	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)
カンピロバクター胃腸炎	0	0	0	0	0	2 (0.7%)
丹毒	0	0	2 (0.7%)	0	0	2 (0.7%)
大腸菌性尿路感染	0	0	0	0	0	2 (0.7%)
眼感染	0	0	2 (0.7%)	0	0	2 (0.7%)
毛包炎	0	1 (2.3%)	1 (0.4%)	0	0	2 (0.7%)
皮膚真菌感染	0	0	1 (0.4%)	0	0	2 (0.7%)
せつ	0	0	0	0	0	2 (0.7%)
ウイルス性胃腸炎	0	0	1 (0.4%)	0	0	2 (0.7%)
消化管感染	0	0	1 (0.4%)	0	0	2 (0.7%)
歯肉炎	0	0	4 (1.4%)	0	0	2 (0.7%)
Ｈ１Ｎ１インフルエンザ	0	1 (2.3%)	1 (0.4%)	0	0	2 (0.7%)
大葉性肺炎	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)
好中球減少性敗血症	0	0	0	0	0	2 (0.7%)
耳下腺炎	0	0	0	0	0	2 (0.7%)
細菌性肺炎	0	0	1 (0.4%)	0	0	2 (0.7%)
ウイルス性気道感染	0	0	0	0	0	2 (0.7%)
敗血症	0	1 (2.3%)	6 (2.1%)	0	0	2 (0.7%)
皮下組織膿瘍	0	0	0	0	0	2 (0.7%)
足部白癬	0	0	3 (1.1%)	0	1 (2.0%)	2 (0.7%)
歯膿瘍	0	0	6 (2.1%)	0	0	2 (0.7%)
歯感染	0	0	2 (0.7%)	0	0	2 (0.7%)
細菌性上気道感染	0	0	0	0	0	2 (0.7%)
急性扁桃炎	0	0	0	0	0	1 (0.4%)
無症候性細菌尿	0	0	0	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
細菌感染	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
カンジダ性亀頭炎	0	0	0	0	0	1 (0.4%)
細菌性気管支炎	0	0	0	0	0	1 (0.4%)
カンピロバクター感染	0	0	0	0	0	1 (0.4%)
カンジダ感染	0	0	2 (0.7%)	0	0	1 (0.4%)
カテーテル留置部位膿瘍	0	0	0	0	0	1 (0.4%)
カテーテル留置部位感染	0	0	0	0	0	1 (0.4%)
慢性副鼻腔炎	0	0	0	0	0	1 (0.4%)
ウイルス性結膜炎	0	0	1 (0.4%)	0	0	1 (0.4%)
コロナウイルス感染	0	0	0	0	0	1 (0.4%)
サイトメガロウイルス感染	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
ウイルス性腸炎	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
喉頭蓋炎	0	0	0	0	0	1 (0.4%)
大腸菌性菌血症	0	0	0	0	0	1 (0.4%)
硬膜外膿瘍	0	0	0	0	0	1 (0.4%)
感染性舌炎	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
感染性脊椎炎	0	0	0	0	0	1 (0.4%)
注入部位蜂巣炎	0	0	0	0	1 (2.0%)	1 (0.4%)
ウイルス性喉頭炎	0	0	0	0	0	1 (0.4%)
リステリア性敗血症	0	0	0	0	0	1 (0.4%)
限局性感染	0	0	5 (1.8%)	0	0	1 (0.4%)
ウイルス性下気道感染	0	0	1 (0.4%)	0	0	1 (0.4%)
粘膜感染	0	0	3 (1.1%)	0	0	1 (0.4%)
鼻膿瘍	0	0	0	0	0	1 (0.4%)
口腔感染	0	0	0	0	0	1 (0.4%)
中咽頭カンジダ症	0	0	0	0	0	1 (0.4%)
外耳炎	0	0	1 (0.4%)	0	0	1 (0.4%)
中耳炎	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
耳管炎	0	0	0	0	0	1 (0.4%)
パラインフルエンザウイルス感染	0	0	1 (0.4%)	0	0	1 (0.4%)
眼窩周囲蜂巣炎	0	0	0	0	0	1 (0.4%)
レンサ球菌性咽頭炎	0	0	1 (0.4%)	0	0	1 (0.4%)
ヘモフィルス性肺炎	0	0	0	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
クレブシエラ菌性肺炎	0	0	0	0	0	1 (0.4%)
レジオネラ菌性肺炎	0	0	1 (0.4%)	0	0	1 (0.4%)
レンサ球菌性肺炎	0	0	0	0	0	1 (0.4%)
前立腺感染	0	0	0	0	0	1 (0.4%)
シュードモナス感染	0	0	0	0	0	1 (0.4%)
腎盂腎炎	0	0	0	0	0	1 (0.4%)
呼吸器モニリア症	0	0	0	0	0	1 (0.4%)
サルモネラ性菌血症	0	0	0	0	1 (2.0%)	1 (0.4%)
軟部組織感染	0	0	0	0	0	1 (0.4%)
扁桃炎	0	0	1 (0.4%)	0	0	1 (0.4%)
気管炎	0	0	1 (0.4%)	0	0	1 (0.4%)
尿道炎	0	0	0	0	1 (2.0%)	1 (0.4%)
子宮膿瘍	0	0	0	0	0	1 (0.4%)
腟感染	0	0	1 (0.4%)	0	0	1 (0.4%)
ウイルス性鼻炎	0	0	0	0	0	1 (0.4%)
ウイルス性上気道感染	0	0	2 (0.7%)	0	0	1 (0.4%)
内臓リーシュマニア症	0	0	0	0	0	1 (0.4%)
創傷感染	0	0	3 (1.1%)	0	0	1 (0.4%)
四肢膿瘍	0	0	1 (0.4%)	0	0	0
アデノウイルス感染	0	0	1 (0.4%)	0	0	0
肛門膿瘍	0	1 (2.3%)	1 (0.4%)	0	0	0
ウイルス性気管支炎	0	0	2 (0.7%)	0	0	0
クロストリジウム・ディフィシレ感染	0	0	2 (0.7%)	0	0	0
細菌性結膜炎	0	0	1 (0.4%)	0	0	0
蓄膿	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
感染性小腸結腸炎	0	0	2 (0.7%)	0	0	0
真菌性眼感染	0	0	1 (0.4%)	0	0	0
熱性感染症	0	0	1 (0.4%)	0	0	0
陰部単純ヘルペス	0	0	1 (0.4%)	0	0	0
真菌性性器感染	0	0	1 (0.4%)	0	0	0
ヘモフィルス感染	0	0	1 (0.4%)	0	0	0
単純ヘルペス	0	1 (2.3%)	1 (0.4%)	0	0	0
麦粒腫	0	0	2 (0.7%)	0	0	0
咬傷感染	0	0	1 (0.4%)	0	0	0

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
感染性筋炎	0	0	1 (0.4%)	0	0	0
真菌性角膜炎	0	0	1 (0.4%)	0	0	0
喉頭炎	0	0	1 (0.4%)	0	0	0
鼻ヘルペス	0	0	1 (0.4%)	0	0	0
壊死性筋膜炎	0	0	1 (0.4%)	0	0	0
口腔ウイルス感染	0	0	1 (0.4%)	0	0	0
骨髄炎	0	2 (4.5%)	2 (0.7%)	0	0	0
爪囲炎	0	0	1 (0.4%)	0	0	0
百日咳	0	0	1 (0.4%)	0	0	0
肺結核	0	1 (2.3%)	1 (0.4%)	0	0	0
歯髄炎	0	0	1 (0.4%)	0	0	0
急性腎盂腎炎	0	1 (2.3%)	1 (0.4%)	0	0	0
皮膚カンジダ	0	0	3 (1.1%)	0	0	0
ブドウ球菌感染	0	0	1 (0.4%)	0	0	0
ブドウ球菌皮膚感染	0	0	1 (0.4%)	0	0	0
尿路性敗血症	0	0	1 (0.4%)	0	0	0
水痘	0	0	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	0	0	1 (0.4%)	0	0	0
外陰腟真菌感染	0	0	1 (0.4%)	0	0	0
外陰部腟炎	0	0	1 (0.4%)	0	0	0
胃腸障害	8 (53.3%)	28 (63.6%)	164 (58.4%)	14 (70.0%)	40 (78.4%)	216 (76.3%)
下痢	2 (13.3%)	6 (13.6%)	69 (24.6%)	4 (20.0%)	16 (31.4%)	121 (42.8%)
便秘	5 (33.3%)	14 (31.8%)	71 (25.3%)	8 (40.0%)	21 (41.2%)	83 (29.3%)
悪心	0	6 (13.6%)	40 (14.2%)	3 (15.0%)	10 (19.6%)	68 (24.0%)
嘔吐	1 (6.7%)	2 (4.5%)	15 (5.3%)	2 (10.0%)	8 (15.7%)	47 (16.6%)
上腹部痛	0	3 (6.8%)	10 (3.6%)	0	3 (5.9%)	21 (7.4%)
腹痛	0	0	11 (3.9%)	0	2 (3.9%)	20 (7.1%)
消化不良	0	0	6 (2.1%)	0	5 (9.8%)	18 (6.4%)
口内炎	0	0	6 (2.1%)	2 (10.0%)	6 (11.8%)	17 (6.0%)
歯痛	0	3 (6.8%)	5 (1.8%)	0	4 (7.8%)	9 (3.2%)
腹部膨満	1 (6.7%)	1 (2.3%)	5 (1.8%)	0	0	7 (2.5%)
口内乾燥	0	0	6 (2.1%)	0	1 (2.0%)	7 (2.5%)
口腔内潰瘍形成	0	2 (4.5%)	4 (1.4%)	0	2 (3.9%)	7 (2.5%)
腹部不快感	0	1 (2.3%)	3 (1.1%)	1 (5.0%)	2 (3.9%)	6 (2.1%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
嚥下障害	0	0	1 (0.4%)	0	0	6 (2.1%)
痔核	0	0	3 (1.1%)	0	0	6 (2.1%)
放屁	0	0	0	0	1 (2.0%)	5 (1.8%)
胃食道逆流性疾患	0	1 (2.3%)	6 (2.1%)	0	1 (2.0%)	5 (1.8%)
胃腸障害	0	0	0	0	0	4 (1.4%)
舌痛	0	1 (2.3%)	4 (1.4%)	0	0	4 (1.4%)
直腸出血	0	0	1 (0.4%)	0	0	4 (1.4%)
嚥下痛	0	0	1 (0.4%)	0	0	3 (1.1%)
口の錯感覚	0	0	2 (0.7%)	0	1 (2.0%)	3 (1.1%)
便通不規則	0	0	0	0	0	2 (0.7%)
大腸炎	0	0	1 (0.4%)	0	0	2 (0.7%)
憩室穿孔	0	0	0	0	0	2 (0.7%)
胃炎	0	1 (2.3%)	1 (0.4%)	0	0	2 (0.7%)
裂孔ヘルニア	0	0	1 (0.4%)	0	0	2 (0.7%)
口の感覚鈍麻	0	0	0	0	0	2 (0.7%)
口腔内痛	0	0	4 (1.4%)	0	0	2 (0.7%)
腹部腫瘤	0	0	0	0	0	1 (0.4%)
下腹部痛	0	0	1 (0.4%)	0	0	1 (0.4%)
腹壁血腫	0	0	0	0	0	1 (0.4%)
裂肛	0	0	0	0	0	1 (0.4%)
肛門出血	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
アフタ性口内炎	1 (6.7%)	1 (2.3%)	2 (0.7%)	1 (5.0%)	1 (2.0%)	1 (0.4%)
胆汁酸吸収不良	0	0	0	0	0	1 (0.4%)
口唇炎	0	0	0	0	0	1 (0.4%)
歯不快感	0	0	0	0	1 (2.0%)	1 (0.4%)
腸憩室	0	0	0	0	0	1 (0.4%)
心窩部不快感	0	0	0	0	0	1 (0.4%)
おくび	0	0	1 (0.4%)	0	0	1 (0.4%)
胃拡張	0	0	0	0	0	1 (0.4%)
胃出血	0	0	0	0	0	1 (0.4%)
出血性胃腸管血管異形成	0	0	0	0	0	1 (0.4%)
吐血	0	0	1 (0.4%)	0	0	1 (0.4%)
血便排泄	0	0	0	0	0	1 (0.4%)
鼠径ヘルニア	0	0	3 (1.1%)	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
口唇びらん	0	0	0	0	0	1 (0.4%)
口唇そう痒症	0	0	0	0	0	1 (0.4%)
口唇腫脹	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
弛緩歯	0	0	0	0	0	1 (0.4%)
非感染性歯肉炎	0	0	0	0	0	1 (0.4%)
口腔粘膜水疱形成	0	0	1 (0.4%)	0	0	1 (0.4%)
肛門周囲痛	0	0	0	0	0	1 (0.4%)
直腸ポリープ	0	0	0	0	0	1 (0.4%)
直腸しぶり	0	0	0	0	0	1 (0.4%)
唾液腺結石	0	0	0	0	0	1 (0.4%)
歯の知覚過敏	0	0	0	0	0	1 (0.4%)
顎下腺腫大	0	0	0	0	0	1 (0.4%)
地図状舌	0	0	1 (0.4%)	0	0	1 (0.4%)
痔瘻	0	0	1 (0.4%)	0	0	0
バレット食道	0	0	1 (0.4%)	0	0	0
呼気臭	0	0	1 (0.4%)	0	0	0
口唇のひび割れ	0	0	1 (0.4%)	0	0	0
潰瘍性大腸炎	0	0	1 (0.4%)	0	0	0
齲歯	0	1 (2.3%)	5 (1.8%)	0	0	0
便失禁	0	0	1 (0.4%)	0	0	0
糞塊	0	0	1 (0.4%)	0	0	0
胃障害	0	0	2 (0.7%)	0	0	0
消化管運動障害	0	0	1 (0.4%)	0	0	0
消化器痛	0	0	1 (0.4%)	0	0	0
歯肉出血	0	0	1 (0.4%)	0	0	0
歯肉潰瘍	0	0	1 (0.4%)	0	0	0
腸閉塞	0	0	1 (0.4%)	0	0	0
腸管穿孔	0	0	1 (0.4%)	0	0	0
過敏性腸症候群	0	0	2 (0.7%)	0	0	0
大腸ポリープ	0	0	1 (0.4%)	0	0	0
下部消化管出血	0	0	1 (0.4%)	0	0	0
メレナ	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	0
口腔内出血	0	1 (2.3%)	1 (0.4%)	0	0	0
食道痛	0	0	1 (0.4%)	0	0	0

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
食道炎	0	1 (2.3%)	1 (0.4%)	0	0	0
膵炎	0	0	1 (0.4%)	0	0	0
歯周の炎症	0	0	1 (0.4%)	0	0	0
ストレス潰瘍	0	1 (2.3%)	1 (0.4%)	0	0	0
舌潰瘍	0	0	1 (0.4%)	0	0	0
歯の脱落	0	0	1 (0.4%)	0	0	0
血液およびリンパ系障害	12 (80.0%)	31 (70.5%)	184 (65.5%)	16 (80.0%)	40 (78.4%)	200 (70.7%)
好中球減少症	6 (40.0%)	19 (43.2%)	121 (43.1%)	12 (60.0%)	34 (66.7%)	168 (59.4%)
貧血	2 (13.3%)	13 (29.5%)	98 (34.9%)	1 (5.0%)	8 (15.7%)	88 (31.1%)
血小板減少症	6 (40.0%)	13 (29.5%)	77 (27.4%)	3 (15.0%)	12 (23.5%)	76 (26.9%)
白血球減少症	2 (13.3%)	6 (13.6%)	17 (6.0%)	3 (15.0%)	10 (19.6%)	21 (7.4%)
リンパ球減少症	8 (53.3%)	8 (18.2%)	15 (5.3%)	8 (40.0%)	8 (15.7%)	17 (6.0%)
発熱性好中球減少症	0	1 (2.3%)	7 (2.5%)	0	2 (3.9%)	16 (5.7%)
リンパ節症	0	0	2 (0.7%)	0	0	2 (0.7%)
凝血異常	0	0	0	0	0	1 (0.4%)
好酸球増加症	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
内出血発生の増加傾向	0	0	0	0	0	1 (0.4%)
骨髄機能不全	0	0	1 (0.4%)	0	0	0
骨髄浮腫	0	0	1 (0.4%)	0	0	0
播種性血管内凝固	0	0	1 (0.4%)	0	0	0
出血性素因	0	0	1 (0.4%)	0	0	0
出血性障害	0	0	1 (0.4%)	0	0	0
過粘稠度症候群	0	0	1 (0.4%)	0	0	0
無胆汁色素尿性黄疸	0	0	1 (0.4%)	0	0	0
白血球増加症	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	0
小球性貧血	0	0	1 (0.4%)	0	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0	0
脾臓障害	0	0	1 (0.4%)	0	0	0
血栓性血小板減少性紫斑病	0	0	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	1 (6.7%)	16 (36.4%)	156 (55.5%)	9 (45.0%)	27 (52.9%)	197 (69.6%)
疲労	0	10 (22.7%)	78 (27.8%)	1 (5.0%)	9 (17.6%)	100 (35.3%)
発熱	1 (6.7%)	2 (4.5%)	31 (11.0%)	4 (20.0%)	10 (19.6%)	57 (20.1%)
無力症	0	2 (4.5%)	36 (12.8%)	0	3 (5.9%)	45 (15.9%)
末梢性浮腫	0	1 (2.3%)	37 (13.2%)	1 (5.0%)	3 (5.9%)	43 (15.2%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
悪寒	0	0	9 (3.2%)	1 (5.0%)	4 (7.8%)	17 (6.0%)
インフルエンザ様疾患	0	0	12 (4.3%)	0	1 (2.0%)	17 (6.0%)
非心臓性胸痛	0	2 (4.5%)	5 (1.8%)	0	2 (3.9%)	11 (3.9%)
倦怠感	0	1 (2.3%)	4 (1.4%)	2 (10.0%)	3 (5.9%)	10 (3.5%)
末梢腫脹	0	0	6 (2.1%)	0	0	8 (2.8%)
胸部不快感	0	1 (2.3%)	1 (0.4%)	0	3 (5.9%)	7 (2.5%)
胸痛	0	0	8 (2.8%)	1 (5.0%)	1 (2.0%)	5 (1.8%)
冷感	0	0	1 (0.4%)	0	3 (5.9%)	5 (1.8%)
全身健康状態低下	0	0	3 (1.1%)	0	0	5 (1.8%)
顔面浮腫	0	1 (2.3%)	3 (1.1%)	0	1 (2.0%)	3 (1.1%)
歩行障害	0	0	3 (1.1%)	0	0	3 (1.1%)
疼痛	0	1 (2.3%)	4 (1.4%)	0	1 (2.0%)	3 (1.1%)
医薬品副作用	0	0	0	0	0	2 (0.7%)
嚢胞	0	0	1 (0.4%)	0	0	2 (0.7%)
薬物不耐性	0	0	0	0	0	2 (0.7%)
熱感	0	0	0	0	0	2 (0.7%)
びくびく感	0	0	0	0	0	2 (0.7%)
浮腫	0	0	3 (1.1%)	1 (5.0%)	1 (2.0%)	2 (0.7%)
腋窩痛	0	0	2 (0.7%)	0	0	1 (0.4%)
カテーテル留置部位関連反応	0	0	0	0	0	1 (0.4%)
運動耐性低下	0	0	0	0	0	1 (0.4%)
溢出	0	0	0	0	0	1 (0.4%)
脂肪組織増加	0	0	0	0	0	1 (0.4%)
高熱	0	0	0	0	0	1 (0.4%)
治癒不良	0	0	0	0	0	1 (0.4%)
注入部位血管外漏出	0	0	0	0	0	1 (0.4%)
注入部位静脈炎	0	0	0	0	0	1 (0.4%)
注入部位発疹	0	0	0	0	0	1 (0.4%)
注射部位内出血	0	0	0	0	0	1 (0.4%)
注射部位紅斑	0	0	0	0	0	1 (0.4%)
注射部位知覚異常	0	0	0	0	0	1 (0.4%)
限局性浮腫	0	0	0	0	0	1 (0.4%)
粘膜の炎症	0	0	0	0	0	1 (0.4%)
多臓器不全	0	0	0	0	1 (2.0%)	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
小結節	0	0	1 (0.4%)	0	0	1 (0.4%)
分泌物分泌	0	0	0	0	0	1 (0.4%)
苦悶感	0	0	1 (0.4%)	0	0	1 (0.4%)
全身性炎症反応症候群	0	0	0	0	0	1 (0.4%)
捻髪音	0	0	1 (0.4%)	0	0	0
不快感	0	0	1 (0.4%)	0	0	0
異常感	0	0	2 (0.7%)	0	0	0
全身性浮腫	0	0	1 (0.4%)	0	0	0
局所腫脹	0	0	2 (0.7%)	0	0	0
粘膜乾燥	0	0	1 (0.4%)	0	0	0
圧痛	0	0	1 (0.4%)	0	0	0
口渇	0	0	1 (0.4%)	0	0	0
呼吸器、胸郭および縦隔障害	4 (26.7%)	15 (34.1%)	114 (40.6%)	10 (50.0%)	29 (56.9%)	170 (60.1%)
咳嗽	1 (6.7%)	3 (6.8%)	35 (12.5%)	0	11 (21.6%)	82 (29.0%)
呼吸困難	0	3 (6.8%)	32 (11.4%)	2 (10.0%)	6 (11.8%)	52 (18.4%)
発声障害	0	0	7 (2.5%)	0	3 (5.9%)	14 (4.9%)
鼻閉	0	0	4 (1.4%)	0	0	14 (4.9%)
気管支痙攣	0	0	1 (0.4%)	0	0	13 (4.6%)
労作性呼吸困難	0	0	5 (1.8%)	0	0	13 (4.6%)
湿性咳嗽	0	1 (2.3%)	8 (2.8%)	0	7 (13.7%)	13 (4.6%)
アレルギー性鼻炎	1 (6.7%)	2 (4.5%)	3 (1.1%)	0	3 (5.9%)	13 (4.6%)
口腔咽頭痛	0	0	10 (3.6%)	0	1 (2.0%)	11 (3.9%)
鼻漏	0	1 (2.3%)	6 (2.1%)	1 (5.0%)	3 (5.9%)	11 (3.9%)
鼻出血	0	2 (4.5%)	12 (4.3%)	0	1 (2.0%)	9 (3.2%)
咽喉刺激感	0	0	0	0	0	9 (3.2%)
喘鳴	0	0	0	0	1 (2.0%)	9 (3.2%)
しゃっくり	2 (13.3%)	5 (11.4%)	9 (3.2%)	3 (15.0%)	4 (7.8%)	8 (2.8%)
肺塞栓症	0	0	11 (3.9%)	0	0	7 (2.5%)
低酸素症	0	0	1 (0.4%)	2 (10.0%)	5 (9.8%)	6 (2.1%)
喉頭浮腫	0	0	0	0	0	6 (2.1%)
肺水腫	0	0	2 (0.7%)	0	1 (2.0%)	5 (1.8%)
胸水	0	0	2 (0.7%)	0	2 (3.9%)	4 (1.4%)
副鼻腔うっ血	0	0	3 (1.1%)	0	0	3 (1.1%)
くしゃみ	0	0	0	0	0	3 (1.1%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
アレルギー性呼吸器症状	0	0	0	0	2 (3.9%)	2 (0.7%)
慢性閉塞性肺疾患	0	0	3 (1.1%)	0	0	2 (0.7%)
肺障害	0	0	2 (0.7%)	0	0	2 (0.7%)
鼻閉塞	0	0	0	0	1 (2.0%)	2 (0.7%)
誤嚥性肺炎	0	0	0	1 (5.0%)	1 (2.0%)	2 (0.7%)
肺臓炎	0	0	0	0	2 (3.9%)	2 (0.7%)
呼吸不全	0	0	1 (0.4%)	0	0	2 (0.7%)
急性肺水腫	0	0	1 (0.4%)	0	0	1 (0.4%)
アレルギー性咽頭炎	0	0	0	0	0	1 (0.4%)
窒息	0	0	0	0	0	1 (0.4%)
気管支拡張症	0	0	0	0	0	1 (0.4%)
喀血	0	0	2 (0.7%)	0	1 (2.0%)	1 (0.4%)
胸水症	0	0	0	0	0	1 (0.4%)
喉頭不快感	0	0	0	0	0	1 (0.4%)
喉頭痛	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
喉頭狭窄	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
喉頭刺激感	0	0	0	0	0	1 (0.4%)
鼻部不快感	0	0	0	0	0	1 (0.4%)
鼻乾燥	0	0	2 (0.7%)	0	0	1 (0.4%)
器質化肺炎	0	0	0	0	0	1 (0.4%)
咽頭紅斑	0	0	1 (0.4%)	0	0	1 (0.4%)
胸膜痛	0	0	1 (0.4%)	0	0	1 (0.4%)
呼気延長	0	0	0	0	0	1 (0.4%)
肺石灰化	0	0	0	0	0	1 (0.4%)
肺高血圧症	0	0	0	0	0	1 (0.4%)
肺腫瘤	0	0	0	0	0	1 (0.4%)
気道うっ血	0	0	0	0	0	1 (0.4%)
副鼻腔障害	0	0	0	0	0	1 (0.4%)
上気道性喘鳴	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
窒息感	0	0	0	0	0	1 (0.4%)
頻呼吸	0	0	0	0	0	1 (0.4%)
咽喉絞扼感	0	0	0	0	0	1 (0.4%)
急性呼吸不全	0	0	1 (0.4%)	0	0	0
無気肺	0	0	1 (0.4%)	0	0	0

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
気管支反応性亢進	0	0	1 (0.4%)	0	0	0
カタル	0	0	5 (1.8%)	0	0	0
間質性肺疾患	0	0	1 (0.4%)	0	0	0
喉頭の炎症	0	0	1 (0.4%)	0	0	0
口腔咽頭不快感	0	0	1 (0.4%)	0	0	0
胸膜炎	0	0	1 (0.4%)	0	0	0
気胸	0	0	1 (0.4%)	0	0	0
鼻痛	0	0	1 (0.4%)	0	0	0
上気道の炎症	0	2 (4.5%)	2 (0.7%)	0	0	0
筋骨格系および結合組織障害	8 (53.3%)	23 (52.3%)	154 (54.8%)	2 (10.0%)	16 (31.4%)	162 (57.2%)
筋痙縮	3 (20.0%)	6 (13.6%)	52 (18.5%)	1 (5.0%)	2 (3.9%)	73 (25.8%)
背部痛	0	5 (11.4%)	48 (17.1%)	2 (10.0%)	5 (9.8%)	50 (17.7%)
関節痛	0	0	21 (7.5%)	0	0	24 (8.5%)
筋力低下	1 (6.7%)	4 (9.1%)	22 (7.8%)	0	1 (2.0%)	23 (8.1%)
四肢痛	1 (6.7%)	4 (9.1%)	30 (10.7%)	0	3 (5.9%)	21 (7.4%)
骨痛	0	1 (2.3%)	12 (4.3%)	0	2 (3.9%)	18 (6.4%)
筋骨格痛	0	3 (6.8%)	16 (5.7%)	0	0	18 (6.4%)
筋肉痛	0	4 (9.1%)	9 (3.2%)	0	3 (5.9%)	16 (5.7%)
筋骨格系胸痛	0	2 (4.5%)	17 (6.0%)	0	1 (2.0%)	15 (5.3%)
頚部痛	1 (6.7%)	1 (2.3%)	11 (3.9%)	0	1 (2.0%)	6 (2.1%)
顎痛	0	0	4 (1.4%)	0	1 (2.0%)	6 (2.1%)
脊椎痛	0	0	6 (2.1%)	0	0	6 (2.1%)
顎骨壊死	1 (6.7%)	2 (4.5%)	4 (1.4%)	0	0	5 (1.8%)
側腹部痛	0	0	1 (0.4%)	0	3 (5.9%)	4 (1.4%)
肢径部痛	0	0	1 (0.4%)	0	0	3 (1.1%)
関節炎	0	0	1 (0.4%)	0	0	2 (0.7%)
出血性関節症	0	0	0	0	0	2 (0.7%)
椎間板突出	0	0	0	0	0	2 (0.7%)
筋肉疲労	0	0	0	0	0	2 (0.7%)
筋骨格硬直	0	0	3 (1.1%)	0	0	2 (0.7%)
ミオパチー	1 (6.7%)	1 (2.3%)	3 (1.1%)	0	0	2 (0.7%)
筋萎縮症	0	0	0	0	0	1 (0.4%)
滑液包炎	0	0	1 (0.4%)	0	0	1 (0.4%)
デュプイトラン拘縮	0	0	0	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
痛風性関節炎	0	0	0	0	0	1 (0.4%)
椎間板圧迫	0	0	0	0	0	1 (0.4%)
関節硬直	0	0	0	0	0	1 (0.4%)
関節腫脹	0	0	6 (2.1%)	0	0	1 (0.4%)
四肢不快感	0	0	0	0	0	1 (0.4%)
中足骨痛	0	0	0	0	0	1 (0.4%)
運動性低下	0	0	0	0	0	1 (0.4%)
筋骨格不快感	0	0	1 (0.4%)	0	0	1 (0.4%)
骨炎	0	0	0	0	0	1 (0.4%)
変形性関節症	0	0	1 (0.4%)	0	0	1 (0.4%)
骨壊死	0	0	0	0	0	1 (0.4%)
脊椎障害	0	0	0	0	0	1 (0.4%)
変形性脊椎症	0	0	1 (0.4%)	0	0	1 (0.4%)
顎関節症候群	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
腱石灰化	0	0	0	0	0	1 (0.4%)
腱痛	0	0	0	0	0	1 (0.4%)
骨脱灰	0	0	1 (0.4%)	0	0	0
軟骨石灰化症	0	0	1 (0.4%)	0	0	0
尾骨痛	0	0	1 (0.4%)	0	0	0
結晶性関節障害	0	0	1 (0.4%)	0	0	0
足変形	0	0	1 (0.4%)	0	0	0
顎障害	0	0	1 (0.4%)	0	0	0
関節滲出液	0	0	1 (0.4%)	0	0	0
筋緊張	0	0	1 (0.4%)	0	0	0
骨粗鬆症	0	0	1 (0.4%)	0	0	0
病的骨折	0	0	2 (0.7%)	0	0	0
足底筋膜炎	0	0	1 (0.4%)	0	0	0
脊柱管狭窄症	0	1 (2.3%)	3 (1.1%)	0	0	0
滑液嚢腫	0	0	1 (0.4%)	0	0	0
腱炎	0	0	2 (0.7%)	0	0	0
開口障害	0	1 (2.3%)	1 (0.4%)	0	0	0
神経系障害	6 (40.0%)	18 (40.9%)	124 (44.1%)	7 (35.0%)	20 (39.2%)	140 (49.5%)
頭痛	1 (6.7%)	2 (4.5%)	19 (6.8%)	1 (5.0%)	6 (11.8%)	37 (13.1%)
振戦	0	1 (2.3%)	24 (8.5%)	0	0	26 (9.2%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
末梢性感覚ニューロパチー	3 (20.0%)	5 (11.4%)	19 (6.8%)	0	3 (5.9%)	23 (8.1%)
浮動性めまい	0	4 (9.1%)	24 (8.5%)	0	0	22 (7.8%)
味覚異常	1 (6.7%)	1 (2.3%)	15 (5.3%)	4 (20.0%)	4 (7.8%)	21 (7.4%)
錯感覚	0	0	10 (3.6%)	0	1 (2.0%)	14 (4.9%)
感覚鈍麻	0	2 (4.5%)	5 (1.8%)	0	2 (3.9%)	13 (4.6%)
末梢性ニューロパチー	0	1 (2.3%)	15 (5.3%)	3 (15.0%)	3 (5.9%)	12 (4.2%)
失神	0	0	2 (0.7%)	0	0	10 (3.5%)
嗜眠	0	0	4 (1.4%)	0	0	6 (2.1%)
失神寸前の状態	0	0	0	0	0	5 (1.8%)
味覚消失	0	0	1 (0.4%)	0	0	4 (1.4%)
認知障害	0	0	2 (0.7%)	0	0	4 (1.4%)
神経痛	0	3 (6.8%)	3 (1.1%)	1 (5.0%)	2 (3.9%)	4 (1.4%)
平衡障害	0	0	2 (0.7%)	0	0	3 (1.1%)
注意力障害	0	0	1 (0.4%)	0	0	3 (1.1%)
知覚過敏	0	0	0	0	0	2 (0.7%)
記憶障害	0	0	8 (2.8%)	0	0	2 (0.7%)
痙攣発作	0	0	0	1 (5.0%)	1 (2.0%)	2 (0.7%)
視野欠損	0	0	0	0	0	2 (0.7%)
健忘	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
無嗅覚	0	0	0	0	0	1 (0.4%)
失声症	0	0	0	0	0	1 (0.4%)
灼熱感	0	0	0	0	0	1 (0.4%)
小脳性運動失調	0	0	0	0	0	1 (0.4%)
脳梗塞	0	0	1 (0.4%)	1 (5.0%)	1 (2.0%)	1 (0.4%)
脳血管発作	0	0	0	0	0	1 (0.4%)
体位性めまい	0	0	1 (0.4%)	0	0	1 (0.4%)
異常感覚	0	0	1 (0.4%)	0	0	1 (0.4%)
構語障害	0	0	0	0	1 (2.0%)	1 (0.4%)
てんかん	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
過眠症	0	0	1 (0.4%)	0	0	1 (0.4%)
運動低下	0	0	0	0	0	1 (0.4%)
レルミット徴候	0	0	0	0	0	1 (0.4%)
筋痙直	0	0	0	0	0	1 (0.4%)
神経系障害	0	0	1 (0.4%)	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
眼振	0	0	0	0	1 (2.0%)	1 (0.4%)
嗅覚錯誤	0	0	0	0	0	1 (0.4%)
腓骨神経麻痺	0	0	0	0	0	1 (0.4%)
下肢静止不能症候群	0	0	2 (0.7%)	0	0	1 (0.4%)
感覚障害	0	0	0	0	0	1 (0.4%)
副鼻腔炎に伴う頭痛	0	0	0	0	0	1 (0.4%)
傾眠	1 (6.7%)	1 (2.3%)	4 (1.4%)	0	0	1 (0.4%)
脊髄浮腫	0	0	0	0	0	1 (0.4%)
一過性脳虚血発作	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.4%)
三叉神経障害	0	0	0	0	0	1 (0.4%)
アカシジア	0	0	2 (0.7%)	0	0	0
失語症	0	0	1 (0.4%)	0	0	0
アテトーゼ	0	1 (2.3%)	1 (0.4%)	0	0	0
頚動脈硬化症	0	0	1 (0.4%)	0	0	0
脳出血	0	0	1 (0.4%)	0	0	0
認知症	0	0	1 (0.4%)	0	0	0
労作性めまい	0	0	1 (0.4%)	0	0	0
統合運動障害	0	0	1 (0.4%)	0	0	0
蟻走感	0	0	1 (0.4%)	0	0	0
不全片麻痺	0	0	1 (0.4%)	0	0	0
味覚減退	0	0	2 (0.7%)	0	0	0
肋間神経痛	0	0	1 (0.4%)	0	0	0
虚血性脳卒中	0	0	1 (0.4%)	0	0	0
意識消失	0	0	1 (0.4%)	0	0	0
片頭痛	0	0	2 (0.7%)	0	0	0
不随意性筋収縮	0	0	1 (0.4%)	0	0	0
末梢性感覚運動ニューロパチー	0	0	1 (0.4%)	0	0	0
ヘルペス後神経痛	0	1 (2.3%)	2 (0.7%)	0	0	0
精神運動亢進	0	0	1 (0.4%)	0	0	0
坐骨神経痛	0	0	3 (1.1%)	0	0	0
感覚運動障害	0	0	1 (0.4%)	0	0	0
脊髄圧迫	0	0	2 (0.7%)	0	0	0
上位運動ニューロンの病変	0	0	1 (0.4%)	0	0	0
第７脳神経麻痺	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	0

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
血管性脳症	0	0	1 (0.4%)	0	0	0
代謝および栄養障害	5 (33.3%)	16 (36.4%)	95 (33.8%)	5 (25.0%)	18 (35.3%)	116 (41.0%)
食欲減退	0	11 (25.0%)	29 (10.3%)	1 (5.0%)	10 (19.6%)	32 (11.3%)
低カリウム血症	0	1 (2.3%)	22 (7.8%)	0	3 (5.9%)	30 (10.6%)
高血糖	1 (6.7%)	1 (2.3%)	19 (6.8%)	4 (20.0%)	6 (11.8%)	25 (8.8%)
低カルシウム血症	0	0	11 (3.9%)	0	1 (2.0%)	18 (6.4%)
低リン酸血症	1 (6.7%)	2 (4.5%)	11 (3.9%)	1 (5.0%)	2 (3.9%)	16 (5.7%)
脱水	0	0	2 (0.7%)	0	0	10 (3.5%)
低マグネシウム血症	0	1 (2.3%)	12 (4.3%)	0	1 (2.0%)	8 (2.8%)
低ナトリウム血症	0	1 (2.3%)	2 (0.7%)	0	1 (2.0%)	8 (2.8%)
高尿酸血症	2 (13.3%)	2 (4.5%)	8 (2.8%)	0	0	7 (2.5%)
高カルシウム血症	0	0	5 (1.8%)	0	1 (2.0%)	5 (1.8%)
高カリウム血症	0	0	2 (0.7%)	0	0	3 (1.1%)
糖尿病	0	0	0	0	0	2 (0.7%)
高コレステロール血症	0	0	1 (0.4%)	0	0	2 (0.7%)
高脂血症	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	2 (0.7%)
低アルブミン血症	0	0	5 (1.8%)	0	0	2 (0.7%)
ビタミンＢ１２欠乏	0	0	3 (1.1%)	0	0	2 (0.7%)
アシドーシス	0	0	0	0	0	1 (0.4%)
悪液質	0	0	0	0	0	1 (0.4%)
電解質失調	0	0	0	0	0	1 (0.4%)
酵素異常	0	0	0	0	1 (2.0%)	1 (0.4%)
体液平衡失調	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
水分過負荷	0	0	0	0	0	1 (0.4%)
体液貯留	0	0	0	0	0	1 (0.4%)
葉酸欠乏	0	0	0	0	0	1 (0.4%)
食物不耐性	0	0	0	0	0	1 (0.4%)
痛風	0	0	8 (2.8%)	0	0	1 (0.4%)
高ナトリウム血症	0	0	1 (0.4%)	0	0	1 (0.4%)
高トリグリセリド血症	0	0	0	0	0	1 (0.4%)
低血糖症	0	0	2 (0.7%)	1 (5.0%)	1 (2.0%)	1 (0.4%)
鉄欠乏	0	0	1 (0.4%)	0	0	1 (0.4%)
１型糖尿病	0	0	0	0	0	1 (0.4%)
ビタミンＤ欠乏	0	0	2 (0.7%)	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
高リン酸塩血症	0	0	1 (0.4%)	0	0	0
食欲亢進	0	0	1 (0.4%)	0	0	0
栄養障害	0	1 (2.3%)	2 (0.7%)	0	0	0
多飲症	0	0	1 (0.4%)	0	0	0
テタニー	0	0	1 (0.4%)	0	0	0
２型糖尿病	0	0	1 (0.4%)	0	0	0
皮膚および皮下組織障害	7 (46.7%)	19 (43.2%)	83 (29.5%)	9 (45.0%)	23 (45.1%)	113 (39.9%)
発疹	2 (13.3%)	2 (4.5%)	29 (10.3%)	4 (20.0%)	8 (15.7%)	35 (12.4%)
そう痒症	2 (13.3%)	6 (13.6%)	29 (10.3%)	1 (5.0%)	6 (11.8%)	28 (9.9%)
多汗症	0	0	8 (2.8%)	0	1 (2.0%)	20 (7.1%)
皮膚乾燥	0	1 (2.3%)	7 (2.5%)	3 (15.0%)	3 (5.9%)	10 (3.5%)
蕁麻疹	0	3 (6.8%)	6 (2.1%)	1 (5.0%)	4 (7.8%)	8 (2.8%)
紅斑	0	0	7 (2.5%)	0	0	6 (2.1%)
斑状丘疹状皮疹	0	0	3 (1.1%)	0	1 (2.0%)	5 (1.8%)
寝汗	0	0	5 (1.8%)	0	0	4 (1.4%)
全身性皮疹	1 (6.7%)	3 (6.8%)	5 (1.8%)	1 (5.0%)	1 (2.0%)	4 (1.4%)
褥瘡性潰瘍	0	0	1 (0.4%)	1 (5.0%)	1 (2.0%)	3 (1.1%)
斑状出血	0	0	1 (0.4%)	0	0	3 (1.1%)
斑状皮疹	0	0	1 (0.4%)	0	0	3 (1.1%)
皮膚病変	0	0	3 (1.1%)	0	0	3 (1.1%)
皮膚潰瘍	0	0	1 (0.4%)	0	1 (2.0%)	3 (1.1%)
顔面腫脹	0	1 (2.3%)	3 (1.1%)	0	1 (2.0%)	3 (1.1%)
脱毛症	0	0	0	0	0	2 (0.7%)
水疱	0	0	0	0	1 (2.0%)	2 (0.7%)
皮膚炎	0	0	2 (0.7%)	0	2 (3.9%)	2 (0.7%)
ざ瘡様皮膚炎	0	0	0	0	1 (2.0%)	2 (0.7%)
湿疹	0	0	1 (0.4%)	0	0	2 (0.7%)
点状出血	0	0	0	0	0	2 (0.7%)
皮膚色素過剰	0	0	0	0	1 (2.0%)	2 (0.7%)
皮膚腫脹	0	0	0	0	0	2 (0.7%)
日光角化症	0	0	2 (0.7%)	0	0	1 (0.4%)
冷汗	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
アレルギー性皮膚炎	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
薬疹	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
多形紅斑	1 (6.7%)	1 (2.3%)	1 (0.4%)	1 (5.0%)	1 (2.0%)	1 (0.4%)
紅色症	0	0	0	0	0	1 (0.4%)
全身紅斑	0	0	0	0	0	1 (0.4%)
毛髪成長異常	0	0	0	0	0	1 (0.4%)
手皮膚炎	0	0	0	0	0	1 (0.4%)
男性型多毛症	0	0	1 (0.4%)	0	0	1 (0.4%)
過角化	0	0	1 (0.4%)	0	0	1 (0.4%)
嵌入爪	0	0	0	0	0	1 (0.4%)
爪甲脱落症	0	0	0	0	0	1 (0.4%)
皮膚疼痛	0	0	0	0	0	1 (0.4%)
アレルギー性そう痒症	0	0	0	0	0	1 (0.4%)
全身性そう痒症	0	0	0	0	1 (2.0%)	1 (0.4%)
丘疹性皮疹	0	0	0	0	0	1 (0.4%)
そう痒性皮疹	0	0	1 (0.4%)	0	0	1 (0.4%)
酒さ	0	0	0	0	0	1 (0.4%)
血管炎性皮疹	0	0	0	0	0	1 (0.4%)
黄色腫	0	0	0	0	1 (2.0%)	1 (0.4%)
接触性皮膚炎	0	1 (2.3%)	1 (0.4%)	0	0	0
多毛症	0	0	1 (0.4%)	0	0	0
乏汗症	0	1 (2.3%)	1 (0.4%)	0	0	0
壊疽性膿皮症	0	1 (2.3%)	1 (0.4%)	0	0	0
小水疱性皮疹	0	1 (2.3%)	1 (0.4%)	0	0	0
皮膚灼熱感	0	0	1 (0.4%)	0	0	0
皮膚障害	0	0	2 (0.7%)	0	0	0
皮膚亀裂	0	0	1 (0.4%)	0	0	0
うっ滞性皮膚炎	0	0	1 (0.4%)	0	0	0
毛細血管拡張症	0	0	1 (0.4%)	0	0	0
乾皮症	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
精神障害	2 (13.3%)	11 (25.0%)	93 (33.1%)	1 (5.0%)	8 (15.7%)	96 (33.9%)
不眠症	2 (13.3%)	9 (20.5%)	55 (19.6%)	1 (5.0%)	7 (13.7%)	55 (19.4%)
不安	0	1 (2.3%)	12 (4.3%)	0	1 (2.0%)	18 (6.4%)
うつ病	0	0	5 (1.8%)	0	0	18 (6.4%)
落ち着きのなさ	0	0	5 (1.8%)	0	1 (2.0%)	8 (2.8%)
激越	0	0	9 (3.2%)	0	0	7 (2.5%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
易刺激性	0	0	5 (1.8%)	0	0	6 (2.1%)
気分変化	0	0	5 (1.8%)	0	0	6 (2.1%)
抑うつ気分	0	1 (2.3%)	2 (0.7%)	0	0	3 (1.1%)
睡眠障害	0	0	4 (1.4%)	0	0	3 (1.1%)
錯乱状態	0	0	7 (2.5%)	0	0	2 (0.7%)
精神障害	0	0	1 (0.4%)	0	0	2 (0.7%)
気分動揺	0	0	1 (0.4%)	0	0	2 (0.7%)
適応障害	0	0	0	0	1 (2.0%)	1 (0.4%)
感情障害	0	0	1 (0.4%)	0	0	1 (0.4%)
精神緩慢	0	0	0	0	0	1 (0.4%)
譫妄	0	1 (2.3%)	5 (1.8%)	0	0	1 (0.4%)
抑うつ症状	0	0	2 (0.7%)	0	0	1 (0.4%)
幻覚	0	0	1 (0.4%)	0	0	1 (0.4%)
精神症状	0	0	0	0	0	1 (0.4%)
涙ぐむ	0	0	0	0	0	1 (0.4%)
まとまりのない会話	0	0	1 (0.4%)	0	0	0
失見当識	0	0	1 (0.4%)	0	0	0
気分変調性障害	0	0	1 (0.4%)	0	0	0
言葉もれ	0	0	1 (0.4%)	0	0	0
リビドー消失	0	0	1 (0.4%)	0	0	0
神経過敏	0	0	5 (1.8%)	0	0	0
精神病性障害	0	0	1 (0.4%)	0	0	0
睡眠時驚愕	0	0	1 (0.4%)	0	0	0
ストレス	0	0	1 (0.4%)	0	0	0
思考異常	0	0	1 (0.4%)	0	0	0
血管障害	0	1 (2.3%)	46 (16.4%)	6 (30.0%)	13 (25.5%)	80 (28.3%)
高血圧	0	0	7 (2.5%)	2 (10.0%)	4 (7.8%)	21 (7.4%)
低血圧	0	0	6 (2.1%)	1 (5.0%)	5 (9.8%)	19 (6.7%)
潮紅	0	1 (2.3%)	5 (1.8%)	1 (5.0%)	1 (2.0%)	8 (2.8%)
深部静脈血栓症	0	0	11 (3.9%)	0	0	5 (1.8%)
静脈炎	0	0	1 (0.4%)	0	0	5 (1.8%)
血腫	0	0	5 (1.8%)	0	0	4 (1.4%)
起立性低血圧	0	0	2 (0.7%)	0	0	4 (1.4%)
塞栓症	0	0	0	1 (5.0%)	1 (2.0%)	3 (1.1%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
ほてり	0	0	2 (0.7%)	0	0	3 (1.1%)
血栓性静脈炎	0	0	0	1 (5.0%)	1 (2.0%)	3 (1.1%)
表在性血栓性静脈炎	0	0	6 (2.1%)	0	0	3 (1.1%)
末梢冷感	0	0	0	0	1 (2.0%)	2 (0.7%)
血栓症	0	0	2 (0.7%)	1 (5.0%)	1 (2.0%)	2 (0.7%)
静脈血栓症	0	0	0	0	0	2 (0.7%)
大動脈拡張	0	0	0	0	0	1 (0.4%)
出血性梗塞	0	0	0	0	0	1 (0.4%)
リンパ浮腫	0	0	0	0	0	1 (0.4%)
末梢動脈狭窄	0	0	0	0	0	1 (0.4%)
表在性静脈炎	0	0	0	0	0	1 (0.4%)
大動脈瘤	0	0	1 (0.4%)	0	0	0
動脈硬化症	0	0	2 (0.7%)	0	0	0
虚血	0	0	1 (0.4%)	0	0	0
蒼白	0	0	1 (0.4%)	0	0	0
血栓後症候群	0	0	1 (0.4%)	0	0	0
レイノー現象	0	0	1 (0.4%)	0	0	0
静脈閉塞	0	0	1 (0.4%)	0	0	0
四肢静脈血栓症	0	0	1 (0.4%)	0	0	0
臨床検査	4 (26.7%)	8 (18.2%)	48 (17.1%)	6 (30.0%)	12 (23.5%)	63 (22.3%)
体重減少	0	0	9 (3.2%)	0	1 (2.0%)	16 (5.7%)
アラニンアミノトランスフェラーゼ増加	2 (13.3%)	4 (9.1%)	10 (3.6%)	5 (25.0%)	7 (13.7%)	15 (5.3%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (6.7%)	3 (6.8%)	9 (3.2%)	3 (15.0%)	4 (7.8%)	9 (3.2%)
血中クレアチニン増加	1 (6.7%)	2 (4.5%)	11 (3.9%)	0	1 (2.0%)	9 (3.2%)
γ－グルタミルトランスフェラーゼ増加	2 (13.3%)	2 (4.5%)	7 (2.5%)	2 (10.0%)	2 (3.9%)	7 (2.5%)
血中アルカリホスファターゼ増加	0	0	5 (1.8%)	3 (15.0%)	3 (5.9%)	6 (2.1%)
心電図ＱＴ延長	0	0	1 (0.4%)	0	1 (2.0%)	5 (1.8%)
免疫グロブリン減少	0	0	0	0	1 (2.0%)	3 (1.1%)
血圧上昇	0	0	0	0	2 (3.9%)	2 (0.7%)
Ｃ－反応性蛋白増加	0	0	2 (0.7%)	0	0	2 (0.7%)
国際標準比増加	0	0	0	0	0	2 (0.7%)
体重増加	0	1 (2.3%)	4 (1.4%)	0	0	2 (0.7%)
アラニンアミノトランスフェラーゼ異常	0	0	0	0	1 (2.0%)	1 (0.4%)
アスパラギン酸アミノトランスフェラーゼ異常	0	0	0	0	1 (2.0%)	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
血中クレアチンホスホキナーゼ増加	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
血中鉄減少	0	0	0	0	0	1 (0.4%)
血中乳酸脱水素酵素減少	0	0	0	0	0	1 (0.4%)
血中乳酸脱水素酵素増加	0	0	1 (0.4%)	0	0	1 (0.4%)
血圧低下	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
心雑音	0	0	0	0	0	1 (0.4%)
腎クレアチニン・クリアランス減少	0	0	2 (0.7%)	0	0	1 (0.4%)
好中球中毒性顆粒存在	0	0	0	0	0	1 (0.4%)
酸素飽和度低下	0	0	0	0	0	1 (0.4%)
前立腺特異性抗原増加	0	0	0	0	0	1 (0.4%)
肺動脈圧上昇	0	0	0	0	0	1 (0.4%)
網状赤血球数増加	0	0	0	0	0	1 (0.4%)
血清フェリチン減少	0	0	0	0	0	1 (0.4%)
トロポニン増加	0	0	0	0	0	1 (0.4%)
抗凝固薬濃度治療量以下	0	0	1 (0.4%)	0	0	0
血中葉酸減少	0	0	1 (0.4%)	0	0	0
体温上昇	0	0	1 (0.4%)	0	0	0
診断法	0	0	1 (0.4%)	0	0	0
フィブリンDダイマー増加	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
糸球体濾過率減少	0	0	2 (0.7%)	0	0	0
ヘリコバクター検査陽性	0	0	1 (0.4%)	0	0	0
静脈雑音	0	0	1 (0.4%)	0	0	0
眼障害	0	5 (11.4%)	35 (12.5%)	1 (5.0%)	8 (15.7%)	57 (20.1%)
霧視	0	2 (4.5%)	14 (5.0%)	1 (5.0%)	5 (9.8%)	19 (6.7%)
白内障	0	1 (2.3%)	8 (2.8%)	0	3 (5.9%)	18 (6.4%)
眼刺激	0	0	1 (0.4%)	0	0	7 (2.5%)
流涙増加	0	0	1 (0.4%)	0	0	7 (2.5%)
眼乾燥	0	1 (2.3%)	3 (1.1%)	0	2 (3.9%)	5 (1.8%)
眼出血	0	0	0	0	0	2 (0.7%)
眼部腫脹	0	0	0	0	0	2 (0.7%)
眼充血	0	0	0	0	0	2 (0.7%)
視力低下	0	0	1 (0.4%)	0	0	2 (0.7%)
視力障害	0	0	0	0	0	2 (0.7%)
眼瞼炎	0	0	0	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
結膜出血	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
眼のアレルギー	0	0	0	0	0	1 (0.4%)
眼脂	0	0	2 (0.7%)	0	0	1 (0.4%)
眼の障害	0	0	0	0	0	1 (0.4%)
眼の炎症	0	0	0	0	0	1 (0.4%)
眼球浮腫	0	0	0	0	0	1 (0.4%)
眼痛	0	0	1 (0.4%)	0	0	1 (0.4%)
眼瞼浮腫	0	0	0	0	0	1 (0.4%)
緑内障	0	0	0	0	0	1 (0.4%)
眼窩周囲浮腫	0	0	1 (0.4%)	0	0	1 (0.4%)
後嚢破裂	0	0	0	0	0	1 (0.4%)
屈折障害	0	0	0	0	0	1 (0.4%)
硝子体浮遊物	0	0	0	0	0	1 (0.4%)
失明	0	0	1 (0.4%)	0	0	0
結膜刺激	0	0	1 (0.4%)	0	0	0
眼瞼下垂	0	0	1 (0.4%)	0	0	0
眼瞼発疹	0	0	1 (0.4%)	0	0	0
水晶体混濁	0	0	1 (0.4%)	0	0	0
黄斑変性	0	0	1 (0.4%)	0	0	0
網膜静脈血栓症	0	0	1 (0.4%)	0	0	0
網膜症	0	0	1 (0.4%)	0	0	0
硝子体剥離	0	0	1 (0.4%)	0	0	0
硝子体出血	0	0	1 (0.4%)	0	0	0
腎および尿路障害	1 (6.7%)	5 (11.4%)	45 (16.0%)	2 (10.0%)	6 (11.8%)	50 (17.7%)
腎機能障害	0	0	13 (4.6%)	2 (10.0%)	2 (3.9%)	20 (7.1%)
頻尿	0	0	3 (1.1%)	0	1 (2.0%)	6 (2.1%)
急性腎不全	1 (6.7%)	2 (4.5%)	15 (5.3%)	0	0	4 (1.4%)
高窒素血症	0	1 (2.3%)	1 (0.4%)	0	1 (2.0%)	3 (1.1%)
慢性腎臓病	0	1 (2.3%)	4 (1.4%)	0	1 (2.0%)	3 (1.1%)
血尿	0	0	1 (0.4%)	0	0	3 (1.1%)
排尿困難	0	0	4 (1.4%)	0	0	2 (0.7%)
腎結石症	0	0	0	0	0	2 (0.7%)
夜間頻尿	0	0	1 (0.4%)	0	0	2 (0.7%)
膀胱結石	0	0	0	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
失禁	0	0	0	0	0	1 (0.4%)
尿意切迫	0	0	0	0	0	1 (0.4%)
腎仙痛	0	0	0	0	1 (2.0%)	1 (0.4%)
腎嚢胞	0	0	0	0	0	1 (0.4%)
腎障害	0	0	0	0	0	1 (0.4%)
腎不全	0	0	5 (1.8%)	0	0	1 (0.4%)
尿道出血	0	0	0	0	0	1 (0.4%)
尿失禁	0	0	2 (0.7%)	0	0	1 (0.4%)
尿路閉塞	0	0	0	0	0	1 (0.4%)
ベンスジョーンズ蛋白尿	0	0	1 (0.4%)	0	0	0
ケトン尿	0	0	1 (0.4%)	0	0	0
下部尿路症状	0	0	1 (0.4%)	0	0	0
排尿異常	0	0	1 (0.4%)	0	0	0
多尿	0	0	1 (0.4%)	0	0	0
腎腫瘤	0	0	1 (0.4%)	0	0	0
尿閉	1 (6.7%)	2 (4.5%)	5 (1.8%)	0	0	0
傷害、中毒および処置合併症	3 (20.0%)	6 (13.6%)	45 (16.0%)	1 (5.0%)	8 (15.7%)	45 (15.9%)
転倒	0	0	8 (2.8%)	0	1 (2.0%)	11 (3.9%)
挫傷	1 (6.7%)	1 (2.3%)	6 (2.1%)	0	0	10 (3.5%)
靭帯捻挫	0	0	0	0	0	4 (1.4%)
脊椎圧迫骨折	0	0	2 (0.7%)	0	1 (2.0%)	4 (1.4%)
裂傷	0	0	2 (0.7%)	0	1 (2.0%)	3 (1.1%)
足骨折	0	0	0	0	1 (2.0%)	2 (0.7%)
関節損傷	0	0	0	0	0	2 (0.7%)
肋骨骨折	0	0	4 (1.4%)	0	0	2 (0.7%)
熱傷	0	0	0	0	0	2 (0.7%)
背部損傷	0	0	1 (0.4%)	0	0	1 (0.4%)
脳ヘルニア	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
鎖骨骨折	0	0	2 (0.7%)	0	0	1 (0.4%)
圧迫骨折	0	1 (2.3%)	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
眼挫傷	0	0	1 (0.4%)	0	0	1 (0.4%)
手骨折	0	0	0	0	0	1 (0.4%)
股関節部骨折	0	0	1 (0.4%)	0	0	1 (0.4%)
肉離れ	0	0	0	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
頚部損傷	0	0	0	0	0	1 (0.4%)
眼窩周囲挫傷	0	0	0	0	0	1 (0.4%)
腓骨神経損傷	0	0	0	0	0	1 (0.4%)
橈骨骨折	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
皮膚擦過傷	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
胸骨損傷	0	0	0	0	0	1 (0.4%)
各種物質毒性	0	0	1 (0.4%)	0	0	1 (0.4%)
上肢骨折	0	0	0	0	0	1 (0.4%)
創合併症	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
創傷出血	0	0	0	0	0	1 (0.4%)
手首関節骨折	0	0	0	0	0	1 (0.4%)
節足動物咬傷	0	0	2 (0.7%)	0	0	0
顔面損傷	0	0	1 (0.4%)	0	0	0
顔面骨骨折	0	0	1 (0.4%)	0	0	0
大腿骨頚部骨折	0	0	1 (0.4%)	0	0	0
上腕骨骨折	0	0	1 (0.4%)	0	0	0
注入に伴う反応	1 (6.7%)	1 (2.3%)	2 (0.7%)	0	0	0
関節脱臼	0	0	2 (0.7%)	0	0	0
四肢損傷	0	0	1 (0.4%)	0	0	0
過量投与	0	0	1 (0.4%)	0	0	0
骨盤骨折	0	0	1 (0.4%)	0	0	0
処置後合併症	0	0	1 (0.4%)	0	0	0
外傷後疼痛	0	0	1 (0.4%)	0	0	0
処置による疼痛	0	0	2 (0.7%)	0	0	0
瘢痕	0	0	1 (0.4%)	0	0	0
引っかき傷	0	0	1 (0.4%)	0	0	0
皮膚創傷	0	0	1 (0.4%)	0	0	0
硬膜下血腫	0	0	1 (0.4%)	0	0	0
腱断裂	0	0	1 (0.4%)	0	0	0
脛骨骨折	0	0	1 (0.4%)	0	0	0
歯牙破折	0	1 (2.3%)	1 (0.4%)	0	0	0
輸血関連呼吸困難	0	1 (2.3%)	1 (0.4%)	0	0	0
外傷性血腫	0	0	1 (0.4%)	0	0	0
創傷	0	0	4 (1.4%)	0	0	0

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
心臓障害	0	1 (2.3%)	25 (8.9%)	2 (10.0%)	6 (11.8%)	41 (14.5%)
心房細動	0	0	7 (2.5%)	1 (5.0%)	1 (2.0%)	9 (3.2%)
頻脈	0	1 (2.3%)	2 (0.7%)	0	2 (3.9%)	9 (3.2%)
狭心症	0	0	1 (0.4%)	1 (5.0%)	2 (3.9%)	7 (2.5%)
動悸	0	0	3 (1.1%)	0	2 (3.9%)	4 (1.4%)
洞性頻脈	0	0	0	0	0	4 (1.4%)
心房粗動	0	0	1 (0.4%)	0	0	2 (0.7%)
左室機能不全	0	0	0	0	0	2 (0.7%)
急性冠動脈症候群	0	0	0	0	0	1 (0.4%)
不整脈	0	0	0	0	0	1 (0.4%)
第一度房室ブロック	0	0	0	0	0	1 (0.4%)
徐脈	0	0	2 (0.7%)	0	0	1 (0.4%)
心アミロイドーシス	0	0	0	0	0	1 (0.4%)
うっ血性心不全	0	0	0	0	0	1 (0.4%)
心肥大	0	0	0	0	0	1 (0.4%)
心肺不全	0	0	0	0	0	1 (0.4%)
伝導障害	0	0	0	0	0	1 (0.4%)
拡張機能障害	0	0	0	0	0	1 (0.4%)
期外収縮	0	0	0	0	0	1 (0.4%)
僧帽弁閉鎖不全症	0	0	0	0	0	1 (0.4%)
心筋梗塞	0	0	1 (0.4%)	0	0	1 (0.4%)
心筋虚血	0	0	1 (0.4%)	0	0	1 (0.4%)
洞性不整脈	0	0	0	0	0	1 (0.4%)
上室性頻脈	0	0	1 (0.4%)	0	0	1 (0.4%)
心室性期外収縮	0	0	1 (0.4%)	0	0	1 (0.4%)
急性心筋梗塞	0	0	3 (1.1%)	0	0	0
心停止	0	0	1 (0.4%)	0	0	0
冠動脈疾患	0	0	1 (0.4%)	0	0	0
心嚢液貯留	0	0	2 (0.7%)	0	0	0
心膜炎	0	0	1 (0.4%)	0	0	0
耳および迷路障害	0	2 (4.5%)	12 (4.3%)	0	3 (5.9%)	18 (6.4%)
耳鳴	0	0	1 (0.4%)	0	1 (2.0%)	8 (2.8%)
回転性めまい	0	1 (2.3%)	6 (2.1%)	0	0	4 (1.4%)
難聴	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
聴力低下	0	0	0	0	0	2 (0.7%)
片耳難聴	0	0	0	0	1 (2.0%)	1 (0.4%)
耳不快感	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
耳出血	0	0	0	0	0	1 (0.4%)
耳痛	0	0	2 (0.7%)	0	0	1 (0.4%)
中耳の炎症	0	1 (2.3%)	1 (0.4%)	0	0	0
頭位性回転性めまい	0	0	1 (0.4%)	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	18 (6.4%)	2 (10.0%)	4 (7.8%)	16 (5.7%)
基底細胞癌	0	0	2 (0.7%)	0	0	2 (0.7%)
脂肪腫	0	0	0	0	0	2 (0.7%)
扁平上皮癌	0	0	3 (1.1%)	0	0	2 (0.7%)
アクロコルドン	0	0	0	0	0	1 (0.4%)
急性単球性白血病	0	0	0	0	0	1 (0.4%)
腺癌	0	0	0	0	1 (2.0%)	1 (0.4%)
乳房の良性新生物	0	0	0	0	1 (2.0%)	1 (0.4%)
甲状腺の良性新生物	0	0	0	0	0	1 (0.4%)
ボーエン病	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
ケラトアカントーマ	0	0	0	0	0	1 (0.4%)
形質細胞性白血病	0	0	2 (0.7%)	0	0	1 (0.4%)
脂漏性角化症	0	0	0	0	0	1 (0.4%)
肛門直腸の良性新生物	0	0	1 (0.4%)	0	0	0
肺の良性新生物	0	0	1 (0.4%)	0	0	0
良性新生物	0	0	1 (0.4%)	0	0	0
膀胱の良性新生物	0	0	1 (0.4%)	0	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0	0
皮膚血管腫	0	0	1 (0.4%)	0	0	0
肺腺癌	0	0	1 (0.4%)	0	0	0
形質細胞腫	0	0	1 (0.4%)	0	0	0
前立腺癌	0	0	1 (0.4%)	0	0	0
直腸腺癌	0	0	1 (0.4%)	0	0	0
シュワン細胞腫	0	0	1 (0.4%)	0	0	0

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
肝胆道系障害	0	1 (2.3%)	7 (2.5%)	2 (10.0%)	2 (3.9%)	11 (3.9%)
高ビリルビン血症	0	1 (2.3%)	2 (0.7%)	0	0	4 (1.4%)
肝機能異常	0	0	0	2 (10.0%)	2 (3.9%)	2 (0.7%)
肝細胞損傷	0	0	0	0	0	2 (0.7%)
胆石症	0	0	0	0	0	1 (0.4%)
脂肪肝	0	0	1 (0.4%)	0	0	1 (0.4%)
肝障害	0	0	3 (1.1%)	0	0	1 (0.4%)
胆管結石	0	0	1 (0.4%)	0	0	0
肝腫瘤	0	0	1 (0.4%)	0	0	0
免疫系障害	0	0	3 (1.1%)	0	0	10 (3.5%)
低ｯグロブリン血症	0	0	0	0	0	4 (1.4%)
季節性アレルギー	0	0	1 (0.4%)	0	0	4 (1.4%)
薬物過敏症	0	0	1 (0.4%)	0	0	1 (0.4%)
免疫抑制	0	0	0	0	0	1 (0.4%)
食物アレルギー	0	0	1 (0.4%)	0	0	0
生殖系および乳房障害	0	2 (4.5%)	17 (6.0%)	1 (5.0%)	1 (2.0%)	10 (3.5%)
勃起不全	0	0	2 (0.7%)	0	0	3 (1.1%)
骨盤痛	0	1 (2.3%)	6 (2.1%)	0	0	2 (0.7%)
乳房嚢胞	0	0	0	0	0	1 (0.4%)
骨盤血腫	0	0	0	0	0	1 (0.4%)
前立腺炎	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.4%)
前立腺腫大	0	0	0	0	0	1 (0.4%)
精巣痛	0	0	0	0	0	1 (0.4%)
腟出血	0	0	2 (0.7%)	0	0	1 (0.4%)
腟逆流	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
萎縮性外陰腟炎	0	0	1 (0.4%)	0	0	0
良性前立腺肥大症	0	0	2 (0.7%)	0	0	0
性器水疱	0	0	1 (0.4%)	0	0	0
精巣腫瘤	0	0	1 (0.4%)	0	0	0
外陰腟痛	0	0	1 (0.4%)	0	0	0
内分泌障害	0	1 (2.3%)	10 (3.6%)	0	0	4 (1.4%)
クッシング様症状	0	1 (2.3%)	4 (1.4%)	0	0	1 (0.4%)
高コルチコイド症	0	0	0	0	0	1 (0.4%)
副甲状腺機能亢進症	0	0	1 (0.4%)	0	0	1 (0.4%)

TSFAE02A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
甲状腺機能亢進症	0	0	0	0	0	1 (0.4%)
クッシング症候群	0	0	1 (0.4%)	0	0	0
甲状腺機能低下症	0	0	1 (0.4%)	0	0	0
下垂体依存性クッシング症候群	0	0	1 (0.4%)	0	0	0
ステロイド離脱症候群	0	0	2 (0.7%)	0	0	0
先天性、家族性および遺伝性障害	0	0	0	0	0	2 (0.7%)
角膜ジストロフィー	0	0	0	0	0	1 (0.4%)
包茎	0	0	0	0	0	1 (0.4%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE02A_3003.SAS] 01JUL2016, 15:20

表 2.7.4-付録-29 Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with toxicity grade 3 or 4 TEAE	148 (62.4%)	185 (76.1%)	206 (73.3%)	260 (81.8%)	102 (99.0%)
MedDRA system organ class/Preferred term					
血液およびリンパ系障害	94 (39.7%)	131 (53.9%)	145 (51.6%)	191 (60.1%)	87 (84.5%)
好中球減少症	10 (4.2%)	31 (12.8%)	104 (37.0%)	174 (54.7%)	79 (76.7%)
血小板減少症	78 (32.9%)	110 (45.3%)	38 (13.5%)	40 (12.6%)	18 (17.5%)
貧血	38 (16.0%)	35 (14.4%)	55 (19.6%)	39 (12.3%)	28 (27.2%)
リンパ球減少症	6 (2.5%)	23 (9.5%)	10 (3.6%)	19 (6.0%)	14 (13.6%)
発熱性好中球減少症	1 (0.4%)	4 (1.6%)	7 (2.5%)	17 (5.3%)	7 (6.8%)
白血球減少症	4 (1.7%)	5 (2.1%)	7 (2.5%)	11 (3.5%)	25 (24.3%)
白血球増加症	0	0	1 (0.4%)	1 (0.3%)	0
骨髄機能不全	0	0	1 (0.4%)	0	0
播種性血管内凝固	0	0	1 (0.4%)	0	0
過粘稠度症候群	0	0	1 (0.4%)	0	0
リンパ節症	0	0	1 (0.4%)	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0
脾臓障害	0	0	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	0	0	1 (0.4%)	0	0
感染症および寄生虫症	45 (19.0%)	52 (21.4%)	64 (22.8%)	86 (27.0%)	29 (28.2%)
肺炎	23 (9.7%)	20 (8.2%)	23 (8.2%)	23 (7.2%)	8 (7.8%)
インフルエンザ	2 (0.8%)	1 (0.4%)	2 (0.7%)	8 (2.5%)	3 (2.9%)
尿路感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	6 (1.9%)	1 (1.0%)
気管支炎	3 (1.3%)	5 (2.1%)	6 (2.1%)	5 (1.6%)	2 (1.9%)
下気道感染	1 (0.4%)	1 (0.4%)	3 (1.1%)	5 (1.6%)	0
気道感染	1 (0.4%)	0	2 (0.7%)	5 (1.6%)	0
上気道感染	2 (0.8%)	4 (1.6%)	3 (1.1%)	4 (1.3%)	3 (2.9%)
インフルエンザ性肺炎	0	0	0	3 (0.9%)	0
虫垂炎	0	0	1 (0.4%)	2 (0.6%)	0
細気管支炎	0	0	0	2 (0.6%)	0
気管支肺炎	1 (0.4%)	2 (0.8%)	0	2 (0.6%)	0
胃腸炎	3 (1.3%)	2 (0.8%)	0	2 (0.6%)	0
Ｈ１Ｎ１インフルエンザ	0	0	0	2 (0.6%)	0
感染	0	0	3 (1.1%)	2 (0.6%)	0
大葉性肺炎	0	0	1 (0.4%)	2 (0.6%)	0
好中球減少性敗血症	0	0	0	2 (0.6%)	0
敗血症	3 (1.3%)	2 (0.8%)	6 (2.1%)	2 (0.6%)	3 (2.9%)
急性扁桃炎	0	0	0	1 (0.3%)	0
細菌感染	0	0	0	1 (0.3%)	0
カンピロバクター胃腸炎	0	0	0	1 (0.3%)	0
蜂巣炎	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
サイトメガロウイルス感染	0	0	0	1 (0.3%)	0
喉頭蓋炎	0	0	0	1 (0.3%)	0
大腸菌性菌血症	0	0	0	1 (0.3%)	0
硬膜外膿瘍	0	0	0	1 (0.3%)	0
ウイルス性胃腸炎	0	0	1 (0.4%)	1 (0.3%)	0
リステリア性敗血症	0	0	0	1 (0.3%)	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
肺感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
鼻膿瘍	0	0	0	1 (0.3%)	0
口腔真菌感染	0	0	0	1 (0.3%)	0
急性中耳炎	0	0	1 (0.4%)	1 (0.3%)	0
パラインフルエンザウイルス感染	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
眼窩周囲蜂巣炎	0	0	0	1 (0.3%)	0
細菌性肺炎	0	0	0	1 (0.3%)	0
ヘモフィルス性肺炎	0	0	0	1 (0.3%)	0
クレブシエラ菌性肺炎	0	0	0	1 (0.3%)	0
レジオネラ菌性肺炎	0	0	1 (0.4%)	1 (0.3%)	0
レンサ球菌性肺炎	0	0	0	1 (0.3%)	0
ウイルス性肺炎	0	0	0	1 (0.3%)	0
シュードモナス感染	0	0	0	1 (0.3%)	0
呼吸器モニリア症	0	0	0	1 (0.3%)	0
ＲＳウイルス感染	0	1 (0.4%)	0	1 (0.3%)	0
サルモネラ性菌血症	0	0	0	1 (0.3%)	0
敗血症性ショック	0	0	2 (0.7%)	1 (0.3%)	0
皮膚感染	0	0	0	1 (0.3%)	0
軟部組織感染	0	0	0	1 (0.3%)	0
扁桃炎	0	0	0	1 (0.3%)	0
細菌性上気道感染	0	0	0	1 (0.3%)	0
子宮膿瘍	0	0	0	1 (0.3%)	0
内臓リーシュマニア症	0	0	0	1 (0.3%)	0
四肢膿瘍	0	0	1 (0.4%)	0	0
アデノウイルス感染	0	0	1 (0.4%)	0	0
肛門膿瘍	0	0	1 (0.4%)	0	0
脳膿瘍	1 (0.4%)	0	0	0	0
ウイルス性気管支炎	0	0	1 (0.4%)	0	0
海綿静脈洞血栓症	1 (0.4%)	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (1.0%)
クロストリジウム・ディフィシレ感染	0	0	1 (0.4%)	0	1 (1.0%)
結膜炎	1 (0.4%)	0	0	0	0
医療機器関連感染	1 (0.4%)	2 (0.8%)	0	0	0
憩室炎	0	0	0	0	1 (1.0%)
心内膜炎	1 (0.4%)	0	0	0	0
感染性小腸結腸炎	0	0	2 (0.7%)	0	0
精巣上体炎	1 (0.4%)	0	0	0	0
丹毒	0	0	1 (0.4%)	0	0
大腸菌性敗血症	1 (0.4%)	0	0	0	0
真菌感染	0	1 (0.4%)	0	0	0
真菌性食道炎	0	1 (0.4%)	0	0	0
壊疽	1 (0.4%)	0	0	0	0
サルモネラ菌性胃腸炎	0	1 (0.4%)	0	0	0
消化管感染	0	0	1 (0.4%)	0	0
ヘモフィルス感染	0	0	1 (0.4%)	0	0
帯状疱疹	1 (0.4%)	4 (1.6%)	1 (0.4%)	0	2 (1.9%)
真菌性角膜炎	0	0	1 (0.4%)	0	0
喉頭炎	0	0	0	0	1 (1.0%)
限局性感染	0	0	1 (0.4%)	0	0
乳腺炎	0	0	0	0	1 (1.0%)
メタニューモウイルス感染	0	1 (0.4%)	0	0	0
壊死性筋膜炎	0	0	1 (0.4%)	0	0
ノカルジア症	1 (0.4%)	0	0	0	0
骨髄炎	0	0	2 (0.7%)	0	0
中耳炎	0	1 (0.4%)	0	0	0
腹膜炎	0	1 (0.4%)	0	0	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
咽頭炎	0	0	1 (0.4%)	0	0
ニューモシスチス・イロベチイ肺炎	0	1 (0.4%)	0	0	0
サイトメガロウイルス性肺炎	0	2 (0.8%)	0	0	0
肺炎球菌性肺炎	0	1 (0.4%)	0	0	0
進行性多巣性白質脳症	0	0	0	0	1 (1.0%)
シュードモナス性敗血症	0	0	0	0	1 (1.0%)
肺敗血症	0	1 (0.4%)	0	0	0
肺結核	0	0	1 (0.4%)	0	0
腎盂腎炎	0	1 (0.4%)	0	0	0
急性腎盂腎炎	0	0	1 (0.4%)	0	0
慢性腎盂腎炎	1 (0.4%)	0	0	0	0
ライノウイルス感染	0	1 (0.4%)	0	0	0
副鼻腔炎	0	3 (1.2%)	0	0	1 (1.0%)
脊髄感染	0	0	0	0	1 (1.0%)
ブドウ球菌性菌血症	1 (0.4%)	0	0	0	0
ステノトロフォモナス感染	1 (0.4%)	0	0	0	0
歯膿瘍	1 (0.4%)	0	0	0	0
歯感染	0	0	0	0	1 (1.0%)
気管気管支炎	1 (0.4%)	0	0	0	0
尿路性敗血症	0	0	1 (0.4%)	0	0
水痘帯状疱疹ウイルス感染	0	0	1 (0.4%)	0	0
代謝および栄養障害	24 (10.1%)	33 (13.6%)	27 (9.6%)	43 (13.5%)	16 (15.5%)
低リン酸血症	1 (0.4%)	5 (2.1%)	6 (2.1%)	12 (3.8%)	2 (1.9%)
高血糖	6 (2.5%)	8 (3.3%)	9 (3.2%)	10 (3.1%)	6 (5.8%)
低カリウム血症	3 (1.3%)	6 (2.5%)	6 (2.1%)	8 (2.5%)	3 (2.9%)
低ナトリウム血症	5 (2.1%)	4 (1.6%)	2 (0.7%)	5 (1.6%)	2 (1.9%)
低カルシウム血症	2 (0.8%)	4 (1.6%)	2 (0.7%)	4 (1.3%)	2 (1.9%)
高カルシウム血症	3 (1.3%)	3 (1.2%)	3 (1.1%)	3 (0.9%)	3 (2.9%)
高尿酸血症	2 (0.8%)	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
食欲減退	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	0
脱水	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
糖尿病	0	1 (0.4%)	0	1 (0.3%)	0
電解質失調	0	0	0	1 (0.3%)	0
低アルブミン血症	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
糖尿病性ケトアシドーシス	1 (0.4%)	0	0	0	0
高カリウム血症	0	1 (0.4%)	1 (0.4%)	0	0
高ナトリウム血症	1 (0.4%)	3 (1.2%)	0	0	0
高リン酸塩血症	0	0	1 (0.4%)	0	0
低マグネシウム血症	0	0	1 (0.4%)	0	0
代謝性アシドーシス	0	1 (0.4%)	0	0	0
腫瘍崩壊症候群	0	1 (0.4%)	0	0	0
２型糖尿病	0	0	1 (0.4%)	0	0
一般・全身障害および投与部位の状態	22 (9.3%)	19 (7.8%)	21 (7.5%)	36 (11.3%)	15 (14.6%)
疲労	8 (3.4%)	11 (4.5%)	7 (2.5%)	18 (5.7%)	10 (9.7%)
無力症	5 (2.1%)	2 (0.8%)	7 (2.5%)	8 (2.5%)	0
発熱	3 (1.3%)	3 (1.2%)	4 (1.4%)	5 (1.6%)	1 (1.0%)
全身健康状態低下	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
倦怠感	0	0	0	2 (0.6%)	0
末梢性浮腫	0	1 (0.4%)	3 (1.1%)	2 (0.6%)	3 (2.9%)
医薬品副作用	0	0	0	1 (0.3%)	0
悪寒	0	0	0	1 (0.3%)	0
運動耐性低下	0	0	0	1 (0.3%)	0
冷感	0	0	0	1 (0.3%)	0
歩行障害	0	0	0	1 (0.3%)	1 (1.0%)
疼痛	2 (0.8%)	2 (0.8%)	0	1 (0.3%)	0
全身性炎症反応症候群	0	0	0	1 (0.3%)	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
胸痛	0	0	1 (0.4%)	0	1 (1.0%)
状態悪化	2 (0.8%)	0	0	0	0
高熱	1 (0.4%)	0	0	0	0
インフルエンザ様疾患	0	0	1 (0.4%)	0	0
非心臓性胸痛	1 (0.4%)	0	0	0	0
浮腫	0	1 (0.4%)	0	0	1 (1.0%)
呼吸器、胸郭および縦隔障害	11 (4.6%)	27 (11.1%)	18 (6.4%)	27 (8.5%)	19 (18.4%)
呼吸困難	2 (0.8%)	9 (3.7%)	2 (0.7%)	9 (2.8%)	7 (6.8%)
肺塞栓症	1 (0.4%)	1 (0.4%)	9 (3.2%)	8 (2.5%)	1 (1.0%)
肺水腫	1 (0.4%)	0	1 (0.4%)	5 (1.6%)	0
喉頭浮腫	0	2 (0.8%)	0	2 (0.6%)	0
胸水	1 (0.4%)	0	0	2 (0.6%)	2 (1.9%)
呼吸不全	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	0
喘鳴	0	0	0	2 (0.6%)	0
急性肺水腫	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
気管支痙攣	0	6 (2.5%)	1 (0.4%)	1 (0.3%)	0
慢性閉塞性肺疾患	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
発声障害	0	0	0	1 (0.3%)	1 (1.0%)
低酸素症	0	0	1 (0.4%)	1 (0.3%)	2 (1.9%)
誤嚥性肺炎	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
急性呼吸不全	0	0	1 (0.4%)	0	0
喘息	0	1 (0.4%)	0	0	1 (1.0%)
無気肺	0	0	1 (0.4%)	0	0
気管支反応性亢進	0	0	0	0	1 (1.0%)
気管支肺症	0	0	0	0	1 (1.0%)
労作性呼吸困難	1 (0.4%)	1 (0.4%)	0	0	0
鼻出血	1 (0.4%)	1 (0.4%)	0	0	0
しゃっくり	1 (0.4%)	0	0	0	1 (1.0%)
胸水症	0	1 (0.4%)	0	0	0
過換気	0	1 (0.4%)	0	0	0
間質性肺疾患	0	0	1 (0.4%)	0	2 (1.9%)
肺障害	0	0	1 (0.4%)	0	1 (1.0%)
鼻閉	0	1 (0.4%)	0	0	0
口腔咽頭腫脹	0	1 (0.4%)	0	0	0
咽頭浮腫	0	1 (0.4%)	0	0	0
気胸	0	0	1 (0.4%)	0	0
湿性咳嗽	0	0	0	0	1 (1.0%)
肺動脈血栓症	0	1 (0.4%)	0	0	0
肺出血	0	1 (0.4%)	0	0	0
呼吸窮迫	0	1 (0.4%)	0	0	0
胃腸障害	9 (3.8%)	18 (7.4%)	16 (5.7%)	26 (8.2%)	8 (7.8%)
下痢	3 (1.3%)	9 (3.7%)	9 (3.2%)	16 (5.0%)	3 (2.9%)
悪心	0	1 (0.4%)	0	4 (1.3%)	0
便秘	2 (0.8%)	0	2 (0.7%)	3 (0.9%)	0
嘔吐	0	0	2 (0.7%)	3 (0.9%)	2 (1.9%)
憩室穿孔	0	1 (0.4%)	0	2 (0.6%)	0
肛門出血	0	0	0	1 (0.3%)	0
大腸炎	0	0	1 (0.4%)	1 (0.3%)	0
嚥下障害	0	0	0	1 (0.3%)	0
胃出血	0	0	0	1 (0.3%)	0
出血性胃腸管血管異形成	0	0	0	1 (0.3%)	0
胃腸障害	0	0	0	1 (0.3%)	0
腹痛	2 (0.8%)	0	0	0	1 (1.0%)
上腹部痛	0	1 (0.4%)	0	0	0
痔瘻	0	0	1 (0.4%)	0	0
潰瘍性大腸炎	0	0	1 (0.4%)	0	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
十二指腸潰瘍	0	1 (0.4%)	0	0	0
胃障害	0	0	1 (0.4%)	0	0
胃炎	1 (0.4%)	0	0	0	0
びらん性胃炎	0	1 (0.4%)	0	0	0
吐血	0	0	1 (0.4%)	0	0
嵌頓臍ヘルニア	1 (0.4%)	0	0	0	0
腸閉塞	0	1 (0.4%)	1 (0.4%)	0	0
口唇腫脹	0	1 (0.4%)	0	0	0
メレナ	0	1 (0.4%)	0	0	0
食道炎	0	0	1 (0.4%)	0	0
急性膵炎	0	1 (0.4%)	0	0	0
慢性膵炎	0	1 (0.4%)	0	0	0
小腸閉塞	0	1 (0.4%)	0	0	2 (1.9%)
上部消化管出血	0	1 (0.4%)	0	0	0
神経系障害	25 (10.5%)	23 (9.5%)	15 (5.3%)	21 (6.6%)	13 (12.6%)
失神	4 (1.7%)	1 (0.4%)	2 (0.7%)	10 (3.1%)	2 (1.9%)
末梢性ニューロパチー	0	0	1 (0.4%)	2 (0.6%)	1 (1.0%)
末梢性感覚ニューロパチー	16 (6.8%)	11 (4.5%)	1 (0.4%)	2 (0.6%)	2 (1.9%)
失神寸前の状態	0	1 (0.4%)	0	2 (0.6%)	0
脳梗塞	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
脳血管発作	0	0	0	1 (0.3%)	0
認知障害	1 (0.4%)	0	0	1 (0.3%)	0
嗜眠	0	0	2 (0.7%)	1 (0.3%)	0
神経系障害	0	0	1 (0.4%)	1 (0.3%)	0
振戦	1 (0.4%)	2 (0.8%)	0	1 (0.3%)	3 (2.9%)
失語症	0	0	1 (0.4%)	0	0
運動失調	0	0	0	0	1 (1.0%)
自律神経ニューロパチー	1 (0.4%)	0	0	0	0
平衡障害	0	1 (0.4%)	0	0	0
頚腕症候群	0	0	0	0	1 (1.0%)
浮動性めまい	0	1 (0.4%)	0	0	2 (1.9%)
塞栓性脳卒中	0	1 (0.4%)	0	0	0
脳症	1 (0.4%)	0	0	0	0
感覚鈍麻	0	0	0	0	1 (1.0%)
肋間神経痛	0	0	1 (0.4%)	0	0
虚血性脳卒中	0	1 (0.4%)	1 (0.4%)	0	0
記憶障害	0	0	1 (0.4%)	0	0
不全単麻痺	1 (0.4%)	0	0	0	0
神経痛	2 (0.8%)	2 (0.8%)	0	0	0
末梢性運動ニューロパチー	2 (0.8%)	2 (0.8%)	0	0	0
ヘルペス後神経痛	0	1 (0.4%)	0	0	0
下肢静止不能症候群	1 (0.4%)	0	0	0	0
感覚運動障害	0	0	1 (0.4%)	0	0
傾眠	0	0	1 (0.4%)	0	0
脊髄圧迫	0	0	1 (0.4%)	0	1 (1.0%)
くも膜下出血	1 (0.4%)	0	0	0	0
血管性脳症	0	0	1 (0.4%)	0	0
血管障害	11 (4.6%)	21 (8.6%)	8 (2.8%)	19 (6.0%)	6 (5.8%)
高血圧	2 (0.8%)	16 (6.6%)	1 (0.4%)	12 (3.8%)	3 (2.9%)
深部静脈血栓症	1 (0.4%)	0	4 (1.4%)	2 (0.6%)	0
低血圧	4 (1.7%)	3 (1.2%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
出血性梗塞	0	0	0	1 (0.3%)	0
起立性低血圧	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	0
末梢動脈狭窄	0	0	0	1 (0.3%)	0
血栓症	0	1 (0.4%)	0	1 (0.3%)	0
大動脈解離	0	0	0	0	1 (1.0%)

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
循環虚脱	1 (0.4%)	0	0	0	0
静脈塞栓症	1 (0.4%)	0	0	0	0
血腫	0	0	0	0	1 (1.0%)
高血圧クリーゼ	0	1 (0.4%)	0	0	0
末梢動脈瘤	0	1 (0.4%)	0	0	0
静脈炎	0	0	1 (0.4%)	0	0
筋骨格系および結合組織障害	12 (5.1%)	18 (7.4%)	18 (6.4%)	18 (5.7%)	18 (17.5%)
背部痛	3 (1.3%)	3 (1.2%)	4 (1.4%)	4 (1.3%)	6 (5.8%)
関節痛	0	4 (1.6%)	1 (0.4%)	3 (0.9%)	2 (1.9%)
骨痛	3 (1.3%)	3 (1.2%)	1 (0.4%)	2 (0.6%)	4 (3.9%)
筋痙縮	0	0	5 (1.8%)	2 (0.6%)	1 (1.0%)
筋骨格痛	0	1 (0.4%)	3 (1.1%)	2 (0.6%)	2 (1.9%)
骨壊死	0	0	0	2 (0.6%)	0
筋萎縮症	0	0	0	1 (0.3%)	0
側腹部痛	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
椎間板突出	0	0	0	1 (0.3%)	0
筋骨格系胸痛	0	1 (0.4%)	0	1 (0.3%)	2 (1.9%)
骨病変	0	1 (0.4%)	0	0	0
結晶性関節障害	0	0	1 (0.4%)	0	0
鼡径部痛	0	1 (0.4%)	0	0	0
運動性低下	1 (0.4%)	0	0	0	0
筋力低下	2 (0.8%)	0	2 (0.7%)	0	4 (3.9%)
筋肉痛	0	2 (0.8%)	0	0	0
顎骨壊死	1 (0.4%)	0	2 (0.7%)	0	1 (1.0%)
四肢痛	2 (0.8%)	4 (1.6%)	1 (0.4%)	0	0
病的骨折	0	2 (0.8%)	1 (0.4%)	0	0
脊柱管狭窄症	1 (0.4%)	0	2 (0.7%)	0	0
脊椎痛	0	3 (1.2%)	1 (0.4%)	0	0
顎関節症候群	0	0	1 (0.4%)	0	0
臨床検査	4 (1.7%)	7 (2.9%)	6 (2.1%)	16 (5.0%)	8 (7.8%)
アラニンアミノトランスフェラーゼ増加	0	4 (1.6%)	3 (1.1%)	8 (2.5%)	4 (3.9%)
γ－グルタミルトランスフェラーゼ増加	3 (1.3%)	1 (0.4%)	1 (0.4%)	5 (1.6%)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.4%)	3 (0.9%)	3 (2.9%)
国際標準比増加	0	0	0	2 (0.6%)	0
血中アルカリホスファターゼ増加	0	0	0	1 (0.3%)	1 (1.0%)
血中クレアチンホスホキナーゼ増加	0	0	0	1 (0.3%)	0
血圧上昇	0	0	0	1 (0.3%)	1 (1.0%)
好中球中毒性顆粒存在	0	0	0	1 (0.3%)	0
抗凝固薬濃度治療量以下	0	0	1 (0.4%)	0	0
血中クレアチニン増加	0	1 (0.4%)	0	0	0
血中乳酸脱水素酵素増加	0	0	1 (0.4%)	0	0
血中リン減少	0	0	0	0	1 (1.0%)
Ｃ－反応性蛋白増加	1 (0.4%)	0	1 (0.4%)	0	0
心電図ＱＴ間隔異常	0	1 (0.4%)	0	0	0
リパーゼ増加	0	1 (0.4%)	0	0	0
サルモネラ検査陽性	0	0	0	0	1 (1.0%)
心臓障害	7 (3.0%)	10 (4.1%)	9 (3.2%)	9 (2.8%)	2 (1.9%)
心房細動	2 (0.8%)	4 (1.6%)	3 (1.1%)	3 (0.9%)	1 (1.0%)
狭心症	0	1 (0.4%)	0	2 (0.6%)	0
急性冠動脈症候群	0	1 (0.4%)	0	1 (0.3%)	0
うっ血性心不全	1 (0.4%)	2 (0.8%)	0	1 (0.3%)	2 (1.9%)
左室機能不全	0	0	0	1 (0.3%)	0
心筋梗塞	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	0
洞性不整脈	0	0	0	1 (0.3%)	0
洞性頻脈	0	0	0	1 (0.3%)	0
急性心筋梗塞	0	1 (0.4%)	3 (1.1%)	0	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
心房粗動	0	1 (0.4%)	1 (0.4%)	0	0
徐脈	1 (0.4%)	0	0	0	0
心不全	1 (0.4%)	2 (0.8%)	0	0	0
心原性ショック	1 (0.4%)	0	0	0	0
冠動脈狭窄	1 (0.4%)	0	0	0	0
僧帽弁閉鎖不全症	0	1 (0.4%)	0	0	0
心膜炎	0	0	1 (0.4%)	0	0
上室性頻脈	0	0	1 (0.4%)	0	0
心室性不整脈	0	1 (0.4%)	0	0	0
心室性期外収縮	1 (0.4%)	0	0	0	0
眼障害	2 (0.8%)	3 (1.2%)	4 (1.4%)	7 (2.2%)	2 (1.9%)
白内障	0	1 (0.4%)	3 (1.1%)	6 (1.9%)	0
後嚢破裂	0	0	0	1 (0.3%)	0
霰粒腫	1 (0.4%)	0	0	0	0
結膜浮腫	0	1 (0.4%)	0	0	0
複視	0	1 (0.4%)	0	0	0
眼出血	0	0	0	0	1 (1.0%)
流涙増加	0	1 (0.4%)	0	0	0
網膜剥離	1 (0.4%)	0	0	0	0
網膜症	0	0	1 (0.4%)	0	0
霧視	0	0	0	0	1 (1.0%)
精神障害	7 (3.0%)	5 (2.1%)	9 (3.2%)	7 (2.2%)	6 (5.8%)
うつ病	1 (0.4%)	0	0	2 (0.6%)	1 (1.0%)
気分変化	0	1 (0.4%)	0	2 (0.6%)	0
不安	1 (0.4%)	0	2 (0.7%)	1 (0.3%)	0
譫妄	2 (0.8%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
不眠症	3 (1.3%)	0	2 (0.7%)	1 (0.3%)	2 (1.9%)
激越	0	1 (0.4%)	1 (0.4%)	0	0
錯乱状態	0	1 (0.4%)	2 (0.7%)	0	3 (2.9%)
抑うつ気分	0	1 (0.4%)	1 (0.4%)	0	0
転導性	1 (0.4%)	0	0	0	0
精神状態変化	0	0	0	0	1 (1.0%)
神経過敏	0	0	1 (0.4%)	0	0
妄想症	1 (0.4%)	0	0	0	0
皮膚および皮下組織障害	0	1 (0.4%)	1 (0.4%)	6 (1.9%)	7 (6.8%)
そう痒症	0	0	0	2 (0.6%)	1 (1.0%)
薬疹	0	0	0	1 (0.3%)	0
全身性皮疹	0	0	0	1 (0.3%)	2 (1.9%)
斑状皮疹	0	0	0	1 (0.3%)	0
斑状丘疹状皮疹	0	0	0	1 (0.3%)	1 (1.0%)
丘疹性皮疹	0	0	0	1 (0.3%)	0
蕁麻疹	0	0	0	1 (0.3%)	0
多形紅斑	0	0	0	0	1 (1.0%)
多汗症	0	1 (0.4%)	0	0	1 (1.0%)
寝汗	0	0	1 (0.4%)	0	0
ばら色粃糠疹	0	0	0	0	1 (1.0%)
傷害、中毒および処置合併症	5 (2.1%)	7 (2.9%)	9 (3.2%)	5 (1.6%)	10 (9.7%)
足骨折	0	0	0	1 (0.3%)	0
手骨折	0	0	0	1 (0.3%)	0
股関節部骨折	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
脊椎骨折	0	1 (0.4%)	0	1 (0.3%)	0
上肢骨折	0	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
足関節部骨折	0	0	0	0	1 (1.0%)
鎖骨骨折	0	0	1 (0.4%)	0	0
圧迫骨折	0	0	1 (0.4%)	0	1 (1.0%)
挫傷	1 (0.4%)	0	0	0	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
毒性物質曝露	0	0	0	0	1 (1.0%)
転倒	0	0	1 (0.4%)	0	6 (5.8%)
大腿骨頚部骨折	0	0	1 (0.4%)	0	0
大腿骨骨折	0	1 (0.4%)	0	0	1 (1.0%)
上腕骨骨折	0	1 (0.4%)	0	0	1 (1.0%)
関節脱臼	0	0	1 (0.4%)	0	0
骨盤骨折	0	0	0	0	1 (1.0%)
処置後合併症	0	0	1 (0.4%)	0	0
恥骨骨折	0	1 (0.4%)	0	0	0
橈骨骨折	0	0	1 (0.4%)	0	0
肋骨骨折	1 (0.4%)	1 (0.4%)	0	0	0
肩甲骨骨折	0	1 (0.4%)	0	0	0
脊椎圧迫骨折	0	0	0	0	1 (1.0%)
硬膜下血腫	1 (0.4%)	0	1 (0.4%)	0	0
胸椎骨折	1 (0.4%)	0	0	0	0
腎および尿路障害	5 (2.1%)	6 (2.5%)	14 (5.0%)	5 (1.6%)	3 (2.9%)
急性腎不全	1 (0.4%)	2 (0.8%)	6 (2.1%)	1 (0.3%)	1 (1.0%)
慢性腎臓病	1 (0.4%)	1 (0.4%)	4 (1.4%)	1 (0.3%)	0
腎不全	2 (0.8%)	0	5 (1.8%)	1 (0.3%)	1 (1.0%)
腎機能障害	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
尿路閉塞	0	0	0	1 (0.3%)	0
血尿	0	2 (0.8%)	0	0	0
骨髄腫円柱腎症	0	1 (0.4%)	0	0	0
肝胆道系障害	1 (0.4%)	0	2 (0.7%)	4 (1.3%)	1 (1.0%)
高ビリルビン血症	0	0	0	2 (0.6%)	1 (1.0%)
肝機能異常	0	0	0	1 (0.3%)	0
肝細胞損傷	0	0	0	1 (0.3%)	0
肝腫瘤	0	0	1 (0.4%)	0	0
虚血性肝炎	1 (0.4%)	0	0	0	0
肝障害	0	0	1 (0.4%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	5 (2.1%)	9 (3.2%)	4 (1.3%)	0
急性単球性白血病	0	0	0	1 (0.3%)	0
胃腺癌	0	0	0	1 (0.3%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.3%)	0
形質細胞性白血病	0	0	1 (0.4%)	1 (0.3%)	0
結腸腺癌	0	1 (0.4%)	0	0	0
基底細胞癌	0	0	1 (0.4%)	0	0
膀胱の良性新生物	0	0	1 (0.4%)	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0
乳癌	0	1 (0.4%)	0	0	0
再発乳癌	1 (0.4%)	0	0	0	0
胃腸管腺腫	0	1 (0.4%)	0	0	0
形質細胞腫	0	1 (0.4%)	1 (0.4%)	0	0
前立腺癌	0	0	1 (0.4%)	0	0
直腸腺癌	0	0	1 (0.4%)	0	0
扁平上皮癌	0	0	2 (0.7%)	0	0
皮膚有棘細胞癌	0	1 (0.4%)	0	0	0
移行上皮癌	0	1 (0.4%)	0	0	0
内分泌障害	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
ステロイド離脱症候群	0	0	1 (0.4%)	1 (0.3%)	0
副腎機能不全	1 (0.4%)	0	0	0	0
クッシング様症状	1 (0.4%)	0	0	0	1 (1.0%)
免疫系障害	0	0	0	1 (0.3%)	0
低ｙグロブリン血症	0	0	0	1 (0.3%)	0

TSFAE03A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
生殖系および乳房障害	0	0	0	1 (0.3%)	0
前立腺腫大	0	0	0	1 (0.3%)	0
耳および迷路障害	0	0	0	0	1 (1.0%)
耳鳴	0	0	0	0	1 (1.0%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE03A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE03A.SAS] 01JUN2016, 10:36

表 2.7.4-付録-30 Number of Subjects with Treatment-emergent Adverse Events with Grade 3 or 4 by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE03: Number of Subjects with Treatment-emergent Adverse Events with Grade 3 or 4 by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: Safety	8
Total number of subjects with toxicity grade 3 or 4 TEAE	8 (100.0%)
MedDRA system organ class/Preferred term	
血液およびリンパ系障害	7 (87.5%)
血小板減少症	6 (75.0%)
リンパ球減少症	5 (62.5%)
白血球減少症	2 (25.0%)
好中球減少症	2 (25.0%)
代謝および栄養障害	4 (50.0%)
高血糖	2 (25.0%)
低カリウム血症	2 (25.0%)
感染症および寄生虫症	2 (25.0%)
帯状疱疹	1 (12.5%)
鼻咽頭炎	1 (12.5%)
一般・全身障害および投与部位の状態	1 (12.5%)
疲労	1 (12.5%)
肝胆道系障害	1 (12.5%)
薬物性肝障害	1 (12.5%)
臨床検査	1 (12.5%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (12.5%)
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)
前立腺癌	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE03.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE03.SAS] 28SEP2016, 04:13

表 2.7.4-付録-31 Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283
Total number of subjects with toxicity grade 3 or 4 TEAE	12 (80.0%)	35 (79.5%)	206 (73.3%)	19 (95.0%)	46 (90.2%)	229 (80.9%)
MedDRA system organ class/Preferred term						
血液およびリンパ系障害	11 (73.3%)	29 (65.9%)	145 (51.6%)	15 (75.0%)	36 (70.6%)	162 (57.2%)
好中球減少症	4 (26.7%)	17 (38.6%)	104 (37.0%)	11 (55.0%)	32 (62.7%)	147 (51.9%)
血小板減少症	2 (13.3%)	7 (15.9%)	38 (13.5%)	1 (5.0%)	5 (9.8%)	36 (12.7%)
貧血	2 (13.3%)	11 (25.0%)	55 (19.6%)	1 (5.0%)	4 (7.8%)	35 (12.4%)
発熱性好中球減少症	0	1 (2.3%)	7 (2.5%)	0	2 (3.9%)	16 (5.7%)
リンパ球減少症	7 (46.7%)	7 (15.9%)	10 (3.6%)	8 (40.0%)	8 (15.7%)	15 (5.3%)
白血球減少症	0	2 (4.5%)	7 (2.5%)	1 (5.0%)	4 (7.8%)	8 (2.8%)
骨髄機能不全	0	0	1 (0.4%)	0	0	0
播種性血管内凝固	0	0	1 (0.4%)	0	0	0
過粘稠度症候群	0	0	1 (0.4%)	0	0	0
白血球増加症	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
リンパ節症	0	0	1 (0.4%)	0	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0	0
脾臓障害	0	0	1 (0.4%)	0	0	0
血栓性血小板減少性紫斑病	0	0	1 (0.4%)	0	0	0
感染症および寄生虫症	2 (13.3%)	11 (25.0%)	64 (22.8%)	5 (25.0%)	10 (19.6%)	80 (28.3%)
肺炎	2 (13.3%)	4 (9.1%)	23 (8.2%)	2 (10.0%)	3 (5.9%)	22 (7.8%)
インフルエンザ	0	0	2 (0.7%)	0	0	8 (2.8%)
下気道感染	0	0	3 (1.1%)	0	0	5 (1.8%)
気道感染	0	0	2 (0.7%)	0	0	5 (1.8%)
尿路感染	0	1 (2.3%)	1 (0.4%)	1 (5.0%)	1 (2.0%)	5 (1.8%)
気管支炎	0	0	6 (2.1%)	0	0	4 (1.4%)
インフルエンザ性肺炎	0	0	0	0	0	3 (1.1%)
上気道感染	0	1 (2.3%)	3 (1.1%)	0	0	3 (1.1%)
虫垂炎	0	0	1 (0.4%)	0	0	2 (0.7%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
細気管支炎	0	0	0	0	1 (2.0%)	2 (0.7%)
気管支肺炎	0	0	0	0	0	2 (0.7%)
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	2 (0.7%)
感染	0	0	3 (1.1%)	0	0	2 (0.7%)
大葉性肺炎	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)
好中球減少性敗血症	0	0	0	0	0	2 (0.7%)
敗血症	0	1 (2.3%)	6 (2.1%)	0	0	2 (0.7%)
急性扁桃炎	0	0	0	0	0	1 (0.4%)
細菌感染	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
カンピロバクター胃腸炎	0	0	0	0	0	1 (0.4%)
蜂巣炎	0	0	1 (0.4%)	0	0	1 (0.4%)
サイトメガロウイルス感染	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
喉頭蓋炎	0	0	0	0	0	1 (0.4%)
大腸菌性菌血症	0	0	0	0	0	1 (0.4%)
硬膜外膿瘍	0	0	0	0	0	1 (0.4%)
胃腸炎	0	0	0	0	0	1 (0.4%)
ウイルス性胃腸炎	0	0	1 (0.4%)	0	0	1 (0.4%)
リステリア性敗血症	0	0	0	0	0	1 (0.4%)
肺感染	0	0	1 (0.4%)	0	0	1 (0.4%)
鼻膿瘍	0	0	0	0	0	1 (0.4%)
口腔真菌感染	0	0	0	0	0	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
パラインフルエンザウイルス感染	0	0	1 (0.4%)	0	0	1 (0.4%)
眼窩周囲蜂巣炎	0	0	0	0	0	1 (0.4%)
細菌性肺炎	0	0	0	0	0	1 (0.4%)
ヘモフィルス性肺炎	0	0	0	0	0	1 (0.4%)
クレブシエラ菌性肺炎	0	0	0	0	0	1 (0.4%)
レジオネラ菌性肺炎	0	0	1 (0.4%)	0	0	1 (0.4%)
レンサ球菌性肺炎	0	0	0	0	0	1 (0.4%)
シュードモナス感染	0	0	0	0	0	1 (0.4%)
呼吸器モニリア症	0	0	0	0	0	1 (0.4%)
ＲＳウイルス感染	0	0	0	0	0	1 (0.4%)
サルモネラ性菌血症	0	0	0	0	1 (2.0%)	1 (0.4%)
敗血症性ショック	0	0	2 (0.7%)	0	0	1 (0.4%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
皮膚感染	0	0	0	0	0	1 (0.4%)
軟部組織感染	0	0	0	0	0	1 (0.4%)
扁桃炎	0	0	0	0	0	1 (0.4%)
細菌性上気道感染	0	0	0	0	0	1 (0.4%)
子宮膿瘍	0	0	0	0	0	1 (0.4%)
内臓リーシュマニア症	0	0	0	0	0	1 (0.4%)
四肢膿瘍	0	0	1 (0.4%)	0	0	0
アデノウイルス感染	0	0	1 (0.4%)	0	0	0
肛門膿瘍	0	1 (2.3%)	1 (0.4%)	0	0	0
ウイルス性気管支炎	0	0	1 (0.4%)	0	0	0
クロストリジウム・ディフィシレ感染	0	0	1 (0.4%)	0	0	0
感染性小腸結腸炎	0	0	2 (0.7%)	0	0	0
丹毒	0	0	1 (0.4%)	0	0	0
消化管感染	0	0	1 (0.4%)	0	0	0
ヘモフィルス感染	0	0	1 (0.4%)	0	0	0
帯状疱疹	0	1 (2.3%)	1 (0.4%)	0	0	0
真菌性角膜炎	0	0	1 (0.4%)	0	0	0
限局性感染	0	0	1 (0.4%)	0	0	0
壊死性筋膜炎	0	0	1 (0.4%)	0	0	0
骨髄炎	0	2 (4.5%)	2 (0.7%)	0	0	0
咽頭炎	0	0	1 (0.4%)	0	0	0
肺結核	0	1 (2.3%)	1 (0.4%)	0	0	0
急性腎盂腎炎	0	1 (2.3%)	1 (0.4%)	0	0	0
尿路性敗血症	0	0	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	0	0	1 (0.4%)	0	0	0
代謝および栄養障害	1 (6.7%)	2 (4.5%)	27 (9.6%)	3 (15.0%)	9 (17.6%)	43 (15.2%)
低リン酸血症	1 (6.7%)	1 (2.3%)	6 (2.1%)	1 (5.0%)	2 (3.9%)	12 (4.2%)
高血糖	0	0	9 (3.2%)	2 (10.0%)	3 (5.9%)	10 (3.5%)
低カリウム血症	0	0	6 (2.1%)	0	1 (2.0%)	8 (2.8%)
低ナトリウム血症	0	1 (2.3%)	2 (0.7%)	0	1 (2.0%)	5 (1.8%)
低カルシウム血症	0	0	2 (0.7%)	0	1 (2.0%)	4 (1.4%)
高カルシウム血症	0	0	3 (1.1%)	0	1 (2.0%)	3 (1.1%)
高尿酸血症	0	0	0	0	0	2 (0.7%)
食欲減退	0	1 (2.3%)	1 (0.4%)	0	1 (2.0%)	1 (0.4%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
脱水	0	0	0	0	0	1 (0.4%)
糖尿病	0	0	0	0	0	1 (0.4%)
電解質失調	0	0	0	0	0	1 (0.4%)
低アルブミン血症	0	0	0	0	0	1 (0.4%)
高カリウム血症	0	0	1 (0.4%)	0	0	0
高リン酸塩血症	0	0	1 (0.4%)	0	0	0
低マグネシウム血症	0	0	1 (0.4%)	0	0	0
２型糖尿病	0	0	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	0	1 (2.3%)	21 (7.5%)	0	4 (7.8%)	36 (12.7%)
疲労	0	0	7 (2.5%)	0	1 (2.0%)	18 (6.4%)
無力症	0	1 (2.3%)	7 (2.5%)	0	1 (2.0%)	8 (2.8%)
発熱	0	0	4 (1.4%)	0	2 (3.9%)	5 (1.8%)
全身健康状態低下	0	0	1 (0.4%)	0	0	2 (0.7%)
倦怠感	0	0	0	0	0	2 (0.7%)
末梢性浮腫	0	0	3 (1.1%)	0	0	2 (0.7%)
医薬品副作用	0	0	0	0	0	1 (0.4%)
悪寒	0	0	0	0	1 (2.0%)	1 (0.4%)
運動耐性低下	0	0	0	0	0	1 (0.4%)
冷感	0	0	0	0	1 (2.0%)	1 (0.4%)
歩行障害	0	0	0	0	0	1 (0.4%)
疼痛	0	0	0	0	0	1 (0.4%)
全身性炎症反応症候群	0	0	0	0	0	1 (0.4%)
胸痛	0	0	1 (0.4%)	0	0	0
インフルエンザ様疾患	0	0	1 (0.4%)	0	0	0
胃腸障害	0	3 (6.8%)	16 (5.7%)	0	4 (7.8%)	25 (8.8%)
下痢	0	2 (4.5%)	9 (3.2%)	0	3 (5.9%)	15 (5.3%)
悪心	0	0	0	0	1 (2.0%)	4 (1.4%)
便秘	0	0	2 (0.7%)	0	0	3 (1.1%)
嘔吐	0	0	2 (0.7%)	0	1 (2.0%)	3 (1.1%)
憩室穿孔	0	0	0	0	0	2 (0.7%)
肛門出血	0	0	0	0	0	1 (0.4%)
大腸炎	0	0	1 (0.4%)	0	0	1 (0.4%)
嚥下障害	0	0	0	0	0	1 (0.4%)
胃出血	0	0	0	0	0	1 (0.4%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
出血性胃腸管血管異形成	0	0	0	0	0	1 (0.4%)
胃腸障害	0	0	0	0	0	1 (0.4%)
痔瘻	0	0	1 (0.4%)	0	0	0
潰瘍性大腸炎	0	0	1 (0.4%)	0	0	0
胃障害	0	0	1 (0.4%)	0	0	0
吐血	0	0	1 (0.4%)	0	0	0
腸閉塞	0	0	1 (0.4%)	0	0	0
食道炎	0	1 (2.3%)	1 (0.4%)	0	0	0
呼吸器、胸郭および縦隔障害	0	0	18 (6.4%)	2 (10.0%)	6 (11.8%)	24 (8.5%)
呼吸困難	0	0	2 (0.7%)	1 (5.0%)	1 (2.0%)	9 (3.2%)
肺塞栓症	0	0	9 (3.2%)	0	0	6 (2.1%)
肺水腫	0	0	1 (0.4%)	0	1 (2.0%)	5 (1.8%)
胸水	0	0	0	0	1 (2.0%)	2 (0.7%)
呼吸不全	0	0	1 (0.4%)	0	0	2 (0.7%)
喘鳴	0	0	0	0	1 (2.0%)	2 (0.7%)
急性肺水腫	0	0	0	0	0	1 (0.4%)
気管支痙攣	0	0	1 (0.4%)	0	0	1 (0.4%)
慢性閉塞性肺疾患	0	0	0	0	0	1 (0.4%)
発声障害	0	0	0	0	0	1 (0.4%)
低酸素症	0	0	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
喉頭浮腫	0	0	0	0	0	1 (0.4%)
誤嚥性肺炎	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
急性呼吸不全	0	0	1 (0.4%)	0	0	0
無気肺	0	0	1 (0.4%)	0	0	0
間質性肺疾患	0	0	1 (0.4%)	0	0	0
肺障害	0	0	1 (0.4%)	0	0	0
気胸	0	0	1 (0.4%)	0	0	0
神経系障害	1 (6.7%)	1 (2.3%)	15 (5.3%)	2 (10.0%)	2 (3.9%)	20 (7.1%)
失神	0	0	2 (0.7%)	0	0	10 (3.5%)
末梢性ニューロパチー	0	0	1 (0.4%)	1 (5.0%)	1 (2.0%)	2 (0.7%)
失神寸前の状態	0	0	0	0	0	2 (0.7%)
脳梗塞	0	0	1 (0.4%)	1 (5.0%)	1 (2.0%)	1 (0.4%)
脳血管発作	0	0	0	0	0	1 (0.4%)
認知障害	0	0	0	0	0	1 (0.4%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
嗜眠	0	0	2 (0.7%)	0	0	1 (0.4%)
神経系障害	0	0	1 (0.4%)	0	0	1 (0.4%)
末梢性感覚ニューロパチー	0	0	1 (0.4%)	0	0	1 (0.4%)
振戦	0	0	0	0	0	1 (0.4%)
失語症	0	0	1 (0.4%)	0	0	0
肋間神経痛	0	0	1 (0.4%)	0	0	0
虚血性脳卒中	0	0	1 (0.4%)	0	0	0
記憶障害	0	0	1 (0.4%)	0	0	0
感覚運動障害	0	0	1 (0.4%)	0	0	0
傾眠	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
脊髄圧迫	0	0	1 (0.4%)	0	0	0
血管性脳症	0	0	1 (0.4%)	0	0	0
血管障害	0	0	8 (2.8%)	0	2 (3.9%)	16 (5.7%)
高血圧	0	0	1 (0.4%)	0	1 (2.0%)	9 (3.2%)
深部静脈血栓症	0	0	4 (1.4%)	0	0	2 (0.7%)
低血圧	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)
出血性梗塞	0	0	0	0	0	1 (0.4%)
起立性低血圧	0	0	1 (0.4%)	0	0	1 (0.4%)
末梢動脈狭窄	0	0	0	0	0	1 (0.4%)
血栓症	0	0	0	0	0	1 (0.4%)
静脈炎	0	0	1 (0.4%)	0	0	0
臨床検査	0	1 (2.3%)	6 (2.1%)	5 (25.0%)	6 (11.8%)	15 (5.3%)
アラニンアミノトランスフェラーゼ増加	0	1 (2.3%)	3 (1.1%)	3 (15.0%)	3 (5.9%)	7 (2.5%)
γ－グルタミルトランスフェラーゼ増加	0	0	1 (0.4%)	2 (10.0%)	2 (3.9%)	5 (1.8%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.4%)	1 (5.0%)	1 (2.0%)	3 (1.1%)
国際標準比増加	0	0	0	0	0	2 (0.7%)
血中アルカリホスファターゼ増加	0	0	0	0	0	1 (0.4%)
血中クレアチンホスホキナーゼ増加	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
血圧上昇	0	0	0	0	1 (2.0%)	1 (0.4%)
好中球中毒性顆粒存在	0	0	0	0	0	1 (0.4%)
抗凝固薬濃度治療量以下	0	0	1 (0.4%)	0	0	0
血中乳酸脱水素酵素増加	0	0	1 (0.4%)	0	0	0
Ｃ－反応性蛋白増加	0	0	1 (0.4%)	0	0	0

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
筋骨格系および結合組織障害	0	1 (2.3%)	18 (6.4%)	0	2 (3.9%)	15 (5.3%)
背部痛	0	0	4 (1.4%)	0	0	4 (1.4%)
関節痛	0	0	1 (0.4%)	0	0	2 (0.7%)
骨痛	0	0	1 (0.4%)	0	0	2 (0.7%)
筋痙縮	0	0	5 (1.8%)	0	0	2 (0.7%)
筋萎縮症	0	0	0	0	0	1 (0.4%)
側腹部痛	0	0	0	0	1 (2.0%)	1 (0.4%)
椎間板突出	0	0	0	0	0	1 (0.4%)
筋骨格系胸痛	0	0	0	0	1 (2.0%)	1 (0.4%)
筋骨格痛	0	0	3 (1.1%)	0	0	1 (0.4%)
骨壊死	0	0	0	0	0	1 (0.4%)
結晶性関節障害	0	0	1 (0.4%)	0	0	0
筋力低下	0	0	2 (0.7%)	0	0	0
顎骨壊死	0	1 (2.3%)	2 (0.7%)	0	0	0
四肢痛	0	0	1 (0.4%)	0	0	0
病的骨折	0	0	1 (0.4%)	0	0	0
脊柱管狭窄症	0	0	2 (0.7%)	0	0	0
脊椎痛	0	0	1 (0.4%)	0	0	0
顎関節症候群	0	0	1 (0.4%)	0	0	0
心臓障害	0	0	9 (3.2%)	0	0	9 (3.2%)
心房細動	0	0	3 (1.1%)	0	0	3 (1.1%)
狭心症	0	0	0	0	0	2 (0.7%)
急性冠動脈症候群	0	0	0	0	0	1 (0.4%)
うっ血性心不全	0	0	0	0	0	1 (0.4%)
左室機能不全	0	0	0	0	0	1 (0.4%)
心筋梗塞	0	0	1 (0.4%)	0	0	1 (0.4%)
洞性不整脈	0	0	0	0	0	1 (0.4%)
洞性頻脈	0	0	0	0	0	1 (0.4%)
急性心筋梗塞	0	0	3 (1.1%)	0	0	0
心房粗動	0	0	1 (0.4%)	0	0	0
心膜炎	0	0	1 (0.4%)	0	0	0
上室性頻脈	0	0	1 (0.4%)	0	0	0
眼障害	0	0	4 (1.4%)	0	2 (3.9%)	7 (2.5%)
白内障	0	0	3 (1.1%)	0	2 (3.9%)	6 (2.1%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
後嚢破裂	0	0	0	0	0	1 (0.4%)
網膜症	0	0	1 (0.4%)	0	0	0
精神障害	0	1 (2.3%)	9 (3.2%)	0	0	7 (2.5%)
うつ病	0	0	0	0	0	2 (0.7%)
気分変化	0	0	0	0	0	2 (0.7%)
不安	0	0	2 (0.7%)	0	0	1 (0.4%)
譫妄	0	0	2 (0.7%)	0	0	1 (0.4%)
不眠症	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.4%)
激越	0	0	1 (0.4%)	0	0	0
錯乱状態	0	0	2 (0.7%)	0	0	0
抑うつ気分	0	0	1 (0.4%)	0	0	0
神経過敏	0	0	1 (0.4%)	0	0	0
皮膚および皮下組織障害	0	0	1 (0.4%)	1 (5.0%)	2 (3.9%)	6 (2.1%)
そう痒症	0	0	0	0	0	2 (0.7%)
薬疹	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
全身性皮疹	0	0	0	0	0	1 (0.4%)
斑状皮疹	0	0	0	0	0	1 (0.4%)
斑状丘疹状皮疹	0	0	0	0	1 (2.0%)	1 (0.4%)
丘疹性皮疹	0	0	0	0	0	1 (0.4%)
蕁麻疹	0	0	0	0	1 (2.0%)	1 (0.4%)
寝汗	0	0	1 (0.4%)	0	0	0
腎および尿路障害	1 (6.7%)	2 (4.5%)	14 (5.0%)	0	0	5 (1.8%)
急性腎不全	1 (6.7%)	1 (2.3%)	6 (2.1%)	0	0	1 (0.4%)
慢性腎臓病	0	1 (2.3%)	4 (1.4%)	0	0	1 (0.4%)
腎不全	0	0	5 (1.8%)	0	0	1 (0.4%)
腎機能障害	0	0	1 (0.4%)	0	0	1 (0.4%)
尿路閉塞	0	0	0	0	0	1 (0.4%)
肝胆道系障害	0	0	2 (0.7%)	1 (5.0%)	1 (2.0%)	4 (1.4%)
高ビリルビン血症	0	0	0	0	0	2 (0.7%)
肝機能異常	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
肝細胞損傷	0	0	0	0	0	1 (0.4%)
肝腫瘤	0	0	1 (0.4%)	0	0	0
肝障害	0	0	1 (0.4%)	0	0	0
傷害、中毒および処置合併症	0	1 (2.3%)	9 (3.2%)	0	0	4 (1.4%)

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
足骨折	0	0	0	0	0	1 (0.4%)
手骨折	0	0	0	0	0	1 (0.4%)
股関節部骨折	0	0	1 (0.4%)	0	0	1 (0.4%)
上肢骨折	0	0	0	0	0	1 (0.4%)
鎖骨骨折	0	0	1 (0.4%)	0	0	0
圧迫骨折	0	1 (2.3%)	1 (0.4%)	0	0	0
転倒	0	0	1 (0.4%)	0	0	0
大腿骨頚部骨折	0	0	1 (0.4%)	0	0	0
関節脱臼	0	0	1 (0.4%)	0	0	0
処置後合併症	0	0	1 (0.4%)	0	0	0
橈骨骨折	0	0	1 (0.4%)	0	0	0
硬膜下血腫	0	0	1 (0.4%)	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	9 (3.2%)	1 (5.0%)	1 (2.0%)	3 (1.1%)
急性単球性白血病	0	0	0	0	0	1 (0.4%)
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
形質細胞性白血病	0	0	1 (0.4%)	0	0	1 (0.4%)
基底細胞癌	0	0	1 (0.4%)	0	0	0
膀胱の良性新生物	0	0	1 (0.4%)	0	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0	0
形質細胞腫	0	0	1 (0.4%)	0	0	0
前立腺癌	0	0	1 (0.4%)	0	0	0
直腸腺癌	0	0	1 (0.4%)	0	0	0
扁平上皮癌	0	0	2 (0.7%)	0	0	0
免疫系障害	0	0	0	0	0	1 (0.4%)
低ｙグロブリン血症	0	0	0	0	0	1 (0.4%)
生殖系および乳房障害	0	0	0	0	0	1 (0.4%)
前立腺腫大	0	0	0	0	0	1 (0.4%)
内分泌障害	0	0	1 (0.4%)	0	0	0
ステロイド離脱症候群	0	0	1 (0.4%)	0	0	0

TSFAE03A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term ; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE03A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE03A_3003.SAS] 30JUN2016, 21:40

表 2.7.4-付録-32 Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
Analysis set: safety	237	243			281	318			103		
Total number of subjects with TEAE related to study treatment	196 (82.7%)	225 (92.6%)	182 (74.9%)	219 (90.1%)	233 (82.9%)	304 (95.6%)	245 (77.0%)	298 (93.7%)	100 (97.1%)	95 (92.2%)	97 (94.2%)
MedDRA system organ class/Preferred term											
血液およびリンパ系障害	92 (38.8%)	143 (58.8%)	95 (39.1%)	138 (56.8%)	146 (52.0%)	215 (67.6%)	81 (25.5%)	214 (67.3%)	84 (81.6%)	56 (54.4%)	84 (81.6%)
好中球減少症	13 (5.5%)	34 (14.0%)	17 (7.0%)	33 (13.6%)	107 (38.1%)	185 (58.2%)	60 (18.9%)	184 (57.9%)	78 (75.7%)	45 (43.7%)	78 (75.7%)
血小板減少症	80 (33.8%)	129 (53.1%)	73 (30.0%)	124 (51.0%)	67 (23.8%)	73 (23.0%)	30 (9.4%)	71 (22.3%)	35 (34.0%)	27 (26.2%)	33 (32.0%)
貧血	28 (11.8%)	33 (13.6%)	22 (9.1%)	31 (12.8%)	55 (19.6%)	58 (18.2%)	15 (4.7%)	57 (17.9%)	45 (43.7%)	32 (31.1%)	43 (41.7%)
白血球減少症	8 (3.4%)	15 (6.2%)	10 (4.1%)	15 (6.2%)	12 (4.3%)	28 (8.8%)	17 (5.3%)	27 (8.5%)	37 (35.9%)	26 (25.2%)	37 (35.9%)
リンパ球減少症	7 (3.0%)	29 (11.9%)	26 (10.7%)	25 (10.3%)	12 (4.3%)	19 (6.0%)	11 (3.5%)	18 (5.7%)	17 (16.5%)	16 (15.5%)	17 (16.5%)
発熱性好中球減少症	1 (0.4%)	2 (0.8%)	2 (0.8%)	2 (0.8%)	6 (2.1%)	15 (4.7%)	5 (1.6%)	15 (4.7%)	6 (5.8%)	4 (3.9%)	6 (5.8%)
好酸球増加症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
血液障害	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
溶血	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
出血性障害	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
白血球増加症	1 (0.4%)	0	0	0	2 (0.7%)	0	0	0	0	0	0
リンパ節症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
リンパ球増加症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
鉄芽球性貧血	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
一般・全身障害および投与部位の状態	65 (27.4%)	96 (39.5%)	59 (24.3%)	81 (33.3%)	90 (32.0%)	176 (55.3%)	93 (29.2%)	157 (49.4%)	71 (68.9%)	58 (56.3%)	58 (56.3%)
疲労	35 (14.8%)	40 (16.5%)	27 (11.1%)	38 (15.6%)	56 (19.9%)	95 (29.9%)	39 (12.3%)	91 (28.6%)	43 (41.7%)	26 (25.2%)	42 (40.8%)
無力症	16 (6.8%)	11 (4.5%)	6 (2.5%)	11 (4.5%)	21 (7.5%)	35 (11.0%)	11 (3.5%)	35 (11.0%)	13 (12.6%)	9 (8.7%)	11 (10.7%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
末梢性浮腫	11 (4.6%)	26 (10.7%)	4 (1.6%)	25 (10.3%)	20 (7.1%)	34 (10.7%)	3 (0.9%)	34 (10.7%)	15 (14.6%)	7 (6.8%)	15 (14.6%)
発熱	5 (2.1%)	25 (10.3%)	17 (7.0%)	19 (7.8%)	7 (2.5%)	28 (8.8%)	25 (7.9%)	19 (6.0%)	17 (16.5%)	16 (15.5%)	8 (7.8%)
倦怠感	2 (0.8%)	4 (1.6%)	2 (0.8%)	3 (1.2%)	2 (0.7%)	8 (2.5%)	2 (0.6%)	8 (2.5%)	1 (1.0%)	0	1 (1.0%)
末梢腫脹	0	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	7 (2.2%)	3 (0.9%)	7 (2.2%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
インフルエンザ様疾患	0	3 (1.2%)	3 (1.2%)	2 (0.8%)	2 (0.7%)	6 (1.9%)	4 (1.3%)	3 (0.9%)	2 (1.9%)	1 (1.0%)	1 (1.0%)
浮腫	4 (1.7%)	13 (5.3%)	0	13 (5.3%)	1 (0.4%)	3 (0.9%)	2 (0.6%)	3 (0.9%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
薬物不耐性	0	0	0	0	0	2 (0.6%)	0	2 (0.6%)	0	0	0
びくびく感	0	0	0	0	0	2 (0.6%)	0	2 (0.6%)	2 (1.9%)	0	2 (1.9%)
医薬品副作用	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
悪寒	2 (0.8%)	10 (4.1%)	10 (4.1%)	1 (0.4%)	3 (1.1%)	15 (4.7%)	14 (4.4%)	1 (0.3%)	19 (18.4%)	19 (18.4%)	4 (3.9%)
運動耐性低下	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
顔面浮腫	0	3 (1.2%)	2 (0.8%)	3 (1.2%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
脂肪組織増加	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
熱感	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	0
歩行障害	0	3 (1.2%)	0	3 (1.2%)	0	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	1 (1.0%)	2 (1.9%)
全身健康状態低下	0	0	0	0	1 (0.4%)	2 (0.6%)	2 (0.6%)	1 (0.3%)	0	0	0
空腹	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
炎症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
多臓器不全	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
疼痛	2 (0.8%)	4 (1.6%)	4 (1.6%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	4 (3.9%)	4 (3.9%)	3 (2.9%)
全身性炎症反応症候群	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
胸部不快感	1 (0.4%)	2 (0.8%)	2 (0.8%)	0	0	5 (1.6%)	5 (1.6%)	0	2 (1.9%)	2 (1.9%)	1 (1.0%)
胸痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
溢出	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
異常感	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
冷感	0	0	0	0	0	5 (1.6%)	5 (1.6%)	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
全身性浮腫	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
高熱	1 (0.4%)	0	0	0	0	1 (0.3%)	1 (0.3%)	0	2 (1.9%)	2 (1.9%)	0
低体温	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
注入部位紅斑	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
注入部位そう痒感	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
注入部位発疹	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
注射部位内出血	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
注射部位紅斑	6 (2.5%)	6 (2.5%)	0	6 (2.5%)	0	0	0	0	0	0	0
注射部位炎症	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
注射部位刺激感	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
注射部位浮腫	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
注射部位疼痛	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
注射部位発疹	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
注射部位反応	2 (0.8%)	4 (1.6%)	0	4 (1.6%)	0	0	0	0	0	0	0
注射部位腫脹	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
局所腫脹	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
限局性浮腫	1 (0.4%)	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
非心臓性胸痛	0	0	0	0	0	2 (0.6%)	2 (0.6%)	0	5 (4.9%)	3 (2.9%)	2 (1.9%)
粘膜浮腫	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
分泌物分泌	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
異物感	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
苦悶感	0	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0	0	0
胃腸障害	72 (30.4%)	100 (41.2%)	50 (20.6%)	85 (35.0%)	90 (32.0%)	173 (54.4%)	86 (27.0%)	150 (47.2%)	56 (54.4%)	30 (29.1%)	50 (48.5%)
下痢	29 (12.2%)	48 (19.8%)	19 (7.8%)	42 (17.3%)	30 (10.7%)	94 (29.6%)	34 (10.7%)	91 (28.6%)	26 (25.2%)	14 (13.6%)	23 (22.3%)
便秘	25 (10.5%)	30 (12.3%)	9 (3.7%)	29 (11.9%)	42 (14.9%)	47 (14.8%)	14 (4.4%)	46 (14.5%)	21 (20.4%)	5 (4.9%)	21 (20.4%)
悪心	11 (4.6%)	25 (10.3%)	16 (6.6%)	16 (6.6%)	15 (5.3%)	44 (13.8%)	31 (9.7%)	27 (8.5%)	20 (19.4%)	18 (17.5%)	14 (13.6%)
上腹部痛	5 (2.1%)	5 (2.1%)	1 (0.4%)	4 (1.6%)	5 (1.8%)	16 (5.0%)	4 (1.3%)	16 (5.0%)	4 (3.9%)	1 (1.0%)	4 (3.9%)
消化不良	11 (4.6%)	4 (1.6%)	2 (0.8%)	2 (0.8%)	4 (1.4%)	11 (3.5%)	1 (0.3%)	10 (3.1%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
口内炎	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	4 (1.4%)	9 (2.8%)	6 (1.9%)	8 (2.5%)	1 (1.0%)	0	1 (1.0%)
嘔吐	5 (2.1%)	18 (7.4%)	12 (4.9%)	7 (2.9%)	2 (0.7%)	27 (8.5%)	26 (8.2%)	8 (2.5%)	10 (9.7%)	9 (8.7%)	6 (5.8%)
腹痛	5 (2.1%)	6 (2.5%)	0	6 (2.5%)	4 (1.4%)	9 (2.8%)	5 (1.6%)	7 (2.2%)	6 (5.8%)	2 (1.9%)	5 (4.9%)
腹部不快感	2 (0.8%)	5 (2.1%)	1 (0.4%)	4 (1.6%)	2 (0.7%)	5 (1.6%)	2 (0.6%)	5 (1.6%)	0	0	0
腹部膨満	5 (2.1%)	5 (2.1%)	1 (0.4%)	5 (2.1%)	3 (1.1%)	5 (1.6%)	1 (0.3%)	5 (1.6%)	2 (1.9%)	0	2 (1.9%)
口内乾燥	0	0	0	0	3 (1.1%)	5 (1.6%)	2 (0.6%)	5 (1.6%)	0	0	0
憩室穿孔	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	0	2 (0.6%)	0	0	0
放屁	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	2 (1.9%)	1 (1.0%)	1 (1.0%)
胃炎	1 (0.4%)	3 (1.2%)	0	3 (1.2%)	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
胃腸障害	1 (0.4%)	0	0	0	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
胃食道逆流性疾患	1 (0.4%)	3 (1.2%)	0	3 (1.2%)	2 (0.7%)	3 (0.9%)	1 (0.3%)	2 (0.6%)	4 (3.9%)	0	4 (3.9%)
口腔内痛	1 (0.4%)	0	0	0	2 (0.7%)	2 (0.6%)	0	2 (0.6%)	0	0	0
腹壁血腫	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
裂肛	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
胆汁酸吸収不良	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
便通不規則	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
大腸炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
心窩部不快感	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
おくび	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
胃拡張	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
胃出血	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
痔核	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
口の感覚鈍麻	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
口腔内潰瘍形成	1 (0.4%)	0	0	0	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
非感染性歯肉炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
口腔粘膜水疱形成	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	1 (1.0%)	2 (1.9%)
口の錯感覚	0	0	0	0	0	2 (0.6%)	2 (0.6%)	1 (0.3%)	0	0	0
肛門出血	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
アフタ性口内炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
齲歯	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
十二指腸潰瘍	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
嚥下障害	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
糞塊	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0	0
胃障害	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
消化管運動障害	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
消化器痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
舌痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
イレウス	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
腸閉塞	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
腸管穿孔	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
口唇そう痒症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
口唇腫脹	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
メレナ	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
嚥下痛	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
食道炎	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
口腔内不快感	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
口腔障害	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
口蓋浮腫	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
膵炎	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0	0
歯の知覚過敏	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
小腸閉塞	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	1 (1.0%)	0	1 (1.0%)
地図状舌	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
舌そう痒症	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
舌潰瘍	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
上部消化管出血	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
感染症および寄生虫症	59 (24.9%)	80 (32.9%)	41 (16.9%)	79 (32.5%)	88 (31.3%)	132 (41.5%)	86 (27.0%)	129 (40.6%)	41 (39.8%)	35 (34.0%)	39 (37.9%)
上気道感染	16 (6.8%)	25 (10.3%)	15 (6.2%)	23 (9.5%)	15 (5.3%)	38 (11.9%)	28 (8.8%)	36 (11.3%)	15 (14.6%)	12 (11.7%)	15 (14.6%)
肺炎	15 (6.3%)	18 (7.4%)	11 (4.5%)	17 (7.0%)	14 (5.0%)	24 (7.5%)	13 (4.1%)	24 (7.5%)	6 (5.8%)	5 (4.9%)	6 (5.8%)
気管支炎	7 (3.0%)	12 (4.9%)	7 (2.9%)	10 (4.1%)	13 (4.6%)	20 (6.3%)	14 (4.4%)	20 (6.3%)	7 (6.8%)	5 (4.9%)	6 (5.8%)
鼻咽頭炎	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	7 (2.5%)	12 (3.8%)	7 (2.2%)	12 (3.8%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
気道感染	1 (0.4%)	0	0	0	8 (2.8%)	12 (3.8%)	8 (2.5%)	11 (3.5%)	0	0	0
下気道感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	5 (1.8%)	7 (2.2%)	3 (0.9%)	7 (2.2%)	0	0	0
帯状疱疹	5 (2.1%)	8 (3.3%)	4 (1.6%)	8 (3.3%)	3 (1.1%)	6 (1.9%)	6 (1.9%)	6 (1.9%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
インフルエンザ	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	5 (1.6%)	4 (1.3%)	5 (1.6%)	2 (1.9%)	1 (1.0%)	2 (1.9%)
口腔カンジダ症	4 (1.7%)	2 (0.8%)	0	2 (0.8%)	2 (0.7%)	5 (1.6%)	0	5 (1.6%)	0	0	0
感染	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	4 (1.3%)	2 (0.6%)	4 (1.3%)	0	0	0
口腔真菌感染	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	3 (1.1%)	4 (1.3%)	1 (0.3%)	4 (1.3%)	0	0	0
副鼻腔炎	2 (0.8%)	6 (2.5%)	2 (0.8%)	6 (2.5%)	2 (0.7%)	4 (1.3%)	2 (0.6%)	4 (1.3%)	4 (3.9%)	3 (2.9%)	4 (3.9%)
尿路感染	1 (0.4%)	5 (2.1%)	1 (0.4%)	4 (1.6%)	1 (0.4%)	4 (1.3%)	2 (0.6%)	4 (1.3%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
ヘルペスウイルス感染	0	0	0	0	0	3 (0.9%)	2 (0.6%)	3 (0.9%)	0	0	0
肺感染	1 (0.4%)	0	0	0	1 (0.4%)	3 (0.9%)	1 (0.3%)	3 (0.9%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
口腔ヘルペス	2 (0.8%)	4 (1.6%)	0	4 (1.6%)	0	3 (0.9%)	3 (0.9%)	3 (0.9%)	1 (1.0%)	0	1 (1.0%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
インフルエンザ性肺炎	0	0	0	0	0	3 (0.9%)	1 (0.3%)	3 (0.9%)	0	0	0
気管支肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
蜂巣炎	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	2 (1.9%)	1 (1.0%)	2 (1.9%)
真菌感染	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
胃腸炎	2 (0.8%)	0	0	0	1 (0.4%)	2 (0.6%)	0	2 (0.6%)	0	0	0
歯肉炎	0	0	0	0	2 (0.7%)	2 (0.6%)	0	2 (0.6%)	0	0	0
咽頭炎	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	4 (1.4%)	2 (0.6%)	2 (0.6%)	2 (0.6%)	0	0	0
ＲＳウイルス感染	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
鼻炎	1 (0.4%)	4 (1.6%)	1 (0.4%)	4 (1.6%)	1 (0.4%)	3 (0.9%)	3 (0.9%)	2 (0.6%)	3 (2.9%)	3 (2.9%)	2 (1.9%)
皮膚感染	1 (0.4%)	0	0	0	3 (1.1%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
ウイルス感染	0	0	0	0	4 (1.4%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
ウイルス性上気道感染	0	1 (0.4%)	0	1 (0.4%)	0	2 (0.6%)	2 (0.6%)	2 (0.6%)	0	0	0
急性扁桃炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
細菌感染	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
細気管支炎	0	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
細菌性気管支炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
カンピロバクター胃腸炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
結膜炎	2 (0.8%)	9 (3.7%)	4 (1.6%)	7 (2.9%)	0	4 (1.3%)	4 (1.3%)	1 (0.3%)	2 (1.9%)	0	2 (1.9%)
コロナウイルス感染	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
サイトメガロウイルス感染	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
大腸菌性菌血症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
ウイルス性胃腸炎	1 (0.4%)	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
リステリア性敗血症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
大葉性肺炎	1 (0.4%)	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
ウイルス性下気道感染	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
粘膜感染	1 (0.4%)	0	0	0	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
中咽頭カンジダ症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
急性中耳炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
耳下腺炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
眼窩周囲蜂巣炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
レンサ球菌性咽頭炎	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
細菌性肺炎	0	0	0	0	0	2 (0.6%)	2 (0.6%)	1 (0.3%)	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
ウイルス性肺炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
腎盂腎炎	0	1 (0.4%)	0	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
膿疱性皮疹	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
呼吸器モニリア症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
敗血症	1 (0.4%)	2 (0.8%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	3 (2.9%)	2 (1.9%)	3 (2.9%)
敗血症性ショック	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
皮下組織膿瘍	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
足部白癬	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
扁桃炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
細菌性上気道感染	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
尿道炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
外陰部腟カンジダ症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
四肢膿瘍	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
急性副鼻腔炎	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
肛門膿瘍	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
体部白癬	1 (0.4%)	0	0	0	0	0	0	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
ウイルス性気管支炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
カンジダ感染	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
細菌性結膜炎	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
膀胱炎	0	0	0	0	3 (1.1%)	0	0	0	0	0	0
医療機器関連感染	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
憩室炎	0	0	0	0	0	0	0	0	2 (1.9%)	2 (1.9%)	2 (1.9%)
耳感染	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
蓄膿	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
感染性小腸結腸炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
丹毒	0	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0	0	0
伝染性紅斑	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
眼感染	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0	0
真菌性眼感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
眼瞼感染	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
熱性感染症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
毛包炎	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
皮膚真菌感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
せつ	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
消化管感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
陰部ヘルペス	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
真菌性性器感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
単純ヘルペス	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
麦粒腫	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
感染性筋炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
注入部位蜂巣炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
真菌性角膜炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
喉頭炎	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	2 (1.9%)	2 (1.9%)	2 (1.9%)
限局性感染	0	0	0	0	2 (0.7%)	0	0	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
乳腺炎	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
鼻ヘルペス	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
食道カンジダ症	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
眼部単純ヘルペス	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
中耳炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
腹膜炎	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
百日咳	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
サイトメガロウイルス性肺炎	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	0	0	0	0	0	0	0
肺炎球菌性肺炎	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
進行性多巣性白質脳症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
シュードモナス性敗血症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
肺敗血症	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
ウイルス性気道感染	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
ライノウイルス感染	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
唾液腺炎	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
皮膚カンジダ	0	0	0	0	2 (0.7%)	0	0	0	0	0	0
ブドウ球菌性咽頭炎	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
癜風	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
真菌性舌感染	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
歯膿瘍	0	0	0	0	4 (1.4%)	0	0	0	0	0	0
歯感染	0	0	0	0	2 (0.7%)	0	0	0	2 (1.9%)	2 (1.9%)	2 (1.9%)
気管気管支炎	1 (0.4%)	0	0	0	0	0	0	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
腟感染	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
水痘	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
ウイルス性咽頭炎	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
ウイルス性ぶどう膜炎	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
外陰腟真菌感染	0	0	0	0	0	0	0	0	2 (1.9%)	1 (1.0%)	2 (1.9%)
外陰部腟炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
創傷感染	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
筋骨格系および結合組織障害	24 (10.1%)	45 (18.5%)	12 (4.9%)	40 (16.5%)	68 (24.2%)	115 (36.2%)	32 (10.1%)	108 (34.0%)	36 (35.0%)	17 (16.5%)	34 (33.0%)
筋痙縮	3 (1.3%)	13 (5.3%)	1 (0.4%)	13 (5.3%)	40 (14.2%)	77 (24.2%)	16 (5.0%)	77 (24.2%)	24 (23.3%)	9 (8.7%)	23 (22.3%)
筋力低下	5 (2.1%)	3 (1.2%)	0	3 (1.2%)	15 (5.3%)	19 (6.0%)	1 (0.3%)	19 (6.0%)	6 (5.8%)	1 (1.0%)	6 (5.8%)
筋肉痛	4 (1.7%)	7 (2.9%)	1 (0.4%)	7 (2.9%)	5 (1.8%)	9 (2.8%)	3 (0.9%)	8 (2.5%)	6 (5.8%)	5 (4.9%)	4 (3.9%)
四肢痛	7 (3.0%)	10 (4.1%)	2 (0.8%)	10 (4.1%)	6 (2.1%)	6 (1.9%)	1 (0.3%)	6 (1.9%)	1 (1.0%)	0	1 (1.0%)
関節痛	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	3 (1.1%)	5 (1.6%)	2 (0.6%)	5 (1.6%)	4 (3.9%)	3 (2.9%)	3 (2.9%)
背部痛	3 (1.3%)	4 (1.6%)	4 (1.6%)	0	1 (0.4%)	8 (2.5%)	7 (2.2%)	5 (1.6%)	4 (3.9%)	3 (2.9%)	2 (1.9%)
骨痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	3 (0.9%)	2 (0.6%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	0
筋肉疲労	0	1 (0.4%)	0	1 (0.4%)	0	2 (0.6%)	0	2 (0.6%)	0	0	0
ミオパチー	2 (0.8%)	7 (2.9%)	1 (0.4%)	7 (2.9%)	3 (1.1%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
骨壊死	0	0	0	0	0	2 (0.6%)	0	2 (0.6%)	0	0	0
筋萎縮症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
側腹部痛	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
出血性関節症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
関節腫脹	0	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	3 (2.9%)	0	3 (2.9%)
運動性低下	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
筋骨格系胸痛	0	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	4 (1.3%)	3 (0.9%)	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
顎骨壊死	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
脊椎障害	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
腱痛	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
デュプイトラン拘縮	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
関節滲出液	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
四肢不快感	2 (0.8%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
筋緊張	0	0	0	0	1 (0.4%)	0	0	0	1 (1.0%)	1 (1.0%)	0
筋攣縮	2 (0.8%)	0	0	0	0	0	0	0	0	0	0
筋骨格痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	2 (0.6%)	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
筋骨格硬直	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
頚部痛	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0	0	0
変形性関節症	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
骨粗鬆症	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
脊椎痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
神経系障害	111 (46.8%)	134 (55.1%)	24 (9.9%)	131 (53.9%)	84 (29.9%)	112 (35.2%)	37 (11.6%)	104 (32.7%)	41 (39.8%)	20 (19.4%)	38 (36.9%)
振戦	7 (3.0%)	2 (0.8%)	0	2 (0.8%)	21 (7.5%)	25 (7.9%)	4 (1.3%)	25 (7.9%)	19 (18.4%)	5 (4.9%)	19 (18.4%)
末梢性感覚ニューロパチー	84 (35.4%)	115 (47.3%)	7 (2.9%)	115 (47.3%)	11 (3.9%)	21 (6.6%)	4 (1.3%)	21 (6.6%)	7 (6.8%)	4 (3.9%)	7 (6.8%)
味覚異常	9 (3.8%)	7 (2.9%)	2 (0.8%)	7 (2.9%)	13 (4.6%)	18 (5.7%)	5 (1.6%)	17 (5.3%)	3 (2.9%)	1 (1.0%)	3 (2.9%)
浮動性めまい	18 (7.6%)	12 (4.9%)	4 (1.6%)	9 (3.7%)	14 (5.0%)	15 (4.7%)	6 (1.9%)	13 (4.1%)	12 (11.7%)	6 (5.8%)	11 (10.7%)
頭痛	6 (2.5%)	9 (3.7%)	5 (2.1%)	6 (2.5%)	10 (3.6%)	18 (5.7%)	13 (4.1%)	9 (2.8%)	7 (6.8%)	5 (4.9%)	6 (5.8%)
末梢性ニューロパチー	0	1 (0.4%)	0	1 (0.4%)	7 (2.5%)	10 (3.1%)	1 (0.3%)	9 (2.8%)	5 (4.9%)	1 (1.0%)	5 (4.9%)
感覚鈍麻	3 (1.3%)	2 (0.8%)	0	2 (0.8%)	2 (0.7%)	6 (1.9%)	0	6 (1.9%)	0	0	0
錯感覚	9 (3.8%)	11 (4.5%)	3 (1.2%)	10 (4.1%)	4 (1.4%)	8 (2.5%)	3 (0.9%)	6 (1.9%)	4 (3.9%)	2 (1.9%)	2 (1.9%)
嗜眠	2 (0.8%)	5 (2.1%)	0	5 (2.1%)	3 (1.1%)	5 (1.6%)	2 (0.6%)	5 (1.6%)	0	0	0
味覚消失	1 (0.4%)	0	0	0	1 (0.4%)	4 (1.3%)	1 (0.3%)	4 (1.3%)	0	0	0
注意力障害	1 (0.4%)	3 (1.2%)	2 (0.8%)	3 (1.2%)	1 (0.4%)	3 (0.9%)	2 (0.6%)	3 (0.9%)	0	0	0
失神	0	0	0	0	0	4 (1.3%)	2 (0.6%)	3 (0.9%)	0	0	0
平衡障害	3 (1.3%)	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
異常感覚	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
記憶障害	0	3 (1.2%)	2 (0.8%)	3 (1.2%)	5 (1.8%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	3 (2.9%)	2 (1.9%)	3 (2.9%)
神経痛	25 (10.5%)	33 (13.6%)	0	33 (13.6%)	2 (0.7%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
失神寸前の状態	1 (0.4%)	3 (1.2%)	1 (0.4%)	3 (1.2%)	0	4 (1.3%)	2 (0.6%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	0
脳血管発作	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
体位性めまい	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
構語障害	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
知覚過敏	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
筋痙直	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
神経系障害	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
嗅覚錯誤	1 (0.4%)	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
精神運動亢進	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
副鼻腔炎に伴う頭痛	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
一過性脳虚血発作	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0	1 (0.3%)	0	0	0
視野欠損	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
アカシジア	0	0	0	0	2 (0.7%)	0	0	0	0	0	0
異痛症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
健忘	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
無嗅覚	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
失語症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
運動失調	2 (0.8%)	0	0	0	0	0	0	0	2 (1.9%)	0	2 (1.9%)
自律神経ニューロパチー	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
灼熱感	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
粘膜の灼熱感	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
脳梗塞	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
脳虚血	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
認知障害	1 (0.4%)	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
塞栓性脳卒中	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
脳症	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
蟻走感	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
頭部不快感	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
不全片麻痺	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
過眠症	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
味覚減退	0	0	0	0	2 (0.7%)	0	0	0	0	0	0
筋緊張低下	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
企図振戦	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
肋間神経痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
虚血性脳卒中	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
意識消失	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
精神的機能障害	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
片頭痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
不随意性筋収縮	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
末梢性運動ニューロパチー	5 (2.1%)	8 (3.3%)	0	8 (3.3%)	0	0	0	0	0	0	0
末梢性感覚運動ニューロパチー	2 (0.8%)	2 (0.8%)	0	2 (0.8%)	0	0	0	0	0	0	0
腓骨神経麻痺	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
ヘルペス後神経痛	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0	0
下肢静止不能症候群	2 (0.8%)	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	0	0	0	0	0	0
傾眠	0	0	0	0	3 (1.1%)	0	0	0	0	0	0
会話障害	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
脊髄圧迫	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
上位運動ニューロンの病変	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
第７脳神経麻痺	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
第６脳神経麻痺	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
血管性脳症	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
精神障害	44 (18.6%)	48 (19.8%)	10 (4.1%)	45 (18.5%)	76 (27.0%)	84 (26.4%)	7 (2.2%)	84 (26.4%)	36 (35.0%)	6 (5.8%)	36 (35.0%)
不眠症	30 (12.7%)	31 (12.8%)	7 (2.9%)	29 (11.9%)	47 (16.7%)	51 (16.0%)	3 (0.9%)	51 (16.0%)	21 (20.4%)	0	21 (20.4%)
うつ病	3 (1.3%)	2 (0.8%)	0	2 (0.8%)	2 (0.7%)	12 (3.8%)	2 (0.6%)	12 (3.8%)	3 (2.9%)	2 (1.9%)	3 (2.9%)
不安	5 (2.1%)	2 (0.8%)	0	2 (0.8%)	8 (2.8%)	10 (3.1%)	1 (0.3%)	9 (2.8%)	10 (9.7%)	3 (2.9%)	10 (9.7%)
激越	5 (2.1%)	4 (1.6%)	1 (0.4%)	4 (1.6%)	8 (2.8%)	7 (2.2%)	0	7 (2.2%)	3 (2.9%)	0	3 (2.9%)
気分変化	0	1 (0.4%)	0	1 (0.4%)	5 (1.8%)	7 (2.2%)	0	7 (2.2%)	0	0	0
易刺激性	4 (1.7%)	3 (1.2%)	0	3 (1.2%)	5 (1.8%)	6 (1.9%)	0	6 (1.9%)	4 (3.9%)	0	4 (3.9%)
抑うつ気分	0	0	0	0	1 (0.4%)	4 (1.3%)	0	4 (1.3%)	0	0	0
落ち着きのなさ	6 (2.5%)	6 (2.5%)	1 (0.4%)	6 (2.5%)	4 (1.4%)	4 (1.3%)	1 (0.3%)	4 (1.3%)	1 (1.0%)	0	1 (1.0%)
気分動揺	0	2 (0.8%)	0	2 (0.8%)	1 (0.4%)	3 (0.9%)	0	3 (0.9%)	1 (1.0%)	0	1 (1.0%)
睡眠障害	2 (0.8%)	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	3 (0.9%)	0	3 (0.9%)	2 (1.9%)	0	2 (1.9%)
精神障害	0	0	0	0	1 (0.4%)	2 (0.6%)	0	2 (0.6%)	0	0	0
感情障害	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
攻撃性	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
錯乱状態	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	1 (1.0%)	2 (1.9%)
感情不安定	0	0	0	0	0	0	0	0	2 (1.9%)	0	2 (1.9%)
譫妄	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
まとまりのない会話	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
転導性	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
気分変調性障害	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
感情的苦悩	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
幻覚	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
リビドー減退	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
言葉もれ	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
リビドー消失	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
精神状態変化	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
神経過敏	1 (0.4%)	0	0	0	5 (1.8%)	0	0	0	0	0	0
妄想症	1 (0.4%)	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
精神的機能代償不全	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
精神病性障害	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
ストレス	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
物質誘発性精神病性障害	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
自殺念慮	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
代謝および栄養障害	34 (14.3%)	53 (21.8%)	18 (7.4%)	50 (20.6%)	43 (15.3%)	66 (20.8%)	19 (6.0%)	64 (20.1%)	27 (26.2%)	15 (14.6%)	25 (24.3%)
高血糖	14 (5.9%)	19 (7.8%)	0	19 (7.8%)	17 (6.0%)	22 (6.9%)	2 (0.6%)	22 (6.9%)	9 (8.7%)	0	9 (8.7%)
食欲減退	7 (3.0%)	11 (4.5%)	6 (2.5%)	10 (4.1%)	9 (3.2%)	21 (6.6%)	8 (2.5%)	19 (6.0%)	8 (7.8%)	4 (3.9%)	7 (6.8%)
低カリウム血症	6 (2.5%)	12 (4.9%)	3 (1.2%)	12 (4.9%)	12 (4.3%)	14 (4.4%)	5 (1.6%)	13 (4.1%)	9 (8.7%)	5 (4.9%)	7 (6.8%)
低カルシウム血症	0	0	0	0	2 (0.7%)	8 (2.5%)	5 (1.6%)	8 (2.5%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
低リン酸血症	3 (1.3%)	4 (1.6%)	4 (1.6%)	3 (1.2%)	6 (2.1%)	7 (2.2%)	1 (0.3%)	7 (2.2%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
低マグネシウム血症	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	3 (0.9%)	1 (0.3%)	3 (0.9%)	3 (2.9%)	2 (1.9%)	2 (1.9%)
脱水	0	1 (0.4%)	0	1 (0.4%)	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
糖尿病	2 (0.8%)	7 (2.9%)	0	7 (2.9%)	0	2 (0.6%)	0	2 (0.6%)	1 (1.0%)	0	1 (1.0%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
低ナトリウム血症	3 (1.3%)	3 (1.2%)	1 (0.4%)	3 (1.2%)	0	2 (0.6%)	2 (0.6%)	2 (0.6%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
体液貯留	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	0	1 (0.3%)	0	1 (0.3%)	0	0	0
葉酸欠乏	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
痛風	0	0	0	0	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
高コレステロール血症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
１型糖尿病	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
コントロール不良の糖尿病	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
糖尿病性ケトアシドーシス	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
水分過負荷	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
高カルシウム血症	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
高クレアチニン血症	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
高カリウム血症	1 (0.4%)	0	0	0	0	0	0	0	2 (1.9%)	2 (1.9%)	2 (1.9%)
高脂血症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
高ナトリウム血症	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
高トリグリセリド血症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
高尿酸血症	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
低アルブミン血症	1 (0.4%)	3 (1.2%)	1 (0.4%)	3 (1.2%)	3 (1.1%)	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	0
低血糖症	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
食欲亢進	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	1 (1.0%)	0	1 (1.0%)
多飲症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
腫瘍崩壊症候群	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
２型糖尿病	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
ビタミンＢ１２欠乏	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
皮膚および皮下組織障害	10 (4.2%)	28 (11.5%)	20 (8.2%)	16 (6.6%)	48 (17.1%)	86 (27.0%)	50 (15.7%)	62 (19.5%)	27 (26.2%)	16 (15.5%)	24 (23.3%)
発疹	0	6 (2.5%)	4 (1.6%)	4 (1.6%)	15 (5.3%)	23 (7.2%)	8 (2.5%)	19 (6.0%)	3 (2.9%)	2 (1.9%)	3 (2.9%)
そう痒症	1 (0.4%)	3 (1.2%)	3 (1.2%)	0	18 (6.4%)	22 (6.9%)	18 (5.7%)	13 (4.1%)	8 (7.8%)	7 (6.8%)	7 (6.8%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
多汗症	3 (1.3%)	3 (1.2%)	1 (0.4%)	2 (0.8%)	4 (1.4%)	16 (5.0%)	11 (3.5%)	8 (2.5%)	5 (4.9%)	3 (2.9%)	3 (2.9%)
斑状丘疹状皮疹	0	4 (1.6%)	3 (1.2%)	2 (0.8%)	2 (0.7%)	5 (1.6%)	4 (1.3%)	4 (1.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
斑状出血	0	0	0	0	1 (0.4%)	3 (0.9%)	0	3 (0.9%)	2 (1.9%)	0	2 (1.9%)
全身性皮疹	0	0	0	0	3 (1.1%)	3 (0.9%)	1 (0.3%)	3 (0.9%)	4 (3.9%)	1 (1.0%)	4 (3.9%)
ざ瘡様皮膚炎	0	0	0	0	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
皮膚乾燥	1 (0.4%)	0	0	0	2 (0.7%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
紅斑	1 (0.4%)	3 (1.2%)	2 (0.8%)	1 (0.4%)	4 (1.4%)	5 (1.6%)	3 (0.9%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	0
点状出血	1 (0.4%)	0	0	0	0	2 (0.6%)	0	2 (0.6%)	0	0	0
斑状皮疹	0	0	0	0	1 (0.4%)	2 (0.6%)	0	2 (0.6%)	0	0	0
日光角化症	0	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
褥瘡性潰瘍	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
皮膚炎	1 (0.4%)	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
アレルギー性皮膚炎	0	2 (0.8%)	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
薬疹	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
湿疹	0	2 (0.8%)	0	2 (0.8%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
多形紅斑	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	2 (1.9%)	1 (1.0%)
紅色症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
全身紅斑	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
毛髪成長異常	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
手皮膚炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
男性型多毛症	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
寝汗	1 (0.4%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
爪甲脱落症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
皮膚疼痛	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
丘疹性皮疹	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
皮膚脆弱性	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
皮膚色素過剰	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
皮膚病変	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
皮膚潰瘍	0	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
顔面腫脹	0	1 (0.4%)	1 (0.4%)	0	3 (1.1%)	1 (0.3%)	0	1 (0.3%)	0	0	0
蕁麻疹	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	5 (1.6%)	5 (1.6%)	1 (0.3%)	0	0	0
血管炎性皮疹	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
脱毛症	1 (0.4%)	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
冷汗	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	0	1 (1.0%)
接触性皮膚炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
毛質異常	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
多毛症	0	0	0	0	1 (0.4%)	0	0	0	1 (1.0%)	0	1 (1.0%)
皮膚粘膜発疹	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
爪破損	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
手掌・足底発赤知覚不全症候群	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0	0
光線過敏性反応	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
粃糠疹	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
ばら色粃糠疹	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
アレルギー性そう痒症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
全身性そう痒症	0	0	0	0	0	0	0	0	2 (1.9%)	1 (1.0%)	2 (1.9%)
壊疽性膿皮症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
紅斑性皮疹	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
そう痒性皮疹	0	0	0	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
皮膚障害	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
皮膚剥脱	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
皮膚亀裂	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
皮膚出血	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
皮膚反応	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
うっ滞性皮膚炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
毛細血管拡張症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	30 (12.7%)	103 (42.4%)	96 (39.5%)	33 (13.6%)	43 (15.3%)	141 (44.3%)	119 (37.4%)	61 (19.2%)	58 (56.3%)	56 (54.4%)	28 (27.2%)
咳嗽	7 (3.0%)	33 (13.6%)	27 (11.1%)	14 (5.8%)	4 (1.4%)	47 (14.8%)	43 (13.5%)	20 (6.3%)	21 (20.4%)	19 (18.4%)	8 (7.8%)
呼吸困難	10 (4.2%)	36 (14.8%)	32 (13.2%)	7 (2.9%)	12 (4.3%)	37 (11.6%)	34 (10.7%)	11 (3.5%)	17 (16.5%)	17 (16.5%)	8 (7.8%)
肺塞栓症	0	0	0	0	11 (3.9%)	9 (2.8%)	1 (0.3%)	9 (2.8%)	1 (1.0%)	0	1 (1.0%)
発声障害	4 (1.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	5 (1.8%)	11 (3.5%)	5 (1.6%)	8 (2.5%)	3 (2.9%)	3 (2.9%)	3 (2.9%)
しゃっくり	3 (1.3%)	0	0	0	6 (2.1%)	7 (2.2%)	1 (0.3%)	6 (1.9%)	3 (2.9%)	1 (1.0%)	3 (2.9%)
湿性咳嗽	1 (0.4%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	2 (0.7%)	7 (2.2%)	5 (1.6%)	5 (1.6%)	5 (4.9%)	5 (4.9%)	4 (3.9%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
アレルギー性鼻炎	0	4 (1.6%)	3 (1.2%)	1 (0.4%)	0	14 (4.4%)	12 (3.8%)	5 (1.6%)	2 (1.9%)	2 (1.9%)	1 (1.0%)
労作性呼吸困難	4 (1.7%)	4 (1.6%)	3 (1.2%)	3 (1.2%)	0	5 (1.6%)	4 (1.3%)	2 (0.6%)	2 (1.9%)	2 (1.9%)	2 (1.9%)
肺臓炎	0	0	0	0	0	2 (0.6%)	2 (0.6%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
肺水腫	1 (0.4%)	0	0	0	0	3 (0.9%)	1 (0.3%)	2 (0.6%)	0	0	0
気管支拡張症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
慢性閉塞性肺疾患	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
鼻出血	4 (1.7%)	5 (2.1%)	3 (1.2%)	5 (2.1%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
胸水症	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0	1 (0.3%)	0	0	0
低酸素症	0	0	0	0	0	6 (1.9%)	6 (1.9%)	1 (0.3%)	4 (3.9%)	3 (2.9%)	2 (1.9%)
肺障害	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
鼻閉	0	11 (4.5%)	11 (4.5%)	1 (0.4%)	0	10 (3.1%)	10 (3.1%)	1 (0.3%)	9 (8.7%)	9 (8.7%)	1 (1.0%)
咽頭紅斑	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
誤嚥性肺炎	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
副鼻腔うっ血	1 (0.4%)	0	0	0	0	2 (0.6%)	1 (0.3%)	1 (0.3%)	1 (1.0%)	1 (1.0%)	0
咽喉刺激感	1 (0.4%)	12 (4.9%)	12 (4.9%)	0	0	9 (2.8%)	9 (2.8%)	1 (0.3%)	8 (7.8%)	8 (7.8%)	1 (1.0%)
喘鳴	0	5 (2.1%)	5 (2.1%)	1 (0.4%)	0	7 (2.2%)	7 (2.2%)	1 (0.3%)	6 (5.8%)	6 (5.8%)	0
アレルギー性咳嗽	0	2 (0.8%)	2 (0.8%)	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
アレルギー性呼吸器症状	0	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0	0	0
窒息	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
喘息	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
気管支反応性亢進	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
慢性気管支炎	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
気管支肺症	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
気管支痙攣	0	22 (9.1%)	22 (9.1%)	0	0	14 (4.4%)	14 (4.4%)	0	0	0	0
カタル	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
喀血	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
間質性肺疾患	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
喉頭不快感	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
喉頭の炎症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
喉頭浮腫	0	2 (0.8%)	2 (0.8%)	0	0	7 (2.2%)	7 (2.2%)	0	2 (1.9%)	2 (1.9%)	0
喉頭狭窄	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
喉頭刺激感	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
鼻部不快感	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
鼻閉塞	0	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	2 (0.6%)	0	0	0	0
器質化肺炎	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
口腔咽頭不快感	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
口腔咽頭痛	1 (0.4%)	3 (1.2%)	2 (0.8%)	2 (0.8%)	5 (1.8%)	1 (0.3%)	1 (0.3%)	0	6 (5.8%)	6 (5.8%)	5 (4.9%)
口腔咽頭腫脹	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
副鼻腔不快感	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
咽頭浮腫	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
胸水	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
胸膜炎	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
胸膜痛	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
呼気延長	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
肺動脈血栓症	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
呼吸不全	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
気道うっ血	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
鼻漏	0	4 (1.6%)	4 (1.6%)	0	0	8 (2.5%)	8 (2.5%)	0	0	0	0
低音性連続性ラ音	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
副鼻腔障害	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
くしゃみ	0	0	0	0	0	2 (0.6%)	2 (0.6%)	0	5 (4.9%)	5 (4.9%)	0
上気道性喘鳴	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
窒息感	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
咽喉絞扼感	0	4 (1.6%)	4 (1.6%)	0	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	0
上気道咳症候群	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	3 (2.9%)	2 (1.9%)	2 (1.9%)
血管障害	18 (7.6%)	34 (14.0%)	23 (9.5%)	25 (10.3%)	27 (9.6%)	63 (19.8%)	29 (9.1%)	42 (13.2%)	21 (20.4%)	13 (12.6%)	13 (12.6%)
高血圧	6 (2.5%)	16 (6.6%)	11 (4.5%)	13 (5.3%)	1 (0.4%)	17 (5.3%)	12 (3.8%)	8 (2.5%)	6 (5.8%)	5 (4.9%)	4 (3.9%)
深部静脈血栓症	0	2 (0.8%)	2 (0.8%)	2 (0.8%)	9 (3.2%)	5 (1.6%)	1 (0.3%)	5 (1.6%)	1 (1.0%)	0	1 (1.0%)
潮紅	2 (0.8%)	4 (1.6%)	2 (0.8%)	2 (0.8%)	5 (1.8%)	9 (2.8%)	6 (1.9%)	4 (1.3%)	6 (5.8%)	4 (3.9%)	3 (2.9%)
静脈炎	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	4 (1.3%)	0	4 (1.3%)	0	0	0
塞栓症	0	0	0	0	0	3 (0.9%)	0	3 (0.9%)	0	0	0
起立性低血圧	4 (1.7%)	3 (1.2%)	0	3 (1.2%)	0	3 (0.9%)	2 (0.6%)	3 (0.9%)	0	0	0
血栓性静脈炎	0	1 (0.4%)	1 (0.4%)	0	0	3 (0.9%)	0	3 (0.9%)	0	0	0
表在性血栓性静脈炎	0	0	0	0	6 (2.1%)	3 (0.9%)	0	3 (0.9%)	2 (1.9%)	1 (1.0%)	1 (1.0%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
ほてり	1 (0.4%)	2 (0.8%)	2 (0.8%)	0	2 (0.7%)	4 (1.3%)	2 (0.6%)	2 (0.6%)	3 (2.9%)	3 (2.9%)	1 (1.0%)
低血圧	3 (1.3%)	5 (2.1%)	5 (2.1%)	2 (0.8%)	2 (0.7%)	9 (2.8%)	8 (2.5%)	2 (0.6%)	1 (1.0%)	0	1 (1.0%)
静脈血栓症	0	0	0	0	0	2 (0.6%)	0	2 (0.6%)	0	0	0
血腫	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
出血性梗塞	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
末梢冷感	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
表在性静脈炎	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
血栓症	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
大動脈解離	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
循環虚脱	2 (0.8%)	0	0	0	0	0	0	0	0	0	0
静脈塞栓症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
充血	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
高血圧クリーゼ	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
蒼白	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
末梢動脈血栓症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
血管拡張	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
四肢静脈血栓症	0	0	0	0	1 (0.4%)	0	0	0	1 (1.0%)	0	1 (1.0%)
臨床検査	10 (4.2%)	24 (9.9%)	13 (5.3%)	22 (9.1%)	24 (8.5%)	42 (13.2%)	24 (7.5%)	39 (12.3%)	16 (15.5%)	10 (9.7%)	13 (12.6%)
アラニンアミノトランスフェラーゼ増加	5 (2.1%)	10 (4.1%)	4 (1.6%)	9 (3.7%)	5 (1.8%)	11 (3.5%)	5 (1.6%)	11 (3.5%)	5 (4.9%)	4 (3.9%)	4 (3.9%)
体重減少	1 (0.4%)	6 (2.5%)	3 (1.2%)	5 (2.1%)	4 (1.4%)	8 (2.5%)	3 (0.9%)	8 (2.5%)	3 (2.9%)	2 (1.9%)	2 (1.9%)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8%)	6 (2.5%)	5 (2.1%)	5 (2.1%)	3 (1.1%)	7 (2.2%)	4 (1.3%)	7 (2.2%)	5 (4.9%)	4 (3.9%)	4 (3.9%)
血中アルカリホスファターゼ増加	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	6 (1.9%)	5 (1.6%)	6 (1.9%)	5 (4.9%)	5 (4.9%)	5 (4.9%)
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	6 (2.5%)	4 (1.6%)	6 (2.5%)	1 (0.4%)	4 (1.3%)	3 (0.9%)	4 (1.3%)	0	0	0
血中クレアチニン増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	4 (1.4%)	3 (0.9%)	1 (0.3%)	3 (0.9%)	0	0	0
心電図ＱＴ延長	0	0	0	0	1 (0.4%)	3 (0.9%)	2 (0.6%)	3 (0.9%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
血圧上昇	0	0	0	0	0	3 (0.9%)	2 (0.6%)	2 (0.6%)	2 (1.9%)	1 (1.0%)	1 (1.0%)
腎クレアチニン・クリアランス減少	0	0	0	0	2 (0.7%)	2 (0.6%)	0	2 (0.6%)	0	0	0
抱合ビリルビン増加	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
血中乳酸脱水素酵素減少	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
血中乳酸脱水素酵素増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
免疫グロブリン減少	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
A型インフルエンザウイルス検査陽性	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
好中球中毒性顆粒存在	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
トロポニン増加	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
体重増加	2 (0.8%)	5 (2.1%)	0	5 (2.1%)	4 (1.4%)	2 (0.6%)	2 (0.6%)	1 (0.3%)	4 (3.9%)	0	4 (3.9%)
血中リン減少	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
体温上昇	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
フィブリンDダイマー増加	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
握力低下	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
心拍数増加	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
ヘリコバクター検査陽性	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
酸素飽和度低下	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
静脈雑音	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
眼障害	18 (7.6%)	27 (11.1%)	15 (6.2%)	17 (7.0%)	14 (5.0%)	44 (13.8%)	17 (5.3%)	34 (10.7%)	14 (13.6%)	7 (6.8%)	12 (11.7%)
白内障	0	1 (0.4%)	0	1 (0.4%)	6 (2.1%)	15 (4.7%)	2 (0.6%)	15 (4.7%)	1 (1.0%)	0	1 (1.0%)
霧視	8 (3.4%)	5 (2.1%)	0	5 (2.1%)	4 (1.4%)	10 (3.1%)	4 (1.3%)	10 (3.1%)	5 (4.9%)	0	5 (4.9%)
眼刺激	1 (0.4%)	0	0	0	0	4 (1.3%)	2 (0.6%)	2 (0.6%)	2 (1.9%)	1 (1.0%)	1 (1.0%)
視力低下	0	1 (0.4%)	0	1 (0.4%)	0	2 (0.6%)	0	2 (0.6%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
視力障害	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	2 (0.6%)	0	2 (0.6%)	2 (1.9%)	1 (1.0%)	2 (1.9%)
結膜出血	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
眼乾燥	4 (1.7%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
眼の障害	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	0	1 (0.3%)	0	0	0
眼出血	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
眼球浮腫	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
屈折障害	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
硝子体浮遊物	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
眼瞼炎	2 (0.8%)	0	0	0	0	0	0	0	0	0	0
霰粒腫	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
結膜刺激	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
結膜浮腫	0	3 (1.2%)	3 (1.2%)	0	0	0	0	0	0	0	0
複視	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	1 (1.0%)	0	1 (1.0%)
眼のアレルギー	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
眼脂	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
眼痛	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
眼そう痒症	1 (0.4%)	0	0	0	0	0	0	0	2 (1.9%)	2 (1.9%)	1 (1.0%)
眼部腫脹	0	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0	0	0
眼瞼浮腫	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
眼瞼発疹	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
流涙増加	0	8 (3.3%)	6 (2.5%)	3 (1.2%)	1 (0.4%)	7 (2.2%)	7 (2.2%)	0	2 (1.9%)	2 (1.9%)	0
水晶体混濁	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
眼充血	0	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0	0	0
眼窩周囲浮腫	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
網膜静脈血栓症	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
網膜症	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
潰瘍性角膜炎	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
硝子体剥離	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
腎および尿路障害	2 (0.8%)	6 (2.5%)	4 (1.6%)	4 (1.6%)	10 (3.6%)	16 (5.0%)	3 (0.9%)	16 (5.0%)	6 (5.8%)	2 (1.9%)	6 (5.8%)
腎機能障害	0	1 (0.4%)	0	1 (0.4%)	5 (1.8%)	11 (3.5%)	2 (0.6%)	11 (3.5%)	0	0	0
高窒素血症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
慢性腎臓病	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
排尿困難	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
腎嚢胞	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
腎不全	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
急性腎不全	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
非感染性膀胱炎	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
血尿	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
失禁	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
中毒性ネフロパシー	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
夜間頻尿	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
頻尿	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
多尿	0	0	0	0	1 (0.4%)	0	0	0	1 (1.0%)	0	1 (1.0%)
腎仙痛	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
尿失禁	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
尿閉	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0
心臓障害	7 (3.0%)	17 (7.0%)	8 (3.3%)	14 (5.8%)	6 (2.1%)	19 (6.0%)	12 (3.8%)	10 (3.1%)	14 (13.6%)	6 (5.8%)	12 (11.7%)
心房細動	1 (0.4%)	4 (1.6%)	2 (0.8%)	4 (1.6%)	2 (0.7%)	3 (0.9%)	0	3 (0.9%)	3 (2.9%)	0	3 (2.9%)
狭心症	1 (0.4%)	0	0	0	1 (0.4%)	3 (0.9%)	2 (0.6%)	2 (0.6%)	2 (1.9%)	2 (1.9%)	1 (1.0%)
徐脈	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	1 (0.3%)	1 (0.3%)	1 (1.0%)	0	1 (1.0%)
伝導障害	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
拡張機能障害	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
心筋虚血	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
動悸	2 (0.8%)	3 (1.2%)	0	3 (1.2%)	0	2 (0.6%)	1 (0.3%)	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
洞性頻脈	0	4 (1.6%)	3 (1.2%)	3 (1.2%)	0	2 (0.6%)	2 (0.6%)	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
急性冠動脈症候群	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
急性心筋梗塞	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
左脚ブロック	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
心不全	2 (0.8%)	3 (1.2%)	0	3 (1.2%)	0	0	0	0	0	0	0
うっ血性心不全	1 (0.4%)	2 (0.8%)	0	2 (0.8%)	0	0	0	0	2 (1.9%)	0	2 (1.9%)
心粗動	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
心膜炎	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
洞性徐脈	0	0	0	0	0	0	0	0	2 (1.9%)	1 (1.0%)	2 (1.9%)
上室性頻脈	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0	0	0
頻脈	0	0	0	0	0	5 (1.6%)	5 (1.6%)	0	1 (1.0%)	1 (1.0%)	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
心室性期外収縮	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0	0
傷害、中毒および処置合併症	2 (0.8%)	4 (1.6%)	2 (0.8%)	3 (1.2%)	4 (1.4%)	9 (2.8%)	1 (0.3%)	8 (2.5%)	9 (8.7%)	6 (5.8%)	7 (6.8%)
挫傷	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	4 (1.3%)	0	4 (1.3%)	3 (2.9%)	2 (1.9%)	3 (2.9%)
脊椎圧迫骨折	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
脊椎骨折	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
各種物質毒性	0	0	0	0	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	0	0	0
創合併症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
アレルギー性輸血反応	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
毒性物質曝露	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
転倒	0	0	0	0	1 (0.4%)	0	0	0	4 (3.9%)	2 (1.9%)	3 (2.9%)
注入に伴う反応	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
眼窩周囲血腫	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
放射線性肺臓炎	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
引っかき傷	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
皮下血腫	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
硬膜下血腫	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
創傷	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
耳および迷路障害	2 (0.8%)	10 (4.1%)	4 (1.6%)	8 (3.3%)	3 (1.1%)	7 (2.2%)	4 (1.3%)	5 (1.6%)	4 (3.9%)	2 (1.9%)	3 (2.9%)
耳鳴	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	3 (0.9%)	1 (0.3%)	3 (0.9%)	2 (1.9%)	0	2 (1.9%)
聴力低下	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
回転性めまい	1 (0.4%)	7 (2.9%)	2 (0.8%)	6 (2.5%)	3 (1.1%)	3 (0.9%)	2 (0.6%)	1 (0.3%)	0	0	0
難聴	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
耳痛	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
耳そう痒症	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	2 (1.9%)	2 (1.9%)	1 (1.0%)
中耳の炎症	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
肝胆道系障害	0	5 (2.1%)	3 (1.2%)	2 (0.8%)	1 (0.4%)	4 (1.3%)	3 (0.9%)	4 (1.3%)	3 (2.9%)	2 (1.9%)	3 (2.9%)
肝機能異常	0	0	0	0	0	2 (0.6%)	2 (0.6%)	2 (0.6%)	0	0	0
肝細胞損傷	0	0	0	0	0	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
胆嚢炎	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
慢性胆嚢炎	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
高ビリルビン血症	0	4 (1.6%)	3 (1.2%)	1 (0.4%)	1 (0.4%)	0	0	0	3 (2.9%)	2 (1.9%)	3 (2.9%)

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
内分泌障害	3 (1.3%)	10 (4.1%)	0	10 (4.1%)	8 (2.8%)	3 (0.9%)	0	3 (0.9%)	3 (2.9%)	0	3 (2.9%)
クッシング様症状	3 (1.3%)	7 (2.9%)	0	7 (2.9%)	4 (1.4%)	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	0	2 (1.9%)
高コルチコイド症	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
ステロイド離脱症候群	0	0	0	0	2 (0.7%)	1 (0.3%)	0	1 (0.3%)	0	0	0
副腎機能不全	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
クッシング症候群	0	2 (0.8%)	0	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0
甲状腺機能低下症	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
下垂体依存性クッシング症候群	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
免疫系障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	4 (1.3%)	4 (1.3%)	2 (0.6%)	3 (2.9%)	3 (2.9%)	1 (1.0%)
免疫抑制	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
続発性免疫不全症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
サイトカイン放出症候群	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
薬物過敏症	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
低ヶグロブリン血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	0
季節性アレルギー	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0	5 (1.8%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	0	0	0
急性単球性白血病	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
基底細胞癌	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
皮膚血管腫	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
前立腺癌	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
扁平上皮癌	0	0	0	0	2 (0.7%)	0	0	0	0	0	0
生殖系および乳房障害	1 (0.4%)	3 (1.2%)	0	3 (1.2%)	3 (1.1%)	2 (0.6%)	0	2 (0.6%)	0	0	0

TSFAE04A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001		
	Vd	DVd			Rd	DRd			DPd		
	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
勃起不全	0	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	2 (0.6%)	0	2 (0.6%)	0	0	0
亀頭包皮炎	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
生殖器痛	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
骨盤痛	0	0	0	0	1 (0.4%)	0	0	0	0	0	0
精巣痛	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0
先天性、家族性および遺伝性障害	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
角膜ジストロフィー	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
肥大型心筋症	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (1.0%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE04A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE04A.SAS] 01JUN2016, 10:37

表 2.7.4-付録-33 Number of Subjects with Drug-Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE06: Number of Subjects with Drug-Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)			
	Related to Treatment	Related to Daratumumab	Related to Bortezomib	Related to Dexamethasone
Analysis set: Safety	8			
Subjects with drug-related TEAE	8 (100.0%)	7 (87.5%)	8 (100.0%)	8 (100.0%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	8 (100.0%)	7 (87.5%)	8 (100.0%)	5 (62.5%)
血小板減少症	7 (87.5%)	6 (75.0%)	7 (87.5%)	1 (12.5%)
リンパ球減少症	5 (62.5%)	5 (62.5%)	4 (50.0%)	5 (62.5%)
白血球減少症	3 (37.5%)	3 (37.5%)	3 (37.5%)	0
好中球減少症	3 (37.5%)	3 (37.5%)	3 (37.5%)	0
貧血	2 (25.0%)	1 (12.5%)	2 (25.0%)	1 (12.5%)
胃腸障害	4 (50.0%)	2 (25.0%)	2 (25.0%)	3 (37.5%)
便秘	2 (25.0%)	1 (12.5%)	2 (25.0%)	2 (25.0%)
胃炎	2 (25.0%)	1 (12.5%)	1 (12.5%)	2 (25.0%)
腹部膨満	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
上腹部痛	1 (12.5%)	0	0	1 (12.5%)
下痢	1 (12.5%)	0	1 (12.5%)	0
消化不良	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
悪心	1 (12.5%)	1 (12.5%)	0	0
嘔吐	1 (12.5%)	1 (12.5%)	0	0
感染症および寄生虫症	4 (50.0%)	4 (50.0%)	4 (50.0%)	4 (50.0%)
気管支炎	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
帯状疱疹	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
インフルエンザ	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
鼻咽頭炎	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
代謝および栄養障害	4 (50.0%)	0	1 (12.5%)	4 (50.0%)
高血糖	3 (37.5%)	0	0	3 (37.5%)
低カリウム血症	2 (25.0%)	0	0	2 (25.0%)
脱水	1 (12.5%)	0	1 (12.5%)	0
呼吸器、胸郭および縦隔障害	4 (50.0%)	4 (50.0%)	1 (12.5%)	1 (12.5%)
低酸素症	2 (25.0%)	2 (25.0%)	0	0
喘鳴	2 (25.0%)	2 (25.0%)	0	0
発声障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
口腔咽頭不快感	1 (12.5%)	1 (12.5%)	0	0
口腔咽頭痛	1 (12.5%)	1 (12.5%)	0	0
一般・全身障害および投与部位の状態	3 (37.5%)	3 (37.5%)	3 (37.5%)	2 (25.0%)
疲労	3 (37.5%)	2 (25.0%)	3 (37.5%)	2 (25.0%)
悪寒	2 (25.0%)	2 (25.0%)	0	0
発熱	1 (12.5%)	1 (12.5%)	0	0
臨床検査	3 (37.5%)	3 (37.5%)	3 (37.5%)	2 (25.0%)
体重減少	2 (25.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)
アラニンアミノトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0	0
血中乳酸脱水素酵素増加	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
血圧上昇	1 (12.5%)	1 (12.5%)	0	0
血中尿素増加	1 (12.5%)	0	1 (12.5%)	0
Ｃ－反応性蛋白増加	1 (12.5%)	1 (12.5%)	0	0

TSFAE06: Number of Subjects with Drug-Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)			
	Related to Treatment	Related to Daratumumab	Related to Bortezomib	Related to Dexamethasone
細胞マーカー増加	1 (12.5%)	0	1 (12.5%)	0
フィブリン分解産物増加	1 (12.5%)	1 (12.5%)	0	0
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0	1 (12.5%)
サーファクタントプロテイン増加	1 (12.5%)	0	1 (12.5%)	0
神経系障害	3 (37.5%)	2 (25.0%)	3 (37.5%)	2 (25.0%)
異常感覚	2 (25.0%)	2 (25.0%)	2 (25.0%)	2 (25.0%)
頭痛	1 (12.5%)	1 (12.5%)	0	0
神経痛	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
末梢性感覚ニューロパチー	1 (12.5%)	0	1 (12.5%)	0
皮膚および皮下組織障害	3 (37.5%)	1 (12.5%)	3 (37.5%)	1 (12.5%)
皮膚炎	1 (12.5%)	0	1 (12.5%)	0
紅斑	1 (12.5%)	0	1 (12.5%)	0
全身性皮疹	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
眼障害	2 (25.0%)	2 (25.0%)	2 (25.0%)	2 (25.0%)
眼精疲労	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
霧視	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
筋骨格系および結合組織障害	2 (25.0%)	0	0	2 (25.0%)
筋力低下	1 (12.5%)	0	0	1 (12.5%)
ミオパチー	1 (12.5%)	0	0	1 (12.5%)
精神障害	2 (25.0%)	1 (12.5%)	1 (12.5%)	2 (25.0%)
短時間睡眠	1 (12.5%)	0	0	1 (12.5%)
不眠症	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
耳および迷路障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
片耳難聴	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
肝胆道系障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
薬物性肝障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
傷害、中毒および処置合併症	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
凍瘡	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
血管障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
高血圧	1 (12.5%)	1 (12.5%)	0	0
低血圧	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population in 'Related to Treatment' column as denominator.
Note: Adverse events related to study treatments are adverse events with a relationship to study treatments of very likely, probably or possible.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE06.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE06.SAS] 28SEP2016, 04:15

表 2.7.4-付録-34 Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
Total[a]							
Analysis set: safety	281			283			
Total number of subjects with TEAE related to study treatment	233 (82.9%)	218 (77.6%)	202 (71.9%)	269 (95.1%)	215 (76.0%)	257 (90.8%)	223 (78.8%)
MedDRA system organ class/Preferred term							
血液およびリンパ系障害	146 (52.0%)	141 (50.2%)	41 (14.6%)	184 (65.0%)	61 (21.6%)	181 (64.0%)	32 (11.3%)
好中球減少症	107 (38.1%)	107 (38.1%)	16 (5.7%)	156 (55.1%)	43 (15.2%)	153 (54.1%)	15 (5.3%)
血小板減少症	67 (23.8%)	65 (23.1%)	10 (3.6%)	63 (22.3%)	23 (8.1%)	61 (21.6%)	5 (1.8%)
貧血	55 (19.6%)	54 (19.2%)	8 (2.8%)	53 (18.7%)	13 (4.6%)	52 (18.4%)	3 (1.1%)
白血球減少症	12 (4.3%)	12 (4.3%)	2 (0.7%)	21 (7.4%)	11 (3.9%)	20 (7.1%)	3 (1.1%)
リンパ球減少症	12 (4.3%)	8 (2.8%)	11 (3.9%)	15 (5.3%)	7 (2.5%)	12 (4.2%)	8 (2.8%)
発熱性好中球減少症	6 (2.1%)	6 (2.1%)	2 (0.7%)	14 (4.9%)	4 (1.4%)	14 (4.9%)	5 (1.8%)
白血球増加症	2 (0.7%)	0	2 (0.7%)	0	0	0	0
好酸球増加症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
出血性障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0
リンパ節症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0	0	0	0
一般・全身障害および投与部位の状態	90 (32.0%)	76 (27.0%)	64 (22.8%)	156 (55.1%)	81 (28.6%)	116 (41.0%)	93 (32.9%)
疲労	56 (19.9%)	49 (17.4%)	33 (11.7%)	83 (29.3%)	35 (12.4%)	74 (26.1%)	41 (14.5%)
無力症	21 (7.5%)	18 (6.4%)	13 (4.6%)	31 (11.0%)	8 (2.8%)	26 (9.2%)	15 (5.3%)
末梢性浮腫	20 (7.1%)	9 (3.2%)	16 (5.7%)	27 (9.5%)	1 (0.4%)	6 (2.1%)	25 (8.8%)
発熱	7 (2.5%)	6 (2.1%)	6 (2.1%)	26 (9.2%)	23 (8.1%)	15 (5.3%)	9 (3.2%)
悪寒	3 (1.1%)	2 (0.7%)	2 (0.7%)	15 (5.3%)	14 (4.9%)	1 (0.4%)	1 (0.4%)
倦怠感	2 (0.7%)	2 (0.7%)	1 (0.4%)	8 (2.8%)	2 (0.7%)	5 (1.8%)	5 (1.8%)
末梢腫脹	3 (1.1%)	2 (0.7%)	2 (0.7%)	6 (2.1%)	2 (0.7%)	1 (0.4%)	6 (2.1%)
インフルエンザ様疾患	2 (0.7%)	2 (0.7%)	1 (0.4%)	6 (2.1%)	4 (1.4%)	3 (1.1%)	3 (1.1%)
胸部不快感	0	0	0	5 (1.8%)	5 (1.8%)	0	0
冷感	0	0	0	5 (1.8%)	5 (1.8%)	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
顔面浮腫	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
全身健康状態低下	1 (0.4%)	1 (0.4%)	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
薬物不耐性	0	0	0	2 (0.7%)	0	0	2 (0.7%)
びくびく感	0	0	0	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
非心臓性胸痛	0	0	0	2 (0.7%)	2 (0.7%)	0	0
浮腫	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
疼痛	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
苦悶感	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
医薬品副作用	0	0	0	1 (0.4%)	0	0	1 (0.4%)
胸痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
運動耐性低下	0	0	0	1 (0.4%)	0	0	1 (0.4%)
溢出	0	0	0	1 (0.4%)	1 (0.4%)	0	0
脂肪組織増加	0	0	0	1 (0.4%)	0	0	1 (0.4%)
異常感	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
熱感	0	0	0	1 (0.4%)	0	0	1 (0.4%)
歩行障害	0	0	0	1 (0.4%)	0	1 (0.4%)	0
全身性浮腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
高熱	0	0	0	1 (0.4%)	1 (0.4%)	0	0
注入部位発疹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
多臓器不全	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
分泌物分泌	0	0	0	1 (0.4%)	1 (0.4%)	0	0
全身性炎症反応症候群	0	0	0	1 (0.4%)	0	1 (0.4%)	0
胃腸障害	90 (32.0%)	80 (28.5%)	44 (15.7%)	152 (53.7%)	74 (26.1%)	108 (38.2%)	62 (21.9%)
下痢	30 (10.7%)	30 (10.7%)	7 (2.5%)	83 (29.3%)	28 (9.9%)	72 (25.4%)	18 (6.4%)
便秘	42 (14.9%)	41 (14.6%)	8 (2.8%)	42 (14.8%)	12 (4.2%)	36 (12.7%)	16 (5.7%)
悪心	15 (5.3%)	14 (5.0%)	6 (2.1%)	37 (13.1%)	25 (8.8%)	22 (7.8%)	9 (3.2%)
嘔吐	2 (0.7%)	2 (0.7%)	0	23 (8.1%)	22 (7.8%)	6 (2.1%)	2 (0.7%)
上腹部痛	5 (1.8%)	2 (0.7%)	4 (1.4%)	15 (5.3%)	3 (1.1%)	4 (1.4%)	14 (4.9%)
消化不良	4 (1.4%)	1 (0.4%)	4 (1.4%)	10 (3.5%)	1 (0.4%)	4 (1.4%)	8 (2.8%)
口内炎	4 (1.4%)	2 (0.7%)	3 (1.1%)	9 (3.2%)	6 (2.1%)	7 (2.5%)	5 (1.8%)
腹痛	4 (1.4%)	3 (1.1%)	2 (0.7%)	8 (2.8%)	5 (1.8%)	6 (2.1%)	2 (0.7%)
口内乾燥	3 (1.1%)	2 (0.7%)	1 (0.4%)	5 (1.8%)	2 (0.7%)	3 (1.1%)	5 (1.8%)
腹部膨満	3 (1.1%)	3 (1.1%)	2 (0.7%)	4 (1.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
腹部不快感	2 (0.7%)	0	2 (0.7%)	3 (1.1%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
胃食道逆流性疾患	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	1 (0.4%)
口腔内潰瘍形成	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	0
口腔内痛	2 (0.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0
憩室穿孔	0	0	0	2 (0.7%)	0	0	2 (0.7%)
放屁	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	0
胃炎	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
胃腸障害	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	0
口腔粘膜水疱形成	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
口の錯感覚	0	0	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	0
腹壁血腫	0	0	0	1 (0.4%)	0	1 (0.4%)	0
裂肛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
アフタ性口内炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
胆汁酸吸収不良	0	0	0	1 (0.4%)	0	1 (0.4%)	0
便通不規則	0	0	0	1 (0.4%)	0	1 (0.4%)	0
大腸炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
齲歯	1 (0.4%)	0	1 (0.4%)	0	0	0	0
嚥下障害	0	0	0	1 (0.4%)	1 (0.4%)	0	0
心窩部不快感	0	0	0	1 (0.4%)	0	0	1 (0.4%)
おくび	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
糞塊	1 (0.4%)	1 (0.4%)	0	0	0	0	0
胃拡張	0	0	0	1 (0.4%)	0	0	1 (0.4%)
胃障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0
胃出血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
消化管運動障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
消化器痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
舌痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
痔核	0	0	0	1 (0.4%)	0	1 (0.4%)	0
口の感覚鈍麻	0	0	0	1 (0.4%)	0	1 (0.4%)	0
腸管穿孔	1 (0.4%)	1 (0.4%)	0	0	0	0	0
口唇そう痒症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
口唇腫脹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
メレナ	1 (0.4%)	1 (0.4%)	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
非感染性歯肉炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
嚥下痛	0	0	0	1 (0.4%)	1 (0.4%)	0	0
膵炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
地図状舌	1 (0.4%)	0	1 (0.4%)	0	0	0	0
舌潰瘍	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
感染症および寄生虫症	88 (31.3%)	66 (23.5%)	83 (29.5%)	118 (41.7%)	72 (25.4%)	95 (33.6%)	97 (34.3%)
上気道感染	15 (5.3%)	11 (3.9%)	14 (5.0%)	33 (11.7%)	25 (8.8%)	27 (9.5%)	27 (9.5%)
肺炎	14 (5.0%)	12 (4.3%)	13 (4.6%)	23 (8.1%)	12 (4.2%)	20 (7.1%)	16 (5.7%)
気管支炎	13 (4.6%)	7 (2.5%)	12 (4.3%)	14 (4.9%)	8 (2.8%)	8 (2.8%)	13 (4.6%)
気道感染	8 (2.8%)	7 (2.5%)	8 (2.8%)	11 (3.9%)	7 (2.5%)	10 (3.5%)	9 (3.2%)
鼻咽頭炎	7 (2.5%)	5 (1.8%)	6 (2.1%)	10 (3.5%)	5 (1.8%)	8 (2.8%)	9 (3.2%)
下気道感染	5 (1.8%)	5 (1.8%)	5 (1.8%)	7 (2.5%)	3 (1.1%)	6 (2.1%)	5 (1.8%)
帯状疱疹	3 (1.1%)	3 (1.1%)	2 (0.7%)	4 (1.4%)	4 (1.4%)	4 (1.4%)	3 (1.1%)
口腔カンジダ症	2 (0.7%)	1 (0.4%)	1 (0.4%)	5 (1.8%)	0	2 (0.7%)	4 (1.4%)
口腔真菌感染	3 (1.1%)	2 (0.7%)	3 (1.1%)	4 (1.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)
インフルエンザ	2 (0.7%)	2 (0.7%)	2 (0.7%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	4 (1.4%)
副鼻腔炎	2 (0.7%)	2 (0.7%)	2 (0.7%)	4 (1.4%)	2 (0.7%)	3 (1.1%)	3 (1.1%)
ウイルス感染	4 (1.4%)	4 (1.4%)	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
感染	2 (0.7%)	2 (0.7%)	1 (0.4%)	3 (1.1%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
皮膚感染	3 (1.1%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
尿路感染	1 (0.4%)	1 (0.4%)	0	4 (1.4%)	2 (0.7%)	2 (0.7%)	4 (1.4%)
歯肉炎	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	0	2 (0.7%)	2 (0.7%)
咽頭炎	4 (1.4%)	4 (1.4%)	4 (1.4%)	0	0	0	0
歯膿瘍	4 (1.4%)	3 (1.1%)	4 (1.4%)	0	0	0	0
気管支肺炎	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
結膜炎	0	0	0	3 (1.1%)	3 (1.1%)	1 (0.4%)	1 (0.4%)
膀胱炎	3 (1.1%)	2 (0.7%)	3 (1.1%)	0	0	0	0
胃腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	2 (0.7%)	1 (0.4%)
ヘルペスウイルス感染	0	0	0	3 (1.1%)	2 (0.7%)	2 (0.7%)	3 (1.1%)
肺感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	0	2 (0.7%)
粘膜感染	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)	0	1 (0.4%)	0
インフルエンザ性肺炎	0	0	0	3 (1.1%)	1 (0.4%)	1 (0.4%)	3 (1.1%)
鼻炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	2 (0.7%)	2 (0.7%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
足部白癬	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
細気管支炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
蜂巣炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
丹毒	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
真菌感染	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
限局性感染	2 (0.7%)	2 (0.7%)	2 (0.7%)	0	0	0	0
口腔ヘルペス	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
細菌性肺炎	0	0	0	2 (0.7%)	2 (0.7%)	0	1 (0.4%)
ＲＳウイルス感染	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
敗血症	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚カンジダ	2 (0.7%)	0	2 (0.7%)	0	0	0	0
歯感染	2 (0.7%)	1 (0.4%)	1 (0.4%)	0	0	0	0
四肢膿瘍	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
急性扁桃炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
肛門膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0	0
細菌感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
ウイルス性気管支炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
カンピロバクター胃腸炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
カンジダ感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
コロナウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
サイトメガロウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
蓄膿	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
感染性小腸結腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
大腸菌性菌血症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
眼感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
真菌性眼感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
熱性感染症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
毛包炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
皮膚真菌感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
真菌性性器感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ヘモフィルス感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
感染性筋炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
注入部位蜂巣炎	0	0	0	1 (0.4%)	1 (0.4%)	0	0
真菌性角膜炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
喉頭炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
リステリア性敗血症	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
大葉性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
ウイルス性下気道感染	0	0	0	1 (0.4%)	0	1 (0.4%)	0
鼻ヘルペス	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
中咽頭カンジダ症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
中耳炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
急性中耳炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
耳下腺炎	0	0	0	1 (0.4%)	0	1 (0.4%)	0
眼窩周囲蜂巣炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
レンサ球菌性咽頭炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
ヘモフィルス性肺炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
レジオネラ菌性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
腎盂腎炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
呼吸器モニリア症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
敗血症性ショック	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ブドウ球菌皮膚感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮下組織膿瘍	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
扁桃炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
細菌性上気道感染	0	0	0	1 (0.4%)	0	0	1 (0.4%)
尿道炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
腟感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
水痘	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
外陰部腟カンジダ症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
外陰部腟炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
創傷感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
神経系障害	84 (29.9%)	62 (22.1%)	56 (19.9%)	98 (34.6%)	33 (11.7%)	73 (25.8%)	51 (18.0%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
振戦	21 (7.5%)	8 (2.8%)	18 (6.4%)	23 (8.1%)	4 (1.4%)	14 (4.9%)	19 (6.7%)
味覚異常	13 (4.6%)	12 (4.3%)	6 (2.1%)	16 (5.7%)	4 (1.4%)	14 (4.9%)	8 (2.8%)
浮動性めまい	14 (5.0%)	13 (4.6%)	6 (2.1%)	13 (4.6%)	6 (2.1%)	5 (1.8%)	8 (2.8%)
頭痛	10 (3.6%)	7 (2.5%)	9 (3.2%)	17 (6.0%)	13 (4.6%)	4 (1.4%)	5 (1.8%)
末梢性感覚ニューロパチー	11 (3.9%)	11 (3.9%)	1 (0.4%)	16 (5.7%)	2 (0.7%)	16 (5.7%)	0
末梢性ニューロパチー	7 (2.5%)	7 (2.5%)	1 (0.4%)	10 (3.5%)	1 (0.4%)	9 (3.2%)	0
錯感覚	4 (1.4%)	4 (1.4%)	1 (0.4%)	5 (1.8%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
嗜眠	3 (1.1%)	2 (0.7%)	3 (1.1%)	5 (1.8%)	2 (0.7%)	5 (1.8%)	3 (1.1%)
感覚鈍麻	2 (0.7%)	1 (0.4%)	2 (0.7%)	5 (1.8%)	0	3 (1.1%)	2 (0.7%)
記憶障害	5 (1.8%)	1 (0.4%)	5 (1.8%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
味覚消失	1 (0.4%)	0	1 (0.4%)	4 (1.4%)	1 (0.4%)	2 (0.7%)	3 (1.1%)
平衡障害	2 (0.7%)	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
注意力障害	1 (0.4%)	1 (0.4%)	0	3 (1.1%)	2 (0.7%)	2 (0.7%)	3 (1.1%)
神経痛	2 (0.7%)	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
失神寸前の状態	0	0	0	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
失神	0	0	0	4 (1.4%)	2 (0.7%)	2 (0.7%)	3 (1.1%)
傾眠	3 (1.1%)	3 (1.1%)	1 (0.4%)	0	0	0	0
アカシジア	2 (0.7%)	0	2 (0.7%)	0	0	0	0
体位性めまい	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
異常感覚	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
味覚減退	2 (0.7%)	1 (0.4%)	2 (0.7%)	0	0	0	0
下肢静止不能症候群	2 (0.7%)	1 (0.4%)	1 (0.4%)	0	0	0	0
健忘	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
失語症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
脳梗塞	1 (0.4%)	1 (0.4%)	0	0	0	0	0
構語障害	0	0	0	1 (0.4%)	0	1 (0.4%)	0
蟻走感	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
知覚過敏	0	0	0	1 (0.4%)	0	1 (0.4%)	0
過眠症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
肋間神経痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0
意識消失	1 (0.4%)	1 (0.4%)	0	0	0	0	0
片頭痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
不随意性筋収縮	1 (0.4%)	1 (0.4%)	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
筋痙直	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
神経系障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
嗅覚錯誤	0	0	0	1 (0.4%)	0	1 (0.4%)	0
ヘルペス後神経痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0
精神運動亢進	1 (0.4%)	0	1 (0.4%)	0	0	0	0
副鼻腔炎に伴う頭痛	0	0	0	1 (0.4%)	0	0	1 (0.4%)
脊髄圧迫	1 (0.4%)	0	1 (0.4%)	0	0	0	0
一過性脳虚血発作	0	0	0	1 (0.4%)	0	0	1 (0.4%)
上位運動ニューロンの病変	1 (0.4%)	1 (0.4%)	0	0	0	0	0
第７脳神経麻痺	1 (0.4%)	1 (0.4%)	0	0	0	0	0
視野欠損	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
筋骨格系および結合組織障害	68 (24.2%)	50 (17.8%)	41 (14.6%)	98 (34.6%)	27 (9.5%)	64 (22.6%)	61 (21.6%)
筋痙縮	40 (14.2%)	33 (11.7%)	21 (7.5%)	62 (21.9%)	11 (3.9%)	52 (18.4%)	33 (11.7%)
筋力低下	15 (5.3%)	3 (1.1%)	14 (5.0%)	19 (6.7%)	1 (0.4%)	2 (0.7%)	18 (6.4%)
筋肉痛	5 (1.8%)	5 (1.8%)	3 (1.1%)	8 (2.8%)	3 (1.1%)	5 (1.8%)	4 (1.4%)
四肢痛	6 (2.1%)	5 (1.8%)	1 (0.4%)	4 (1.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
背部痛	1 (0.4%)	1 (0.4%)	0	8 (2.8%)	7 (2.5%)	4 (1.4%)	1 (0.4%)
関節痛	3 (1.1%)	3 (1.1%)	0	4 (1.4%)	2 (0.7%)	3 (1.1%)	4 (1.4%)
筋骨格系胸痛	2 (0.7%)	0	2 (0.7%)	4 (1.4%)	3 (1.1%)	0	1 (0.4%)
ミオパチー	3 (1.1%)	2 (0.7%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	0	2 (0.7%)
骨痛	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	2 (0.7%)
関節腫脹	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
筋肉疲労	0	0	0	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
筋骨格痛	0	0	0	2 (0.7%)	2 (0.7%)	0	0
頚部痛	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
筋萎縮症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
デュプイトラン拘縮	0	0	0	1 (0.4%)	1 (0.4%)	0	0
側腹部痛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
出血性関節症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
関節滲出液	1 (0.4%)	1 (0.4%)	0	0	0	0	0
運動性低下	0	0	0	1 (0.4%)	0	0	1 (0.4%)
筋緊張	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
筋骨格硬直	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
骨壊死	0	0	0	1 (0.4%)	0	0	1 (0.4%)
顎骨壊死	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
骨粗鬆症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
脊柱管狭窄症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
脊椎障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
脊椎痛	1 (0.4%)	0	1 (0.4%)	0	0	0	0
腱痛	0	0	0	1 (0.4%)	0	0	1 (0.4%)
呼吸器、胸郭および縦隔障害	43 (15.3%)	30 (10.7%)	28 (10.0%)	121 (42.8%)	103 (36.4%)	33 (11.7%)	35 (12.4%)
呼吸困難	12 (4.3%)	8 (2.8%)	5 (1.8%)	35 (12.4%)	32 (11.3%)	8 (2.8%)	7 (2.5%)
咳嗽	4 (1.4%)	4 (1.4%)	2 (0.7%)	35 (12.4%)	32 (11.3%)	11 (3.9%)	8 (2.8%)
肺塞栓症	11 (3.9%)	11 (3.9%)	4 (1.4%)	7 (2.5%)	1 (0.4%)	7 (2.5%)	2 (0.7%)
気管支痙攣	0	0	0	13 (4.6%)	13 (4.6%)	0	0
発声障害	5 (1.8%)	1 (0.4%)	4 (1.4%)	8 (2.8%)	3 (1.1%)	0	5 (1.8%)
しゃっくり	6 (2.1%)	2 (0.7%)	5 (1.8%)	7 (2.5%)	1 (0.4%)	0	6 (2.1%)
アレルギー性鼻炎	0	0	0	10 (3.5%)	8 (2.8%)	4 (1.4%)	3 (1.1%)
鼻閉	0	0	0	8 (2.8%)	8 (2.8%)	0	0
湿性咳嗽	2 (0.7%)	2 (0.7%)	2 (0.7%)	6 (2.1%)	5 (1.8%)	4 (1.4%)	4 (1.4%)
鼻漏	0	0	0	8 (2.8%)	8 (2.8%)	0	0
咽喉刺激感	0	0	0	8 (2.8%)	8 (2.8%)	1 (0.4%)	0
喘鳴	0	0	0	7 (2.5%)	7 (2.5%)	1 (0.4%)	0
低酸素症	0	0	0	6 (2.1%)	6 (2.1%)	1 (0.4%)	1 (0.4%)
喉頭浮腫	0	0	0	6 (2.1%)	6 (2.1%)	0	0
口腔咽頭痛	5 (1.8%)	2 (0.7%)	5 (1.8%)	1 (0.4%)	1 (0.4%)	0	0
労作性呼吸困難	0	0	0	5 (1.8%)	4 (1.4%)	1 (0.4%)	2 (0.7%)
鼻出血	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	0
肺水腫	0	0	0	3 (1.1%)	1 (0.4%)	0	2 (0.7%)
アレルギー性呼吸器症状	0	0	0	2 (0.7%)	2 (0.7%)	0	0
肺障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
鼻閉塞	0	0	0	2 (0.7%)	2 (0.7%)	0	0
肺臓炎	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
くしゃみ	0	0	0	2 (0.7%)	2 (0.7%)	0	0
窒息	0	0	0	1 (0.4%)	1 (0.4%)	0	0
気管支拡張症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
カタル	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
慢性閉塞性肺疾患	0	0	0	1 (0.4%)	0	1 (0.4%)	0
胸水症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
喉頭不快感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
喉頭の炎症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
喉頭狭窄	0	0	0	1 (0.4%)	1 (0.4%)	0	0
喉頭刺激感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
鼻部不快感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
咽頭紅斑	0	0	0	1 (0.4%)	0	0	1 (0.4%)
誤嚥性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
呼気延長	0	0	0	1 (0.4%)	1 (0.4%)	0	0
副鼻腔うっ血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
副鼻腔障害	0	0	0	1 (0.4%)	1 (0.4%)	0	0
上気道性喘鳴	0	0	0	1 (0.4%)	1 (0.4%)	0	0
窒息感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
咽喉絞扼感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
精神障害	76 (27.0%)	9 (3.2%)	73 (26.0%)	74 (26.1%)	6 (2.1%)	13 (4.6%)	72 (25.4%)
不眠症	47 (16.7%)	3 (1.1%)	46 (16.4%)	46 (16.3%)	2 (0.7%)	4 (1.4%)	45 (15.9%)
不安	8 (2.8%)	1 (0.4%)	7 (2.5%)	10 (3.5%)	1 (0.4%)	1 (0.4%)	9 (3.2%)
激越	8 (2.8%)	0	8 (2.8%)	6 (2.1%)	0	0	6 (2.1%)
うつ病	2 (0.7%)	0	2 (0.7%)	11 (3.9%)	2 (0.7%)	5 (1.8%)	9 (3.2%)
易刺激性	5 (1.8%)	1 (0.4%)	4 (1.4%)	6 (2.1%)	0	0	6 (2.1%)
気分変化	5 (1.8%)	0	5 (1.8%)	6 (2.1%)	0	0	6 (2.1%)
落ち着きのなさ	4 (1.4%)	1 (0.4%)	4 (1.4%)	4 (1.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)
神経過敏	5 (1.8%)	0	5 (1.8%)	0	0	0	0
睡眠障害	3 (1.1%)	2 (0.7%)	3 (1.1%)	2 (0.7%)	0	0	2 (0.7%)
抑うつ気分	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	0	1 (0.4%)	3 (1.1%)
錯乱状態	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
精神障害	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	0	0	2 (0.7%)
気分動揺	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	0	1 (0.4%)	2 (0.7%)
感情障害	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
譫妄	1 (0.4%)	0	1 (0.4%)	0	0	0	0
まとまりのない会話	1 (0.4%)	1 (0.4%)	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
気分変調性障害	1 (0.4%)	0	1 (0.4%)	0	0	0	0
幻覚	1 (0.4%)	0	1 (0.4%)	0	0	0	0
言葉もれ	1 (0.4%)	0	1 (0.4%)	0	0	0	0
リビドー消失	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
精神病性障害	1 (0.4%)	0	1 (0.4%)	0	0	0	0
ストレス	1 (0.4%)	0	1 (0.4%)	0	0	0	0
皮膚および皮下組織障害	48 (17.1%)	39 (13.9%)	26 (9.3%)	80 (28.3%)	49 (17.3%)	46 (16.3%)	26 (9.2%)
そう痒症	18 (6.4%)	18 (6.4%)	0	22 (7.8%)	18 (6.4%)	13 (4.6%)	1 (0.4%)
発疹	15 (5.3%)	10 (3.6%)	6 (2.1%)	20 (7.1%)	7 (2.5%)	16 (5.7%)	2 (0.7%)
多汗症	4 (1.4%)	1 (0.4%)	4 (1.4%)	14 (4.9%)	11 (3.9%)	2 (0.7%)	4 (1.4%)
紅斑	4 (1.4%)	2 (0.7%)	2 (0.7%)	5 (1.8%)	3 (1.1%)	0	2 (0.7%)
斑状丘疹状皮疹	2 (0.7%)	2 (0.7%)	0	5 (1.8%)	4 (1.4%)	2 (0.7%)	3 (1.1%)
全身性皮疹	3 (1.1%)	3 (1.1%)	1 (0.4%)	3 (1.1%)	1 (0.4%)	3 (1.1%)	0
蕁麻疹	1 (0.4%)	1 (0.4%)	0	5 (1.8%)	5 (1.8%)	1 (0.4%)	0
皮膚乾燥	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
顔面腫脹	3 (1.1%)	0	3 (1.1%)	1 (0.4%)	0	0	1 (0.4%)
斑状出血	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
寝汗	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
斑状皮疹	1 (0.4%)	1 (0.4%)	0	2 (0.7%)	0	2 (0.7%)	0
日光角化症	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ざ瘡様皮膚炎	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
アレルギー性皮膚炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
湿疹	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
多形紅斑	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
男性型多毛症	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
点状出血	0	0	0	2 (0.7%)	0	0	2 (0.7%)
そう痒性皮疹	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
皮膚潰瘍	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
脱毛症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
冷汗	0	0	0	1 (0.4%)	1 (0.4%)	0	0
褥瘡性潰瘍	0	0	0	1 (0.4%)	0	0	1 (0.4%)
接触性皮膚炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
薬疹	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
紅色症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
全身紅斑	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
毛髪成長異常	0	0	0	1 (0.4%)	0	0	1 (0.4%)
手皮膚炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
多毛症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
爪甲脱落症	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
皮膚疼痛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
アレルギー性そう痒症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
壊疽性膿皮症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
丘疹性皮疹	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
皮膚亀裂	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚色素過剰	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
皮膚病変	0	0	0	1 (0.4%)	0	1 (0.4%)	0
うっ滞性皮膚炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
毛細血管拡張症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
血管炎性皮疹	0	0	0	1 (0.4%)	0	1 (0.4%)	0
代謝および栄養障害	43 (15.3%)	22 (7.8%)	38 (13.5%)	61 (21.6%)	17 (6.0%)	32 (11.3%)	46 (16.3%)
高血糖	17 (6.0%)	2 (0.7%)	17 (6.0%)	20 (7.1%)	1 (0.4%)	2 (0.7%)	20 (7.1%)
食欲減退	9 (3.2%)	9 (3.2%)	6 (2.1%)	19 (6.7%)	7 (2.5%)	17 (6.0%)	6 (2.1%)
低カリウム血症	12 (4.3%)	7 (2.5%)	9 (3.2%)	14 (4.9%)	5 (1.8%)	7 (2.5%)	10 (3.5%)
低リン酸血症	6 (2.1%)	3 (1.1%)	4 (1.4%)	7 (2.5%)	1 (0.4%)	5 (1.8%)	3 (1.1%)
低カルシウム血症	2 (0.7%)	0	2 (0.7%)	8 (2.8%)	5 (1.8%)	6 (2.1%)	6 (2.1%)
低マグネシウム血症	2 (0.7%)	2 (0.7%)	2 (0.7%)	3 (1.1%)	1 (0.4%)	1 (0.4%)	3 (1.1%)
低アルブミン血症	3 (1.1%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	0	0
脱水	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
糖尿病	0	0	0	2 (0.7%)	0	0	2 (0.7%)
痛風	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	0	0	0
低ナトリウム血症	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	0
水分過負荷	0	0	0	1 (0.4%)	1 (0.4%)	0	0
体液貯留	0	0	0	1 (0.4%)	0	0	1 (0.4%)
葉酸欠乏	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
高コレステロール血症	0	0	0	1 (0.4%)	0	0	1 (0.4%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
高脂血症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
高尿酸血症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
食欲亢進	1 (0.4%)	0	1 (0.4%)	0	0	0	0
多飲症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
１型糖尿病	0	0	0	1 (0.4%)	0	0	1 (0.4%)
２型糖尿病	1 (0.4%)	0	1 (0.4%)	0	0	0	0
血管障害	27 (9.6%)	20 (7.1%)	11 (3.9%)	55 (19.4%)	24 (8.5%)	30 (10.6%)	15 (5.3%)
深部静脈血栓症	9 (3.2%)	9 (3.2%)	3 (1.1%)	5 (1.8%)	1 (0.4%)	5 (1.8%)	2 (0.7%)
高血圧	1 (0.4%)	0	1 (0.4%)	13 (4.6%)	10 (3.5%)	1 (0.4%)	5 (1.8%)
潮紅	5 (1.8%)	0	5 (1.8%)	8 (2.8%)	5 (1.8%)	1 (0.4%)	3 (1.1%)
低血圧	2 (0.7%)	2 (0.7%)	0	7 (2.5%)	6 (2.1%)	1 (0.4%)	0
表在性血栓性静脈炎	6 (2.1%)	5 (1.8%)	1 (0.4%)	3 (1.1%)	0	3 (1.1%)	1 (0.4%)
ほてり	2 (0.7%)	0	2 (0.7%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
静脈炎	1 (0.4%)	1 (0.4%)	0	4 (1.4%)	0	4 (1.4%)	1 (0.4%)
塞栓症	0	0	0	3 (1.1%)	0	3 (1.1%)	1 (0.4%)
起立性低血圧	0	0	0	3 (1.1%)	2 (0.7%)	3 (1.1%)	1 (0.4%)
血栓性静脈炎	0	0	0	3 (1.1%)	0	3 (1.1%)	1 (0.4%)
血栓症	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
血腫	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
静脈血栓症	0	0	0	2 (0.7%)	0	2 (0.7%)	0
出血性梗塞	0	0	0	1 (0.4%)	0	1 (0.4%)	0
蒼白	1 (0.4%)	1 (0.4%)	0	0	0	0	0
末梢冷感	0	0	0	1 (0.4%)	0	1 (0.4%)	0
表在性静脈炎	0	0	0	1 (0.4%)	0	1 (0.4%)	0
四肢静脈血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
臨床検査	24 (8.5%)	20 (7.1%)	11 (3.9%)	31 (11.0%)	17 (6.0%)	27 (9.5%)	14 (4.9%)
アラニンアミノトランスフェラーゼ増加	5 (1.8%)	5 (1.8%)	2 (0.7%)	9 (3.2%)	5 (1.8%)	9 (3.2%)	3 (1.1%)
体重減少	4 (1.4%)	4 (1.4%)	1 (0.4%)	8 (2.8%)	3 (1.1%)	6 (2.1%)	5 (1.8%)
アスパラギン酸アミノトランスフェラーゼ増加	3 (1.1%)	3 (1.1%)	2 (0.7%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
血中クレアチニン増加	4 (1.4%)	4 (1.4%)	1 (0.4%)	2 (0.7%)	0	2 (0.7%)	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
体重増加	4 (1.4%)	0	4 (1.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
心電図ＱＴ延長	1 (0.4%)	1 (0.4%)	0	3 (1.1%)	2 (0.7%)	3 (1.1%)	0
血中アルカリホスファターゼ増加	0	0	0	3 (1.1%)	3 (1.1%)	3 (1.1%)	3 (1.1%)
腎クレアチニン・クリアランス減少	2 (0.7%)	2 (0.7%)	0	0	0	0	0
血中乳酸脱水素酵素減少	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
血圧上昇	0	0	0	1 (0.4%)	0	0	1 (0.4%)
体温上昇	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
フィブリンＤダイマー増加	1 (0.4%)	1 (0.4%)	0	0	0	0	0
ヘリコバクター検査陽性	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
免疫グロブリン減少	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
好中球中毒性顆粒存在	0	0	0	1 (0.4%)	0	1 (0.4%)	0
酸素飽和度低下	0	0	0	1 (0.4%)	1 (0.4%)	0	0
トロポニン増加	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
静脈雑音	1 (0.4%)	1 (0.4%)	0	0	0	0	0
眼障害	14 (5.0%)	6 (2.1%)	12 (4.3%)	40 (14.1%)	15 (5.3%)	9 (3.2%)	29 (10.2%)
白内障	6 (2.1%)	0	6 (2.1%)	14 (4.9%)	1 (0.4%)	2 (0.7%)	14 (4.9%)
霧視	4 (1.4%)	1 (0.4%)	4 (1.4%)	10 (3.5%)	4 (1.4%)	5 (1.8%)	8 (2.8%)
流涙増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	6 (2.1%)	6 (2.1%)	0	0
眼刺激	0	0	0	4 (1.4%)	2 (0.7%)	1 (0.4%)	2 (0.7%)
眼乾燥	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
眼部腫脹	0	0	0	2 (0.7%)	2 (0.7%)	0	0
視力低下	0	0	0	2 (0.7%)	0	0	2 (0.7%)
視力障害	0	0	0	2 (0.7%)	0	0	2 (0.7%)
結膜刺激	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
眼のアレルギー	0	0	0	1 (0.4%)	1 (0.4%)	0	0
眼の障害	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
眼出血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
眼球浮腫	0	0	0	1 (0.4%)	0	0	1 (0.4%)
眼瞼発疹	1 (0.4%)	1 (0.4%)	0	0	0	0	0
水晶体混濁	1 (0.4%)	0	1 (0.4%)	0	0	0	0
眼充血	0	0	0	1 (0.4%)	1 (0.4%)	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
眼窩周囲浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0
網膜静脈血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
硝子体浮遊物	0	0	0	1 (0.4%)	0	0	1 (0.4%)
腎および尿路障害	10 (3.6%)	7 (2.5%)	5 (1.8%)	15 (5.3%)	3 (1.1%)	14 (4.9%)	3 (1.1%)
腎機能障害	5 (1.8%)	5 (1.8%)	1 (0.4%)	10 (3.5%)	2 (0.7%)	10 (3.5%)	0
急性腎不全	2 (0.7%)	2 (0.7%)	0	0	0	0	0
腎不全	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
高窒素血症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
慢性腎臓病	0	0	0	1 (0.4%)	0	1 (0.4%)	0
排尿困難	0	0	0	1 (0.4%)	0	0	1 (0.4%)
頻尿	1 (0.4%)	0	1 (0.4%)	0	0	0	0
多尿	1 (0.4%)	0	1 (0.4%)	0	0	0	0
腎嚢胞	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
尿失禁	1 (0.4%)	0	1 (0.4%)	0	0	0	0
尿閉	1 (0.4%)	0	1 (0.4%)	0	0	0	0
心臓障害	6 (2.1%)	5 (1.8%)	3 (1.1%)	18 (6.4%)	11 (3.9%)	4 (1.4%)	8 (2.8%)
心房細動	2 (0.7%)	1 (0.4%)	1 (0.4%)	3 (1.1%)	0	1 (0.4%)	2 (0.7%)
頻脈	0	0	0	5 (1.8%)	5 (1.8%)	0	0
狭心症	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
徐脈	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	1 (0.4%)
動悸	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.4%)
洞性頻脈	0	0	0	2 (0.7%)	2 (0.7%)	0	1 (0.4%)
上室性頻脈	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0	0	0	0
伝導障害	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
拡張機能障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
心筋虚血	0	0	0	1 (0.4%)	0	1 (0.4%)	0
心膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0
心室性期外収縮	1 (0.4%)	1 (0.4%)	0	0	0	0	0
傷害、中毒および処置合併症	4 (1.4%)	1 (0.4%)	4 (1.4%)	7 (2.5%)	0	2 (0.7%)	6 (2.1%)
挫傷	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	0	1 (0.4%)	4 (1.4%)
各種物質毒性	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
転倒	1 (0.4%)	0	1 (0.4%)	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
引っかき傷	1 (0.4%)	0	1 (0.4%)	0	0	0	0
脊椎圧迫骨折	0	0	0	1 (0.4%)	0	0	1 (0.4%)
創合併症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
内分泌障害	8 (2.8%)	0	8 (2.8%)	2 (0.7%)	0	0	2 (0.7%)
クッシング様症状	4 (1.4%)	0	4 (1.4%)	1 (0.4%)	0	0	1 (0.4%)
ステロイド離脱症候群	2 (0.7%)	0	2 (0.7%)	0	0	0	0
クッシング症候群	1 (0.4%)	0	1 (0.4%)	0	0	0	0
高コルチコイド症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
下垂体依存性クッシング症候群	1 (0.4%)	0	1 (0.4%)	0	0	0	0
耳および迷路障害	3 (1.1%)	2 (0.7%)	3 (1.1%)	6 (2.1%)	4 (1.4%)	4 (1.4%)	2 (0.7%)
回転性めまい	3 (1.1%)	2 (0.7%)	3 (1.1%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
耳鳴	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
聴力低下	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5 (1.8%)	4 (1.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
扁平上皮癌	2 (0.7%)	2 (0.7%)	0	0	0	0	0
急性単球性白血病	0	0	0	1 (0.4%)	0	1 (0.4%)	0
基底細胞癌	1 (0.4%)	1 (0.4%)	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚血管腫	1 (0.4%)	0	1 (0.4%)	0	0	0	0
前立腺癌	1 (0.4%)	1 (0.4%)	0	0	0	0	0
肝胆道系障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
肝機能異常	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	2 (0.7%)
肝細胞損傷	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
高ビリルビン血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
生殖系および乳房障害	3 (1.1%)	3 (1.1%)	1 (0.4%)	2 (0.7%)	0	2 (0.7%)	0
勃起不全	2 (0.7%)	2 (0.7%)	0	2 (0.7%)	0	2 (0.7%)	0
骨盤痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
免疫系障害	0	0	0	3 (1.1%)	3 (1.1%)	1 (0.4%)	1 (0.4%)
薬物過敏症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
低γグロブリン血症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
免疫抑制	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
先天性、家族性および遺伝性障害	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
角膜ジストロフィー	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
Japanese							
Analysis set: safety	15			20			
Total number of subjects with TEAE related to study treatment	15 (100.0%)	14 (93.3%)	15 (100.0%)	20 (100.0%)	15 (75.0%)	20 (100.0%)	16 (80.0%)
MedDRA system organ class/Preferred term							
血液およびリンパ系障害	11 (73.3%)	8 (53.3%)	10 (66.7%)	15 (75.0%)	8 (40.0%)	14 (70.0%)	6 (30.0%)
好中球減少症	5 (33.3%)	5 (33.3%)	1 (6.7%)	12 (60.0%)	4 (20.0%)	11 (55.0%)	1 (5.0%)
血小板減少症	6 (40.0%)	5 (33.3%)	2 (13.3%)	3 (15.0%)	0	3 (15.0%)	0
貧血	1 (6.7%)	1 (6.7%)	0	1 (5.0%)	0	1 (5.0%)	0
白血球減少症	2 (13.3%)	2 (13.3%)	1 (6.7%)	3 (15.0%)	2 (10.0%)	2 (10.0%)	0
リンパ球減少症	7 (46.7%)	4 (26.7%)	7 (46.7%)	7 (35.0%)	4 (20.0%)	7 (35.0%)	5 (25.0%)
発熱性好中球減少症	0	0	0	0	0	0	0
白血球増加症	1 (6.7%)	0	1 (6.7%)	0	0	0	0
好酸球増加症	0	0	0	1 (5.0%)	0	1 (5.0%)	0
出血性障害	0	0	0	0	0	0	0
リンパ節症	0	0	0	0	0	0	0
鉄芽球性貧血	0	0	0	0	0	0	0
一般・全身障害および投与部位の状態	1 (6.7%)	1 (6.7%)	1 (6.7%)	7 (35.0%)	4 (20.0%)	3 (15.0%)	4 (20.0%)
疲労	0	0	0	1 (5.0%)	0	0	1 (5.0%)
無力症	0	0	0	0	0	0	0
末梢性浮腫	0	0	0	1 (5.0%)	0	0	1 (5.0%)
発熱	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (10.0%)	1 (5.0%)	1 (5.0%)	0
悪寒	0	0	0	1 (5.0%)	1 (5.0%)	0	0
倦怠感	0	0	0	2 (10.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
末梢腫脹	0	0	0	0	0	0	0
インフルエンザ様疾患	0	0	0	0	0	0	0
胸部不快感	0	0	0	0	0	0	0
冷感	0	0	0	0	0	0	0
顔面浮腫	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
全身健康状態低下	0	0	0	0	0	0	0
薬物不耐性	0	0	0	0	0	0	0
びくびく感	0	0	0	0	0	0	0
非心臓性胸痛	0	0	0	0	0	0	0
浮腫	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
疼痛	0	0	0	0	0	0	0
苦悶感	0	0	0	0	0	0	0
医薬品副作用	0	0	0	0	0	0	0
胸痛	0	0	0	0	0	0	0
運動耐性低下	0	0	0	0	0	0	0
溢出	0	0	0	0	0	0	0
脂肪組織増加	0	0	0	0	0	0	0
異常感	0	0	0	0	0	0	0
熱感	0	0	0	0	0	0	0
歩行障害	0	0	0	0	0	0	0
全身性浮腫	0	0	0	0	0	0	0
高熱	0	0	0	0	0	0	0
注入部位発疹	0	0	0	0	0	0	0
多臓器不全	0	0	0	0	0	0	0
分泌物分泌	0	0	0	0	0	0	0
全身性炎症反応症候群	0	0	0	0	0	0	0
胃腸障害	5 (33.3%)	4 (26.7%)	2 (13.3%)	4 (20.0%)	2 (10.0%)	4 (20.0%)	1 (5.0%)
下痢	0	0	0	1 (5.0%)	0	1 (5.0%)	0
便秘	3 (20.0%)	2 (13.3%)	1 (6.7%)	2 (10.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)
悪心	0	0	0	1 (5.0%)	0	1 (5.0%)	0
嘔吐	0	0	0	0	0	0	0
上腹部痛	0	0	0	0	0	0	0
消化不良	0	0	0	0	0	0	0
口内炎	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	0
腹痛	0	0	0	0	0	0	0
口内乾燥	0	0	0	0	0	0	0
腹部膨満	1 (6.7%)	1 (6.7%)	1 (6.7%)	0	0	0	0
腹部不快感	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
胃食道逆流性疾患	0	0	0	0	0	0	0
口腔内潰瘍形成	0	0	0	0	0	0	0
口腔内痛	0	0	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0	0
放屁	0	0	0	0	0	0	0
胃炎	0	0	0	0	0	0	0
胃腸障害	0	0	0	0	0	0	0
口腔粘膜水疱形成	0	0	0	0	0	0	0
口の錯感覚	0	0	0	0	0	0	0
腹壁血腫	0	0	0	0	0	0	0
裂肛	0	0	0	0	0	0	0
アフタ性口内炎	0	0	0	0	0	0	0
胆汁酸吸収不良	0	0	0	0	0	0	0
便通不規則	0	0	0	0	0	0	0
大腸炎	0	0	0	0	0	0	0
齲歯	0	0	0	0	0	0	0
嚥下障害	0	0	0	0	0	0	0
心窩部不快感	0	0	0	0	0	0	0
おくび	0	0	0	0	0	0	0
糞塊	0	0	0	0	0	0	0
胃拡張	0	0	0	0	0	0	0
胃障害	0	0	0	0	0	0	0
胃出血	0	0	0	0	0	0	0
消化管運動障害	0	0	0	0	0	0	0
消化器痛	0	0	0	0	0	0	0
舌痛	0	0	0	0	0	0	0
痔核	0	0	0	0	0	0	0
口の感覚鈍麻	0	0	0	0	0	0	0
腸管穿孔	0	0	0	0	0	0	0
口唇そう痒症	0	0	0	0	0	0	0
口唇腫脹	0	0	0	0	0	0	0
メレナ	1 (6.7%)	1 (6.7%)	0	0	0	0	0
非感染性歯肉炎	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
嚥下痛	0	0	0	0	0	0	0
膵炎	0	0	0	0	0	0	0
地図状舌	0	0	0	0	0	0	0
舌潰瘍	0	0	0	0	0	0	0
感染症および寄生虫症	7 (46.7%)	6 (40.0%)	7 (46.7%)	7 (35.0%)	5 (25.0%)	6 (30.0%)	7 (35.0%)
上気道感染	0	0	0	0	0	0	0
肺炎	2 (13.3%)	2 (13.3%)	2 (13.3%)	1 (5.0%)	0	0	1 (5.0%)
気管支炎	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
気道感染	0	0	0	0	0	0	0
鼻咽頭炎	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)
下気道感染	0	0	0	0	0	0	0
帯状疱疹	1 (6.7%)	1 (6.7%)	1 (6.7%)	0	0	0	0
口腔カンジダ症	0	0	0	0	0	0	0
口腔真菌感染	0	0	0	0	0	0	0
インフルエンザ	0	0	0	0	0	0	0
副鼻腔炎	0	0	0	0	0	0	0
ウイルス感染	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	0
皮膚感染	0	0	0	1 (5.0%)	0	1 (5.0%)	1 (5.0%)
尿路感染	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
歯肉炎	0	0	0	0	0	0	0
咽頭炎	0	0	0	0	0	0	0
歯膿瘍	0	0	0	0	0	0	0
気管支肺炎	1 (6.7%)	0	1 (6.7%)	0	0	0	0
結膜炎	0	0	0	0	0	0	0
膀胱炎	0	0	0	0	0	0	0
胃腸炎	0	0	0	0	0	0	0
ヘルペスウイルス感染	0	0	0	0	0	0	0
肺感染	0	0	0	0	0	0	0
粘膜感染	0	0	0	0	0	0	0
インフルエンザ性肺炎	0	0	0	0	0	0	0
鼻炎	0	0	0	0	0	0	0
足部白癬	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
細気管支炎	0	0	0	0	0	0	0
蜂巣炎	0	0	0	0	0	0	0
丹毒	0	0	0	0	0	0	0
真菌感染	0	0	0	0	0	0	0
限局性感染	0	0	0	0	0	0	0
口腔ヘルペス	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0
ＲＳウイルス感染	0	0	0	0	0	0	0
敗血症	0	0	0	0	0	0	0
皮膚カンジダ	0	0	0	0	0	0	0
歯感染	0	0	0	0	0	0	0
四肢膿瘍	0	0	0	0	0	0	0
急性扁桃炎	0	0	0	0	0	0	0
肛門膿瘍	0	0	0	0	0	0	0
細菌感染	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
細菌性気管支炎	0	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	0	0	0
カンピロバクター胃腸炎	0	0	0	0	0	0	0
カンジダ感染	0	0	0	0	0	0	0
コロナウイルス感染	0	0	0	0	0	0	0
サイトメガロウイルス感染	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
蓄膿	1 (6.7%)	1 (6.7%)	1 (6.7%)	0	0	0	0
感染性小腸結腸炎	0	0	0	0	0	0	0
大腸菌性菌血症	0	0	0	0	0	0	0
眼感染	0	0	0	0	0	0	0
真菌性眼感染	0	0	0	0	0	0	0
熱性感染症	0	0	0	0	0	0	0
毛包炎	0	0	0	0	0	0	0
皮膚真菌感染	0	0	0	0	0	0	0
真菌性性器感染	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	0	0	0
感染性筋炎	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
注入部位蜂巣炎	0	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0	0
喉頭炎	0	0	0	0	0	0	0
リステリア性敗血症	0	0	0	0	0	0	0
大葉性肺炎	0	0	0	0	0	0	0
ウイルス性下気道感染	0	0	0	0	0	0	0
鼻ヘルペス	0	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0	0
中咽頭カンジダ症	0	0	0	0	0	0	0
中耳炎	1 (6.7%)	1 (6.7%)	1 (6.7%)	0	0	0	0
急性中耳炎	0	0	0	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0	0	0	0
耳下腺炎	0	0	0	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0	0	0	0
レンサ球菌性咽頭炎	0	0	0	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	0	0
腎盂腎炎	0	0	0	0	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0	0	0	0
皮下組織膿瘍	0	0	0	0	0	0	0
扁桃炎	0	0	0	0	0	0	0
細菌性上気道感染	0	0	0	0	0	0	0
尿道炎	0	0	0	0	0	0	0
腟感染	0	0	0	0	0	0	0
水痘	0	0	0	0	0	0	0
外陰部腟カンジダ症	0	0	0	0	0	0	0
外陰部腟炎	0	0	0	0	0	0	0
創傷感染	0	0	0	0	0	0	0
神経系障害	3 (20.0%)	3 (20.0%)	1 (6.7%)	3 (15.0%)	1 (5.0%)	3 (15.0%)	1 (5.0%)
振戦	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
味覚異常	1 (6.7%)	1 (6.7%)	0	1 (5.0%)	0	1 (5.0%)	1 (5.0%)
浮動性めまい	0	0	0	0	0	0	0
頭痛	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (5.0%)	1 (5.0%)	0	0
末梢性感覚ニューロパチー	2 (13.3%)	2 (13.3%)	1 (6.7%)	0	0	0	0
末梢性ニューロパチー	0	0	0	3 (15.0%)	0	3 (15.0%)	0
錯感覚	0	0	0	0	0	0	0
嗜眠	0	0	0	0	0	0	0
感覚鈍麻	0	0	0	0	0	0	0
記憶障害	0	0	0	0	0	0	0
味覚消失	0	0	0	0	0	0	0
平衡障害	0	0	0	0	0	0	0
注意力障害	0	0	0	0	0	0	0
神経痛	0	0	0	0	0	0	0
失神寸前の状態	0	0	0	0	0	0	0
失神	0	0	0	0	0	0	0
傾眠	0	0	0	0	0	0	0
アカシジア	0	0	0	0	0	0	0
体位性めまい	0	0	0	0	0	0	0
異常感覚	0	0	0	0	0	0	0
味覚減退	0	0	0	0	0	0	0
下肢静止不能症候群	0	0	0	0	0	0	0
健忘	0	0	0	0	0	0	0
失語症	0	0	0	0	0	0	0
脳梗塞	0	0	0	0	0	0	0
構語障害	0	0	0	0	0	0	0
蟻走感	0	0	0	0	0	0	0
知覚過敏	0	0	0	0	0	0	0
過眠症	0	0	0	0	0	0	0
肋間神経痛	0	0	0	0	0	0	0
意識消失	0	0	0	0	0	0	0
片頭痛	0	0	0	0	0	0	0
不随意性筋収縮	0	0	0	0	0	0	0
筋痙直	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
神経系障害	0	0	0	0	0	0	0
嗅覚錯誤	0	0	0	0	0	0	0
ヘルペス後神経痛	0	0	0	0	0	0	0
精神運動亢進	0	0	0	0	0	0	0
副鼻腔炎に伴う頭痛	0	0	0	0	0	0	0
脊髄圧迫	0	0	0	0	0	0	0
一過性脳虚血発作	0	0	0	0	0	0	0
上位運動ニューロンの病変	0	0	0	0	0	0	0
第７脳神経麻痺	0	0	0	0	0	0	0
視野欠損	0	0	0	0	0	0	0
筋骨格系および結合組織障害	4 (26.7%)	3 (20.0%)	2 (13.3%)	0	0	0	0
筋痙縮	2 (13.3%)	2 (13.3%)	0	0	0	0	0
筋力低下	1 (6.7%)	0	1 (6.7%)	0	0	0	0
筋肉痛	0	0	0	0	0	0	0
四肢痛	0	0	0	0	0	0	0
背部痛	0	0	0	0	0	0	0
関節痛	0	0	0	0	0	0	0
筋骨格系胸痛	0	0	0	0	0	0	0
ミオパチー	1 (6.7%)	1 (6.7%)	1 (6.7%)	0	0	0	0
骨痛	0	0	0	0	0	0	0
関節腫脹	0	0	0	0	0	0	0
筋肉疲労	0	0	0	0	0	0	0
筋骨格痛	0	0	0	0	0	0	0
頚部痛	0	0	0	0	0	0	0
筋萎縮症	0	0	0	0	0	0	0
デュプイトラン拘縮	0	0	0	0	0	0	0
側腹部痛	0	0	0	0	0	0	0
出血性関節症	0	0	0	0	0	0	0
関節滲出液	0	0	0	0	0	0	0
運動性低下	0	0	0	0	0	0	0
筋緊張	0	0	0	0	0	0	0
筋骨格硬直	0	0	0	0	0	0	0
骨壊死	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
顎骨壊死	0	0	0	0	0	0	0
骨粗鬆症	0	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	0	0	0
脊椎障害	0	0	0	0	0	0	0
脊椎痛	0	0	0	0	0	0	0
腱痛	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	2 (13.3%)	2 (13.3%)	1 (6.7%)	8 (40.0%)	6 (30.0%)	1 (5.0%)	3 (15.0%)
呼吸困難	0	0	0	2 (10.0%)	2 (10.0%)	0	0
咳嗽	0	0	0	0	0	0	0
肺塞栓症	0	0	0	0	0	0	0
気管支痙攣	0	0	0	0	0	0	0
発声障害	0	0	0	0	0	0	0
しゃっくり	2 (13.3%)	2 (13.3%)	1 (6.7%)	3 (15.0%)	0	0	3 (15.0%)
アレルギー性鼻炎	0	0	0	0	0	0	0
鼻閉	0	0	0	0	0	0	0
湿性咳嗽	0	0	0	0	0	0	0
鼻漏	0	0	0	1 (5.0%)	1 (5.0%)	0	0
咽喉刺激感	0	0	0	0	0	0	0
喘鳴	0	0	0	0	0	0	0
低酸素症	0	0	0	2 (10.0%)	2 (10.0%)	1 (5.0%)	1 (5.0%)
喉頭浮腫	0	0	0	0	0	0	0
口腔咽頭痛	0	0	0	0	0	0	0
労作性呼吸困難	0	0	0	0	0	0	0
鼻出血	0	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0	0
アレルギー性呼吸器症状	0	0	0	0	0	0	0
肺障害	0	0	0	0	0	0	0
鼻閉塞	0	0	0	0	0	0	0
肺臓炎	0	0	0	0	0	0	0
くしゃみ	0	0	0	0	0	0	0
窒息	0	0	0	0	0	0	0
気管支拡張症	0	0	0	0	0	0	0
カタル	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
慢性閉塞性肺疾患	0	0	0	0	0	0	0
胸水症	0	0	0	0	0	0	0
喉頭不快感	0	0	0	0	0	0	0
喉頭の炎症	0	0	0	0	0	0	0
喉頭狭窄	0	0	0	1 (5.0%)	1 (5.0%)	0	0
喉頭刺激感	0	0	0	0	0	0	0
鼻部不快感	0	0	0	0	0	0	0
咽頭紅斑	0	0	0	0	0	0	0
誤嚥性肺炎	0	0	0	0	0	0	0
呼気延長	0	0	0	0	0	0	0
副鼻腔うっ血	0	0	0	0	0	0	0
副鼻腔障害	0	0	0	0	0	0	0
上気道性喘鳴	0	0	0	1 (5.0%)	1 (5.0%)	0	0
窒息感	0	0	0	0	0	0	0
咽喉絞扼感	0	0	0	0	0	0	0
精神障害	2 (13.3%)	0	2 (13.3%)	0	0	0	0
不眠症	2 (13.3%)	0	2 (13.3%)	0	0	0	0
不安	0	0	0	0	0	0	0
激越	0	0	0	0	0	0	0
うつ病	0	0	0	0	0	0	0
易刺激性	0	0	0	0	0	0	0
気分変化	0	0	0	0	0	0	0
落ち着きのなさ	0	0	0	0	0	0	0
神経過敏	0	0	0	0	0	0	0
睡眠障害	0	0	0	0	0	0	0
抑うつ気分	0	0	0	0	0	0	0
錯乱状態	0	0	0	0	0	0	0
精神障害	0	0	0	0	0	0	0
気分動揺	0	0	0	0	0	0	0
感情障害	0	0	0	0	0	0	0
譫妄	0	0	0	0	0	0	0
まとまりのない会話	0	0	0	0	0	0	0
気分変調性障害	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
幻覚	0	0	0	0	0	0	0
言葉もれ	0	0	0	0	0	0	0
リビドー消失	0	0	0	0	0	0	0
精神病性障害	0	0	0	0	0	0	0
ストレス	0	0	0	0	0	0	0
皮膚および皮下組織障害	5 (33.3%)	5 (33.3%)	0	6 (30.0%)	1 (5.0%)	6 (30.0%)	0
そう痒症	1 (6.7%)	1 (6.7%)	0	0	0	0	0
発疹	2 (13.3%)	2 (13.3%)	0	3 (15.0%)	0	3 (15.0%)	0
多汗症	0	0	0	0	0	0	0
紅斑	0	0	0	0	0	0	0
斑状丘疹状皮疹	0	0	0	0	0	0	0
全身性皮疹	1 (6.7%)	1 (6.7%)	0	1 (5.0%)	0	1 (5.0%)	0
蕁麻疹	0	0	0	0	0	0	0
皮膚乾燥	0	0	0	0	0	0	0
顔面腫脹	0	0	0	0	0	0	0
斑状出血	0	0	0	0	0	0	0
寝汗	0	0	0	0	0	0	0
斑状皮疹	0	0	0	0	0	0	0
日光角化症	0	0	0	0	0	0	0
皮膚炎	0	0	0	0	0	0	0
ざ瘡様皮膚炎	0	0	0	0	0	0	0
アレルギー性皮膚炎	0	0	0	0	0	0	0
湿疹	0	0	0	0	0	0	0
多形紅斑	1 (6.7%)	1 (6.7%)	0	1 (5.0%)	0	1 (5.0%)	0
男性型多毛症	0	0	0	0	0	0	0
点状出血	0	0	0	0	0	0	0
そう痒性皮疹	0	0	0	0	0	0	0
皮膚潰瘍	0	0	0	0	0	0	0
脱毛症	0	0	0	0	0	0	0
冷汗	0	0	0	0	0	0	0
褥瘡性潰瘍	0	0	0	0	0	0	0
接触性皮膚炎	0	0	0	0	0	0	0
薬疹	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
紅色症	0	0	0	0	0	0	0
全身紅斑	0	0	0	0	0	0	0
毛髪成長異常	0	0	0	0	0	0	0
手皮膚炎	0	0	0	0	0	0	0
多毛症	0	0	0	0	0	0	0
爪甲脱落症	0	0	0	0	0	0	0
皮膚疼痛	0	0	0	0	0	0	0
アレルギー性そう痒症	0	0	0	0	0	0	0
壊疽性膿皮症	0	0	0	0	0	0	0
丘疹性皮疹	0	0	0	0	0	0	0
皮膚亀裂	0	0	0	0	0	0	0
皮膚色素過剰	0	0	0	0	0	0	0
皮膚病変	0	0	0	0	0	0	0
うっ滞性皮膚炎	0	0	0	0	0	0	0
毛細血管拡張症	0	0	0	0	0	0	0
血管炎性皮疹	0	0	0	0	0	0	0
代謝および栄養障害	4 (26.7%)	1 (6.7%)	4 (26.7%)	3 (15.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)
高血糖	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (10.0%)	0	0	2 (10.0%)
食欲減退	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	0
低カリウム血症	0	0	0	0	0	0	0
低リン酸血症	1 (6.7%)	0	1 (6.7%)	0	0	0	0
低カルシウム血症	0	0	0	0	0	0	0
低マグネシウム血症	0	0	0	0	0	0	0
低アルブミン血症	0	0	0	0	0	0	0
脱水	0	0	0	0	0	0	0
糖尿病	0	0	0	0	0	0	0
痛風	0	0	0	0	0	0	0
低ナトリウム血症	0	0	0	0	0	0	0
水分過負荷	0	0	0	0	0	0	0
体液貯留	0	0	0	0	0	0	0
葉酸欠乏	0	0	0	0	0	0	0
高コレステロール血症	0	0	0	0	0	0	0
高脂血症	1 (6.7%)	0	1 (6.7%)	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
高尿酸血症	1 (6.7%)	0	1 (6.7%)	0	0	0	0
食欲亢進	0	0	0	0	0	0	0
多飲症	0	0	0	0	0	0	0
１型糖尿病	0	0	0	0	0	0	0
２型糖尿病	0	0	0	0	0	0	0
血管障害	0	0	0	4 (20.0%)	2 (10.0%)	1 (5.0%)	2 (10.0%)
深部静脈血栓症	0	0	0	0	0	0	0
高血圧	0	0	0	1 (5.0%)	0	0	1 (5.0%)
潮紅	0	0	0	1 (5.0%)	1 (5.0%)	0	0
低血圧	0	0	0	1 (5.0%)	1 (5.0%)	0	0
表在性血栓性静脈炎	0	0	0	0	0	0	0
ほてり	0	0	0	0	0	0	0
静脈炎	0	0	0	0	0	0	0
塞栓症	0	0	0	1 (5.0%)	0	1 (5.0%)	1 (5.0%)
起立性低血圧	0	0	0	0	0	0	0
血栓性静脈炎	0	0	0	1 (5.0%)	0	1 (5.0%)	1 (5.0%)
血栓症	0	0	0	0	0	0	0
血腫	0	0	0	0	0	0	0
静脈血栓症	0	0	0	0	0	0	0
出血性梗塞	0	0	0	0	0	0	0
蒼白	0	0	0	0	0	0	0
末梢冷感	0	0	0	0	0	0	0
表在性静脈炎	0	0	0	0	0	0	0
四肢静脈血栓症	0	0	0	0	0	0	0
臨床検査	2 (13.3%)	2 (13.3%)	1 (6.7%)	4 (20.0%)	3 (15.0%)	4 (20.0%)	3 (15.0%)
アラニンアミノトランスフェラーゼ増加	1 (6.7%)	1 (6.7%)	1 (6.7%)	4 (20.0%)	3 (15.0%)	4 (20.0%)	3 (15.0%)
体重減少	0	0	0	0	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)
血中クレアチニン増加	0	0	0	0	0	0	0
γ－グルタミルトランスフェラーゼ増加	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
体重増加	0	0	0	0	0	0	0
心電図ＱＴ延長	0	0	0	0	0	0	0
血中アルカリホスファターゼ増加	0	0	0	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)
腎クレアチニン・クリアランス減少	0	0	0	0	0	0	0
血中乳酸脱水素酵素減少	0	0	0	0	0	0	0
血圧上昇	0	0	0	0	0	0	0
体温上昇	0	0	0	0	0	0	0
フィブリンＤダイマー増加	1 (6.7%)	1 (6.7%)	0	0	0	0	0
ヘリコバクター検査陽性	0	0	0	0	0	0	0
免疫グロブリン減少	0	0	0	0	0	0	0
好中球中毒性顆粒存在	0	0	0	0	0	0	0
酸素飽和度低下	0	0	0	0	0	0	0
トロポニン増加	0	0	0	0	0	0	0
静脈雑音	0	0	0	0	0	0	0
眼障害	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
白内障	0	0	0	0	0	0	0
霧視	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
流涙増加	0	0	0	0	0	0	0
眼刺激	0	0	0	0	0	0	0
眼乾燥	0	0	0	0	0	0	0
眼部腫脹	0	0	0	0	0	0	0
視力低下	0	0	0	0	0	0	0
視力障害	0	0	0	0	0	0	0
結膜刺激	0	0	0	0	0	0	0
眼のアレルギー	0	0	0	0	0	0	0
眼の障害	0	0	0	0	0	0	0
眼出血	0	0	0	0	0	0	0
眼球浮腫	0	0	0	0	0	0	0
眼瞼発疹	0	0	0	0	0	0	0
水晶体混濁	0	0	0	0	0	0	0
眼充血	0	0	0	0	0	0	0
眼窩周囲浮腫	0	0	0	0	0	0	0
網膜静脈血栓症	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
硝子体浮遊物	0	0	0	0	0	0	0
腎および尿路障害	1 (6.7%)	1 (6.7%)	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	0
腎機能障害	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	0
急性腎不全	1 (6.7%)	1 (6.7%)	0	0	0	0	0
腎不全	0	0	0	0	0	0	0
高窒素血症	0	0	0	0	0	0	0
慢性腎臓病	0	0	0	0	0	0	0
排尿困難	0	0	0	0	0	0	0
頻尿	0	0	0	0	0	0	0
多尿	0	0	0	0	0	0	0
腎嚢胞	0	0	0	0	0	0	0
尿失禁	0	0	0	0	0	0	0
尿閉	0	0	0	0	0	0	0
心臓障害	0	0	0	0	0	0	0
心房細動	0	0	0	0	0	0	0
頻脈	0	0	0	0	0	0	0
狭心症	0	0	0	0	0	0	0
徐脈	0	0	0	0	0	0	0
動悸	0	0	0	0	0	0	0
洞性頻脈	0	0	0	0	0	0	0
上室性頻脈	0	0	0	0	0	0	0
急性心筋梗塞	0	0	0	0	0	0	0
伝導障害	0	0	0	0	0	0	0
拡張機能障害	0	0	0	0	0	0	0
心筋虚血	0	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0	0
心室性期外収縮	0	0	0	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0	0	0	0
挫傷	0	0	0	0	0	0	0
各種物質毒性	0	0	0	0	0	0	0
転倒	0	0	0	0	0	0	0
引っかき傷	0	0	0	0	0	0	0
脊椎圧迫骨折	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
創合併症	0	0	0	0	0	0	0
内分泌障害	0	0	0	0	0	0	0
クッシング様症状	0	0	0	0	0	0	0
ステロイド離脱症候群	0	0	0	0	0	0	0
クッシング症候群	0	0	0	0	0	0	0
高コルチコイド症	0	0	0	0	0	0	0
下垂体依存性クッシング症候群	0	0	0	0	0	0	0
耳および迷路障害	0	0	0	0	0	0	0
回転性めまい	0	0	0	0	0	0	0
耳鳴	0	0	0	0	0	0	0
聴力低下	0	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
扁平上皮癌	0	0	0	0	0	0	0
急性単球性白血病	0	0	0	0	0	0	0
基底細胞癌	0	0	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
皮膚血管腫	0	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0	0
肝胆道系障害	0	0	0	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)
肝機能異常	0	0	0	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)
肝細胞損傷	0	0	0	0	0	0	0
高ビリルビン血症	0	0	0	0	0	0	0
生殖系および乳房障害	0	0	0	0	0	0	0
勃起不全	0	0	0	0	0	0	0
骨盤痛	0	0	0	0	0	0	0
免疫系障害	0	0	0	0	0	0	0
薬物過敏症	0	0	0	0	0	0	0
低ｯグロブリン血症	0	0	0	0	0	0	0
免疫抑制	0	0	0	0	0	0	0
先天性、家族性および遺伝性障害	0	0	0	0	0	0	0
角膜ジストロフィー	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
East Asian[b] Analysis set: safety	44			51			
Total number of subjects with TEAE related to study treatment	30 (68.2%)	28 (63.6%)	27 (61.4%)	48 (94.1%)	39 (76.5%)	47 (92.2%)	32 (62.7%)
MedDRA system organ class/Preferred term							
血液およびリンパ系障害	22 (50.0%)	19 (43.2%)	10 (22.7%)	38 (74.5%)	17 (33.3%)	37 (72.5%)	8 (15.7%)
好中球減少症	14 (31.8%)	14 (31.8%)	1 (2.3%)	32 (62.7%)	10 (19.6%)	31 (60.8%)	2 (3.9%)
血小板減少症	13 (29.5%)	12 (27.3%)	2 (4.5%)	9 (17.6%)	3 (5.9%)	9 (17.6%)	0
貧血	4 (9.1%)	4 (9.1%)	0	3 (5.9%)	1 (2.0%)	3 (5.9%)	0
白血球減少症	4 (9.1%)	4 (9.1%)	1 (2.3%)	10 (19.6%)	8 (15.7%)	9 (17.6%)	1 (2.0%)
リンパ球減少症	7 (15.9%)	4 (9.1%)	7 (15.9%)	7 (13.7%)	4 (7.8%)	7 (13.7%)	5 (9.8%)
発熱性好中球減少症	1 (2.3%)	1 (2.3%)	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
白血球増加症	1 (2.3%)	0	1 (2.3%)	0	0	0	0
好酸球増加症	0	0	0	1 (2.0%)	0	1 (2.0%)	0
出血性障害	0	0	0	0	0	0	0
リンパ節症	0	0	0	0	0	0	0
鉄芽球性貧血	0	0	0	0	0	0	0
一般・全身障害および投与部位の状態	8 (18.2%)	5 (11.4%)	7 (15.9%)	19 (37.3%)	14 (27.5%)	9 (17.6%)	11 (21.6%)
疲労	7 (15.9%)	3 (6.8%)	6 (13.6%)	6 (11.8%)	2 (3.9%)	5 (9.8%)	5 (9.8%)
無力症	0	0	0	2 (3.9%)	1 (2.0%)	1 (2.0%)	2 (3.9%)
末梢性浮腫	1 (2.3%)	1 (2.3%)	0	2 (3.9%)	0	0	2 (3.9%)
発熱	1 (2.3%)	1 (2.3%)	1 (2.3%)	6 (11.8%)	5 (9.8%)	4 (7.8%)	2 (3.9%)
悪寒	0	0	0	3 (5.9%)	3 (5.9%)	0	0
倦怠感	0	0	0	2 (3.9%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
末梢腫脹	0	0	0	0	0	0	0
インフルエンザ様疾患	0	0	0	0	0	0	0
胸部不快感	0	0	0	2 (3.9%)	2 (3.9%)	0	0
冷感	0	0	0	3 (5.9%)	3 (5.9%)	0	0
顔面浮腫	0	0	0	0	0	0	0
全身健康状態低下	0	0	0	0	0	0	0
薬物不耐性	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
びくびく感	0	0	0	0	0	0	0
非心臓性胸痛	0	0	0	0	0	0	0
浮腫	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
疼痛	0	0	0	1 (2.0%)	0	1 (2.0%)	0
苦悶感	0	0	0	0	0	0	0
医薬品副作用	0	0	0	0	0	0	0
胸痛	0	0	0	0	0	0	0
運動耐性低下	0	0	0	0	0	0	0
溢出	0	0	0	0	0	0	0
脂肪組織増加	0	0	0	0	0	0	0
異常感	0	0	0	0	0	0	0
熱感	0	0	0	0	0	0	0
歩行障害	0	0	0	0	0	0	0
全身性浮腫	0	0	0	0	0	0	0
高熱	0	0	0	0	0	0	0
注入部位発疹	0	0	0	0	0	0	0
多臓器不全	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
分泌物分泌	0	0	0	0	0	0	0
全身性炎症反応症候群	0	0	0	0	0	0	0
胃腸障害	7 (15.9%)	5 (11.4%)	4 (9.1%)	14 (27.5%)	8 (15.7%)	11 (21.6%)	5 (9.8%)
下痢	0	0	0	5 (9.8%)	1 (2.0%)	5 (9.8%)	0
便秘	4 (9.1%)	3 (6.8%)	2 (4.5%)	5 (9.8%)	2 (3.9%)	5 (9.8%)	3 (5.9%)
悪心	1 (2.3%)	0	1 (2.3%)	3 (5.9%)	1 (2.0%)	2 (3.9%)	0
嘔吐	0	0	0	3 (5.9%)	3 (5.9%)	0	0
上腹部痛	1 (2.3%)	0	1 (2.3%)	1 (2.0%)	0	0	1 (2.0%)
消化不良	0	0	0	0	0	0	0
口内炎	0	0	0	3 (5.9%)	3 (5.9%)	3 (5.9%)	2 (3.9%)
腹痛	0	0	0	0	0	0	0
口内乾燥	0	0	0	0	0	0	0
腹部膨満	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0
腹部不快感	1 (2.3%)	0	1 (2.3%)	0	0	0	0
胃食道逆流性疾患	0	0	0	0	0	0	0
口腔内潰瘍形成	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
口腔内痛	0	0	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0	0
放屁	0	0	0	1 (2.0%)	0	1 (2.0%)	0
胃炎	0	0	0	0	0	0	0
胃腸障害	0	0	0	0	0	0	0
口腔粘膜水疱形成	0	0	0	0	0	0	0
口の錯感覚	0	0	0	0	0	0	0
腹壁血腫	0	0	0	0	0	0	0
裂肛	0	0	0	0	0	0	0
アフタ性口内炎	0	0	0	0	0	0	0
胆汁酸吸収不良	0	0	0	0	0	0	0
便通不規則	0	0	0	0	0	0	0
大腸炎	0	0	0	0	0	0	0
齲歯	0	0	0	0	0	0	0
嚥下障害	0	0	0	0	0	0	0
心窩部不快感	0	0	0	0	0	0	0
おくび	0	0	0	0	0	0	0
糞塊	0	0	0	0	0	0	0
胃拡張	0	0	0	0	0	0	0
胃障害	0	0	0	0	0	0	0
胃出血	0	0	0	0	0	0	0
消化管運動障害	0	0	0	0	0	0	0
消化器痛	0	0	0	0	0	0	0
舌痛	0	0	0	0	0	0	0
痔核	0	0	0	0	0	0	0
口の感覚鈍麻	0	0	0	0	0	0	0
腸管穿孔	0	0	0	0	0	0	0
口唇そう痒症	0	0	0	0	0	0	0
口唇腫脹	0	0	0	1 (2.0%)	1 (2.0%)	0	0
メレナ	1 (2.3%)	1 (2.3%)	0	0	0	0	0
非感染性歯肉炎	0	0	0	0	0	0	0
嚥下痛	0	0	0	0	0	0	0
膵炎	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
地図状舌	0	0	0	0	0	0	0
舌潰瘍	0	0	0	0	0	0	0
感染症および寄生虫症	10 (22.7%)	8 (18.2%)	9 (20.5%)	16 (31.4%)	12 (23.5%)	15 (29.4%)	14 (27.5%)
上気道感染	1 (2.3%)	0	1 (2.3%)	6 (11.8%)	5 (9.8%)	6 (11.8%)	6 (11.8%)
肺炎	2 (4.5%)	2 (4.5%)	2 (4.5%)	2 (3.9%)	0	1 (2.0%)	1 (2.0%)
気管支炎	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
気道感染	0	0	0	0	0	0	0
鼻咽頭炎	1 (2.3%)	1 (2.3%)	1 (2.3%)	2 (3.9%)	2 (3.9%)	2 (3.9%)	2 (3.9%)
下気道感染	0	0	0	0	0	0	0
帯状疱疹	2 (4.5%)	2 (4.5%)	1 (2.3%)	3 (5.9%)	3 (5.9%)	3 (5.9%)	2 (3.9%)
口腔カンジダ症	0	0	0	0	0	0	0
口腔真菌感染	0	0	0	0	0	0	0
インフルエンザ	0	0	0	0	0	0	0
副鼻腔炎	0	0	0	0	0	0	0
ウイルス感染	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	0
皮膚感染	0	0	0	1 (2.0%)	0	1 (2.0%)	1 (2.0%)
尿路感染	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
歯肉炎	0	0	0	0	0	0	0
咽頭炎	0	0	0	0	0	0	0
歯膿瘍	0	0	0	0	0	0	0
気管支肺炎	1 (2.3%)	0	1 (2.3%)	0	0	0	0
結膜炎	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
膀胱炎	0	0	0	0	0	0	0
胃腸炎	0	0	0	0	0	0	0
ヘルペスウイルス感染	0	0	0	0	0	0	0
肺感染	0	0	0	0	0	0	0
粘膜感染	0	0	0	0	0	0	0
インフルエンザ性肺炎	0	0	0	0	0	0	0
鼻炎	0	0	0	0	0	0	0
足部白癬	0	0	0	0	0	0	0
細気管支炎	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
蜂巣炎	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
丹毒	0	0	0	0	0	0	0
真菌感染	0	0	0	0	0	0	0
限局性感染	0	0	0	0	0	0	0
口腔ヘルペス	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0
ＲＳウイルス感染	0	0	0	0	0	0	0
敗血症	0	0	0	0	0	0	0
皮膚カンジダ	0	0	0	0	0	0	0
歯感染	0	0	0	0	0	0	0
四肢膿瘍	0	0	0	0	0	0	0
急性扁桃炎	0	0	0	0	0	0	0
肛門膿瘍	1 (2.3%)	1 (2.3%)	0	0	0	0	0
細菌感染	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
細菌性気管支炎	0	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	0	0	0
カンピロバクター胃腸炎	0	0	0	0	0	0	0
カンジダ感染	0	0	0	0	0	0	0
コロナウイルス感染	0	0	0	0	0	0	0
サイトメガロウイルス感染	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
蓄膿	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0
感染性小腸結腸炎	0	0	0	0	0	0	0
大腸菌性菌血症	0	0	0	0	0	0	0
眼感染	0	0	0	0	0	0	0
真菌性眼感染	0	0	0	0	0	0	0
熱性感染症	0	0	0	0	0	0	0
毛包炎	1 (2.3%)	0	1 (2.3%)	0	0	0	0
皮膚真菌感染	0	0	0	0	0	0	0
真菌性性器感染	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	0	0	0
感染性筋炎	0	0	0	0	0	0	0
注入部位蜂巣炎	0	0	0	1 (2.0%)	1 (2.0%)	0	0
真菌性角膜炎	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
喉頭炎	0	0	0	0	0	0	0
リステリア性敗血症	0	0	0	0	0	0	0
大葉性肺炎	0	0	0	0	0	0	0
ウイルス性下気道感染	0	0	0	0	0	0	0
鼻ヘルペス	0	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0	0
中咽頭カンジダ症	0	0	0	0	0	0	0
中耳炎	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0
急性中耳炎	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
パラインフルエンザウイルス感染	0	0	0	0	0	0	0
耳下腺炎	0	0	0	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0	0	0	0
レンサ球菌性咽頭炎	0	0	0	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	0	0
腎盂腎炎	0	0	0	0	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0	0	0	0
皮下組織膿瘍	0	0	0	0	0	0	0
扁桃炎	0	0	0	0	0	0	0
細菌性上気道感染	0	0	0	0	0	0	0
尿道炎	0	0	0	1 (2.0%)	0	0	1 (2.0%)
膣感染	0	0	0	0	0	0	0
水痘	0	0	0	0	0	0	0
外陰部膣カンジダ症	0	0	0	0	0	0	0
外陰部膣炎	0	0	0	0	0	0	0
創傷感染	0	0	0	0	0	0	0
神経系障害	6 (13.6%)	6 (13.6%)	2 (4.5%)	7 (13.7%)	2 (3.9%)	7 (13.7%)	2 (3.9%)
振戦	0	0	0	0	0	0	0
味覚異常	1 (2.3%)	1 (2.3%)	0	1 (2.0%)	0	1 (2.0%)	1 (2.0%)
浮動性めまい	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
頭痛	1 (2.3%)	1 (2.3%)	1 (2.3%)	1 (2.0%)	1 (2.0%)	0	0
末梢性感覚ニューロパチー	2 (4.5%)	2 (4.5%)	1 (2.3%)	1 (2.0%)	0	1 (2.0%)	0
末梢性ニューロパチー	0	0	0	3 (5.9%)	0	3 (5.9%)	0
錯感覚	0	0	0	0	0	0	0
嗜眠	0	0	0	0	0	0	0
感覚鈍麻	1 (2.3%)	1 (2.3%)	1 (2.3%)	2 (3.9%)	0	2 (3.9%)	0
記憶障害	0	0	0	0	0	0	0
味覚消失	0	0	0	0	0	0	0
平衡障害	0	0	0	0	0	0	0
注意力障害	0	0	0	0	0	0	0
神経痛	2 (4.5%)	2 (4.5%)	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
失神寸前の状態	0	0	0	0	0	0	0
失神	0	0	0	0	0	0	0
傾眠	0	0	0	0	0	0	0
アカシジア	0	0	0	0	0	0	0
体位性めまい	0	0	0	0	0	0	0
異常感覚	0	0	0	0	0	0	0
味覚減退	0	0	0	0	0	0	0
下肢静止不能症候群	0	0	0	0	0	0	0
健忘	0	0	0	0	0	0	0
失語症	0	0	0	0	0	0	0
脳梗塞	0	0	0	0	0	0	0
構語障害	0	0	0	1 (2.0%)	0	1 (2.0%)	0
蟻走感	0	0	0	0	0	0	0
知覚過敏	0	0	0	0	0	0	0
過眠症	0	0	0	0	0	0	0
肋間神経痛	0	0	0	0	0	0	0
意識消失	0	0	0	0	0	0	0
片頭痛	0	0	0	0	0	0	0
不随意性筋収縮	0	0	0	0	0	0	0
筋痙直	0	0	0	0	0	0	0
神経系障害	0	0	0	0	0	0	0
嗅覚錯誤	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
ヘルペス後神経痛	1 (2.3%)	1 (2.3%)	0	0	0	0	0
精神運動亢進	0	0	0	0	0	0	0
副鼻腔炎に伴う頭痛	0	0	0	0	0	0	0
脊髄圧迫	0	0	0	0	0	0	0
一過性脳虚血発作	0	0	0	0	0	0	0
上位運動ニューロンの病変	0	0	0	0	0	0	0
第７脳神経麻痺	0	0	0	0	0	0	0
視野欠損	0	0	0	0	0	0	0
筋骨格系および結合組織障害	7 (15.9%)	4 (9.1%)	5 (11.4%)	5 (9.8%)	1 (2.0%)	2 (3.9%)	2 (3.9%)
筋痙縮	4 (9.1%)	2 (4.5%)	2 (4.5%)	1 (2.0%)	0	0	1 (2.0%)
筋力低下	2 (4.5%)	0	2 (4.5%)	0	0	0	0
筋肉痛	1 (2.3%)	1 (2.3%)	0	1 (2.0%)	0	1 (2.0%)	0
四肢痛	0	0	0	1 (2.0%)	0	1 (2.0%)	0
背部痛	0	0	0	1 (2.0%)	0	0	1 (2.0%)
関節痛	0	0	0	0	0	0	0
筋骨格系胸痛	0	0	0	1 (2.0%)	1 (2.0%)	0	0
ミオパチー	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0
骨痛	0	0	0	0	0	0	0
関節腫脹	0	0	0	0	0	0	0
筋肉疲労	0	0	0	0	0	0	0
筋骨格痛	0	0	0	0	0	0	0
頚部痛	0	0	0	0	0	0	0
筋萎縮症	0	0	0	0	0	0	0
デュプイトラン拘縮	0	0	0	0	0	0	0
側腹部痛	0	0	0	0	0	0	0
出血性関節症	0	0	0	0	0	0	0
関節滲出液	0	0	0	0	0	0	0
運動性低下	0	0	0	0	0	0	0
筋緊張	0	0	0	0	0	0	0
筋骨格硬直	0	0	0	0	0	0	0
骨壊死	0	0	0	0	0	0	0
顎骨壊死	0	0	0	0	0	0	0
骨粗鬆症	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
脊柱管狭窄症	0	0	0	0	0	0	0
脊椎障害	0	0	0	0	0	0	0
脊椎痛	0	0	0	0	0	0	0
腱痛	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	2 (4.5%)	2 (4.5%)	1 (2.3%)	23 (45.1%)	21 (41.2%)	7 (13.7%)	8 (15.7%)
呼吸困難	0	0	0	6 (11.8%)	6 (11.8%)	1 (2.0%)	1 (2.0%)
咳嗽	0	0	0	3 (5.9%)	3 (5.9%)	2 (3.9%)	2 (3.9%)
肺塞栓症	0	0	0	0	0	0	0
気管支痙攣	0	0	0	0	0	0	0
発声障害	0	0	0	2 (3.9%)	1 (2.0%)	0	1 (2.0%)
しゃっくり	2 (4.5%)	2 (4.5%)	1 (2.3%)	4 (7.8%)	0	0	4 (7.8%)
アレルギー性鼻炎	0	0	0	2 (3.9%)	2 (3.9%)	1 (2.0%)	1 (2.0%)
鼻閉	0	0	0	0	0	0	0
湿性咳嗽	0	0	0	5 (9.8%)	4 (7.8%)	4 (7.8%)	4 (7.8%)
鼻漏	0	0	0	2 (3.9%)	2 (3.9%)	0	0
咽喉刺激感	0	0	0	0	0	0	0
喘鳴	0	0	0	1 (2.0%)	1 (2.0%)	0	0
低酸素症	0	0	0	5 (9.8%)	5 (9.8%)	1 (2.0%)	1 (2.0%)
喉頭浮腫	0	0	0	0	0	0	0
口腔咽頭痛	0	0	0	0	0	0	0
労作性呼吸困難	0	0	0	0	0	0	0
鼻出血	0	0	0	0	0	0	0
肺水腫	0	0	0	1 (2.0%)	1 (2.0%)	0	0
アレルギー性呼吸器症状	0	0	0	2 (3.9%)	2 (3.9%)	0	0
肺障害	0	0	0	0	0	0	0
鼻閉塞	0	0	0	1 (2.0%)	1 (2.0%)	0	0
肺臓炎	0	0	0	2 (3.9%)	2 (3.9%)	2 (3.9%)	1 (2.0%)
くしゃみ	0	0	0	0	0	0	0
窒息	0	0	0	0	0	0	0
気管支拡張症	0	0	0	0	0	0	0
カタル	0	0	0	0	0	0	0
慢性閉塞性肺疾患	0	0	0	0	0	0	0
胸水症	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
喉頭不快感	0	0	0	0	0	0	0
喉頭の炎症	0	0	0	0	0	0	0
喉頭狭窄	0	0	0	1 (2.0%)	1 (2.0%)	0	0
喉頭刺激感	0	0	0	0	0	0	0
鼻部不快感	0	0	0	0	0	0	0
咽頭紅斑	0	0	0	0	0	0	0
誤嚥性肺炎	0	0	0	0	0	0	0
呼気延長	0	0	0	0	0	0	0
副鼻腔うっ血	0	0	0	0	0	0	0
副鼻腔障害	0	0	0	0	0	0	0
上気道性喘鳴	0	0	0	1 (2.0%)	1 (2.0%)	0	0
窒息感	0	0	0	0	0	0	0
咽喉絞扼感	0	0	0	0	0	0	0
精神障害	5 (11.4%)	1 (2.3%)	5 (11.4%)	3 (5.9%)	0	1 (2.0%)	3 (5.9%)
不眠症	5 (11.4%)	1 (2.3%)	5 (11.4%)	3 (5.9%)	0	1 (2.0%)	3 (5.9%)
不安	0	0	0	0	0	0	0
激越	0	0	0	0	0	0	0
うつ病	0	0	0	0	0	0	0
易刺激性	0	0	0	0	0	0	0
気分変化	0	0	0	0	0	0	0
落ち着きのなさ	0	0	0	0	0	0	0
神経過敏	0	0	0	0	0	0	0
睡眠障害	0	0	0	0	0	0	0
抑うつ気分	0	0	0	0	0	0	0
錯乱状態	0	0	0	0	0	0	0
精神障害	0	0	0	0	0	0	0
気分動揺	0	0	0	0	0	0	0
感情障害	0	0	0	0	0	0	0
譫妄	0	0	0	0	0	0	0
まとまりのない会話	0	0	0	0	0	0	0
気分変調性障害	0	0	0	0	0	0	0
幻覚	0	0	0	0	0	0	0
言葉もれ	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
リビドー消失	0	0	0	0	0	0	0
精神病性障害	0	0	0	0	0	0	0
ストレス	0	0	0	0	0	0	0
皮膚および皮下組織障害	7 (15.9%)	7 (15.9%)	2 (4.5%)	13 (25.5%)	7 (13.7%)	10 (19.6%)	2 (3.9%)
そう痒症	1 (2.3%)	1 (2.3%)	0	2 (3.9%)	2 (3.9%)	0	0
発疹	2 (4.5%)	2 (4.5%)	0	3 (5.9%)	0	3 (5.9%)	0
多汗症	0	0	0	0	0	0	0
紅斑	0	0	0	0	0	0	0
斑状丘疹状皮疹	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	0
全身性皮疹	1 (2.3%)	1 (2.3%)	0	1 (2.0%)	0	1 (2.0%)	0
蕁麻疹	0	0	0	2 (3.9%)	2 (3.9%)	1 (2.0%)	0
皮膚乾燥	0	0	0	0	0	0	0
顔面腫脹	1 (2.3%)	0	1 (2.3%)	0	0	0	0
斑状出血	0	0	0	0	0	0	0
寝汗	0	0	0	0	0	0	0
斑状皮疹	0	0	0	0	0	0	0
日光角化症	0	0	0	0	0	0	0
皮膚炎	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
ざ瘡様皮膚炎	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
アレルギー性皮膚炎	0	0	0	1 (2.0%)	0	1 (2.0%)	0
湿疹	0	0	0	0	0	0	0
多形紅斑	1 (2.3%)	1 (2.3%)	0	1 (2.0%)	0	1 (2.0%)	0
男性型多毛症	0	0	0	0	0	0	0
点状出血	0	0	0	0	0	0	0
そう痒性皮疹	0	0	0	0	0	0	0
皮膚潰瘍	0	0	0	0	0	0	0
脱毛症	0	0	0	0	0	0	0
冷汗	0	0	0	1 (2.0%)	1 (2.0%)	0	0
褥瘡性潰瘍	0	0	0	0	0	0	0
接触性皮膚炎	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0
薬疹	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	0
紅色症	0	0	0	0	0	0	0
全身紅斑	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
毛髪成長異常	0	0	0	0	0	0	0
手皮膚炎	0	0	0	0	0	0	0
多毛症	0	0	0	0	0	0	0
爪甲脱落症	0	0	0	0	0	0	0
皮膚疼痛	0	0	0	0	0	0	0
アレルギー性そう痒症	0	0	0	0	0	0	0
壊疽性膿皮症	1 (2.3%)	1 (2.3%)	0	0	0	0	0
丘疹性皮疹	0	0	0	0	0	0	0
皮膚亀裂	0	0	0	0	0	0	0
皮膚色素過剰	0	0	0	0	0	0	0
皮膚病変	0	0	0	0	0	0	0
うっ滞性皮膚炎	0	0	0	0	0	0	0
毛細血管拡張症	0	0	0	0	0	0	0
血管炎性皮疹	0	0	0	0	0	0	0
代謝および栄養障害	5 (11.4%)	2 (4.5%)	4 (9.1%)	8 (15.7%)	3 (5.9%)	5 (9.8%)	4 (7.8%)
高血糖	1 (2.3%)	1 (2.3%)	1 (2.3%)	3 (5.9%)	0	0	3 (5.9%)
食欲減退	1 (2.3%)	1 (2.3%)	0	5 (9.8%)	3 (5.9%)	5 (9.8%)	1 (2.0%)
低カリウム血症	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
低リン酸血症	1 (2.3%)	0	1 (2.3%)	0	0	0	0
低カルシウム血症	0	0	0	0	0	0	0
低マグネシウム血症	0	0	0	0	0	0	0
低アルブミン血症	0	0	0	0	0	0	0
脱水	0	0	0	0	0	0	0
糖尿病	0	0	0	0	0	0	0
痛風	0	0	0	0	0	0	0
低ナトリウム血症	0	0	0	0	0	0	0
水分過負荷	0	0	0	0	0	0	0
体液貯留	0	0	0	0	0	0	0
葉酸欠乏	0	0	0	0	0	0	0
高コレステロール血症	0	0	0	0	0	0	0
高脂血症	1 (2.3%)	0	1 (2.3%)	0	0	0	0
高尿酸血症	1 (2.3%)	0	1 (2.3%)	0	0	0	0
食欲亢進	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
多飲症	0	0	0	0	0	0	0
１型糖尿病	0	0	0	0	0	0	0
２型糖尿病	0	0	0	0	0	0	0
血管障害	1 (2.3%)	0	1 (2.3%)	8 (15.7%)	6 (11.8%)	1 (2.0%)	2 (3.9%)
深部静脈血栓症	0	0	0	0	0	0	0
高血圧	0	0	0	2 (3.9%)	1 (2.0%)	0	1 (2.0%)
潮紅	1 (2.3%)	0	1 (2.3%)	1 (2.0%)	1 (2.0%)	0	0
低血圧	0	0	0	4 (7.8%)	4 (7.8%)	0	0
表在性血栓性静脈炎	0	0	0	0	0	0	0
ほてり	0	0	0	0	0	0	0
静脈炎	0	0	0	0	0	0	0
塞栓症	0	0	0	1 (2.0%)	0	1 (2.0%)	1 (2.0%)
起立性低血圧	0	0	0	0	0	0	0
血栓性静脈炎	0	0	0	1 (2.0%)	0	1 (2.0%)	1 (2.0%)
血栓症	0	0	0	0	0	0	0
血腫	0	0	0	0	0	0	0
静脈血栓症	0	0	0	0	0	0	0
出血性梗塞	0	0	0	0	0	0	0
蒼白	0	0	0	0	0	0	0
末梢冷感	0	0	0	0	0	0	0
表在性静脈炎	0	0	0	0	0	0	0
四肢静脈血栓症	0	0	0	0	0	0	0
臨床検査	4 (9.1%)	3 (6.8%)	2 (4.5%)	8 (15.7%)	4 (7.8%)	7 (13.7%)	4 (7.8%)
アラニンアミノトランスフェラーゼ増加	1 (2.3%)	1 (2.3%)	1 (2.3%)	6 (11.8%)	3 (5.9%)	6 (11.8%)	3 (5.9%)
体重減少	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (2.3%)	1 (2.3%)	1 (2.3%)	3 (5.9%)	2 (3.9%)	3 (5.9%)	2 (3.9%)
血中クレアチニン増加	1 (2.3%)	1 (2.3%)	0	1 (2.0%)	0	1 (2.0%)	0
γ－グルタミルトランスフェラーゼ増加	1 (2.3%)	1 (2.3%)	1 (2.3%)	2 (3.9%)	2 (3.9%)	2 (3.9%)	2 (3.9%)
体重増加	1 (2.3%)	0	1 (2.3%)	0	0	0	0
心電図ＱＴ延長	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
血中アルカリホスファターゼ増加	0	0	0	2 (3.9%)	2 (3.9%)	2 (3.9%)	2 (3.9%)
腎クレアチニン・クリアランス減少	0	0	0	0	0	0	0
血中乳酸脱水素酵素減少	0	0	0	0	0	0	0
血圧上昇	0	0	0	1 (2.0%)	0	0	1 (2.0%)
体温上昇	0	0	0	0	0	0	0
フィブリンDダイマー増加	1 (2.3%)	1 (2.3%)	0	0	0	0	0
ヘリコバクター検査陽性	0	0	0	0	0	0	0
免疫グロブリン減少	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	0
好中球中毒性顆粒存在	0	0	0	0	0	0	0
酸素飽和度低下	0	0	0	0	0	0	0
トロポニン増加	0	0	0	0	0	0	0
静脈雑音	0	0	0	0	0	0	0
眼障害	0	0	0	2 (3.9%)	1 (2.0%)	1 (2.0%)	2 (3.9%)
白内障	0	0	0	1 (2.0%)	0	0	1 (2.0%)
霧視	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
流涙増加	0	0	0	0	0	0	0
眼刺激	0	0	0	0	0	0	0
眼乾燥	0	0	0	0	0	0	0
眼部腫脹	0	0	0	0	0	0	0
視力低下	0	0	0	0	0	0	0
視力障害	0	0	0	0	0	0	0
結膜刺激	0	0	0	0	0	0	0
眼のアレルギー	0	0	0	0	0	0	0
眼の障害	0	0	0	0	0	0	0
眼出血	0	0	0	0	0	0	0
眼球浮腫	0	0	0	0	0	0	0
眼瞼発疹	0	0	0	0	0	0	0
水晶体混濁	0	0	0	0	0	0	0
眼充血	0	0	0	0	0	0	0
眼窩周囲浮腫	0	0	0	0	0	0	0
網膜静脈血栓症	0	0	0	0	0	0	0
硝子体浮遊物	0	0	0	0	0	0	0
腎および尿路障害	1 (2.3%)	1 (2.3%)	0	2 (3.9%)	1 (2.0%)	2 (3.9%)	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
腎機能障害	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	0
急性腎不全	1 (2.3%)	1 (2.3%)	0	0	0	0	0
腎不全	0	0	0	0	0	0	0
高窒素血症	0	0	0	0	0	0	0
慢性腎臓病	0	0	0	1 (2.0%)	0	1 (2.0%)	0
排尿困難	0	0	0	0	0	0	0
頻尿	0	0	0	0	0	0	0
多尿	0	0	0	0	0	0	0
腎嚢胞	0	0	0	0	0	0	0
尿失禁	0	0	0	0	0	0	0
尿閉	0	0	0	0	0	0	0
心臓障害	0	0	0	3 (5.9%)	3 (5.9%)	0	0
心房細動	0	0	0	0	0	0	0
頻脈	0	0	0	2 (3.9%)	2 (3.9%)	0	0
狭心症	0	0	0	1 (2.0%)	1 (2.0%)	0	0
徐脈	0	0	0	0	0	0	0
動悸	0	0	0	1 (2.0%)	1 (2.0%)	0	0
洞性頻脈	0	0	0	0	0	0	0
上室性頻脈	0	0	0	0	0	0	0
急性心筋梗塞	0	0	0	0	0	0	0
伝導障害	0	0	0	0	0	0	0
拡張機能障害	0	0	0	0	0	0	0
心筋虚血	0	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0	0
心室性期外収縮	0	0	0	0	0	0	0
傷害、中毒および処置合併症	0	0	0	2 (3.9%)	0	1 (2.0%)	1 (2.0%)
挫傷	0	0	0	0	0	0	0
各種物質毒性	0	0	0	0	0	0	0
転倒	0	0	0	0	0	0	0
引っかき傷	0	0	0	0	0	0	0
脊椎圧迫骨折	0	0	0	1 (2.0%)	0	0	1 (2.0%)
創合併症	0	0	0	1 (2.0%)	0	1 (2.0%)	0
内分泌障害	1 (2.3%)	0	1 (2.3%)	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
クッシング様症状	1 (2.3%)	0	1 (2.3%)	0	0	0	0
ステロイド離脱症候群	0	0	0	0	0	0	0
クッシング症候群	0	0	0	0	0	0	0
高コルチコイド症	0	0	0	0	0	0	0
下垂体依存性クッシング症候群	0	0	0	0	0	0	0
耳および迷路障害	0	0	0	0	0	0	0
回転性めまい	0	0	0	0	0	0	0
耳鳴	0	0	0	0	0	0	0
聴力低下	0	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
扁平上皮癌	0	0	0	0	0	0	0
急性単球性白血病	0	0	0	0	0	0	0
基底細胞癌	0	0	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
皮膚血管腫	0	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0	0
肝胆道系障害	1 (2.3%)	1 (2.3%)	1 (2.3%)	2 (3.9%)	2 (3.9%)	2 (3.9%)	2 (3.9%)
肝機能異常	0	0	0	2 (3.9%)	2 (3.9%)	2 (3.9%)	2 (3.9%)
肝細胞損傷	0	0	0	0	0	0	0
高ビリルビン血症	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0
生殖系および乳房障害	0	0	0	0	0	0	0
勃起不全	0	0	0	0	0	0	0
骨盤痛	0	0	0	0	0	0	0
免疫系障害	0	0	0	0	0	0	0
薬物過敏症	0	0	0	0	0	0	0
低γグロブリン血症	0	0	0	0	0	0	0
免疫抑制	0	0	0	0	0	0	0
先天性、家族性および遺伝性障害	0	0	0	0	0	0	0
角膜ジストロフィー	0	0	0	0	0	0	0

TSFAE04A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone; LEN = lenalidomide; DEX = dexamethasone; DARA = daratumumab.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE04A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE04A_3003.SAS] 05JUL2016, 08:33

表 2.7.4-付録-35 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Total number of subjects with TEAEs	22 (95.7%)	55 (100.0%)	154 (98.7%)	3 (100.0%)	234 (98.7%)
MedDRA system organ class / Preferred term					
一般・全身障害および投与部位の状態	11 (47.8%)	36 (65.5%)	106 (67.9%)	0	153 (64.6%)
疲労	2 (8.7%)	20 (36.4%)	59 (37.8%)	0	81 (34.2%)
発熱	8 (34.8%)	20 (36.4%)	29 (18.6%)	0	57 (24.1%)
悪寒	0	9 (16.4%)	16 (10.3%)	0	25 (10.5%)
無力症	0	3 (5.5%)	12 (7.7%)	0	15 (6.3%)
末梢性浮腫	1 (4.3%)	5 (9.1%)	11 (7.1%)	0	17 (7.2%)
胸痛	2 (8.7%)	1 (1.8%)	9 (5.8%)	0	12 (5.1%)
疼痛	0	2 (3.6%)	8 (5.1%)	0	10 (4.2%)
インフルエンザ様疾患	3 (13.0%)	1 (1.8%)	7 (4.5%)	0	11 (4.6%)
非心臓性胸痛	0	2 (3.6%)	6 (3.8%)	0	8 (3.4%)
全身健康状態低下	0	1 (1.8%)	5 (3.2%)	0	6 (2.5%)
注射部位内出血	0	0	3 (1.9%)	0	3 (1.3%)
局所腫脹	0	0	3 (1.9%)	0	3 (1.3%)
倦怠感	0	0	3 (1.9%)	0	3 (1.3%)
胸部不快感	0	3 (5.5%)	2 (1.3%)	0	5 (2.1%)
顔面浮腫	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
全身性浮腫	0	0	2 (1.3%)	0	2 (0.8%)
浮腫	0	0	2 (1.3%)	0	2 (0.8%)
腋窩痛	0	0	1 (0.6%)	0	1 (0.4%)
医療機器の問題	0	0	1 (0.6%)	0	1 (0.4%)
顔面痛	0	0	1 (0.6%)	0	1 (0.4%)
歩行障害	0	0	1 (0.6%)	0	1 (0.4%)
低体温	0	0	1 (0.6%)	0	1 (0.4%)
注入部位内出血	0	0	1 (0.6%)	0	1 (0.4%)
注射部位浮腫	0	0	1 (0.6%)	0	1 (0.4%)
注射部位反応	0	0	1 (0.6%)	0	1 (0.4%)
限局性浮腫	0	0	1 (0.6%)	0	1 (0.4%)
腫瘤	0	0	1 (0.6%)	0	1 (0.4%)
恥骨上痛	0	0	1 (0.6%)	0	1 (0.4%)
急性期反応	0	1 (1.8%)	0	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
呼吸器、胸郭および縦隔障害	8 (34.8%)	32 (58.2%)	95 (60.9%)	2 (66.7%)	137 (57.8%)
咳嗽	5 (21.7%)	12 (21.8%)	31 (19.9%)	1 (33.3%)	49 (20.7%)
鼻閉	0	5 (9.1%)	25 (16.0%)	1 (33.3%)	31 (13.1%)
呼吸困難	1 (4.3%)	11 (20.0%)	22 (14.1%)	0	34 (14.3%)
口腔咽頭痛	0	3 (5.5%)	15 (9.6%)	0	18 (7.6%)
アレルギー性鼻炎	1 (4.3%)	12 (21.8%)	11 (7.1%)	0	24 (10.1%)
咽喉刺激感	0	1 (1.8%)	10 (6.4%)	0	11 (4.6%)
労作性呼吸困難	0	1 (1.8%)	8 (5.1%)	0	9 (3.8%)
鼻出血	0	2 (3.6%)	8 (5.1%)	0	10 (4.2%)
湿性咳嗽	0	4 (7.3%)	8 (5.1%)	0	12 (5.1%)
喘鳴	0	1 (1.8%)	6 (3.8%)	0	7 (3.0%)
気管支痙攣	1 (4.3%)	1 (1.8%)	5 (3.2%)	1 (33.3%)	8 (3.4%)
胸水	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
副鼻腔うっ血	0	0	4 (2.6%)	0	4 (1.7%)
くしゃみ	0	0	4 (2.6%)	0	4 (1.7%)
低酸素症	0	0	3 (1.9%)	0	3 (1.3%)
咽喉絞扼感	0	0	3 (1.9%)	0	3 (1.3%)
上気道咳症候群	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
呼吸不全	0	0	2 (1.3%)	0	2 (0.8%)
急性肺水腫	0	0	1 (0.6%)	0	1 (0.4%)
アレルギー性咳嗽	0	0	1 (0.6%)	0	1 (0.4%)
慢性閉塞性肺疾患	0	0	1 (0.6%)	0	1 (0.4%)
発声障害	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
上気道分泌増加	0	0	1 (0.6%)	0	1 (0.4%)
喉頭浮腫	0	0	1 (0.6%)	0	1 (0.4%)
アレルギー性喉頭炎	0	3 (5.5%)	1 (0.6%)	0	4 (1.7%)
鼻部障害	0	0	1 (0.6%)	0	1 (0.4%)
誤嚥性肺炎	0	0	1 (0.6%)	0	1 (0.4%)
肺うっ血	0	0	1 (0.6%)	0	1 (0.4%)
肺塞栓症	0	0	1 (0.6%)	0	1 (0.4%)
肺水腫	0	0	1 (0.6%)	0	1 (0.4%)
鼻漏	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
喉頭の炎症	0	1 (1.8%)	0	0	1 (0.4%)
筋骨格系および結合組織障害	6 (26.1%)	30 (54.5%)	89 (57.1%)	1 (33.3%)	126 (53.2%)
背部痛	1 (4.3%)	8 (14.5%)	33 (21.2%)	1 (33.3%)	43 (18.1%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
関節痛	2 (8.7%)	5 (9.1%)	25 (16.0%)	0	32 (13.5%)
四肢痛	1 (4.3%)	1 (1.8%)	23 (14.7%)	0	25 (10.5%)
筋骨格系胸痛	0	5 (9.1%)	16 (10.3%)	0	21 (8.9%)
骨痛	1 (4.3%)	6 (10.9%)	14 (9.0%)	0	21 (8.9%)
筋骨格痛	0	3 (5.5%)	13 (8.3%)	0	16 (6.8%)
筋痙縮	0	2 (3.6%)	10 (6.4%)	0	12 (5.1%)
筋肉痛	0	6 (10.9%)	6 (3.8%)	0	12 (5.1%)
単径部痛	0	0	4 (2.6%)	0	4 (1.7%)
頚部痛	0	0	3 (1.9%)	0	3 (1.3%)
病的骨折	0	0	3 (1.9%)	0	3 (1.3%)
脊椎痛	0	0	3 (1.9%)	0	3 (1.3%)
筋力低下	0	0	2 (1.3%)	0	2 (0.8%)
骨炎	0	0	2 (1.3%)	0	2 (0.8%)
脊柱管狭窄症	0	0	2 (1.3%)	0	2 (0.8%)
骨侵食	0	0	1 (0.6%)	0	1 (0.4%)
骨病変	0	0	1 (0.6%)	0	1 (0.4%)
関節可動域低下	0	0	1 (0.6%)	0	1 (0.4%)
四肢不快感	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
運動性低下	0	0	1 (0.6%)	0	1 (0.4%)
筋肉疲労	0	0	1 (0.6%)	0	1 (0.4%)
筋骨格不快感	0	0	1 (0.6%)	0	1 (0.4%)
顎骨壊死	0	0	1 (0.6%)	0	1 (0.4%)
顎痛	0	0	1 (0.6%)	0	1 (0.4%)
腱炎	0	0	1 (0.6%)	0	1 (0.4%)
側腹部痛	0	1 (1.8%)	0	0	1 (0.4%)
脊柱後弯症	1 (4.3%)	0	0	0	1 (0.4%)
筋骨格硬直	0	1 (1.8%)	0	0	1 (0.4%)
ミオパチー	0	1 (1.8%)	0	0	1 (0.4%)
骨壊死	0	1 (1.8%)	0	0	1 (0.4%)
骨粗鬆症性骨折	0	1 (1.8%)	0	0	1 (0.4%)
胃腸障害	9 (39.1%)	27 (49.1%)	85 (54.5%)	2 (66.7%)	123 (51.9%)
悪心	3 (13.0%)	10 (18.2%)	40 (25.6%)	0	53 (22.4%)
下痢	2 (8.7%)	13 (23.6%)	24 (15.4%)	1 (33.3%)	40 (16.9%)
便秘	1 (4.3%)	6 (10.9%)	22 (14.1%)	0	29 (12.2%)
嘔吐	1 (4.3%)	8 (14.5%)	20 (12.8%)	1 (33.3%)	30 (12.7%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
腹痛	2 (8.7%)	1 (1.8%)	9 (5.8%)	0	12 (5.1%)
消化不良	0	3 (5.5%)	4 (2.6%)	0	7 (3.0%)
口内炎	0	3 (5.5%)	4 (2.6%)	0	7 (3.0%)
歯痛	0	0	4 (2.6%)	0	4 (1.7%)
腹部膨満	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
放屁	0	0	3 (1.9%)	0	3 (1.3%)
口の感覚鈍麻	0	0	3 (1.9%)	0	3 (1.3%)
腹部不快感	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
上腹部痛	0	0	2 (1.3%)	0	2 (0.8%)
便失禁	0	0	2 (1.3%)	0	2 (0.8%)
胃食道逆流性疾患	0	0	2 (1.3%)	0	2 (0.8%)
歯肉出血	0	0	2 (1.3%)	0	2 (0.8%)
口腔内痛	0	0	2 (1.3%)	0	2 (0.8%)
水疱性出血性口峡炎	0	0	1 (0.6%)	0	1 (0.4%)
大腸炎	0	0	1 (0.6%)	0	1 (0.4%)
憩室	0	0	1 (0.6%)	0	1 (0.4%)
嚥下障害	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
胃炎	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
歯肉腫脹	0	0	1 (0.6%)	0	1 (0.4%)
舌炎	0	0	1 (0.6%)	0	1 (0.4%)
血便排泄	0	0	1 (0.6%)	0	1 (0.4%)
痔核	0	0	1 (0.6%)	0	1 (0.4%)
大腸閉塞	0	0	1 (0.6%)	0	1 (0.4%)
口唇出血	0	0	1 (0.6%)	0	1 (0.4%)
口腔内潰瘍形成	1 (4.3%)	0	1 (0.6%)	0	2 (0.8%)
口腔粘膜変色	0	0	1 (0.6%)	0	1 (0.4%)
膵炎	0	0	1 (0.6%)	0	1 (0.4%)
口の錯感覚	0	0	1 (0.6%)	0	1 (0.4%)
舌苔	0	0	1 (0.6%)	0	1 (0.4%)
歯の発育障害	0	0	1 (0.6%)	0	1 (0.4%)
歯の障害	0	0	1 (0.6%)	0	1 (0.4%)
アフタ性口内炎	0	3 (5.5%)	0	0	3 (1.3%)
口内乾燥	1 (4.3%)	2 (3.6%)	0	0	3 (1.3%)
舌痛	0	1 (1.8%)	0	0	1 (0.4%)
口唇浮腫	1 (4.3%)	0	0	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
食道炎	1 (4.3%)	0	0	0	1 (0.4%)
感染症および寄生虫症	7 (30.4%)	32 (58.2%)	85 (54.5%)	1 (33.3%)	125 (52.7%)
上気道感染	0	12 (21.8%)	27 (17.3%)	0	39 (16.5%)
鼻咽頭炎	2 (8.7%)	9 (16.4%)	18 (11.5%)	1 (33.3%)	30 (12.7%)
肺炎	1 (4.3%)	4 (7.3%)	13 (8.3%)	0	18 (7.6%)
副鼻腔炎	1 (4.3%)	1 (1.8%)	9 (5.8%)	0	11 (4.6%)
尿路感染	0	2 (3.6%)	7 (4.5%)	1 (33.3%)	10 (4.2%)
気管支炎	0	0	5 (3.2%)	0	5 (2.1%)
結膜炎	0	0	3 (1.9%)	0	3 (1.3%)
帯状疱疹	1 (4.3%)	4 (7.3%)	3 (1.9%)	0	8 (3.4%)
大葉性肺炎	0	0	3 (1.9%)	0	3 (1.3%)
口腔カンジダ症	0	3 (5.5%)	3 (1.9%)	0	6 (2.5%)
カンジダ感染	0	2 (3.6%)	2 (1.3%)	0	4 (1.7%)
単純ヘルペス	0	0	2 (1.3%)	0	2 (0.8%)
感染	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
インフルエンザ	0	3 (5.5%)	2 (1.3%)	0	5 (2.1%)
パラインフルエンザウイルス感染	0	0	2 (1.3%)	0	2 (0.8%)
咽頭炎	0	0	2 (1.3%)	0	2 (0.8%)
鼻炎	0	0	2 (1.3%)	0	2 (0.8%)
軟部組織感染	0	0	2 (1.3%)	0	2 (0.8%)
水痘	0	0	2 (1.3%)	0	2 (0.8%)
蜂巣炎	0	0	1 (0.6%)	0	1 (0.4%)
膀胱炎	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
サイトメガロウイルス性脈絡網膜炎	0	0	1 (0.6%)	0	1 (0.4%)
医療機器関連感染	0	0	1 (0.6%)	0	1 (0.4%)
耳感染	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
胃腸炎	1 (4.3%)	1 (1.8%)	1 (0.6%)	0	3 (1.3%)
ウイルス性胃腸炎	0	0	1 (0.6%)	0	1 (0.4%)
性器感染	0	0	1 (0.6%)	0	1 (0.4%)
Ｈ１Ｎ１インフルエンザ	0	0	1 (0.6%)	0	1 (0.4%)
麦粒腫	0	0	1 (0.6%)	0	1 (0.4%)
下気道感染	0	0	1 (0.6%)	0	1 (0.4%)
粘膜感染	0	0	1 (0.6%)	0	1 (0.4%)
眼部単純ヘルペス	0	0	1 (0.6%)	0	1 (0.4%)
口腔真菌感染	0	0	1 (0.6%)	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
口腔ヘルペス	0	0	1 (0.6%)	0	1 (0.4%)
爪囲炎	0	0	1 (0.6%)	0	1 (0.4%)
レンサ球菌性肺炎	0	0	1 (0.6%)	0	1 (0.4%)
腎盂腎炎	0	0	1 (0.6%)	0	1 (0.4%)
気道感染	0	0	1 (0.6%)	0	1 (0.4%)
敗血症	0	0	1 (0.6%)	0	1 (0.4%)
レンサ球菌感染	0	0	1 (0.6%)	0	1 (0.4%)
歯感染	0	0	1 (0.6%)	0	1 (0.4%)
ウイルス性上気道感染	0	0	1 (0.6%)	0	1 (0.4%)
外陰腟真菌感染	0	0	1 (0.6%)	0	1 (0.4%)
菌血症	0	1 (1.8%)	0	0	1 (0.4%)
真菌感染	0	1 (1.8%)	0	0	1 (0.4%)
真菌性消化管感染	0	1 (1.8%)	0	0	1 (0.4%)
肺感染	0	1 (1.8%)	0	0	1 (0.4%)
メタニューモウイルス感染	0	1 (1.8%)	0	0	1 (0.4%)
ＲＳウイルス感染	0	2 (3.6%)	0	0	2 (0.8%)
細菌性尿路感染	0	1 (1.8%)	0	0	1 (0.4%)
ウイルス感染	1 (4.3%)	0	0	0	1 (0.4%)
外陰部腟カンジダ症	1 (4.3%)	0	0	0	1 (0.4%)
血液およびリンパ系障害	9 (39.1%)	21 (38.2%)	76 (48.7%)	0	106 (44.7%)
貧血	4 (17.4%)	12 (21.8%)	39 (25.0%)	0	55 (23.2%)
好中球減少症	1 (4.3%)	3 (5.5%)	34 (21.8%)	0	38 (16.0%)
血小板減少症	3 (13.0%)	10 (18.2%)	31 (19.9%)	0	44 (18.6%)
白血球減少症	0	2 (3.6%)	14 (9.0%)	0	16 (6.8%)
リンパ球減少症	2 (8.7%)	7 (12.7%)	9 (5.8%)	0	18 (7.6%)
ヘモグロビン血症	0	0	1 (0.6%)	0	1 (0.4%)
内出血発生の増加傾向	0	0	1 (0.6%)	0	1 (0.4%)
汎血球減少症	0	0	1 (0.6%)	0	1 (0.4%)
赤血球凝集	0	0	1 (0.6%)	0	1 (0.4%)
溶血	3 (13.0%)	0	0	0	3 (1.3%)
単球減少症	3 (13.0%)	0	0	0	3 (1.3%)
代謝および栄養障害	2 (8.7%)	16 (29.1%)	64 (41.0%)	0	82 (34.6%)
食欲減退	1 (4.3%)	5 (9.1%)	23 (14.7%)	0	29 (12.2%)
高カルシウム血症	0	4 (7.3%)	18 (11.5%)	0	22 (9.3%)
高血糖	0	4 (7.3%)	13 (8.3%)	0	17 (7.2%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
低カリウム血症	0	4 (7.3%)	12 (7.7%)	0	16 (6.8%)
低マグネシウム血症	0	2 (3.6%)	9 (5.8%)	0	11 (4.6%)
低ナトリウム血症	1 (4.3%)	6 (10.9%)	8 (5.1%)	0	15 (6.3%)
高カリウム血症	0	1 (1.8%)	5 (3.2%)	0	6 (2.5%)
酵素異常	1 (4.3%)	3 (5.5%)	4 (2.6%)	0	8 (3.4%)
高尿酸血症	0	2 (3.6%)	4 (2.6%)	0	6 (2.5%)
低アルブミン血症	0	4 (7.3%)	4 (2.6%)	0	8 (3.4%)
低カルシウム血症	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
糖尿病	0	0	1 (0.6%)	0	1 (0.4%)
高ナトリウム血症	0	0	1 (0.6%)	0	1 (0.4%)
高リン酸塩血症	0	0	1 (0.6%)	0	1 (0.4%)
低血糖症	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
栄養障害	0	0	1 (0.6%)	0	1 (0.4%)
ビタミンＢ１２欠乏	0	0	1 (0.6%)	0	1 (0.4%)
体液貯留	0	1 (1.8%)	0	0	1 (0.4%)
低リン酸血症	0	2 (3.6%)	0	0	2 (0.8%)
代謝性アシドーシス	0	1 (1.8%)	0	0	1 (0.4%)
神経系障害	6 (26.1%)	25 (45.5%)	50 (32.1%)	0	81 (34.2%)
頭痛	2 (8.7%)	4 (7.3%)	15 (9.6%)	0	21 (8.9%)
浮動性めまい	3 (13.0%)	6 (10.9%)	13 (8.3%)	0	22 (9.3%)
末梢性感覚ニューロパチー	1 (4.3%)	7 (12.7%)	6 (3.8%)	0	14 (5.9%)
感覚鈍麻	1 (4.3%)	1 (1.8%)	5 (3.2%)	0	7 (3.0%)
傾眠	0	1 (1.8%)	5 (3.2%)	0	6 (2.5%)
振戦	0	2 (3.6%)	4 (2.6%)	0	6 (2.5%)
味覚異常	0	4 (7.3%)	3 (1.9%)	0	7 (3.0%)
錯感覚	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
下肢静止不能症候群	0	0	2 (1.3%)	0	2 (0.8%)
意識変容状態	0	0	1 (0.6%)	0	1 (0.4%)
手根管症候群	0	0	1 (0.6%)	0	1 (0.4%)
意識レベルの低下	0	0	1 (0.6%)	0	1 (0.4%)
脳症	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
知覚過敏	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
嗜眠	0	0	1 (0.6%)	0	1 (0.4%)
記憶障害	0	0	1 (0.6%)	0	1 (0.4%)
神経痛	0	0	1 (0.6%)	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
嗅覚錯誤	0	0	1 (0.6%)	0	1 (0.4%)
脊髄圧迫	0	0	1 (0.6%)	0	1 (0.4%)
失神	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
第７脳神経麻痺	0	0	1 (0.6%)	0	1 (0.4%)
無感覚	0	1 (1.8%)	0	0	1 (0.4%)
坐骨神経痛	0	1 (1.8%)	0	0	1 (0.4%)
第６脳神経麻痺	0	1 (1.8%)	0	0	1 (0.4%)
皮膚および皮下組織障害	3 (13.0%)	16 (29.1%)	35 (22.4%)	0	54 (22.8%)
そう痒症	1 (4.3%)	4 (7.3%)	5 (3.2%)	0	10 (4.2%)
多汗症	0	3 (5.5%)	3 (1.9%)	0	6 (2.5%)
寝汗	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
発疹	2 (8.7%)	7 (12.7%)	3 (1.9%)	0	12 (5.1%)
斑状丘疹状皮疹	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
皮膚嚢腫	0	0	2 (1.3%)	0	2 (0.8%)
ざ瘡様皮膚炎	0	0	2 (1.3%)	0	2 (0.8%)
接触性皮膚炎	0	0	2 (1.3%)	0	2 (0.8%)
皮膚乾燥	0	0	2 (1.3%)	0	2 (0.8%)
湿疹	0	0	2 (1.3%)	0	2 (0.8%)
紅斑	1 (4.3%)	0	2 (1.3%)	0	3 (1.3%)
点状出血	0	0	2 (1.3%)	0	2 (0.8%)
褥瘡性潰瘍	0	0	1 (0.6%)	0	1 (0.4%)
薬疹	0	0	1 (0.6%)	0	1 (0.4%)
皮脂欠乏性湿疹	0	0	1 (0.6%)	0	1 (0.4%)
手掌・足底発赤知覚不全症候群	0	0	1 (0.6%)	0	1 (0.4%)
色素沈着障害	0	0	1 (0.6%)	0	1 (0.4%)
全身性そう痒症	0	0	1 (0.6%)	0	1 (0.4%)
乾癬	0	0	1 (0.6%)	0	1 (0.4%)
斑状皮疹	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
丘疹性皮疹	0	0	1 (0.6%)	0	1 (0.4%)
皮膚剥脱	0	0	1 (0.6%)	0	1 (0.4%)
皮膚色素過剰	0	0	1 (0.6%)	0	1 (0.4%)
皮膚潰瘍	0	0	1 (0.6%)	0	1 (0.4%)
蕁麻疹	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
脱毛症	0	1 (1.8%)	0	0	1 (0.4%)
爪変色	0	1 (1.8%)	0	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
血管障害	5 (21.7%)	14 (25.5%)	29 (18.6%)	0	48 (20.3%)
高血圧	2 (8.7%)	10 (18.2%)	15 (9.6%)	0	27 (11.4%)
低血圧	2 (8.7%)	1 (1.8%)	7 (4.5%)	0	10 (4.2%)
血腫	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
潮紅	2 (8.7%)	1 (1.8%)	3 (1.9%)	0	6 (2.5%)
深部静脈血栓症	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
ほてり	0	2 (3.6%)	1 (0.6%)	0	3 (1.3%)
表在性静脈炎	0	0	1 (0.6%)	0	1 (0.4%)
レイノー現象	0	0	1 (0.6%)	0	1 (0.4%)
四肢静脈血栓症	0	0	1 (0.6%)	0	1 (0.4%)
傷害、中毒および処置合併症	1 (4.3%)	3 (5.5%)	28 (17.9%)	0	32 (13.5%)
挫傷	0	1 (1.8%)	5 (3.2%)	0	6 (2.5%)
転倒	0	0	5 (3.2%)	0	5 (2.1%)
肋骨骨折	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
上腕骨骨折	0	0	2 (1.3%)	0	2 (0.8%)
裂傷	0	0	2 (1.3%)	0	2 (0.8%)
腰椎骨折	0	0	2 (1.3%)	0	2 (0.8%)
脊椎圧迫骨折	1 (4.3%)	0	2 (1.3%)	0	3 (1.3%)
骨挫傷	0	0	1 (0.6%)	0	1 (0.4%)
擦過傷	0	0	1 (0.6%)	0	1 (0.4%)
足骨折	0	0	1 (0.6%)	0	1 (0.4%)
骨折	0	0	1 (0.6%)	0	1 (0.4%)
肉離れ	0	0	1 (0.6%)	0	1 (0.4%)
眼窩周囲挫傷	0	0	1 (0.6%)	0	1 (0.4%)
処置による疼痛	0	0	1 (0.6%)	0	1 (0.4%)
硬膜下血腫	0	0	1 (0.6%)	0	1 (0.4%)
腱断裂	0	0	1 (0.6%)	0	1 (0.4%)
輸血反応	0	0	1 (0.6%)	0	1 (0.4%)
上肢骨折	0	0	1 (0.6%)	0	1 (0.4%)
創傷	0	0	1 (0.6%)	0	1 (0.4%)
手首関節骨折	0	0	1 (0.6%)	0	1 (0.4%)
四肢外傷性切断	0	1 (1.8%)	0	0	1 (0.4%)
精神障害	0	9 (16.4%)	28 (17.9%)	0	37 (15.6%)
不安	0	0	9 (5.8%)	0	9 (3.8%)
錯乱状態	0	1 (1.8%)	7 (4.5%)	0	8 (3.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
不眠症	0	4 (7.3%)	7 (4.5%)	0	11 (4.6%)
激越	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
譫妄	0	0	3 (1.9%)	0	3 (1.3%)
うつ病	0	2 (3.6%)	3 (1.9%)	0	5 (2.1%)
気分変化	0	0	2 (1.3%)	0	2 (0.8%)
摂食障害	0	0	1 (0.6%)	0	1 (0.4%)
幻覚	0	0	1 (0.6%)	0	1 (0.4%)
精神状態変化	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
気分動揺	0	1 (1.8%)	0	0	1 (0.4%)
神経過敏	0	1 (1.8%)	0	0	1 (0.4%)
腎および尿路障害	11 (47.8%)	15 (27.3%)	25 (16.0%)	1 (33.3%)	52 (21.9%)
腎機能障害	1 (4.3%)	8 (14.5%)	11 (7.1%)	0	20 (8.4%)
排尿困難	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
頻尿	1 (4.3%)	0	2 (1.3%)	0	3 (1.3%)
蛋白尿	10 (43.5%)	3 (5.5%)	2 (1.3%)	1 (33.3%)	16 (6.8%)
尿閉	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
非感染性膀胱炎	0	0	1 (0.6%)	0	1 (0.4%)
血尿	0	2 (3.6%)	1 (0.6%)	0	3 (1.3%)
夜間頻尿	0	0	1 (0.6%)	0	1 (0.4%)
腎不全	0	0	1 (0.6%)	0	1 (0.4%)
腎静脈血栓症	0	0	1 (0.6%)	0	1 (0.4%)
尿失禁	0	3 (5.5%)	1 (0.6%)	0	4 (1.7%)
尿路閉塞	0	0	1 (0.6%)	0	1 (0.4%)
高窒素血症	0	1 (1.8%)	0	0	1 (0.4%)
膀胱痙縮	0	1 (1.8%)	0	0	1 (0.4%)
尿意切迫	0	1 (1.8%)	0	0	1 (0.4%)
急性腎不全	0	1 (1.8%)	0	0	1 (0.4%)
臨床検査	10 (43.5%)	7 (12.7%)	20 (12.8%)	0	37 (15.6%)
体重減少	0	4 (7.3%)	7 (4.5%)	0	11 (4.6%)
体重増加	0	1 (1.8%)	4 (2.6%)	0	5 (2.1%)
交差適合試験不適合	0	0	3 (1.9%)	0	3 (1.3%)
国際標準比増加	0	1 (1.8%)	3 (1.9%)	0	4 (1.7%)
血中クレアチンホスホキナーゼ増加	1 (4.3%)	0	1 (0.6%)	0	2 (0.8%)
血中テストステロン減少	0	0	1 (0.6%)	0	1 (0.4%)
心電図異常Q波	0	0	1 (0.6%)	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
心電図ＱＴ延長	5 (21.7%)	0	1 (0.6%)	0	6 (2.5%)
心電図異常Ｔ波	0	0	1 (0.6%)	0	1 (0.4%)
酸素飽和度異常	0	0	1 (0.6%)	0	1 (0.4%)
尿量減少	0	0	1 (0.6%)	0	1 (0.4%)
遊離ヘモグロビン陽性	5 (21.7%)	0	0	0	5 (2.1%)
ハプトグロビン減少	1 (4.3%)	0	0	0	1 (0.4%)
心拍数増加	0	1 (1.8%)	0	0	1 (0.4%)
リンパ球数減少	1 (4.3%)	1 (1.8%)	0	0	2 (0.8%)
眼障害	1 (4.3%)	10 (18.2%)	13 (8.3%)	0	24 (10.1%)
霧視	0	2 (3.6%)	7 (4.5%)	0	9 (3.8%)
眼乾燥	0	0	2 (1.3%)	0	2 (0.8%)
眼そう痒症	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
眼充血	1 (4.3%)	0	2 (1.3%)	0	3 (1.3%)
白内障	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
結膜出血	0	0	1 (0.6%)	0	1 (0.4%)
複視	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
睫毛乱生	0	0	1 (0.6%)	0	1 (0.4%)
眼部腫脹	0	1 (1.8%)	0	0	1 (0.4%)
眼瞼機能障害	0	1 (1.8%)	0	0	1 (0.4%)
眼瞼下垂	0	1 (1.8%)	0	0	1 (0.4%)
眼瞼発疹	0	1 (1.8%)	0	0	1 (0.4%)
光視症	0	1 (1.8%)	0	0	1 (0.4%)
視力障害	0	1 (1.8%)	0	0	1 (0.4%)
硝子体浮遊物	0	1 (1.8%)	0	0	1 (0.4%)
心臓障害	4 (17.4%)	2 (3.6%)	11 (7.1%)	0	17 (7.2%)
動悸	1 (4.3%)	0	5 (3.2%)	0	6 (2.5%)
洞性頻脈	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
頻脈	2 (8.7%)	1 (1.8%)	2 (1.3%)	0	5 (2.1%)
狭心症	0	0	1 (0.6%)	0	1 (0.4%)
心房粗動	0	0	1 (0.6%)	0	1 (0.4%)
徐脈	0	0	1 (0.6%)	0	1 (0.4%)
左脚ブロック	0	0	1 (0.6%)	0	1 (0.4%)
うっ血性心不全	0	0	1 (0.6%)	0	1 (0.4%)
心肺停止	0	0	1 (0.6%)	0	1 (0.4%)
心房細動	1 (4.3%)	0	0	0	1 (0.4%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
上室性期外収縮	1 (4.3%)	0	0	0	1 (0.4%)
肝胆道系障害	1 (4.3%)	4 (7.3%)	8 (5.1%)	0	13 (5.5%)
肝機能異常	1 (4.3%)	3 (5.5%)	6 (3.8%)	0	10 (4.2%)
肝不全	0	0	1 (0.6%)	0	1 (0.4%)
高ビリルビン血症	0	0	1 (0.6%)	0	1 (0.4%)
黄疸	0	0	1 (0.6%)	0	1 (0.4%)
脂肪肝	0	1 (1.8%)	0	0	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3%)	3 (5.5%)	6 (3.8%)	0	10 (4.2%)
基底細胞癌	0	1 (1.8%)	2 (1.3%)	0	3 (1.3%)
腫瘍疼痛	0	0	2 (1.3%)	0	2 (0.8%)
肛門直腸ヒト乳頭腫ウイルス感染	0	0	1 (0.6%)	0	1 (0.4%)
皮膚癌	0	0	1 (0.6%)	0	1 (0.4%)
皮膚良性新生物	1 (4.3%)	0	0	0	1 (0.4%)
形質細胞性白血病	0	1 (1.8%)	0	0	1 (0.4%)
皮膚乳頭腫	0	1 (1.8%)	0	0	1 (0.4%)
耳および迷路障害	0	3 (5.5%)	5 (3.2%)	0	8 (3.4%)
耳痛	0	0	2 (1.3%)	0	2 (0.8%)
耳の障害	0	0	1 (0.6%)	0	1 (0.4%)
耳鳴	0	0	1 (0.6%)	0	1 (0.4%)
回転性めまい	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
耳垢栓塞	0	1 (1.8%)	0	0	1 (0.4%)
耳不快感	0	1 (1.8%)	0	0	1 (0.4%)
生殖系および乳房障害	0	3 (5.5%)	4 (2.6%)	1 (33.3%)	8 (3.4%)
生殖器痛	0	0	1 (0.6%)	0	1 (0.4%)
乳頭痛	0	0	1 (0.6%)	0	1 (0.4%)
性器浮腫	0	0	1 (0.6%)	0	1 (0.4%)
陰茎浮腫	0	0	1 (0.6%)	0	1 (0.4%)
腟出血	0	0	1 (0.6%)	0	1 (0.4%)
血精液症	0	1 (1.8%)	0	0	1 (0.4%)
骨盤痛	0	1 (1.8%)	0	0	1 (0.4%)
前立腺炎	0	1 (1.8%)	0	1 (33.3%)	2 (0.8%)
免疫系障害	3 (13.0%)	2 (3.6%)	3 (1.9%)	0	8 (3.4%)
アレルギー性浮腫	0	0	1 (0.6%)	0	1 (0.4%)
サイトカイン放出症候群	1 (4.3%)	1 (1.8%)	1 (0.6%)	0	3 (1.3%)

TSFAE02: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
季節性アレルギー	0	0	1 (0.6%)	0	1 (0.4%)
過敏症	2 (8.7%)	1 (1.8%)	0	0	3 (1.3%)
先天性、家族性および遺伝性障害	0	0	1 (0.6%)	0	1 (0.4%)
あざ	0	0	1 (0.6%)	0	1 (0.4%)

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae02.sas] 16MAR2015, 12:02

表 2.7.4-付録-36 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
Analysis set: all treated	23						55					
Total number of subjects with TEAEs	22 (95.7%)	1 (4.3%)	12 (52.2%)	7 (30.4%)	1 (4.3%)	1 (4.3%)	55 (100.0%)	3 (5.5%)	21 (38.2%)	21 (38.2%)	10 (18.2%)	0
MedDRA system organ class/Preferred term												
一般・全身障害および投与部位の状態	11 (47.8%)	9 (39.1%)	2 (8.7%)	0	0	0	36 (65.5%)	12 (21.8%)	18 (32.7%)	5 (9.1%)	1 (1.8%)	0
疲労	2 (8.7%)	2 (8.7%)	0	0	0	0	20 (36.4%)	7 (12.7%)	12 (21.8%)	1 (1.8%)	0	0
発熱	8 (34.8%)	6 (26.1%)	2 (8.7%)	0	0	0	20 (36.4%)	13 (23.6%)	6 (10.9%)	1 (1.8%)	0	0
悪寒	0	0	0	0	0	0	9 (16.4%)	4 (7.3%)	4 (7.3%)	1 (1.8%)	0	0
無力症	0	0	0	0	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
末梢性浮腫	1 (4.3%)	1 (4.3%)	0	0	0	0	5 (9.1%)	4 (7.3%)	1 (1.8%)	0	0	0
胸痛	2 (8.7%)	2 (8.7%)	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
疼痛	0	0	0	0	0	0	2 (3.6%)	2 (3.6%)	0	0	0	0
インフルエンザ様疾患	3 (13.0%)	3 (13.0%)	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
非心臓性胸痛	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
全身健康状態低下	0	0	0	0	0	0	1 (1.8%)	0	0	0	1 (1.8%)	0
注射部位内出血	0	0	0	0	0	0	0	0	0	0	0	0
局所腫脹	0	0	0	0	0	0	0	0	0	0	0	0
倦怠感	0	0	0	0	0	0	0	0	0	0	0	0
胸部不快感	0	0	0	0	0	0	3 (5.5%)	0	3 (5.5%)	0	0	0
顔面浮腫	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
全身性浮腫	0	0	0	0	0	0	0	0	0	0	0	0
浮腫	0	0	0	0	0	0	0	0	0	0	0	0
腋窩痛	0	0	0	0	0	0	0	0	0	0	0	0
医療機器の問題	0	0	0	0	0	0	0	0	0	0	0	0
顔面痛	0	0	0	0	0	0	0	0	0	0	0	0
歩行障害	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
低体温	0	0	0	0	0	0	0	0	0	0	0	0
注入部位内出血	0	0	0	0	0	0	0	0	0	0	0	0
注射部位浮腫	0	0	0	0	0	0	0	0	0	0	0	0
注射部位反応	0	0	0	0	0	0	0	0	0	0	0	0
限局性浮腫	0	0	0	0	0	0	0	0	0	0	0	0
腫瘤	0	0	0	0	0	0	0	0	0	0	0	0
恥骨上痛	0	0	0	0	0	0	0	0	0	0	0	0
急性期反応	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
呼吸器、胸郭および縦隔障害	8 (34.8%)	7 (30.4%)	0	1 (4.3%)	0	0	32 (58.2%)	10 (18.2%)	21 (38.2%)	1 (1.8%)	0	0
咳嗽	5 (21.7%)	5 (21.7%)	0	0	0	0	12 (21.8%)	7 (12.7%)	5 (9.1%)	0	0	0
鼻閉	0	0	0	0	0	0	5 (9.1%)	3 (5.5%)	2 (3.6%)	0	0	0
呼吸困難	1 (4.3%)	1 (4.3%)	0	0	0	0	11 (20.0%)	7 (12.7%)	4 (7.3%)	0	0	0
口腔咽頭痛	0	0	0	0	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
アレルギー性鼻炎	1 (4.3%)	1 (4.3%)	0	0	0	0	12 (21.8%)	0	12 (21.8%)	0	0	0
咽喉刺激感	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
労作性呼吸困難	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
鼻出血	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
湿性咳嗽	0	0	0	0	0	0	4 (7.3%)	3 (5.5%)	1 (1.8%)	0	0	0
喘鳴	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
気管支痙攣	1 (4.3%)	0	0	1 (4.3%)	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
胸水	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
副鼻腔うっ血	0	0	0	0	0	0	0	0	0	0	0	0
くしゃみ	0	0	0	0	0	0	0	0	0	0	0	0
低酸素症	0	0	0	0	0	0	0	0	0	0	0	0
咽喉絞扼感	0	0	0	0	0	0	0	0	0	0	0	0
上気道咳症候群	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
呼吸不全	0	0	0	0	0	0	0	0	0	0	0	0
急性肺水腫	0	0	0	0	0	0	0	0	0	0	0	0
アレルギー性咳嗽	0	0	0	0	0	0	0	0	0	0	0	0
慢性閉塞性肺疾患	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
発声障害	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
上気道分泌増加	0	0	0	0	0	0	0	0	0	0	0	0
喉頭浮腫	0	0	0	0	0	0	0	0	0	0	0	0
アレルギー性喉頭炎	0	0	0	0	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
鼻部障害	0	0	0	0	0	0	0	0	0	0	0	0
誤嚥性肺炎	0	0	0	0	0	0	0	0	0	0	0	0
肺うっ血	0	0	0	0	0	0	0	0	0	0	0	0
肺塞栓症	0	0	0	0	0	0	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0	0	0	0	0	0	0
鼻漏	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
喉頭の炎症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
筋骨格系および結合組織障害	6 (26.1%)	2 (8.7%)	3 (13.0%)	1 (4.3%)	0	0	30 (54.5%)	12 (21.8%)	13 (23.6%)	5 (9.1%)	0	0
背部痛	1 (4.3%)	0	1 (4.3%)	0	0	0	8 (14.5%)	2 (3.6%)	3 (5.5%)	3 (5.5%)	0	0
関節痛	2 (8.7%)	1 (4.3%)	1 (4.3%)	0	0	0	5 (9.1%)	4 (7.3%)	1 (1.8%)	0	0	0
四肢痛	1 (4.3%)	1 (4.3%)	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
筋骨格系胸痛	0	0	0	0	0	0	5 (9.1%)	1 (1.8%)	4 (7.3%)	0	0	0
骨痛	1 (4.3%)	0	1 (4.3%)	0	0	0	6 (10.9%)	2 (3.6%)	4 (7.3%)	0	0	0
筋骨格痛	0	0	0	0	0	0	3 (5.5%)	1 (1.8%)	1 (1.8%)	1 (1.8%)	0	0
筋痙縮	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
筋肉痛	0	0	0	0	0	0	6 (10.9%)	2 (3.6%)	4 (7.3%)	0	0	0
単径部痛	0	0	0	0	0	0	0	0	0	0	0	0
頚部痛	0	0	0	0	0	0	0	0	0	0	0	0
病的骨折	0	0	0	0	0	0	0	0	0	0	0	0
脊椎痛	0	0	0	0	0	0	0	0	0	0	0	0
筋力低下	0	0	0	0	0	0	0	0	0	0	0	0
骨炎	0	0	0	0	0	0	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	0	0	0	0	0	0	0	0
骨侵食	0	0	0	0	0	0	0	0	0	0	0	0
骨病変	0	0	0	0	0	0	0	0	0	0	0	0
関節可動域低下	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
四肢不快感	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
運動性低下	0	0	0	0	0	0	0	0	0	0	0	0
筋肉疲労	0	0	0	0	0	0	0	0	0	0	0	0
筋骨格不快感	0	0	0	0	0	0	0	0	0	0	0	0
顎骨壊死	0	0	0	0	0	0	0	0	0	0	0	0
顎痛	0	0	0	0	0	0	0	0	0	0	0	0
腱炎	0	0	0	0	0	0	0	0	0	0	0	0
側腹部痛	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
脊柱後弯症	1 (4.3%)	0	0	1 (4.3%)	0	0	0	0	0	0	0	0
筋骨格硬直	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
ミオパチー	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
骨壊死	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
骨粗鬆症性骨折	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
胃腸障害	9 (39.1%)	6 (26.1%)	2 (8.7%)	0	0	1 (4.3%)	27 (49.1%)	15 (27.3%)	11 (20.0%)	1 (1.8%)	0	0
悪心	3 (13.0%)	3 (13.0%)	0	0	0	0	10 (18.2%)	5 (9.1%)	4 (7.3%)	1 (1.8%)	0	0
下痢	2 (8.7%)	2 (8.7%)	0	0	0	0	13 (23.6%)	9 (16.4%)	4 (7.3%)	0	0	0
便秘	1 (4.3%)	0	1 (4.3%)	0	0	0	6 (10.9%)	3 (5.5%)	3 (5.5%)	0	0	0
嘔吐	1 (4.3%)	1 (4.3%)	0	0	0	0	8 (14.5%)	6 (10.9%)	1 (1.8%)	1 (1.8%)	0	0
腹痛	2 (8.7%)	1 (4.3%)	0	0	0	1 (4.3%)	1 (1.8%)	1 (1.8%)	0	0	0	0
消化不良	0	0	0	0	0	0	3 (5.5%)	1 (1.8%)	2 (3.6%)	0	0	0
口内炎	0	0	0	0	0	0	3 (5.5%)	3 (5.5%)	0	0	0	0
歯痛	0	0	0	0	0	0	0	0	0	0	0	0
腹部膨満	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
放屁	0	0	0	0	0	0	0	0	0	0	0	0
口の感覚鈍麻	0	0	0	0	0	0	0	0	0	0	0	0
腹部不快感	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
上腹部痛	0	0	0	0	0	0	0	0	0	0	0	0
便失禁	0	0	0	0	0	0	0	0	0	0	0	0
胃食道逆流性疾患	0	0	0	0	0	0	0	0	0	0	0	0
歯肉出血	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
口腔内痛	0	0	0	0	0	0	0	0	0	0	0	0
水疱性出血性口峡炎	0	0	0	0	0	0	0	0	0	0	0	0
大腸炎	0	0	0	0	0	0	0	0	0	0	0	0
憩室	0	0	0	0	0	0	0	0	0	0	0	0
嚥下障害	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
胃炎	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
歯肉腫脹	0	0	0	0	0	0	0	0	0	0	0	0
舌炎	0	0	0	0	0	0	0	0	0	0	0	0
血便排泄	0	0	0	0	0	0	0	0	0	0	0	0
痔核	0	0	0	0	0	0	0	0	0	0	0	0
大腸閉塞	0	0	0	0	0	0	0	0	0	0	0	0
口唇出血	0	0	0	0	0	0	0	0	0	0	0	0
口腔内潰瘍形成	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
口腔粘膜変色	0	0	0	0	0	0	0	0	0	0	0	0
膵炎	0	0	0	0	0	0	0	0	0	0	0	0
口の錯感覚	0	0	0	0	0	0	0	0	0	0	0	0
舌苔	0	0	0	0	0	0	0	0	0	0	0	0
歯の発育障害	0	0	0	0	0	0	0	0	0	0	0	0
歯の障害	0	0	0	0	0	0	0	0	0	0	0	0
アフタ性口内炎	0	0	0	0	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
口内乾燥	1 (4.3%)	1 (4.3%)	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
舌痛	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
口唇浮腫	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
食道炎	1 (4.3%)	0	1 (4.3%)	0	0	0	0	0	0	0	0	0
感染症および寄生虫症	7 (30.4%)	2 (8.7%)	5 (21.7%)	0	0	0	32 (58.2%)	7 (12.7%)	21 (38.2%)	4 (7.3%)	0	0
上気道感染	0	0	0	0	0	0	12 (21.8%)	1 (1.8%)	11 (20.0%)	0	0	0
鼻咽頭炎	2 (8.7%)	1 (4.3%)	1 (4.3%)	0	0	0	9 (16.4%)	8 (14.5%)	1 (1.8%)	0	0	0
肺炎	1 (4.3%)	0	1 (4.3%)	0	0	0	4 (7.3%)	0	1 (1.8%)	3 (5.5%)	0	0
副鼻腔炎	1 (4.3%)	1 (4.3%)	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
尿路感染	0	0	0	0	0	0	2 (3.6%)	0	2 (3.6%)	0	0	0
気管支炎	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
結膜炎	0	0	0	0	0	0	0	0	0	0	0	0
帯状疱疹	1 (4.3%)	0	1 (4.3%)	0	0	0	4 (7.3%)	1 (1.8%)	3 (5.5%)	0	0	0
大葉性肺炎	0	0	0	0	0	0	0	0	0	0	0	0
口腔カンジダ症	0	0	0	0	0	0	3 (5.5%)	0	3 (5.5%)	0	0	0
カンジダ感染	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
単純ヘルペス	0	0	0	0	0	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
インフルエンザ	0	0	0	0	0	0	3 (5.5%)	1 (1.8%)	2 (3.6%)	0	0	0
パラインフルエンザウイルス感染	0	0	0	0	0	0	0	0	0	0	0	0
咽頭炎	0	0	0	0	0	0	0	0	0	0	0	0
鼻炎	0	0	0	0	0	0	0	0	0	0	0	0
軟部組織感染	0	0	0	0	0	0	0	0	0	0	0	0
水痘	0	0	0	0	0	0	0	0	0	0	0	0
蜂巣炎	0	0	0	0	0	0	0	0	0	0	0	0
膀胱炎	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
サイトメガロウイルス性脈絡網膜炎	0	0	0	0	0	0	0	0	0	0	0	0
医療機器関連感染	0	0	0	0	0	0	0	0	0	0	0	0
耳感染	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
胃腸炎	1 (4.3%)	0	1 (4.3%)	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
ウイルス性胃腸炎	0	0	0	0	0	0	0	0	0	0	0	0
性器感染	0	0	0	0	0	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	0	0	0	0	0	0	0
麦粒腫	0	0	0	0	0	0	0	0	0	0	0	0
下気道感染	0	0	0	0	0	0	0	0	0	0	0	0
粘膜感染	0	0	0	0	0	0	0	0	0	0	0	0
眼部単純ヘルペス	0	0	0	0	0	0	0	0	0	0	0	0
口腔真菌感染	0	0	0	0	0	0	0	0	0	0	0	0
口腔ヘルペス	0	0	0	0	0	0	0	0	0	0	0	0
爪囲炎	0	0	0	0	0	0	0	0	0	0	0	0
レンサ球菌性肺炎	0	0	0	0	0	0	0	0	0	0	0	0
腎盂腎炎	0	0	0	0	0	0	0	0	0	0	0	0
気道感染	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
敗血症	0	0	0	0	0	0	0	0	0	0	0	0
レンサ球菌感染	0	0	0	0	0	0	0	0	0	0	0	0
歯感染	0	0	0	0	0	0	0	0	0	0	0	0
ウイルス性上気道感染	0	0	0	0	0	0	0	0	0	0	0	0
外陰腟真菌感染	0	0	0	0	0	0	0	0	0	0	0	0
菌血症	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
真菌感染	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
真菌性消化管感染	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
肺感染	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
メタニューモウイルス感染	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
ＲＳウイルス感染	0	0	0	0	0	0	2 (3.6%)	0	2 (3.6%)	0	0	0
細菌性尿路感染	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
ウイルス感染	1 (4.3%)	0	1 (4.3%)	0	0	0	0	0	0	0	0	0
外陰部腟カンジダ症	1 (4.3%)	0	1 (4.3%)	0	0	0	0	0	0	0	0	0
血液およびリンパ系障害	9 (39.1%)	3 (13.0%)	4 (17.4%)	1 (4.3%)	1 (4.3%)	0	21 (38.2%)	1 (1.8%)	4 (7.3%)	7 (12.7%)	9 (16.4%)	0
貧血	4 (17.4%)	0	3 (13.0%)	1 (4.3%)	0	0	12 (21.8%)	1 (1.8%)	5 (9.1%)	6 (10.9%)	0	0
好中球減少症	1 (4.3%)	0	0	1 (4.3%)	0	0	3 (5.5%)	0	2 (3.6%)	1 (1.8%)	0	0
血小板減少症	3 (13.0%)	0	1 (4.3%)	1 (4.3%)	1 (4.3%)	0	10 (18.2%)	2 (3.6%)	0	2 (3.6%)	6 (10.9%)	0
白血球減少症	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
リンパ球減少症	2 (8.7%)	1 (4.3%)	1 (4.3%)	0	0	0	7 (12.7%)	0	2 (3.6%)	2 (3.6%)	3 (5.5%)	0
ヘモグロビン血症	0	0	0	0	0	0	0	0	0	0	0	0
内出血発生の増加傾向	0	0	0	0	0	0	0	0	0	0	0	0
赤血球凝集	0	0	0	0	0	0	0	0	0	0	0	0
溶血	3 (13.0%)	3 (13.0%)	0	0	0	0	0	0	0	0	0	0
単球減少症	3 (13.0%)	3 (13.0%)	0	0	0	0	0	0	0	0	0	0
代謝および栄養障害	2 (8.7%)	2 (8.7%)	0	0	0	0	16 (29.1%)	4 (7.3%)	5 (9.1%)	5 (9.1%)	2 (3.6%)	0
食欲減退	1 (4.3%)	1 (4.3%)	0	0	0	0	5 (9.1%)	2 (3.6%)	3 (5.5%)	0	0	0
高カルシウム血症	0	0	0	0	0	0	4 (7.3%)	1 (1.8%)	1 (1.8%)	1 (1.8%)	1 (1.8%)	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
高血糖	0	0	0	0	0	0	4 (7.3%)	3 (5.5%)	0	1 (1.8%)	0	0
低カリウム血症	0	0	0	0	0	0	4 (7.3%)	3 (5.5%)	0	1 (1.8%)	0	0
低マグネシウム血症	0	0	0	0	0	0	2 (3.6%)	2 (3.6%)	0	0	0	0
低ナトリウム血症	1 (4.3%)	1 (4.3%)	0	0	0	0	6 (10.9%)	3 (5.5%)	0	3 (5.5%)	0	0
高カリウム血症	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
酵素異常	1 (4.3%)	1 (4.3%)	0	0	0	0	3 (5.5%)	1 (1.8%)	2 (3.6%)	0	0	0
高尿酸血症	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	0	0	1 (1.8%)	0
低アルブミン血症	0	0	0	0	0	0	4 (7.3%)	2 (3.6%)	2 (3.6%)	0	0	0
低カルシウム血症	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
糖尿病	0	0	0	0	0	0	0	0	0	0	0	0
高ナトリウム血症	0	0	0	0	0	0	0	0	0	0	0	0
高リン酸塩血症	0	0	0	0	0	0	0	0	0	0	0	0
低血糖症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
栄養障害	0	0	0	0	0	0	0	0	0	0	0	0
ビタミンＢ１２欠乏	0	0	0	0	0	0	0	0	0	0	0	0
体液貯留	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
低リン酸血症	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
代謝性アシドーシス	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
神経系障害	6 (26.1%)	4 (17.4%)	2 (8.7%)	0	0	0	25 (45.5%)	12 (21.8%)	10 (18.2%)	3 (5.5%)	0	0
頭痛	2 (8.7%)	2 (8.7%)	0	0	0	0	4 (7.3%)	1 (1.8%)	3 (5.5%)	0	0	0
浮動性めまい	3 (13.0%)	2 (8.7%)	1 (4.3%)	0	0	0	6 (10.9%)	5 (9.1%)	1 (1.8%)	0	0	0
末梢性感覚ニューロパチー	1 (4.3%)	0	1 (4.3%)	0	0	0	7 (12.7%)	2 (3.6%)	5 (9.1%)	0	0	0
感覚鈍麻	1 (4.3%)	1 (4.3%)	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
傾眠	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
振戦	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
味覚異常	0	0	0	0	0	0	4 (7.3%)	3 (5.5%)	1 (1.8%)	0	0	0
錯感覚	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
下肢静止不能症候群	0	0	0	0	0	0	0	0	0	0	0	0
意識変容状態	0	0	0	0	0	0	0	0	0	0	0	0
手根管症候群	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
意識レベルの低下	0	0	0	0	0	0	0	0	0	0	0	0
脳症	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
知覚過敏	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
嗜眠	0	0	0	0	0	0	0	0	0	0	0	0
記憶障害	0	0	0	0	0	0	0	0	0	0	0	0
神経痛	0	0	0	0	0	0	0	0	0	0	0	0
嗅覚錯誤	0	0	0	0	0	0	0	0	0	0	0	0
脊髄圧迫	0	0	0	0	0	0	0	0	0	0	0	0
失神	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
第７脳神経麻痺	0	0	0	0	0	0	0	0	0	0	0	0
無感覚	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
坐骨神経痛	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
第６脳神経麻痺	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
皮膚および皮下組織障害	3 (13.0%)	3 (13.0%)	0	0	0	0	16 (29.1%)	12 (21.8%)	4 (7.3%)	0	0	0
そう痒症	1 (4.3%)	1 (4.3%)	0	0	0	0	4 (7.3%)	2 (3.6%)	2 (3.6%)	0	0	0
多汗症	0	0	0	0	0	0	3 (5.5%)	3 (5.5%)	0	0	0	0
寝汗	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
発疹	2 (8.7%)	2 (8.7%)	0	0	0	0	7 (12.7%)	5 (9.1%)	2 (3.6%)	0	0	0
斑状丘疹状皮疹	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
皮膚嚢腫	0	0	0	0	0	0	0	0	0	0	0	0
ざ瘡様皮膚炎	0	0	0	0	0	0	0	0	0	0	0	0
接触性皮膚炎	0	0	0	0	0	0	0	0	0	0	0	0
皮膚乾燥	0	0	0	0	0	0	0	0	0	0	0	0
湿疹	0	0	0	0	0	0	0	0	0	0	0	0
紅斑	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
点状出血	0	0	0	0	0	0	0	0	0	0	0	0
褥瘡性潰瘍	0	0	0	0	0	0	0	0	0	0	0	0
薬疹	0	0	0	0	0	0	0	0	0	0	0	0
皮脂欠乏性湿疹	0	0	0	0	0	0	0	0	0	0	0	0
手掌・足底発赤知覚不全症候群	0	0	0	0	0	0	0	0	0	0	0	0
色素沈着障害	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
全身性そう痒症	0	0	0	0	0	0	0	0	0	0	0	0
乾癬	0	0	0	0	0	0	0	0	0	0	0	0
斑状皮疹	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
丘疹性皮疹	0	0	0	0	0	0	0	0	0	0	0	0
皮膚剥脱	0	0	0	0	0	0	0	0	0	0	0	0
皮膚色素過剰	0	0	0	0	0	0	0	0	0	0	0	0
皮膚潰瘍	0	0	0	0	0	0	0	0	0	0	0	0
蕁麻疹	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
脱毛症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
爪変色	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
血管障害	5 (21.7%)	2 (8.7%)	3 (13.0%)	0	0	0	14 (25.5%)	4 (7.3%)	6 (10.9%)	4 (7.3%)	0	0
高血圧	2 (8.7%)	0	2 (8.7%)	0	0	0	10 (18.2%)	1 (1.8%)	5 (9.1%)	4 (7.3%)	0	0
低血圧	2 (8.7%)	1 (4.3%)	1 (4.3%)	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
血腫	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
潮紅	2 (8.7%)	2 (8.7%)	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
深部静脈血栓症	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
ほてり	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
表在性静脈炎	0	0	0	0	0	0	0	0	0	0	0	0
レイノー現象	0	0	0	0	0	0	0	0	0	0	0	0
四肢静脈血栓症	0	0	0	0	0	0	0	0	0	0	0	0
傷害、中毒および処置合併症	1 (4.3%)	0	0	1 (4.3%)	0	0	3 (5.5%)	1 (1.8%)	1 (1.8%)	1 (1.8%)	0	0
挫傷	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
転倒	0	0	0	0	0	0	0	0	0	0	0	0
肋骨骨折	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
上腕骨骨折	0	0	0	0	0	0	0	0	0	0	0	0
裂傷	0	0	0	0	0	0	0	0	0	0	0	0
腰椎骨折	0	0	0	0	0	0	0	0	0	0	0	0
脊椎圧迫骨折	1 (4.3%)	0	0	1 (4.3%)	0	0	0	0	0	0	0	0
骨挫傷	0	0	0	0	0	0	0	0	0	0	0	0
擦過傷	0	0	0	0	0	0	0	0	0	0	0	0
足骨折	0	0	0	0	0	0	0	0	0	0	0	0
骨折	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Toxicity Grade						Toxicity Grade					
	Total	1	2	3	4	5	Total	1	2	3	4	5
肉離れ	0	0	0	0	0	0	0	0	0	0	0	0
眼窩周囲挫傷	0	0	0	0	0	0	0	0	0	0	0	0
処置による疼痛	0	0	0	0	0	0	0	0	0	0	0	0
硬膜下血腫	0	0	0	0	0	0	0	0	0	0	0	0
腱断裂	0	0	0	0	0	0	0	0	0	0	0	0
輸血反応	0	0	0	0	0	0	0	0	0	0	0	0
上肢骨折	0	0	0	0	0	0	0	0	0	0	0	0
創傷	0	0	0	0	0	0	0	0	0	0	0	0
手首関節骨折	0	0	0	0	0	0	0	0	0	0	0	0
四肢外傷性切断	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
精神障害	0	0	0	0	0	0	9 (16.4%)	6 (10.9%)	3 (5.5%)	0	0	0
不安	0	0	0	0	0	0	0	0	0	0	0	0
錯乱状態	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
不眠症	0	0	0	0	0	0	4 (7.3%)	4 (7.3%)	0	0	0	0
激越	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
譫妄	0	0	0	0	0	0	0	0	0	0	0	0
うつ病	0	0	0	0	0	0	2 (3.6%)	0	2 (3.6%)	0	0	0
気分変化	0	0	0	0	0	0	0	0	0	0	0	0
摂食障害	0	0	0	0	0	0	0	0	0	0	0	0
幻覚	0	0	0	0	0	0	0	0	0	0	0	0
精神状態変化	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
気分動揺	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
神経過敏	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
腎および尿路障害	11 (47.8%)	6 (26.1%)	5 (21.7%)	0	0	0	15 (27.3%)	7 (12.7%)	6 (10.9%)	2 (3.6%)	0	0
腎機能障害	1 (4.3%)	0	1 (4.3%)	0	0	0	8 (14.5%)	2 (3.6%)	5 (9.1%)	1 (1.8%)	0	0
排尿困難	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
頻尿	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
蛋白尿	10 (43.5%)	6 (26.1%)	4 (17.4%)	0	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
尿閉	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
非感染性膀胱炎	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
血尿	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
夜間頻尿	0	0	0	0	0	0	0	0	0	0	0	0
腎不全	0	0	0	0	0	0	0	0	0	0	0	0
腎静脈血栓症	0	0	0	0	0	0	0	0	0	0	0	0
尿失禁	0	0	0	0	0	0	3 (5.5%)	1 (1.8%)	2 (3.6%)	0	0	0
尿路閉塞	0	0	0	0	0	0	0	0	0	0	0	0
高窒素血症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
膀胱痙縮	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
尿意切迫	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
急性腎不全	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
臨床検査	10 (43.5%)	5 (21.7%)	3 (13.0%)	2 (8.7%)	0	0	7 (12.7%)	3 (5.5%)	2 (3.6%)	2 (3.6%)	0	0
体重減少	0	0	0	0	0	0	4 (7.3%)	2 (3.6%)	2 (3.6%)	0	0	0
体重増加	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
国際標準比増加	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
血中クレアチンホスホキナーゼ増加	1 (4.3%)	0	0	1 (4.3%)	0	0	0	0	0	0	0	0
血中テストステロン減少	0	0	0	0	0	0	0	0	0	0	0	0
心電図異常Q波	0	0	0	0	0	0	0	0	0	0	0	0
心電図ＱＴ延長	5 (21.7%)	2 (8.7%)	2 (8.7%)	1 (4.3%)	0	0	0	0	0	0	0	0
心電図異常Ｔ波	0	0	0	0	0	0	0	0	0	0	0	0
酸素飽和度異常	0	0	0	0	0	0	0	0	0	0	0	0
尿量減少	0	0	0	0	0	0	0	0	0	0	0	0
遊離ヘモグロビン陽性	5 (21.7%)	4 (17.4%)	1 (4.3%)	0	0	0	0	0	0	0	0	0
ハプトグロビン減少	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
心拍数増加	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
リンパ球数減少	1 (4.3%)	1 (4.3%)	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
眼障害	1 (4.3%)	1 (4.3%)	0	0	0	0	10 (18.2%)	8 (14.5%)	1 (1.8%)	1 (1.8%)	0	0
霧視	0	0	0	0	0	0	2 (3.6%)	1 (1.8%)	1 (1.8%)	0	0	0
眼乾燥	0	0	0	0	0	0	0	0	0	0	0	0
眼そう痒症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
眼充血	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
白内障	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
結膜出血	0	0	0	0	0	0	0	0	0	0	0	0
複視	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
睫毛乱生	0	0	0	0	0	0	0	0	0	0	0	0
眼部腫脹	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
眼瞼機能障害	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
眼瞼下垂	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
眼瞼発疹	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
光視症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
視力障害	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
硝子体浮遊物	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
心臓障害	4 (17.4%)	3 (13.0%)	1 (4.3%)	0	0	0	2 (3.6%)	2 (3.6%)	0	0	0	0
動悸	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
洞性頻脈	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
頻脈	2 (8.7%)	2 (8.7%)	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
狭心症	0	0	0	0	0	0	0	0	0	0	0	0
心房粗動	0	0	0	0	0	0	0	0	0	0	0	0
徐脈	0	0	0	0	0	0	0	0	0	0	0	0
左脚ブロック	0	0	0	0	0	0	0	0	0	0	0	0
うっ血性心不全	0	0	0	0	0	0	0	0	0	0	0	0
心肺停止	0	0	0	0	0	0	0	0	0	0	0	0
心房細動	1 (4.3%)	0	1 (4.3%)	0	0	0	0	0	0	0	0	0
上室性期外収縮	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
肝胆道系障害	1 (4.3%)	0	0	1 (4.3%)	0	0	4 (7.3%)	3 (5.5%)	1 (1.8%)	0	0	0
肝機能異常	1 (4.3%)	0	0	1 (4.3%)	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
肝不全	0	0	0	0	0	0	0	0	0	0	0	0
高ビリルビン血症	0	0	0	0	0	0	0	0	0	0	0	0
黄疸	0	0	0	0	0	0	0	0	0	0	0	0
脂肪肝	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
耳および迷路障害	0	0	0	0	0	0	3 (5.5%)	2 (3.6%)	1 (1.8%)	0	0	0
耳痛	0	0	0	0	0	0	0	0	0	0	0	0
耳の障害	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
耳鳴	0	0	0	0	0	0	0	0	0	0	0	0
回転性めまい	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
耳垢栓塞	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
耳不快感	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3%)	1 (4.3%)	0	0	0	0	3 (5.5%)	1 (1.8%)	1 (1.8%)	1 (1.8%)	0	0
腫瘍疼痛	0	0	0	0	0	0	0	0	0	0	0	0
肛門直腸ヒト乳頭腫ウイルス感染	0	0	0	0	0	0	0	0	0	0	0	0
基底細胞癌	0	0	0	0	0	0	1 (1.8%)	0	1 (1.8%)	0	0	0
皮膚癌	0	0	0	0	0	0	0	0	0	0	0	0
皮膚良性新生物	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
皮膚乳頭腫	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
生殖系および乳房障害	0	0	0	0	0	0	3 (5.5%)	2 (3.6%)	0	1 (1.8%)	0	0
生殖器痛	0	0	0	0	0	0	0	0	0	0	0	0
乳頭痛	0	0	0	0	0	0	0	0	0	0	0	0
性器浮腫	0	0	0	0	0	0	0	0	0	0	0	0
陰茎浮腫	0	0	0	0	0	0	0	0	0	0	0	0
腟出血	0	0	0	0	0	0	0	0	0	0	0	0
血精液症	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
骨盤痛	0	0	0	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
前立腺炎	0	0	0	0	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
免疫系障害	3 (13.0%)	0	2 (8.7%)	1 (4.3%)	0	0	2 (3.6%)	1 (1.8%)	0	1 (1.8%)	0	0
アレルギー性浮腫	0	0	0	0	0	0	0	0	0	0	0	0
サイトカイン放出症候群	1 (4.3%)	0	1 (4.3%)	0	0	0	1 (1.8%)	0	0	1 (1.8%)	0	0
季節性アレルギー	0	0	0	0	0	0	0	0	0	0	0	0
過敏症	2 (8.7%)	0	1 (4.3%)	1 (4.3%)	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0
先天性、家族性および遺伝性障害	0	0	0	0	0	0	0	0	0	0	0	0
あざ	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART1OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Toxicity Grade						Toxicity Grade					
	Total	1	2	3	4	5	Total	1	2	3	4	5

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02EPART1OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae02e.sas] 16MAR2015, 16:20

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
Analysis set: all treated	156						3					
Total number of subjects with TEAEs	154 (98.7%)	10 (6.4%)	56 (35.9%)	59 (37.8%)	19 (12.2%)	10 (6.4%)	3 (100.0%)	0	2 (66.7%)	1 (33.3%)	0	0
MedDRA system organ class/Preferred term												
一般・全身障害および投与部位の状態	106 (67.9%)	46 (29.5%)	47 (30.1%)	8 (5.1%)	0	5 (3.2%)	0	0	0	0	0	0
疲労	59 (37.8%)	32 (20.5%)	24 (15.4%)	3 (1.9%)	0	0	0	0	0	0	0	0
発熱	29 (18.6%)	19 (12.2%)	8 (5.1%)	2 (1.3%)	0	0	0	0	0	0	0	0
悪寒	16 (10.3%)	8 (5.1%)	8 (5.1%)	0	0	0	0	0	0	0	0	0
無力症	12 (7.7%)	5 (3.2%)	6 (3.8%)	1 (0.6%)	0	0	0	0	0	0	0	0
末梢性浮腫	11 (7.1%)	5 (3.2%)	5 (3.2%)	1 (0.6%)	0	0	0	0	0	0	0	0
胸痛	9 (5.8%)	6 (3.8%)	3 (1.9%)	0	0	0	0	0	0	0	0	0
疼痛	8 (5.1%)	5 (3.2%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0
インフルエンザ様疾患	7 (4.5%)	4 (2.6%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0
非心臓性胸痛	6 (3.8%)	5 (3.2%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
全身健康状態低下	5 (3.2%)	0	0	0	0	5 (3.2%)	0	0	0	0	0	0
注射部位内出血	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
局所腫脹	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
倦怠感	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
胸部不快感	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
顔面浮腫	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
全身性浮腫	2 (1.3%)	0	2 (1.3%)	0	0	0	0	0	0	0	0	0
浮腫	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
腋窩痛	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
医療機器の問題	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
顔面痛	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
歩行障害	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
低体温	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
注入部位内出血	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Toxicity Grade						Toxicity Grade					
	Total	1	2	3	4	5	Total	1	2	3	4	5
注射部位浮腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
注射部位反応	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
限局性浮腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
腫瘤	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
恥骨上痛	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
急性期反応	0	0	0	0	0	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	95 (60.9%)	44 (28.2%)	42 (26.9%)	8 (5.1%)	0	1 (0.6%)	2 (66.7%)	1 (33.3%)	1 (33.3%)	0	0	0
咳嗽	31 (19.9%)	22 (14.1%)	9 (5.8%)	0	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0
鼻閉	25 (16.0%)	14 (9.0%)	11 (7.1%)	0	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0
呼吸困難	22 (14.1%)	12 (7.7%)	9 (5.8%)	1 (0.6%)	0	0	0	0	0	0	0	0
口腔咽頭痛	15 (9.6%)	14 (9.0%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
アレルギー性鼻炎	11 (7.1%)	3 (1.9%)	8 (5.1%)	0	0	0	0	0	0	0	0	0
咽喉刺激感	10 (6.4%)	8 (5.1%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
労作性呼吸困難	8 (5.1%)	7 (4.5%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
鼻出血	8 (5.1%)	8 (5.1%)	0	0	0	0	0	0	0	0	0	0
湿性咳嗽	8 (5.1%)	4 (2.6%)	4 (2.6%)	0	0	0	0	0	0	0	0	0
喘鳴	6 (3.8%)	4 (2.6%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
気管支痙攣	5 (3.2%)	0	3 (1.9%)	2 (1.3%)	0	0	1 (33.3%)	0	1 (33.3%)	0	0	0
胸水	4 (2.6%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
副鼻腔うっ血	4 (2.6%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
くしゃみ	4 (2.6%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
低酸素症	3 (1.9%)	0	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0
咽喉絞扼感	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
上気道咳症候群	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
呼吸不全	2 (1.3%)	0	0	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0
急性肺水腫	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
アレルギー性咳嗽	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
慢性閉塞性肺疾患	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
発声障害	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
上気道分泌増加	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
喉頭浮腫	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
アレルギー性喉頭炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
鼻部障害	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
誤嚥性肺炎	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
肺うっ血	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
肺塞栓症	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
肺水腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
鼻漏	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
喉頭の炎症	0	0	0	0	0	0	0	0	0	0	0	0
筋骨格系および結合組織障害	89 (57.1%)	36 (23.1%)	41 (26.3%)	10 (6.4%)	2 (1.3%)	0	1 (33.3%)	1 (33.3%)	0	0	0	0
背部痛	33 (21.2%)	11 (7.1%)	19 (12.2%)	3 (1.9%)	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0
関節痛	25 (16.0%)	13 (8.3%)	12 (7.7%)	0	0	0	0	0	0	0	0	0
四肢痛	23 (14.7%)	14 (9.0%)	8 (5.1%)	1 (0.6%)	0	0	0	0	0	0	0	0
筋骨格系胸痛	16 (10.3%)	4 (2.6%)	10 (6.4%)	2 (1.3%)	0	0	0	0	0	0	0	0
骨痛	14 (9.0%)	8 (5.1%)	5 (3.2%)	1 (0.6%)	0	0	0	0	0	0	0	0
筋骨格痛	13 (8.3%)	4 (2.6%)	8 (5.1%)	1 (0.6%)	0	0	0	0	0	0	0	0
筋痙縮	10 (6.4%)	8 (5.1%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
筋肉痛	6 (3.8%)	4 (2.6%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
鼡径部痛	4 (2.6%)	1 (0.6%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0
頚部痛	3 (1.9%)	1 (0.6%)	0	2 (1.3%)	0	0	0	0	0	0	0	0
病的骨折	3 (1.9%)	0	1 (0.6%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0
脊椎痛	3 (1.9%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
筋力低下	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
骨炎	2 (1.3%)	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
脊柱管狭窄症	2 (1.3%)	0	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0
骨侵食	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
骨病変	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
関節可動域低下	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
四肢不快感	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
運動性低下	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
筋肉疲労	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
筋骨格不快感	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
顎骨壊死	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
顎痛	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
腱炎	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
側腹部痛	0	0	0	0	0	0	0	0	0	0	0	0
脊柱後弯症	0	0	0	0	0	0	0	0	0	0	0	0
筋骨格硬直	0	0	0	0	0	0	0	0	0	0	0	0
ミオパチー	0	0	0	0	0	0	0	0	0	0	0	0
骨壊死	0	0	0	0	0	0	0	0	0	0	0	0
骨粗鬆症性骨折	0	0	0	0	0	0	0	0	0	0	0	0
胃腸障害	85 (54.5%)	46 (29.5%)	36 (23.1%)	2 (1.3%)	1 (0.6%)	0	2 (66.7%)	2 (66.7%)	0	0	0	0
悪心	40 (25.6%)	29 (18.6%)	11 (7.1%)	0	0	0	0	0	0	0	0	0
下痢	24 (15.4%)	16 (10.3%)	8 (5.1%)	0	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0
便秘	22 (14.1%)	12 (7.7%)	10 (6.4%)	0	0	0	0	0	0	0	0	0
嘔吐	20 (12.8%)	11 (7.1%)	9 (5.8%)	0	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0
腹痛	9 (5.8%)	5 (3.2%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0
消化不良	4 (2.6%)	1 (0.6%)	3 (1.9%)	0	0	0	0	0	0	0	0	0
口内炎	4 (2.6%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
歯痛	4 (2.6%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
腹部膨満	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
放屁	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
口の感覚鈍麻	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
腹部不快感	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
上腹部痛	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
便失禁	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
胃食道逆流性疾患	2 (1.3%)	0	2 (1.3%)	0	0	0	0	0	0	0	0	0
歯肉出血	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
口腔内痛	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
水疱性出血性口峡炎	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
大腸炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
憩室	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
嚥下障害	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
胃炎	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
歯肉腫脹	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
舌炎	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
血便排泄	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
痔核	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
大腸閉塞	1 (0.6%)	0	0	0	1 (0.6%)	0	0	0	0	0	0	0
口唇出血	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
口腔内潰瘍形成	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
口腔粘膜変色	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
膵炎	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
口の錯感覚	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
舌苔	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
歯の発育障害	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
歯の障害	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
アフタ性口内炎	0	0	0	0	0	0	0	0	0	0	0	0
口内乾燥	0	0	0	0	0	0	0	0	0	0	0	0
舌痛	0	0	0	0	0	0	0	0	0	0	0	0
口唇浮腫	0	0	0	0	0	0	0	0	0	0	0	0
食道炎	0	0	0	0	0	0	0	0	0	0	0	0
感染症および寄生虫症	85 (54.5%)	17 (10.9%)	52 (33.3%)	14 (9.0%)	1 (0.6%)	1 (0.6%)	1 (33.3%)	0	0	1 (33.3%)	0	0
上気道感染	27 (17.3%)	3 (1.9%)	23 (14.7%)	1 (0.6%)	0	0	0	0	0	0	0	0
鼻咽頭炎	18 (11.5%)	14 (9.0%)	4 (2.6%)	0	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
肺炎	13 (8.3%)	0	4 (2.6%)	8 (5.1%)	0	1 (0.6%)	0	0	0	0	0	0
副鼻腔炎	9 (5.8%)	2 (1.3%)	7 (4.5%)	0	0	0	0	0	0	0	0	0
尿路感染	7 (4.5%)	1 (0.6%)	6 (3.8%)	0	0	0	1 (33.3%)	0	0	1 (33.3%)	0	0
気管支炎	5 (3.2%)	1 (0.6%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0	0
結膜炎	3 (1.9%)	1 (0.6%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
帯状疱疹	3 (1.9%)	0	1 (0.6%)	2 (1.3%)	0	0	0	0	0	0	0	0
大葉性肺炎	3 (1.9%)	0	1 (0.6%)	2 (1.3%)	0	0	0	0	0	0	0	0
口腔カンジダ症	3 (1.9%)	1 (0.6%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
カンジダ感染	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
単純ヘルペス	2 (1.3%)	0	2 (1.3%)	0	0	0	0	0	0	0	0	0
感染	2 (1.3%)	0	2 (1.3%)	0	0	0	0	0	0	0	0	0
インフルエンザ	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
パラインフルエンザウイルス感染	2 (1.3%)	0	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
咽頭炎	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
鼻炎	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
軟部組織感染	2 (1.3%)	0	0	2 (1.3%)	0	0	0	0	0	0	0	0
水痘	2 (1.3%)	0	2 (1.3%)	0	0	0	0	0	0	0	0	0
蜂巣炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
膀胱炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
サイトメガロウイルス性脈絡網膜炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
医療機器関連感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
耳感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
胃腸炎	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
ウイルス性胃腸炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
性器感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
麦粒腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
下気道感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
粘膜感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
眼部単純ヘルペス	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
口腔真菌感染	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
口腔ヘルペス	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
爪囲炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
レンサ球菌性肺炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
腎盂腎炎	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
気道感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
敗血症	1 (0.6%)	0	0	0	1 (0.6%)	0	0	0	0	0	0	0
レンサ球菌感染	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
歯感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
ウイルス性上気道感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
外陰腟真菌感染	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
菌血症	0	0	0	0	0	0	0	0	0	0	0	0
真菌感染	0	0	0	0	0	0	0	0	0	0	0	0
真菌性消化管感染	0	0	0	0	0	0	0	0	0	0	0	0
肺感染	0	0	0	0	0	0	0	0	0	0	0	0
メタニューモウイルス感染	0	0	0	0	0	0	0	0	0	0	0	0
ＲＳウイルス感染	0	0	0	0	0	0	0	0	0	0	0	0
細菌性尿路感染	0	0	0	0	0	0	0	0	0	0	0	0
ウイルス感染	0	0	0	0	0	0	0	0	0	0	0	0
外陰部腟カンジダ症	0	0	0	0	0	0	0	0	0	0	0	0
血液およびリンパ系障害	76 (48.7%)	10 (6.4%)	13 (8.3%)	39 (25.0%)	14 (9.0%)	0	0	0	0	0	0	0
貧血	39 (25.0%)	0	12 (7.7%)	27 (17.3%)	0	0	0	0	0	0	0	0
好中球減少症	34 (21.8%)	6 (3.8%)	9 (5.8%)	15 (9.6%)	4 (2.6%)	0	0	0	0	0	0	0
血小板減少症	31 (19.9%)	6 (3.8%)	3 (1.9%)	13 (8.3%)	9 (5.8%)	0	0	0	0	0	0	0
白血球減少症	14 (9.0%)	3 (1.9%)	4 (2.6%)	7 (4.5%)	0	0	0	0	0	0	0	0
リンパ球減少症	9 (5.8%)	0	0	6 (3.8%)	3 (1.9%)	0	0	0	0	0	0	0
ヘモグロビン血症	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
内出血発生の増加傾向	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
赤血球凝集	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
溶血	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
単球減少症	0	0	0	0	0	0	0	0	0	0	0	0
代謝および栄養障害	64 (41.0%)	27 (17.3%)	23 (14.7%)	9 (5.8%)	4 (2.6%)	1 (0.6%)	0	0	0	0	0	0
食欲減退	23 (14.7%)	14 (9.0%)	8 (5.1%)	1 (0.6%)	0	0	0	0	0	0	0	0
高カルシウム血症	18 (11.5%)	6 (3.8%)	6 (3.8%)	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0
高血糖	13 (8.3%)	6 (3.8%)	3 (1.9%)	4 (2.6%)	0	0	0	0	0	0	0	0
低カリウム血症	12 (7.7%)	8 (5.1%)	3 (1.9%)	0	1 (0.6%)	0	0	0	0	0	0	0
低マグネシウム血症	9 (5.8%)	6 (3.8%)	3 (1.9%)	0	0	0	0	0	0	0	0	0
低ナトリウム血症	8 (5.1%)	8 (5.1%)	0	0	0	0	0	0	0	0	0	0
高カリウム血症	5 (3.2%)	4 (2.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0
酵素異常	4 (2.6%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
高尿酸血症	4 (2.6%)	3 (1.9%)	0	0	1 (0.6%)	0	0	0	0	0	0	0
低アルブミン血症	4 (2.6%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
低カルシウム血症	3 (1.9%)	1 (0.6%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
糖尿病	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
高ナトリウム血症	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
高リン酸塩血症	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
低血糖症	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
栄養障害	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
ビタミンＢ１２欠乏	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
体液貯留	0	0	0	0	0	0	0	0	0	0	0	0
低リン酸血症	0	0	0	0	0	0	0	0	0	0	0	0
代謝性アシドーシス	0	0	0	0	0	0	0	0	0	0	0	0
神経系障害	50 (32.1%)	29 (18.6%)	14 (9.0%)	6 (3.8%)	1 (0.6%)	0	0	0	0	0	0	0
頭痛	15 (9.6%)	10 (6.4%)	3 (1.9%)	2 (1.3%)	0	0	0	0	0	0	0	0
浮動性めまい	13 (8.3%)	10 (6.4%)	3 (1.9%)	0	0	0	0	0	0	0	0	0
末梢性感覚ニューロパチー	6 (3.8%)	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0
感覚鈍麻	5 (3.2%)	2 (1.3%)	3 (1.9%)	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
傾眠	5 (3.2%)	2 (1.3%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0
振戦	4 (2.6%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
味覚異常	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
錯感覚	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
下肢静止不能症候群	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
意識変容状態	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
手根管症候群	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
意識レベルの低下	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
脳症	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
知覚過敏	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
嗜眠	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
記憶障害	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
神経痛	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
嗅覚錯誤	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
脊髄圧迫	1 (0.6%)	0	0	0	1 (0.6%)	0	0	0	0	0	0	0
失神	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
第７脳神経麻痺	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
無感覚	0	0	0	0	0	0	0	0	0	0	0	0
坐骨神経痛	0	0	0	0	0	0	0	0	0	0	0	0
第６脳神経麻痺	0	0	0	0	0	0	0	0	0	0	0	0
皮膚および皮下組織障害	35 (22.4%)	29 (18.6%)	6 (3.8%)	0	0	0	0	0	0	0	0	0
そう痒症	5 (3.2%)	4 (2.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
多汗症	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
寝汗	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
発疹	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
斑状丘疹状皮疹	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
皮膚嚢腫	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
ざ瘡様皮膚炎	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
接触性皮膚炎	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
皮膚乾燥	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
湿疹	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
紅斑	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
点状出血	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
褥瘡性潰瘍	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
薬疹	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
皮脂欠乏性湿疹	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
手掌・足底発赤知覚不全症候群	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
色素沈着障害	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
全身性そう痒症	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
乾癬	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
斑状皮疹	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
丘疹性皮疹	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
皮膚剥脱	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
皮膚色素過剰	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
皮膚潰瘍	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
蕁麻疹	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
脱毛症	0	0	0	0	0	0	0	0	0	0	0	0
爪変色	0	0	0	0	0	0	0	0	0	0	0	0
血管障害	29 (18.6%)	10 (6.4%)	9 (5.8%)	10 (6.4%)	0	0	0	0	0	0	0	0
高血圧	15 (9.6%)	3 (1.9%)	4 (2.6%)	8 (5.1%)	0	0	0	0	0	0	0	0
低血圧	7 (4.5%)	3 (1.9%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0	0
血腫	4 (2.6%)	4 (2.6%)	0	0	0	0	0	0	0	0	0	0
潮紅	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
深部静脈血栓症	2 (1.3%)	0	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
ほてり	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
表在性静脈炎	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
レイノー現象	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
四肢静脈血栓症	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
傷害、中毒および処置合併症	28 (17.9%)	14 (9.0%)	9 (5.8%)	5 (3.2%)	0	0	0	0	0	0	0	0
挫傷	5 (3.2%)	5 (3.2%)	0	0	0	0	0	0	0	0	0	0
転倒	5 (3.2%)	3 (1.9%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
肋骨骨折	3 (1.9%)	0	3 (1.9%)	0	0	0	0	0	0	0	0	0
上腕骨骨折	2 (1.3%)	0	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
裂傷	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
腰椎骨折	2 (1.3%)	0	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
脊椎圧迫骨折	2 (1.3%)	0	0	2 (1.3%)	0	0	0	0	0	0	0	0
骨挫傷	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
擦過傷	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
足骨折	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
骨折	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
肉離れ	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
眼窩周囲挫傷	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
処置による疼痛	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
硬膜下血腫	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
腱断裂	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
輸血反応	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
上肢骨折	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
創傷	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
手首関節骨折	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
四肢外傷性切断	0	0	0	0	0	0	0	0	0	0	0	0
精神障害	28 (17.9%)	14 (9.0%)	10 (6.4%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0
不安	9 (5.8%)	5 (3.2%)	4 (2.6%)	0	0	0	0	0	0	0	0	0
錯乱状態	7 (4.5%)	3 (1.9%)	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0
不眠症	7 (4.5%)	4 (2.6%)	3 (1.9%)	0	0	0	0	0	0	0	0	0
激越	3 (1.9%)	1 (0.6%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
譫妄	3 (1.9%)	1 (0.6%)	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0
うつ病	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
気分変化	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
摂食障害	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
幻覚	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
精神状態変化	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
気分動揺	0	0	0	0	0	0	0	0	0	0	0	0
神経過敏	0	0	0	0	0	0	0	0	0	0	0	0
腎および尿路障害	25 (16.0%)	13 (8.3%)	6 (3.8%)	6 (3.8%)	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
腎機能障害	11 (7.1%)	6 (3.8%)	3 (1.9%)	2 (1.3%)	0	0	0	0	0	0	0	0
排尿困難	3 (1.9%)	3 (1.9%)	0	0	0	0	0	0	0	0	0	0
頻尿	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
蛋白尿	2 (1.3%)	1 (0.6%)	0	1 (0.6%)	0	0	1 (33.3%)	1 (33.3%)	0	0	0	0
尿閉	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
非感染性膀胱炎	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
血尿	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
夜間頻尿	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
腎不全	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
腎静脈血栓症	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
尿失禁	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
尿路閉塞	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
高窒素血症	0	0	0	0	0	0	0	0	0	0	0	0
膀胱痙縮	0	0	0	0	0	0	0	0	0	0	0	0
尿意切迫	0	0	0	0	0	0	0	0	0	0	0	0
急性腎不全	0	0	0	0	0	0	0	0	0	0	0	0
臨床検査	17 (10.9%)	8 (5.1%)	5 (3.2%)	4 (2.6%)	0	0	0	0	0	0	0	0
体重減少	7 (4.5%)	5 (3.2%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
体重増加	4 (2.6%)	3 (1.9%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
国際標準比増加	3 (1.9%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0
血中クレアチンホスホキナーゼ増加	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
血中テストステロン減少	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
心電図異常Q波	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
心電図ＱＴ延長	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
心電図異常Ｔ波	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
酸素飽和度異常	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
尿量減少	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
遊離ヘモグロビン陽性	0	0	0	0	0	0	0	0	0	0	0	0
ハプトグロビン減少	0	0	0	0	0	0	0	0	0	0	0	0
心拍数増加	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
リンパ球数減少	0	0	0	0	0	0	0	0	0	0	0	0
眼障害	13 (8.3%)	12 (7.7%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
霧視	7 (4.5%)	7 (4.5%)	0	0	0	0	0	0	0	0	0	0
眼乾燥	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
眼そう痒症	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
眼充血	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
白内障	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
結膜出血	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
複視	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
睫毛乱生	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
眼部腫脹	0	0	0	0	0	0	0	0	0	0	0	0
眼瞼機能障害	0	0	0	0	0	0	0	0	0	0	0	0
眼瞼下垂	0	0	0	0	0	0	0	0	0	0	0	0
眼瞼発疹	0	0	0	0	0	0	0	0	0	0	0	0
光視症	0	0	0	0	0	0	0	0	0	0	0	0
視力障害	0	0	0	0	0	0	0	0	0	0	0	0
硝子体浮遊物	0	0	0	0	0	0	0	0	0	0	0	0
心臓障害	11 (7.1%)	4 (2.6%)	4 (2.6%)	2 (1.3%)	0	1 (0.6%)	0	0	0	0	0	0
動悸	5 (3.2%)	3 (1.9%)	2 (1.3%)	0	0	0	0	0	0	0	0	0
洞性頻脈	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
頻脈	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
狭心症	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
心房粗動	1 (0.6%)	0	0	1 (0.6%)	0	0	0	0	0	0	0	0
徐脈	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
左脚ブロック	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
うっ血性心不全	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
心肺停止	1 (0.6%)	0	0	0	0	1 (0.6%)	0	0	0	0	0	0
心房細動	0	0	0	0	0	0	0	0	0	0	0	0
上室性期外収縮	0	0	0	0	0	0	0	0	0	0	0	0
肝胆道系障害	8 (5.1%)	5 (3.2%)	1 (0.6%)	0	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0
肝機能異常	6 (3.8%)	4 (2.6%)	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0
肝不全	1 (0.6%)	0	0	0	0	1 (0.6%)	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
高ビリルビン血症	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
黄疸	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
脂肪肝	0	0	0	0	0	0	0	0	0	0	0	0
耳および迷路障害	5 (3.2%)	4 (2.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
耳痛	2 (1.3%)	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
耳の障害	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
耳鳴	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
回転性めまい	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
耳垢栓塞	0	0	0	0	0	0	0	0	0	0	0	0
耳不快感	0	0	0	0	0	0	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5 (3.2%)	4 (2.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
腫瘍疼痛	2 (1.3%)	2 (1.3%)	0	0	0	0	0	0	0	0	0	0
肛門直腸ヒト乳頭腫ウイルス感染	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
基底細胞癌	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
皮膚癌	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
皮膚良性新生物	0	0	0	0	0	0	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0	0	0	0	0	0	0
皮膚乳頭腫	0	0	0	0	0	0	0	0	0	0	0	0
生殖系および乳房障害	4 (2.6%)	4 (2.6%)	0	0	0	0	1 (33.3%)	0	1 (33.3%)	0	0	0
生殖器痛	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
乳頭痛	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
性器浮腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
陰茎浮腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
腟出血	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
血精液症	0	0	0	0	0	0	0	0	0	0	0	0
骨盤痛	0	0	0	0	0	0	0	0	0	0	0	0
前立腺炎	0	0	0	0	0	0	1 (33.3%)	0	1 (33.3%)	0	0	0
免疫系障害	3 (1.9%)	2 (1.3%)	1 (0.6%)	0	0	0	0	0	0	0	0	0
アレルギー性浮腫	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0

TSFAE02EPART2OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
		Toxicity Grade						Toxicity Grade				
	Total	1	2	3	4	5	Total	1	2	3	4	5
サイトカイン放出症候群	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
季節性アレルギー	1 (0.6%)	0	1 (0.6%)	0	0	0	0	0	0	0	0	0
過敏症	0	0	0	0	0	0	0	0	0	0	0	0
先天性、家族性および遺伝性障害	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0
あざ	1 (0.6%)	1 (0.6%)	0	0	0	0	0	0	0	0	0	0

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02EPART2OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae02e.sas] 16MAR2015, 16:20

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
Analysis set: all treated	237					
Total number of subjects with TEAEs	234 (98.7%)	14 (5.9%)	91 (38.4%)	88 (37.1%)	30 (12.7%)	11 (4.6%)
MedDRA system organ class/Preferred term						
一般・全身障害および投与部位の状態	153 (64.6%)	67 (28.3%)	67 (28.3%)	13 (5.5%)	1 (0.4%)	5 (2.1%)
疲労	81 (34.2%)	41 (17.3%)	36 (15.2%)	4 (1.7%)	0	0
発熱	57 (24.1%)	38 (16.0%)	16 (6.8%)	3 (1.3%)	0	0
悪寒	25 (10.5%)	12 (5.1%)	12 (5.1%)	1 (0.4%)	0	0
無力症	15 (6.3%)	7 (3.0%)	7 (3.0%)	1 (0.4%)	0	0
末梢性浮腫	17 (7.2%)	10 (4.2%)	6 (2.5%)	1 (0.4%)	0	0
胸痛	12 (5.1%)	8 (3.4%)	3 (1.3%)	1 (0.4%)	0	0
疼痛	10 (4.2%)	7 (3.0%)	2 (0.8%)	1 (0.4%)	0	0
インフルエンザ様疾患	11 (4.6%)	8 (3.4%)	2 (0.8%)	1 (0.4%)	0	0
非心臓性胸痛	8 (3.4%)	6 (2.5%)	2 (0.8%)	0	0	0
全身健康状態低下	6 (2.5%)	0	0	0	1 (0.4%)	5 (2.1%)
注射部位内出血	3 (1.3%)	3 (1.3%)	0	0	0	0
局所腫脹	3 (1.3%)	3 (1.3%)	0	0	0	0
倦怠感	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0
胸部不快感	5 (2.1%)	1 (0.4%)	4 (1.7%)	0	0	0
顔面浮腫	3 (1.3%)	2 (0.8%)	0	1 (0.4%)	0	0
全身性浮腫	2 (0.8%)	0	2 (0.8%)	0	0	0
浮腫	2 (0.8%)	2 (0.8%)	0	0	0	0
腋窩痛	1 (0.4%)	1 (0.4%)	0	0	0	0
医療機器の問題	1 (0.4%)	1 (0.4%)	0	0	0	0
顔面痛	1 (0.4%)	1 (0.4%)	0	0	0	0
歩行障害	1 (0.4%)	0	1 (0.4%)	0	0	0
低体温	1 (0.4%)	0	1 (0.4%)	0	0	0
注入部位内出血	1 (0.4%)	1 (0.4%)	0	0	0	0
注射部位浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0
注射部位反応	1 (0.4%)	0	1 (0.4%)	0	0	0
限局性浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0
腫瘤	1 (0.4%)	1 (0.4%)	0	0	0	0
恥骨上痛	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
急性期反応	1 (0.4%)	1 (0.4%)	0	0	0	0
呼吸器、胸郭および縦隔障害	137 (57.8%)	62 (26.2%)	64 (27.0%)	10 (4.2%)	0	1 (0.4%)
咳嗽	49 (20.7%)	35 (14.8%)	14 (5.9%)	0	0	0
鼻閉	31 (13.1%)	18 (7.6%)	13 (5.5%)	0	0	0
呼吸困難	34 (14.3%)	20 (8.4%)	13 (5.5%)	1 (0.4%)	0	0
口腔咽頭痛	18 (7.6%)	16 (6.8%)	2 (0.8%)	0	0	0
アレルギー性鼻炎	24 (10.1%)	4 (1.7%)	20 (8.4%)	0	0	0
咽喉刺激感	11 (4.6%)	9 (3.8%)	2 (0.8%)	0	0	0
労作性呼吸困難	9 (3.8%)	8 (3.4%)	1 (0.4%)	0	0	0
鼻出血	10 (4.2%)	9 (3.8%)	1 (0.4%)	0	0	0
湿性咳嗽	12 (5.1%)	7 (3.0%)	5 (2.1%)	0	0	0
喘鳴	7 (3.0%)	4 (1.7%)	3 (1.3%)	0	0	0
気管支痙攣	8 (3.4%)	1 (0.4%)	4 (1.7%)	3 (1.3%)	0	0
胸水	5 (2.1%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	0
副鼻腔うっ血	4 (1.7%)	3 (1.3%)	1 (0.4%)	0	0	0
くしゃみ	4 (1.7%)	2 (0.8%)	2 (0.8%)	0	0	0
低酸素症	3 (1.3%)	0	2 (0.8%)	1 (0.4%)	0	0
咽喉絞扼感	3 (1.3%)	3 (1.3%)	0	0	0	0
上気道咳症候群	4 (1.7%)	4 (1.7%)	0	0	0	0
呼吸不全	2 (0.8%)	0	0	1 (0.4%)	0	1 (0.4%)
急性肺水腫	1 (0.4%)	0	0	1 (0.4%)	0	0
アレルギー性咳嗽	1 (0.4%)	0	1 (0.4%)	0	0	0
慢性閉塞性肺疾患	1 (0.4%)	0	1 (0.4%)	0	0	0
発声障害	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
上気道分泌増加	1 (0.4%)	0	1 (0.4%)	0	0	0
喉頭浮腫	1 (0.4%)	0	1 (0.4%)	0	0	0
アレルギー性喉頭炎	4 (1.7%)	2 (0.8%)	2 (0.8%)	0	0	0
鼻部障害	1 (0.4%)	0	1 (0.4%)	0	0	0
誤嚥性肺炎	1 (0.4%)	0	0	1 (0.4%)	0	0
肺うっ血	1 (0.4%)	1 (0.4%)	0	0	0	0
肺塞栓症	1 (0.4%)	0	0	1 (0.4%)	0	0
肺水腫	1 (0.4%)	1 (0.4%)	0	0	0	0
鼻漏	2 (0.8%)	2 (0.8%)	0	0	0	0
喉頭の炎症	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
筋骨格系および結合組織障害	126 (53.2%)	51 (21.5%)	57 (24.1%)	16 (6.8%)	2 (0.8%)	0
背部痛	43 (18.1%)	14 (5.9%)	23 (9.7%)	6 (2.5%)	0	0
関節痛	32 (13.5%)	18 (7.6%)	14 (5.9%)	0	0	0
四肢痛	25 (10.5%)	16 (6.8%)	8 (3.4%)	1 (0.4%)	0	0
筋骨格系胸痛	21 (8.9%)	5 (2.1%)	14 (5.9%)	2 (0.8%)	0	0
骨痛	21 (8.9%)	10 (4.2%)	10 (4.2%)	1 (0.4%)	0	0
筋骨格痛	16 (6.8%)	5 (2.1%)	9 (3.8%)	2 (0.8%)	0	0
筋痙縮	12 (5.1%)	9 (3.8%)	3 (1.3%)	0	0	0
筋肉痛	12 (5.1%)	6 (2.5%)	6 (2.5%)	0	0	0
胂径部痛	4 (1.7%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0
頚部痛	3 (1.3%)	1 (0.4%)	0	2 (0.8%)	0	0
病的骨折	3 (1.3%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
脊椎痛	3 (1.3%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
筋力低下	2 (0.8%)	2 (0.8%)	0	0	0	0
骨炎	2 (0.8%)	1 (0.4%)	0	1 (0.4%)	0	0
脊柱管狭窄症	2 (0.8%)	0	1 (0.4%)	0	1 (0.4%)	0
骨侵食	1 (0.4%)	1 (0.4%)	0	0	0	0
骨病変	1 (0.4%)	0	1 (0.4%)	0	0	0
関節可動域低下	1 (0.4%)	1 (0.4%)	0	0	0	0
四肢不快感	2 (0.8%)	2 (0.8%)	0	0	0	0
運動性低下	1 (0.4%)	0	1 (0.4%)	0	0	0
筋肉疲労	1 (0.4%)	1 (0.4%)	0	0	0	0
筋骨格不快感	1 (0.4%)	1 (0.4%)	0	0	0	0
顎骨壊死	1 (0.4%)	0	1 (0.4%)	0	0	0
顎痛	1 (0.4%)	0	1 (0.4%)	0	0	0
腱炎	1 (0.4%)	1 (0.4%)	0	0	0	0
側腹部痛	1 (0.4%)	1 (0.4%)	0	0	0	0
脊柱後弯症	1 (0.4%)	0	0	1 (0.4%)	0	0
筋骨格硬直	1 (0.4%)	1 (0.4%)	0	0	0	0
ミオパチー	1 (0.4%)	0	1 (0.4%)	0	0	0
骨壊死	1 (0.4%)	1 (0.4%)	0	0	0	0
骨粗鬆症性骨折	1 (0.4%)	0	0	1 (0.4%)	0	0
胃腸障害	123 (51.9%)	69 (29.1%)	49 (20.7%)	3 (1.3%)	1 (0.4%)	1 (0.4%)
悪心	53 (22.4%)	37 (15.6%)	15 (6.3%)	1 (0.4%)	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
下痢	40 (16.9%)	28 (11.8%)	12 (5.1%)	0	0	0
便秘	29 (12.2%)	15 (6.3%)	14 (5.9%)	0	0	0
嘔吐	30 (12.7%)	19 (8.0%)	10 (4.2%)	1 (0.4%)	0	0
腹痛	12 (5.1%)	7 (3.0%)	2 (0.8%)	2 (0.8%)	0	1 (0.4%)
消化不良	7 (3.0%)	2 (0.8%)	5 (2.1%)	0	0	0
口内炎	7 (3.0%)	5 (2.1%)	2 (0.8%)	0	0	0
歯痛	4 (1.7%)	3 (1.3%)	1 (0.4%)	0	0	0
腹部膨満	4 (1.7%)	4 (1.7%)	0	0	0	0
放屁	3 (1.3%)	3 (1.3%)	0	0	0	0
口の感覚鈍麻	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0
腹部不快感	3 (1.3%)	3 (1.3%)	0	0	0	0
上腹部痛	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
便失禁	2 (0.8%)	2 (0.8%)	0	0	0	0
胃食道逆流性疾患	2 (0.8%)	0	2 (0.8%)	0	0	0
歯肉出血	2 (0.8%)	2 (0.8%)	0	0	0	0
口腔内痛	2 (0.8%)	2 (0.8%)	0	0	0	0
水疱性出血性口峡炎	1 (0.4%)	1 (0.4%)	0	0	0	0
大腸炎	1 (0.4%)	0	1 (0.4%)	0	0	0
憩室	1 (0.4%)	1 (0.4%)	0	0	0	0
嚥下障害	2 (0.8%)	0	2 (0.8%)	0	0	0
胃炎	2 (0.8%)	2 (0.8%)	0	0	0	0
歯肉腫脹	1 (0.4%)	0	1 (0.4%)	0	0	0
舌炎	1 (0.4%)	1 (0.4%)	0	0	0	0
血便排泄	1 (0.4%)	1 (0.4%)	0	0	0	0
痔核	1 (0.4%)	0	1 (0.4%)	0	0	0
大腸閉塞	1 (0.4%)	0	0	0	1 (0.4%)	0
口唇出血	1 (0.4%)	1 (0.4%)	0	0	0	0
口腔内潰瘍形成	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
口腔粘膜変色	1 (0.4%)	1 (0.4%)	0	0	0	0
膵炎	1 (0.4%)	0	0	1 (0.4%)	0	0
口の錯感覚	1 (0.4%)	1 (0.4%)	0	0	0	0
舌苔	1 (0.4%)	1 (0.4%)	0	0	0	0
歯の発育障害	1 (0.4%)	1 (0.4%)	0	0	0	0
歯の障害	1 (0.4%)	0	1 (0.4%)	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
アフタ性口内炎	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0
口内乾燥	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0
舌痛	1 (0.4%)	1 (0.4%)	0	0	0	0
口唇浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0
食道炎	1 (0.4%)	0	1 (0.4%)	0	0	0
感染症および寄生虫症	125 (52.7%)	26 (11.0%)	78 (32.9%)	19 (8.0%)	1 (0.4%)	1 (0.4%)
上気道感染	39 (16.5%)	4 (1.7%)	34 (14.3%)	1 (0.4%)	0	0
鼻咽頭炎	30 (12.7%)	24 (10.1%)	6 (2.5%)	0	0	0
肺炎	18 (7.6%)	0	6 (2.5%)	11 (4.6%)	0	1 (0.4%)
副鼻腔炎	11 (4.6%)	3 (1.3%)	8 (3.4%)	0	0	0
尿路感染	10 (4.2%)	1 (0.4%)	8 (3.4%)	1 (0.4%)	0	0
気管支炎	5 (2.1%)	1 (0.4%)	3 (1.3%)	1 (0.4%)	0	0
結膜炎	3 (1.3%)	1 (0.4%)	2 (0.8%)	0	0	0
帯状疱疹	8 (3.4%)	1 (0.4%)	5 (2.1%)	2 (0.8%)	0	0
大葉性肺炎	3 (1.3%)	0	1 (0.4%)	2 (0.8%)	0	0
口腔カンジダ症	6 (2.5%)	1 (0.4%)	5 (2.1%)	0	0	0
カンジダ感染	4 (1.7%)	2 (0.8%)	2 (0.8%)	0	0	0
単純ヘルペス	2 (0.8%)	0	2 (0.8%)	0	0	0
感染	3 (1.3%)	0	3 (1.3%)	0	0	0
インフルエンザ	5 (2.1%)	3 (1.3%)	2 (0.8%)	0	0	0
パラインフルエンザウイルス感染	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0	0
咽頭炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
鼻炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
軟部組織感染	2 (0.8%)	0	0	2 (0.8%)	0	0
水痘	2 (0.8%)	0	2 (0.8%)	0	0	0
蜂巣炎	1 (0.4%)	0	1 (0.4%)	0	0	0
膀胱炎	2 (0.8%)	0	2 (0.8%)	0	0	0
サイトメガロウイルス性脈絡網膜炎	1 (0.4%)	0	1 (0.4%)	0	0	0
医療機器関連感染	1 (0.4%)	0	1 (0.4%)	0	0	0
耳感染	2 (0.8%)	0	2 (0.8%)	0	0	0
胃腸炎	3 (1.3%)	1 (0.4%)	2 (0.8%)	0	0	0
ウイルス性胃腸炎	1 (0.4%)	0	1 (0.4%)	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
性器感染	1 (0.4%)	0	1 (0.4%)	0	0	0
Ｈ１Ｎ１インフルエンザ	1 (0.4%)	0	0	1 (0.4%)	0	0
麦粒腫	1 (0.4%)	1 (0.4%)	0	0	0	0
下気道感染	1 (0.4%)	0	1 (0.4%)	0	0	0
粘膜感染	1 (0.4%)	0	1 (0.4%)	0	0	0
眼部単純ヘルペス	1 (0.4%)	0	1 (0.4%)	0	0	0
口腔真菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0
口腔ヘルペス	1 (0.4%)	0	1 (0.4%)	0	0	0
爪囲炎	1 (0.4%)	0	1 (0.4%)	0	0	0
レンサ球菌性肺炎	1 (0.4%)	0	1 (0.4%)	0	0	0
腎盂腎炎	1 (0.4%)	0	0	1 (0.4%)	0	0
気道感染	1 (0.4%)	0	1 (0.4%)	0	0	0
敗血症	1 (0.4%)	0	0	0	1 (0.4%)	0
レンサ球菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0
歯感染	1 (0.4%)	0	1 (0.4%)	0	0	0
ウイルス性上気道感染	1 (0.4%)	0	1 (0.4%)	0	0	0
外陰腟真菌感染	1 (0.4%)	0	1 (0.4%)	0	0	0
菌血症	1 (0.4%)	0	0	1 (0.4%)	0	0
真菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0
真菌性消化管感染	1 (0.4%)	0	1 (0.4%)	0	0	0
肺感染	1 (0.4%)	0	1 (0.4%)	0	0	0
メタニューモウイルス感染	1 (0.4%)	1 (0.4%)	0	0	0	0
ＲＳウイルス感染	2 (0.8%)	0	2 (0.8%)	0	0	0
細菌性尿路感染	1 (0.4%)	0	1 (0.4%)	0	0	0
ウイルス感染	1 (0.4%)	0	1 (0.4%)	0	0	0
外陰部腟カンジダ症	1 (0.4%)	0	1 (0.4%)	0	0	0
血液およびリンパ系障害	106 (44.7%)	14 (5.9%)	21 (8.9%)	47 (19.8%)	24 (10.1%)	0
貧血	55 (23.2%)	1 (0.4%)	20 (8.4%)	34 (14.3%)	0	0
好中球減少症	38 (16.0%)	6 (2.5%)	11 (4.6%)	17 (7.2%)	4 (1.7%)	0
血小板減少症	44 (18.6%)	8 (3.4%)	4 (1.7%)	16 (6.8%)	16 (6.8%)	0
白血球減少症	16 (6.8%)	4 (1.7%)	5 (2.1%)	7 (3.0%)	0	0
リンパ球減少症	18 (7.6%)	1 (0.4%)	3 (1.3%)	8 (3.4%)	6 (2.5%)	0
ヘモグロビン血症	1 (0.4%)	0	1 (0.4%)	0	0	0
内出血発生の増加傾向	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
赤血球凝集	1 (0.4%)	1 (0.4%)	0	0	0	0
溶血	3 (1.3%)	3 (1.3%)	0	0	0	0
単球減少症	3 (1.3%)	3 (1.3%)	0	0	0	0
代謝および栄養障害	82 (34.6%)	33 (13.9%)	28 (11.8%)	14 (5.9%)	6 (2.5%)	1 (0.4%)
食欲減退	29 (12.2%)	17 (7.2%)	11 (4.6%)	1 (0.4%)	0	0
高カルシウム血症	22 (9.3%)	7 (3.0%)	7 (3.0%)	4 (1.7%)	3 (1.3%)	1 (0.4%)
高血糖	17 (7.2%)	9 (3.8%)	3 (1.3%)	5 (2.1%)	0	0
低カリウム血症	16 (6.8%)	11 (4.6%)	3 (1.3%)	1 (0.4%)	1 (0.4%)	0
低マグネシウム血症	11 (4.6%)	8 (3.4%)	3 (1.3%)	0	0	0
低ナトリウム血症	15 (6.3%)	12 (5.1%)	0	3 (1.3%)	0	0
高カリウム血症	6 (2.5%)	4 (1.7%)	1 (0.4%)	1 (0.4%)	0	0
酵素異常	8 (3.4%)	4 (1.7%)	4 (1.7%)	0	0	0
高尿酸血症	6 (2.5%)	4 (1.7%)	0	0	2 (0.8%)	0
低アルブミン血症	8 (3.4%)	4 (1.7%)	4 (1.7%)	0	0	0
低カルシウム血症	4 (1.7%)	1 (0.4%)	3 (1.3%)	0	0	0
糖尿病	1 (0.4%)	0	0	1 (0.4%)	0	0
高ナトリウム血症	1 (0.4%)	1 (0.4%)	0	0	0	0
高リン酸塩血症	1 (0.4%)	1 (0.4%)	0	0	0	0
低血糖症	2 (0.8%)	2 (0.8%)	0	0	0	0
栄養障害	1 (0.4%)	0	1 (0.4%)	0	0	0
ビタミンＢ１２欠乏	1 (0.4%)	1 (0.4%)	0	0	0	0
体液貯留	1 (0.4%)	1 (0.4%)	0	0	0	0
低リン酸血症	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
代謝性アシドーシス	1 (0.4%)	0	1 (0.4%)	0	0	0
神経系障害	81 (34.2%)	45 (19.0%)	26 (11.0%)	9 (3.8%)	1 (0.4%)	0
頭痛	21 (8.9%)	13 (5.5%)	6 (2.5%)	2 (0.8%)	0	0
浮動性めまい	22 (9.3%)	17 (7.2%)	5 (2.1%)	0	0	0
末梢性感覚ニューロパチー	14 (5.9%)	5 (2.1%)	9 (3.8%)	0	0	0
感覚鈍麻	7 (3.0%)	4 (1.7%)	3 (1.3%)	0	0	0
傾眠	6 (2.5%)	2 (0.8%)	3 (1.3%)	1 (0.4%)	0	0
振戦	6 (2.5%)	4 (1.7%)	2 (0.8%)	0	0	0
味覚異常	7 (3.0%)	5 (2.1%)	2 (0.8%)	0	0	0
錯感覚	4 (1.7%)	3 (1.3%)	1 (0.4%)	0	0	0
下肢静止不能症候群	2 (0.8%)	2 (0.8%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
意識変容状態	1 (0.4%)	1 (0.4%)	0	0	0	0
手根管症候群	1 (0.4%)	1 (0.4%)	0	0	0	0
意識レベルの低下	1 (0.4%)	0	0	1 (0.4%)	0	0
脳症	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0	0
知覚過敏	2 (0.8%)	2 (0.8%)	0	0	0	0
嗜眠	1 (0.4%)	0	1 (0.4%)	0	0	0
記憶障害	1 (0.4%)	1 (0.4%)	0	0	0	0
神経痛	1 (0.4%)	0	1 (0.4%)	0	0	0
嗅覚錯誤	1 (0.4%)	1 (0.4%)	0	0	0	0
脊髄圧迫	1 (0.4%)	0	0	0	1 (0.4%)	0
失神	2 (0.8%)	0	0	2 (0.8%)	0	0
第７脳神経麻痺	1 (0.4%)	0	1 (0.4%)	0	0	0
無感覚	1 (0.4%)	0	0	1 (0.4%)	0	0
坐骨神経痛	1 (0.4%)	1 (0.4%)	0	0	0	0
第６脳神経麻痺	1 (0.4%)	0	0	1 (0.4%)	0	0
皮膚および皮下組織障害	54 (22.8%)	44 (18.6%)	10 (4.2%)	0	0	0
そう痒症	10 (4.2%)	7 (3.0%)	3 (1.3%)	0	0	0
多汗症	6 (2.5%)	6 (2.5%)	0	0	0	0
寝汗	4 (1.7%)	4 (1.7%)	0	0	0	0
発疹	12 (5.1%)	10 (4.2%)	2 (0.8%)	0	0	0
斑状丘疹状皮疹	4 (1.7%)	4 (1.7%)	0	0	0	0
皮膚嚢腫	2 (0.8%)	2 (0.8%)	0	0	0	0
ざ瘡様皮膚炎	2 (0.8%)	2 (0.8%)	0	0	0	0
接触性皮膚炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
皮膚乾燥	2 (0.8%)	2 (0.8%)	0	0	0	0
湿疹	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
紅斑	3 (1.3%)	3 (1.3%)	0	0	0	0
点状出血	2 (0.8%)	2 (0.8%)	0	0	0	0
褥瘡性潰瘍	1 (0.4%)	0	1 (0.4%)	0	0	0
薬疹	1 (0.4%)	1 (0.4%)	0	0	0	0
皮脂欠乏性湿疹	1 (0.4%)	0	1 (0.4%)	0	0	0
手掌・足底発赤知覚不全症候群	1 (0.4%)	1 (0.4%)	0	0	0	0
色素沈着障害	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
全身性そう痒症	1 (0.4%)	1 (0.4%)	0	0	0	0
乾癬	1 (0.4%)	1 (0.4%)	0	0	0	0
斑状皮疹	2 (0.8%)	0	2 (0.8%)	0	0	0
丘疹性皮疹	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚剥脱	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚色素過剰	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚潰瘍	1 (0.4%)	1 (0.4%)	0	0	0	0
蕁麻疹	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
脱毛症	1 (0.4%)	1 (0.4%)	0	0	0	0
爪変色	1 (0.4%)	1 (0.4%)	0	0	0	0
血管障害	48 (20.3%)	16 (6.8%)	18 (7.6%)	14 (5.9%)	0	0
高血圧	27 (11.4%)	4 (1.7%)	11 (4.6%)	12 (5.1%)	0	0
低血圧	10 (4.2%)	4 (1.7%)	5 (2.1%)	1 (0.4%)	0	0
血腫	5 (2.1%)	5 (2.1%)	0	0	0	0
潮紅	6 (2.5%)	6 (2.5%)	0	0	0	0
深部静脈血栓症	3 (1.3%)	0	2 (0.8%)	1 (0.4%)	0	0
ほてり	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0
表在性静脈炎	1 (0.4%)	1 (0.4%)	0	0	0	0
レイノー現象	1 (0.4%)	0	1 (0.4%)	0	0	0
四肢静脈血栓症	1 (0.4%)	0	1 (0.4%)	0	0	0
傷害、中毒および処置合併症	32 (13.5%)	15 (6.3%)	10 (4.2%)	7 (3.0%)	0	0
挫傷	6 (2.5%)	6 (2.5%)	0	0	0	0
転倒	5 (2.1%)	3 (1.3%)	1 (0.4%)	1 (0.4%)	0	0
肋骨骨折	4 (1.7%)	0	4 (1.7%)	0	0	0
上腕骨骨折	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0	0
裂傷	2 (0.8%)	2 (0.8%)	0	0	0	0
腰椎骨折	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0	0
脊椎圧迫骨折	3 (1.3%)	0	0	3 (1.3%)	0	0
骨挫傷	1 (0.4%)	1 (0.4%)	0	0	0	0
擦過傷	1 (0.4%)	1 (0.4%)	0	0	0	0
足骨折	1 (0.4%)	0	1 (0.4%)	0	0	0
骨折	1 (0.4%)	0	1 (0.4%)	0	0	0
肉離れ	1 (0.4%)	1 (0.4%)	0	0	0	0
眼窩周囲挫傷	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
処置による疼痛	1 (0.4%)	1 (0.4%)	0	0	0	0
硬膜下血腫	1 (0.4%)	0	0	1 (0.4%)	0	0
腱断裂	1 (0.4%)	0	1 (0.4%)	0	0	0
輸血反応	1 (0.4%)	1 (0.4%)	0	0	0	0
上肢骨折	1 (0.4%)	0	1 (0.4%)	0	0	0
創傷	1 (0.4%)	1 (0.4%)	0	0	0	0
手首関節骨折	1 (0.4%)	0	0	1 (0.4%)	0	0
四肢外傷性切断	1 (0.4%)	0	0	1 (0.4%)	0	0
精神障害	37 (15.6%)	20 (8.4%)	13 (5.5%)	3 (1.3%)	1 (0.4%)	0
不安	9 (3.8%)	5 (2.1%)	4 (1.7%)	0	0	0
錯乱状態	8 (3.4%)	4 (1.7%)	2 (0.8%)	2 (0.8%)	0	0
不眠症	11 (4.6%)	8 (3.4%)	3 (1.3%)	0	0	0
激越	4 (1.7%)	2 (0.8%)	2 (0.8%)	0	0	0
譫妄	3 (1.3%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0
うつ病	5 (2.1%)	2 (0.8%)	3 (1.3%)	0	0	0
気分変化	2 (0.8%)	2 (0.8%)	0	0	0	0
摂食障害	1 (0.4%)	0	1 (0.4%)	0	0	0
幻覚	1 (0.4%)	1 (0.4%)	0	0	0	0
精神状態変化	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0	0
気分動揺	1 (0.4%)	0	1 (0.4%)	0	0	0
神経過敏	1 (0.4%)	1 (0.4%)	0	0	0	0
腎および尿路障害	52 (21.9%)	27 (11.4%)	17 (7.2%)	8 (3.4%)	0	0
腎機能障害	20 (8.4%)	8 (3.4%)	9 (3.8%)	3 (1.3%)	0	0
排尿困難	4 (1.7%)	4 (1.7%)	0	0	0	0
頻尿	3 (1.3%)	3 (1.3%)	0	0	0	0
蛋白尿	16 (6.8%)	10 (4.2%)	5 (2.1%)	1 (0.4%)	0	0
尿閉	3 (1.3%)	1 (0.4%)	2 (0.8%)	0	0	0
非感染性膀胱炎	1 (0.4%)	0	1 (0.4%)	0	0	0
血尿	3 (1.3%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
夜間頻尿	1 (0.4%)	1 (0.4%)	0	0	0	0
腎不全	1 (0.4%)	0	0	1 (0.4%)	0	0
腎静脈血栓症	1 (0.4%)	0	1 (0.4%)	0	0	0
尿失禁	4 (1.7%)	2 (0.8%)	2 (0.8%)	0	0	0
尿路閉塞	1 (0.4%)	0	0	1 (0.4%)	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
高窒素血症	1 (0.4%)	1 (0.4%)	0	0	0	0
膀胱痙縮	1 (0.4%)	0	1 (0.4%)	0	0	0
尿意切迫	1 (0.4%)	1 (0.4%)	0	0	0	0
急性腎不全	1 (0.4%)	0	0	1 (0.4%)	0	0
臨床検査	34 (14.3%)	16 (6.8%)	10 (4.2%)	8 (3.4%)	0	0
体重減少	11 (4.6%)	7 (3.0%)	3 (1.3%)	1 (0.4%)	0	0
体重増加	5 (2.1%)	4 (1.7%)	1 (0.4%)	0	0	0
国際標準比増加	4 (1.7%)	1 (0.4%)	1 (0.4%)	2 (0.8%)	0	0
血中クレアチンホスホキナーゼ増加	2 (0.8%)	0	0	2 (0.8%)	0	0
血中テストステロン減少	1 (0.4%)	0	1 (0.4%)	0	0	0
心電図異常Q波	1 (0.4%)	0	1 (0.4%)	0	0	0
心電図ＱＴ延長	6 (2.5%)	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0
心電図異常Ｔ波	1 (0.4%)	1 (0.4%)	0	0	0	0
酸素飽和度異常	1 (0.4%)	0	0	1 (0.4%)	0	0
尿量減少	1 (0.4%)	0	1 (0.4%)	0	0	0
遊離ヘモグロビン陽性	5 (2.1%)	4 (1.7%)	1 (0.4%)	0	0	0
ハプトグロビン減少	1 (0.4%)	1 (0.4%)	0	0	0	0
心拍数増加	1 (0.4%)	1 (0.4%)	0	0	0	0
リンパ球数減少	2 (0.8%)	1 (0.4%)	0	1 (0.4%)	0	0
眼障害	24 (10.1%)	21 (8.9%)	2 (0.8%)	1 (0.4%)	0	0
霧視	9 (3.8%)	8 (3.4%)	1 (0.4%)	0	0	0
眼乾燥	2 (0.8%)	2 (0.8%)	0	0	0	0
眼そう痒症	3 (1.3%)	3 (1.3%)	0	0	0	0
眼充血	3 (1.3%)	3 (1.3%)	0	0	0	0
白内障	2 (0.8%)	2 (0.8%)	0	0	0	0
結膜出血	1 (0.4%)	1 (0.4%)	0	0	0	0
複視	2 (0.8%)	2 (0.8%)	0	0	0	0
睫毛乱生	1 (0.4%)	0	1 (0.4%)	0	0	0
眼部腫脹	1 (0.4%)	0	0	1 (0.4%)	0	0
眼瞼機能障害	1 (0.4%)	1 (0.4%)	0	0	0	0
眼瞼下垂	1 (0.4%)	1 (0.4%)	0	0	0	0
眼瞼発疹	1 (0.4%)	1 (0.4%)	0	0	0	0
光視症	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
視力障害	1 (0.4%)	1 (0.4%)	0	0	0	0
硝子体浮遊物	1 (0.4%)	1 (0.4%)	0	0	0	0
心臓障害	17 (7.2%)	9 (3.8%)	5 (2.1%)	2 (0.8%)	0	1 (0.4%)
動悸	6 (2.5%)	4 (1.7%)	2 (0.8%)	0	0	0
洞性頻脈	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0
頻脈	5 (2.1%)	4 (1.7%)	1 (0.4%)	0	0	0
狭心症	1 (0.4%)	0	0	1 (0.4%)	0	0
心房粗動	1 (0.4%)	0	0	1 (0.4%)	0	0
徐脈	1 (0.4%)	1 (0.4%)	0	0	0	0
左脚ブロック	1 (0.4%)	1 (0.4%)	0	0	0	0
うっ血性心不全	1 (0.4%)	1 (0.4%)	0	0	0	0
心肺停止	1 (0.4%)	0	0	0	0	1 (0.4%)
心房細動	1 (0.4%)	0	1 (0.4%)	0	0	0
上室性期外収縮	1 (0.4%)	1 (0.4%)	0	0	0	0
肝胆道系障害	13 (5.5%)	8 (3.4%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肝機能異常	10 (4.2%)	6 (2.5%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	0
肝不全	1 (0.4%)	0	0	0	0	1 (0.4%)
高ビリルビン血症	1 (0.4%)	1 (0.4%)	0	0	0	0
黄疸	1 (0.4%)	1 (0.4%)	0	0	0	0
脂肪肝	1 (0.4%)	1 (0.4%)	0	0	0	0
耳および迷路障害	8 (3.4%)	6 (2.5%)	2 (0.8%)	0	0	0
耳痛	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
耳の障害	1 (0.4%)	1 (0.4%)	0	0	0	0
耳鳴	1 (0.4%)	1 (0.4%)	0	0	0	0
回転性めまい	2 (0.8%)	2 (0.8%)	0	0	0	0
耳垢栓塞	1 (0.4%)	0	1 (0.4%)	0	0	0
耳不快感	1 (0.4%)	1 (0.4%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	9 (3.8%)	6 (2.5%)	2 (0.8%)	1 (0.4%)	0	0
腫瘍疼痛	2 (0.8%)	2 (0.8%)	0	0	0	0
肛門直腸ヒト乳頭腫ウイルス感染	1 (0.4%)	1 (0.4%)	0	0	0	0
基底細胞癌	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0

TSFAE02EPART3OF3: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Toxicity Grade					
	Total	1	2	3	4	5
皮膚癌	1 (0.4%)	0	1 (0.4%)	0	0	0
皮膚良性新生物	1 (0.4%)	1 (0.4%)	0	0	0	0
形質細胞性白血病	1 (0.4%)	0	0	1 (0.4%)	0	0
皮膚乳頭腫	1 (0.4%)	1 (0.4%)	0	0	0	0
生殖系および乳房障害	8 (3.4%)	6 (2.5%)	1 (0.4%)	1 (0.4%)	0	0
生殖器痛	1 (0.4%)	1 (0.4%)	0	0	0	0
乳頭痛	1 (0.4%)	1 (0.4%)	0	0	0	0
性器浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0
陰茎浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0
腟出血	1 (0.4%)	1 (0.4%)	0	0	0	0
血精液症	1 (0.4%)	1 (0.4%)	0	0	0	0
骨盤痛	1 (0.4%)	0	0	1 (0.4%)	0	0
前立腺炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0
免疫系障害	8 (3.4%)	3 (1.3%)	3 (1.3%)	2 (0.8%)	0	0
アレルギー性浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0
サイトカイン放出症候群	3 (1.3%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
季節性アレルギー	1 (0.4%)	0	1 (0.4%)	0	0	0
過敏症	3 (1.3%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
先天性、家族性および遺伝性障害	1 (0.4%)	1 (0.4%)	0	0	0	0
あざ	1 (0.4%)	1 (0.4%)	0	0	0	0

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02EPART3OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae02e.sas] 16MAR2015, 16:20

表 2.7.4-付録-37 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
Analysis set: all treated	23			55			156		
Total number of subjects treated within window[a]	23	23	0	55	55	11	156	156	52
Total number of subjects with TEAEs	22 (95.7%)	22 (95.7%)	-	55 (100.0%)	55 (100.0%)	8 (72.7%)	154 (98.7%)	154 (98.7%)	37 (71.2%)
MedDRA system organ class/Preferred term									
一般・全身障害および投与部位の状態	11 (47.8%)	11 (47.8%)	-	36 (65.5%)	35 (63.6%)	3 (27.3%)	106 (67.9%)	104 (66.7%)	7 (13.5%)
疲労	2 (8.7%)	2 (8.7%)	-	20 (36.4%)	19 (34.5%)	1 (9.1%)	59 (37.8%)	58 (37.2%)	1 (1.9%)
発熱	8 (34.8%)	8 (34.8%)	-	20 (36.4%)	19 (34.5%)	1 (9.1%)	29 (18.6%)	28 (17.9%)	1 (1.9%)
悪寒	0	0	-	9 (16.4%)	9 (16.4%)	0	16 (10.3%)	16 (10.3%)	0
無力症	0	0	-	3 (5.5%)	3 (5.5%)	0	12 (7.7%)	12 (7.7%)	0
末梢性浮腫	1 (4.3%)	1 (4.3%)	-	5 (9.1%)	5 (9.1%)	0	11 (7.1%)	10 (6.4%)	1 (1.9%)
胸痛	2 (8.7%)	2 (8.7%)	-	1 (1.8%)	0	1 (9.1%)	9 (5.8%)	6 (3.8%)	3 (5.8%)
疼痛	0	0	-	2 (3.6%)	2 (3.6%)	0	8 (5.1%)	8 (5.1%)	0
インフルエンザ様疾患	3 (13.0%)	3 (13.0%)	-	1 (1.8%)	1 (1.8%)	0	7 (4.5%)	7 (4.5%)	0
非心臓性胸痛	0	0	-	2 (3.6%)	2 (3.6%)	0	6 (3.8%)	6 (3.8%)	0
全身健康状態低下	0	0	-	1 (1.8%)	1 (1.8%)	0	5 (3.2%)	5 (3.2%)	0
注射部位内出血	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
局所腫脹	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
倦怠感	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
胸部不快感	0	0	-	3 (5.5%)	3 (5.5%)	0	2 (1.3%)	2 (1.3%)	0
顔面浮腫	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
全身性浮腫	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
浮腫	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
腋窩痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
医療機器の問題	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
顔面痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
歩行障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
低体温	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
注入部位内出血	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
注射部位浮腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
注射部位反応	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
限局性浮腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腫瘤	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
恥骨上痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
急性期反応	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
呼吸器、胸郭および縦隔障害	8 (34.8%)	8 (34.8%)	-	32 (58.2%)	31 (56.4%)	3 (27.3%)	95 (60.9%)	94 (60.3%)	7 (13.5%)
咳嗽	5 (21.7%)	5 (21.7%)	-	12 (21.8%)	10 (18.2%)	3 (27.3%)	31 (19.9%)	29 (18.6%)	5 (9.6%)
鼻閉	0	0	-	5 (9.1%)	5 (9.1%)	0	25 (16.0%)	23 (14.7%)	2 (3.8%)
呼吸困難	1 (4.3%)	1 (4.3%)	-	11 (20.0%)	11 (20.0%)	1 (9.1%)	22 (14.1%)	22 (14.1%)	0
口腔咽頭痛	0	0	-	3 (5.5%)	3 (5.5%)	0	15 (9.6%)	13 (8.3%)	2 (3.8%)
アレルギー性鼻炎	1 (4.3%)	1 (4.3%)	-	12 (21.8%)	12 (21.8%)	0	11 (7.1%)	11 (7.1%)	0
咽喉刺激感	0	0	-	1 (1.8%)	1 (1.8%)	0	10 (6.4%)	10 (6.4%)	0
労作性呼吸困難	0	0	-	1 (1.8%)	0	1 (9.1%)	8 (5.1%)	8 (5.1%)	0
鼻出血	0	0	-	2 (3.6%)	2 (3.6%)	0	8 (5.1%)	8 (5.1%)	0
湿性咳嗽	0	0	-	4 (7.3%)	4 (7.3%)	0	8 (5.1%)	8 (5.1%)	0
喘鳴	0	0	-	1 (1.8%)	1 (1.8%)	0	6 (3.8%)	6 (3.8%)	0
気管支痙攣	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	5 (3.2%)	5 (3.2%)	0
胸水	0	0	-	1 (1.8%)	1 (1.8%)	0	4 (2.6%)	4 (2.6%)	0
副鼻腔うっ血	0	0	-	0	0	0	4 (2.6%)	4 (2.6%)	1 (1.9%)
くしゃみ	0	0	-	0	0	0	4 (2.6%)	4 (2.6%)	0
低酸素症	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
咽喉絞扼感	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
上気道咳症候群	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
呼吸不全	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
急性肺水腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
アレルギー性咳嗽	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
慢性閉塞性肺疾患	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
発声障害	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
上気道分泌増加	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
喉頭浮腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
アレルギー性喉頭炎	0	0	-	3 (5.5%)	3 (5.5%)	0	1 (0.6%)	1 (0.6%)	0
鼻部障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
誤嚥性肺炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
肺うっ血	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
肺塞栓症	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
肺水腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
鼻漏	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
喉頭の炎症	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
筋骨格系および結合組織障害	6 (26.1%)	6 (26.1%)	-	30 (54.5%)	30 (54.5%)	1 (9.1%)	89 (57.1%)	86 (55.1%)	10 (19.2%)
背部痛	1 (4.3%)	1 (4.3%)	-	8 (14.5%)	8 (14.5%)	0	33 (21.2%)	31 (19.9%)	2 (3.8%)
関節痛	2 (8.7%)	2 (8.7%)	-	5 (9.1%)	5 (9.1%)	0	25 (16.0%)	23 (14.7%)	2 (3.8%)
四肢痛	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	23 (14.7%)	22 (14.1%)	2 (3.8%)
筋骨格系胸痛	0	0	-	5 (9.1%)	5 (9.1%)	0	16 (10.3%)	13 (8.3%)	3 (5.8%)
骨痛	1 (4.3%)	1 (4.3%)	-	6 (10.9%)	6 (10.9%)	0	14 (9.0%)	13 (8.3%)	1 (1.9%)
筋骨格痛	0	0	-	3 (5.5%)	3 (5.5%)	0	13 (8.3%)	13 (8.3%)	0
筋痙縮	0	0	-	2 (3.6%)	2 (3.6%)	1 (9.1%)	10 (6.4%)	10 (6.4%)	0
筋肉痛	0	0	-	6 (10.9%)	6 (10.9%)	0	6 (3.8%)	6 (3.8%)	0
肢径部痛	0	0	-	0	0	0	4 (2.6%)	3 (1.9%)	1 (1.9%)
頚部痛	0	0	-	0	0	0	3 (1.9%)	2 (1.3%)	1 (1.9%)
病的骨折	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
脊椎痛	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
筋力低下	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
骨炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
脊柱管狭窄症	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
骨侵食	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
骨病変	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
関節可動域低下	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
四肢不快感	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
運動性低下	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
筋肉疲労	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
筋骨格不快感	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
顎骨壊死	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
顎痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腱炎	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
側腹部痛	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
脊柱後弯症	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
筋骨格硬直	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
ミオパチー	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
骨粗鬆症性骨折	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
胃腸障害	9 (39.1%)	9 (39.1%)	-	27 (49.1%)	26 (47.3%)	5 (45.5%)	85 (54.5%)	82 (52.6%)	11 (21.2%)
悪心	3 (13.0%)	3 (13.0%)	-	10 (18.2%)	9 (16.4%)	1 (9.1%)	40 (25.6%)	38 (24.4%)	4 (7.7%)
下痢	2 (8.7%)	2 (8.7%)	-	13 (23.6%)	13 (23.6%)	1 (9.1%)	24 (15.4%)	23 (14.7%)	1 (1.9%)
便秘	1 (4.3%)	1 (4.3%)	-	6 (10.9%)	4 (7.3%)	2 (18.2%)	22 (14.1%)	21 (13.5%)	1 (1.9%)
嘔吐	1 (4.3%)	1 (4.3%)	-	8 (14.5%)	8 (14.5%)	0	20 (12.8%)	18 (11.5%)	2 (3.8%)
腹痛	2 (8.7%)	2 (8.7%)	-	1 (1.8%)	1 (1.8%)	0	9 (5.8%)	9 (5.8%)	0
消化不良	0	0	-	3 (5.5%)	3 (5.5%)	0	4 (2.6%)	3 (1.9%)	1 (1.9%)
口内炎	0	0	-	3 (5.5%)	3 (5.5%)	0	4 (2.6%)	4 (2.6%)	0
歯痛	0	0	-	0	0	0	4 (2.6%)	3 (1.9%)	1 (1.9%)
腹部膨満	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
放屁	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
口の感覚鈍麻	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
腹部不快感	0	0	-	1 (1.8%)	0	1 (9.1%)	2 (1.3%)	2 (1.3%)	0
上腹部痛	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
便失禁	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
胃食道逆流性疾患	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
歯肉出血	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
口腔内痛	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
水疱性出血性口峡炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
大腸炎	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
憩室	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
嚥下障害	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
胃炎	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
歯肉腫脹	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
舌炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
血便排泄	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
痔核	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
大腸閉塞	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口唇出血	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口腔内潰瘍形成	1 (4.3%)	1 (4.3%)	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口腔粘膜変色	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
膵炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
口の錯感覚	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
舌苔	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
歯の発育障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
歯の障害	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
アフタ性口内炎	0	0	-	3 (5.5%)	2 (3.6%)	1 (9.1%)	0	0	0
口内乾燥	1 (4.3%)	1 (4.3%)	-	2 (3.6%)	2 (3.6%)	0	0	0	0
舌痛	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
口唇浮腫	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
食道炎	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
感染症および寄生虫症	7 (30.4%)	7 (30.4%)	-	32 (58.2%)	31 (56.4%)	4 (36.4%)	85 (54.5%)	79 (50.6%)	20 (38.5%)
上気道感染	0	0	-	12 (21.8%)	12 (21.8%)	0	27 (17.3%)	23 (14.7%)	9 (17.3%)
鼻咽頭炎	2 (8.7%)	2 (8.7%)	-	9 (16.4%)	8 (14.5%)	2 (18.2%)	18 (11.5%)	16 (10.3%)	3 (5.8%)
肺炎	1 (4.3%)	1 (4.3%)	-	4 (7.3%)	4 (7.3%)	0	13 (8.3%)	10 (6.4%)	3 (5.8%)
副鼻腔炎	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	9 (5.8%)	9 (5.8%)	1 (1.9%)
尿路感染	0	0	-	2 (3.6%)	2 (3.6%)	0	7 (4.5%)	4 (2.6%)	3 (5.8%)
気管支炎	0	0	-	0	0	0	5 (3.2%)	4 (2.6%)	2 (3.8%)
結膜炎	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
帯状疱疹	1 (4.3%)	1 (4.3%)	-	4 (7.3%)	4 (7.3%)	0	3 (1.9%)	2 (1.3%)	1 (1.9%)
大葉性肺炎	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
口腔カンジダ症	0	0	-	3 (5.5%)	3 (5.5%)	0	3 (1.9%)	3 (1.9%)	0
カンジダ感染	0	0	-	2 (3.6%)	1 (1.8%)	1 (9.1%)	2 (1.3%)	2 (1.3%)	0
単純ヘルペス	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
感染	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
インフルエンザ	0	0	-	3 (5.5%)	2 (3.6%)	1 (9.1%)	2 (1.3%)	2 (1.3%)	0
パラインフルエンザウイルス感染	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
咽頭炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
鼻炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
軟部組織感染	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
水痘	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
蜂巣炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
膀胱炎	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	0	1 (1.9%)
サイトメガロウイルス性脈絡網膜炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
医療機器関連感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
耳感染	0	0	-	1 (1.8%)	0	1 (9.1%)	1 (0.6%)	1 (0.6%)	0
胃腸炎	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	0	1 (9.1%)	1 (0.6%)	0	1 (1.9%)
ウイルス性胃腸炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
性器感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
Ｈ１Ｎ１インフルエンザ	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
麦粒腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
下気道感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
粘膜感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
眼部単純ヘルペス	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口腔真菌感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口腔ヘルペス	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
爪囲炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	1 (1.9%)
レンサ球菌性肺炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腎盂腎炎	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
気道感染	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
敗血症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
レンサ球菌感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
歯感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
ウイルス性上気道感染	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
外陰腟真菌感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
菌血症	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
真菌感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
真菌性消化管感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
肺感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
メタニューモウイルス感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
ＲＳウイルス感染	0	0	-	2 (3.6%)	2 (3.6%)	0	0	0	0
細菌性尿路感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
ウイルス感染	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
外陰部腟カンジダ症	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
血液およびリンパ系障害	9 (39.1%)	9 (39.1%)	-	21 (38.2%)	21 (38.2%)	1 (9.1%)	76 (48.7%)	76 (48.7%)	1 (1.9%)
貧血	4 (17.4%)	4 (17.4%)	-	12 (21.8%)	11 (20.0%)	1 (9.1%)	39 (25.0%)	39 (25.0%)	0
好中球減少症	1 (4.3%)	1 (4.3%)	-	3 (5.5%)	3 (5.5%)	0	34 (21.8%)	34 (21.8%)	0
血小板減少症	3 (13.0%)	3 (13.0%)	-	10 (18.2%)	10 (18.2%)	1 (9.1%)	31 (19.9%)	31 (19.9%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
白血球減少症	0	0	-	2 (3.6%)	2 (3.6%)	0	14 (9.0%)	14 (9.0%)	1 (1.9%)
リンパ球減少症	2 (8.7%)	2 (8.7%)	-	7 (12.7%)	7 (12.7%)	0	9 (5.8%)	9 (5.8%)	0
ヘモグロビン血症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
内出血発生の増加傾向	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
汎血球減少症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
赤血球凝集	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
溶血	3 (13.0%)	3 (13.0%)	-	0	0	0	0	0	0
単球減少症	3 (13.0%)	3 (13.0%)	-	0	0	0	0	0	0
代謝および栄養障害	2 (8.7%)	2 (8.7%)	-	16 (29.1%)	15 (27.3%)	1 (9.1%)	64 (41.0%)	61 (39.1%)	8 (15.4%)
食欲減退	1 (4.3%)	1 (4.3%)	-	5 (9.1%)	4 (7.3%)	1 (9.1%)	23 (14.7%)	22 (14.1%)	2 (3.8%)
高カルシウム血症	0	0	-	4 (7.3%)	4 (7.3%)	0	18 (11.5%)	17 (10.9%)	2 (3.8%)
高血糖	0	0	-	4 (7.3%)	4 (7.3%)	0	13 (8.3%)	13 (8.3%)	1 (1.9%)
低カリウム血症	0	0	-	4 (7.3%)	4 (7.3%)	0	12 (7.7%)	10 (6.4%)	3 (5.8%)
低マグネシウム血症	0	0	-	2 (3.6%)	2 (3.6%)	0	9 (5.8%)	9 (5.8%)	0
低ナトリウム血症	1 (4.3%)	1 (4.3%)	-	6 (10.9%)	6 (10.9%)	0	8 (5.1%)	8 (5.1%)	0
高カリウム血症	0	0	-	1 (1.8%)	1 (1.8%)	0	5 (3.2%)	4 (2.6%)	1 (1.9%)
酵素異常	1 (4.3%)	1 (4.3%)	-	3 (5.5%)	3 (5.5%)	0	4 (2.6%)	4 (2.6%)	0
高尿酸血症	0	0	-	2 (3.6%)	2 (3.6%)	0	4 (2.6%)	3 (1.9%)	1 (1.9%)
低アルブミン血症	0	0	-	4 (7.3%)	4 (7.3%)	0	4 (2.6%)	4 (2.6%)	0
低カルシウム血症	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	1 (1.9%)
糖尿病	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
高ナトリウム血症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
高リン酸塩血症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
低血糖症	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
栄養障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
ビタミンＢ１２欠乏	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
体液貯留	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
低リン酸血症	0	0	-	2 (3.6%)	2 (3.6%)	0	0	0	0
代謝性アシドーシス	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
神経系障害	6 (26.1%)	6 (26.1%)	-	25 (45.5%)	24 (43.6%)	1 (9.1%)	50 (32.1%)	46 (29.5%)	8 (15.4%)
頭痛	2 (8.7%)	2 (8.7%)	-	4 (7.3%)	4 (7.3%)	0	15 (9.6%)	14 (9.0%)	1 (1.9%)
浮動性めまい	3 (13.0%)	3 (13.0%)	-	6 (10.9%)	6 (10.9%)	0	13 (8.3%)	12 (7.7%)	2 (3.8%)
末梢性感覚ニューロパチー	1 (4.3%)	1 (4.3%)	-	7 (12.7%)	7 (12.7%)	0	6 (3.8%)	6 (3.8%)	1 (1.9%)
感覚鈍麻	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	5 (3.2%)	3 (1.9%)	2 (3.8%)

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	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
傾眠	0	0	-	1 (1.8%)	1 (1.8%)	0	5 (3.2%)	5 (3.2%)	0
振戦	0	0	-	2 (3.6%)	1 (1.8%)	1 (9.1%)	4 (2.6%)	3 (1.9%)	1 (1.9%)
味覚異常	0	0	-	4 (7.3%)	4 (7.3%)	0	3 (1.9%)	1 (0.6%)	2 (3.8%)
錯感覚	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	2 (1.3%)	1 (1.9%)
下肢静止不能症候群	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
意識変容状態	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
手根管症候群	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
意識レベルの低下	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
脳症	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
知覚過敏	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
嗜眠	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
記憶障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
神経痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
嗅覚錯誤	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
脊髄圧迫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
失神	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
第７脳神経麻痺	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
無感覚	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
坐骨神経痛	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
第６脳神経麻痺	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
皮膚および皮下組織障害	3 (13.0%)	3 (13.0%)	-	16 (29.1%)	14 (25.5%)	2 (18.2%)	35 (22.4%)	33 (21.2%)	3 (5.8%)
そう痒症	1 (4.3%)	1 (4.3%)	-	4 (7.3%)	4 (7.3%)	0	5 (3.2%)	4 (2.6%)	1 (1.9%)
多汗症	0	0	-	3 (5.5%)	3 (5.5%)	0	3 (1.9%)	3 (1.9%)	0
寝汗	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
発疹	2 (8.7%)	2 (8.7%)	-	7 (12.7%)	6 (10.9%)	1 (9.1%)	3 (1.9%)	3 (1.9%)	0
斑状丘疹状皮疹	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
皮膚嚢腫	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
ざ瘡様皮膚炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
接触性皮膚炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
皮膚乾燥	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
湿疹	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
紅斑	1 (4.3%)	1 (4.3%)	-	0	0	0	2 (1.3%)	2 (1.3%)	0
点状出血	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
褥瘡性潰瘍	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

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	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
薬疹	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
皮脂欠乏性湿疹	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
手掌・足底発赤知覚不全症候群	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
色素沈着障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
全身性そう痒症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
乾癬	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
斑状皮疹	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
丘疹性皮疹	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
皮膚剥脱	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
皮膚色素過剰	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
皮膚潰瘍	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
蕁麻疹	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
脱毛症	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
爪変色	0	0	-	1 (1.8%)	0	1 (9.1%)	0	0	0
血管障害	5 (21.7%)	5 (21.7%)	-	14 (25.5%)	14 (25.5%)	0	29 (18.6%)	27 (17.3%)	2 (3.8%)
高血圧	2 (8.7%)	2 (8.7%)	-	10 (18.2%)	10 (18.2%)	0	15 (9.6%)	15 (9.6%)	0
低血圧	2 (8.7%)	2 (8.7%)	-	1 (1.8%)	1 (1.8%)	0	7 (4.5%)	6 (3.8%)	1 (1.9%)
血腫	0	0	-	1 (1.8%)	1 (1.8%)	0	4 (2.6%)	4 (2.6%)	0
潮紅	2 (8.7%)	2 (8.7%)	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
深部静脈血栓症	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
ほてり	0	0	-	2 (3.6%)	2 (3.6%)	0	1 (0.6%)	1 (0.6%)	0
表在性静脈炎	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
レイノー現象	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
四肢静脈血栓症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
傷害、中毒および処置合併症	1 (4.3%)	1 (4.3%)	-	3 (5.5%)	3 (5.5%)	0	28 (17.9%)	24 (15.4%)	4 (7.7%)
挫傷	0	0	-	1 (1.8%)	1 (1.8%)	0	5 (3.2%)	5 (3.2%)	0
転倒	0	0	-	0	0	0	5 (3.2%)	4 (2.6%)	1 (1.9%)
肋骨骨折	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
上腕骨骨折	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
裂傷	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
腰椎骨折	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
脊椎圧迫骨折	1 (4.3%)	1 (4.3%)	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
骨挫傷	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)

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	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
擦過傷	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
足骨折	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
骨折	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
肉離れ	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
眼窩周囲挫傷	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
処置による疼痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
硬膜下血腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腱断裂	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
輸血反応	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
上肢骨折	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
創傷	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
手首関節骨折	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
四肢外傷性切断	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
精神障害	0	0	-	9 (16.4%)	9 (16.4%)	0	28 (17.9%)	26 (16.7%)	2 (3.8%)
不安	0	0	-	0	0	0	9 (5.8%)	9 (5.8%)	0
錯乱状態	0	0	-	1 (1.8%)	1 (1.8%)	0	7 (4.5%)	7 (4.5%)	0
不眠症	0	0	-	4 (7.3%)	4 (7.3%)	0	7 (4.5%)	6 (3.8%)	1 (1.9%)
激越	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
譫妄	0	0	-	0	0	0	3 (1.9%)	2 (1.3%)	1 (1.9%)
うつ病	0	0	-	2 (3.6%)	2 (3.6%)	0	3 (1.9%)	3 (1.9%)	0
気分変化	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
摂食障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
幻覚	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
精神状態変化	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
気分動揺	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
神経過敏	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
腎および尿路障害	11 (47.8%)	11 (47.8%)	-	15 (27.3%)	14 (25.5%)	2 (18.2%)	25 (16.0%)	23 (14.7%)	3 (5.8%)
腎機能障害	1 (4.3%)	1 (4.3%)	-	8 (14.5%)	8 (14.5%)	0	11 (7.1%)	10 (6.4%)	2 (3.8%)
排尿困難	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	2 (1.3%)	1 (1.9%)
頻尿	1 (4.3%)	1 (4.3%)	-	0	0	0	2 (1.3%)	2 (1.3%)	0
蛋白尿	10 (43.5%)	10 (43.5%)	-	3 (5.5%)	3 (5.5%)	0	2 (1.3%)	2 (1.3%)	0
尿閉	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
非感染性膀胱炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
血尿	0	0	-	2 (3.6%)	2 (3.6%)	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
夜間頻尿	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腎不全	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腎静脈血栓症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
尿失禁	0	0	-	3 (5.5%)	3 (5.5%)	0	1 (0.6%)	1 (0.6%)	0
尿路閉塞	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
高窒素血症	0	0	-	1 (1.8%)	0	1 (9.1%)	0	0	0
膀胱痙縮	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
尿意切迫	0	0	-	1 (1.8%)	0	1 (9.1%)	0	0	0
急性腎不全	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
臨床検査	10 (43.5%)	10 (43.5%)	-	7 (12.7%)	7 (12.7%)	0	20 (12.8%)	20 (12.8%)	1 (1.9%)
体重減少	0	0	-	4 (7.3%)	4 (7.3%)	0	7 (4.5%)	7 (4.5%)	0
体重増加	0	0	-	1 (1.8%)	1 (1.8%)	0	4 (2.6%)	4 (2.6%)	0
交差適合試験不適合	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
国際標準比増加	0	0	-	1 (1.8%)	1 (1.8%)	0	3 (1.9%)	3 (1.9%)	0
血中クレアチンホスホキナーゼ増加	1 (4.3%)	1 (4.3%)	-	0	0	0	1 (0.6%)	1 (0.6%)	0
血中テストステロン減少	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
心電図異常Q波	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
心電図ＱＴ延長	5 (21.7%)	5 (21.7%)	-	0	0	0	1 (0.6%)	1 (0.6%)	0
心電図異常Ｔ波	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
酸素飽和度異常	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
尿量減少	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
遊離ヘモグロビン陽性	5 (21.7%)	5 (21.7%)	-	0	0	0	0	0	0
ハプトグロビン減少	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
心拍数増加	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
リンパ球数減少	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	0	0	0
眼障害	1 (4.3%)	1 (4.3%)	-	10 (18.2%)	9 (16.4%)	1 (9.1%)	13 (8.3%)	13 (8.3%)	0
霧視	0	0	-	2 (3.6%)	2 (3.6%)	0	7 (4.5%)	7 (4.5%)	0
眼乾燥	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
眼そう痒症	0	0	-	1 (1.8%)	0	1 (9.1%)	2 (1.3%)	2 (1.3%)	0
眼充血	1 (4.3%)	1 (4.3%)	-	0	0	0	2 (1.3%)	2 (1.3%)	0
白内障	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
結膜出血	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
複視	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
睫毛乱生	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
眼部腫脹	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
眼瞼機能障害	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
眼瞼下垂	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
眼瞼発疹	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
光視症	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
視力障害	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
硝子体浮遊物	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
心臓障害	4 (17.4%)	4 (17.4%)	-	2 (3.6%)	2 (3.6%)	0	11 (7.1%)	11 (7.1%)	0
動悸	1 (4.3%)	1 (4.3%)	-	0	0	0	5 (3.2%)	5 (3.2%)	0
洞性頻脈	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
頻脈	2 (8.7%)	2 (8.7%)	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
狭心症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
心房粗動	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
徐脈	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
左脚ブロック	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
うっ血性心不全	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
心肺停止	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
心房細動	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
上室性期外収縮	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
肝胆道系障害	1 (4.3%)	1 (4.3%)	-	4 (7.3%)	4 (7.3%)	0	8 (5.1%)	8 (5.1%)	0
肝機能異常	1 (4.3%)	1 (4.3%)	-	3 (5.5%)	3 (5.5%)	0	6 (3.8%)	6 (3.8%)	0
肝不全	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
高ビリルビン血症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
黄疸	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
脂肪肝	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3%)	1 (4.3%)	-	3 (5.5%)	2 (3.6%)	1 (9.1%)	6 (3.8%)	6 (3.8%)	0
基底細胞癌	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
腫瘍疼痛	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
肛門直腸ヒト乳頭腫ウイルス感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
皮膚癌	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

TSFAE02DPART1OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
皮膚良性新生物	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
形質細胞性白血病	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
皮膚乳頭腫	0	0	-	1 (1.8%)	0	1 (9.1%)	0	0	0
耳および迷路障害	0	0	-	3 (5.5%)	3 (5.5%)	0	5 (3.2%)	4 (2.6%)	1 (1.9%)
耳痛	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
耳の障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
耳鳴	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
回転性めまい	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
耳垢栓塞	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
耳不快感	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
生殖系および乳房障害	0	0	-	3 (5.5%)	3 (5.5%)	0	4 (2.6%)	4 (2.6%)	0
生殖器痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
乳頭痛	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
性器浮腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
陰茎浮腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腟出血	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
血精液症	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
骨盤痛	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
前立腺炎	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
免疫系障害	3 (13.0%)	3 (13.0%)	-	2 (3.6%)	2 (3.6%)	0	3 (1.9%)	3 (1.9%)	0
アレルギー性浮腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
サイトカイン放出症候群	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0
季節性アレルギー	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
過敏症	2 (8.7%)	2 (8.7%)	-	1 (1.8%)	1 (1.8%)	0	0	0	0
先天性、家族性および遺伝性障害	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
あざ	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

Keys: TEAE = treatment-emergent adverse event.
[a]Includes subjects either treated or experienced any TEAE within the specific window.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects treated within each window as denominator.

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
Analysis set: all treated	3			237		
Total number of subjects treated within window[a]	3	3	0	237	237	63
Total number of subjects with TEAEs	3 (100.0%)	3 (100.0%)	-	234 (98.7%)	234 (98.7%)	45 (71.4%)
MedDRA system organ class/Preferred term						
一般・全身障害および投与部位の状態	0	0	-	153 (64.6%)	150 (63.3%)	10 (15.9%)
疲労	0	0	-	81 (34.2%)	79 (33.3%)	2 (3.2%)
発熱	0	0	-	57 (24.1%)	55 (23.2%)	2 (3.2%)
悪寒	0	0	-	25 (10.5%)	25 (10.5%)	0
無力症	0	0	-	15 (6.3%)	15 (6.3%)	0
末梢性浮腫	0	0	-	17 (7.2%)	16 (6.8%)	1 (1.6%)
胸痛	0	0	-	12 (5.1%)	8 (3.4%)	4 (6.3%)
疼痛	0	0	-	10 (4.2%)	10 (4.2%)	0
インフルエンザ様疾患	0	0	-	11 (4.6%)	11 (4.6%)	0
非心臓性胸痛	0	0	-	8 (3.4%)	8 (3.4%)	0
全身健康状態低下	0	0	-	6 (2.5%)	6 (2.5%)	0
注射部位内出血	0	0	-	3 (1.3%)	3 (1.3%)	0
局所腫脹	0	0	-	3 (1.3%)	3 (1.3%)	0
倦怠感	0	0	-	3 (1.3%)	3 (1.3%)	0
胸部不快感	0	0	-	5 (2.1%)	5 (2.1%)	0
顔面浮腫	0	0	-	3 (1.3%)	3 (1.3%)	0
全身性浮腫	0	0	-	2 (0.8%)	2 (0.8%)	0
浮腫	0	0	-	2 (0.8%)	2 (0.8%)	0
腋窩痛	0	0	-	1 (0.4%)	1 (0.4%)	0
医療機器の問題	0	0	-	1 (0.4%)	0	1 (1.6%)
顔面痛	0	0	-	1 (0.4%)	1 (0.4%)	0
歩行障害	0	0	-	1 (0.4%)	1 (0.4%)	0
低体温	0	0	-	1 (0.4%)	1 (0.4%)	0
注入部位内出血	0	0	-	1 (0.4%)	1 (0.4%)	0
注射部位浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0
注射部位反応	0	0	-	1 (0.4%)	1 (0.4%)	0
限局性浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
腫瘤	0	0	-	1 (0.4%)	1 (0.4%)	0
恥骨上痛	0	0	-	1 (0.4%)	1 (0.4%)	0
急性期反応	0	0	-	1 (0.4%)	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	2 (66.7%)	2 (66.7%)	-	137 (57.8%)	135 (57.0%)	10 (15.9%)
咳嗽	1 (33.3%)	1 (33.3%)	-	49 (20.7%)	45 (19.0%)	8 (12.7%)
鼻閉	1 (33.3%)	1 (33.3%)	-	31 (13.1%)	29 (12.2%)	2 (3.2%)
呼吸困難	0	0	-	34 (14.3%)	34 (14.3%)	1 (1.6%)
口腔咽頭痛	0	0	-	18 (7.6%)	16 (6.8%)	2 (3.2%)
アレルギー性鼻炎	0	0	-	24 (10.1%)	24 (10.1%)	0
咽喉刺激感	0	0	-	11 (4.6%)	11 (4.6%)	0
労作性呼吸困難	0	0	-	9 (3.8%)	8 (3.4%)	1 (1.6%)
鼻出血	0	0	-	10 (4.2%)	10 (4.2%)	0
湿性咳嗽	0	0	-	12 (5.1%)	12 (5.1%)	0
喘鳴	0	0	-	7 (3.0%)	7 (3.0%)	0
気管支痙攣	1 (33.3%)	1 (33.3%)	-	8 (3.4%)	8 (3.4%)	0
胸水	0	0	-	5 (2.1%)	5 (2.1%)	0
副鼻腔うっ血	0	0	-	4 (1.7%)	4 (1.7%)	1 (1.6%)
くしゃみ	0	0	-	4 (1.7%)	4 (1.7%)	0
低酸素症	0	0	-	3 (1.3%)	3 (1.3%)	0
咽喉絞扼感	0	0	-	3 (1.3%)	3 (1.3%)	0
上気道咳症候群	0	0	-	4 (1.7%)	4 (1.7%)	0
呼吸不全	0	0	-	2 (0.8%)	2 (0.8%)	0
急性肺水腫	0	0	-	1 (0.4%)	1 (0.4%)	0
アレルギー性咳嗽	0	0	-	1 (0.4%)	1 (0.4%)	0
慢性閉塞性肺疾患	0	0	-	1 (0.4%)	1 (0.4%)	0
発声障害	0	0	-	2 (0.8%)	2 (0.8%)	0
上気道分泌増加	0	0	-	1 (0.4%)	1 (0.4%)	0
喉頭浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0
アレルギー性喉頭炎	0	0	-	4 (1.7%)	4 (1.7%)	0
鼻部障害	0	0	-	1 (0.4%)	1 (0.4%)	0
誤嚥性肺炎	0	0	-	1 (0.4%)	1 (0.4%)	0
肺うっ血	0	0	-	1 (0.4%)	1 (0.4%)	0
肺塞栓症	0	0	-	1 (0.4%)	0	1 (1.6%)
肺水腫	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
鼻漏	0	0	-	2 (0.8%)	2 (0.8%)	0
喉頭の炎症	0	0	-	1 (0.4%)	1 (0.4%)	0
筋骨格系および結合組織障害	1 (33.3%)	1 (33.3%)	-	126 (53.2%)	123 (51.9%)	11 (17.5%)
背部痛	1 (33.3%)	1 (33.3%)	-	43 (18.1%)	41 (17.3%)	2 (3.2%)
関節痛	0	0	-	32 (13.5%)	30 (12.7%)	2 (3.2%)
四肢痛	0	0	-	25 (10.5%)	24 (10.1%)	2 (3.2%)
筋骨格系胸痛	0	0	-	21 (8.9%)	18 (7.6%)	3 (4.8%)
骨痛	0	0	-	21 (8.9%)	20 (8.4%)	1 (1.6%)
筋骨格痛	0	0	-	16 (6.8%)	16 (6.8%)	0
筋痙縮	0	0	-	12 (5.1%)	12 (5.1%)	1 (1.6%)
筋肉痛	0	0	-	12 (5.1%)	12 (5.1%)	0
単径部痛	0	0	-	4 (1.7%)	3 (1.3%)	1 (1.6%)
頚部痛	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
病的骨折	0	0	-	3 (1.3%)	3 (1.3%)	0
脊椎痛	0	0	-	3 (1.3%)	3 (1.3%)	0
筋力低下	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
骨炎	0	0	-	2 (0.8%)	2 (0.8%)	0
脊柱管狭窄症	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
骨侵食	0	0	-	1 (0.4%)	1 (0.4%)	0
骨病変	0	0	-	1 (0.4%)	1 (0.4%)	0
関節可動域低下	0	0	-	1 (0.4%)	1 (0.4%)	0
四肢不快感	0	0	-	2 (0.8%)	2 (0.8%)	0
運動性低下	0	0	-	1 (0.4%)	1 (0.4%)	0
筋肉疲労	0	0	-	1 (0.4%)	1 (0.4%)	0
筋骨格不快感	0	0	-	1 (0.4%)	1 (0.4%)	0
顎骨壊死	0	0	-	1 (0.4%)	1 (0.4%)	0
顎痛	0	0	-	1 (0.4%)	1 (0.4%)	0
腱炎	0	0	-	1 (0.4%)	0	1 (1.6%)
側腹部痛	0	0	-	1 (0.4%)	1 (0.4%)	0
脊柱後弯症	0	0	-	1 (0.4%)	1 (0.4%)	0
筋骨格硬直	0	0	-	1 (0.4%)	1 (0.4%)	0
〃オパチー	0	0	-	1 (0.4%)	1 (0.4%)	0
骨粗鬆症性骨折	0	0	-	1 (0.4%)	1 (0.4%)	0
胃腸障害	2 (66.7%)	2 (66.7%)	-	123 (51.9%)	119 (50.2%)	16 (25.4%)

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
悪心	0	0	-	53 (22.4%)	50 (21.1%)	5 (7.9%)
下痢	1 (33.3%)	1 (33.3%)	-	40 (16.9%)	39 (16.5%)	2 (3.2%)
便秘	0	0	-	29 (12.2%)	26 (11.0%)	3 (4.8%)
嘔吐	1 (33.3%)	1 (33.3%)	-	30 (12.7%)	28 (11.8%)	2 (3.2%)
腹痛	0	0	-	12 (5.1%)	12 (5.1%)	0
消化不良	0	0	-	7 (3.0%)	6 (2.5%)	1 (1.6%)
口内炎	0	0	-	7 (3.0%)	7 (3.0%)	0
歯痛	0	0	-	4 (1.7%)	3 (1.3%)	1 (1.6%)
腹部膨満	0	0	-	4 (1.7%)	4 (1.7%)	0
放屁	0	0	-	3 (1.3%)	3 (1.3%)	0
口の感覚鈍麻	0	0	-	3 (1.3%)	3 (1.3%)	0
腹部不快感	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
上腹部痛	0	0	-	2 (0.8%)	2 (0.8%)	0
便失禁	0	0	-	2 (0.8%)	2 (0.8%)	0
胃食道逆流性疾患	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
歯肉出血	0	0	-	2 (0.8%)	2 (0.8%)	0
口腔内痛	0	0	-	2 (0.8%)	2 (0.8%)	0
水疱性出血性口峡炎	0	0	-	1 (0.4%)	1 (0.4%)	0
大腸炎	0	0	-	1 (0.4%)	0	1 (1.6%)
憩室	0	0	-	1 (0.4%)	0	1 (1.6%)
嚥下障害	0	0	-	2 (0.8%)	2 (0.8%)	0
胃炎	0	0	-	2 (0.8%)	2 (0.8%)	0
歯肉腫脹	0	0	-	1 (0.4%)	1 (0.4%)	0
舌炎	0	0	-	1 (0.4%)	1 (0.4%)	0
血便排泄	0	0	-	1 (0.4%)	1 (0.4%)	0
痔核	0	0	-	1 (0.4%)	1 (0.4%)	0
大腸閉塞	0	0	-	1 (0.4%)	1 (0.4%)	0
口唇出血	0	0	-	1 (0.4%)	1 (0.4%)	0
口腔内潰瘍形成	0	0	-	2 (0.8%)	2 (0.8%)	0
口腔粘膜変色	0	0	-	1 (0.4%)	1 (0.4%)	0
膵炎	0	0	-	1 (0.4%)	1 (0.4%)	0
口の錯感覚	0	0	-	1 (0.4%)	1 (0.4%)	0
舌苔	0	0	-	1 (0.4%)	1 (0.4%)	0
歯の発育障害	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
歯の障害	0	0	-	1 (0.4%)	0	1 (1.6%)
アフタ性口内炎	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
口内乾燥	0	0	-	3 (1.3%)	3 (1.3%)	0
舌痛	0	0	-	1 (0.4%)	1 (0.4%)	0
口唇浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0
食道炎	0	0	-	1 (0.4%)	1 (0.4%)	0
感染症および寄生虫症	1 (33.3%)	1 (33.3%)	-	125 (52.7%)	118 (49.8%)	24 (38.1%)
上気道感染	0	0	-	39 (16.5%)	35 (14.8%)	9 (14.3%)
鼻咽頭炎	1 (33.3%)	1 (33.3%)	-	30 (12.7%)	27 (11.4%)	5 (7.9%)
肺炎	0	0	-	18 (7.6%)	15 (6.3%)	3 (4.8%)
副鼻腔炎	0	0	-	11 (4.6%)	11 (4.6%)	1 (1.6%)
尿路感染	1 (33.3%)	1 (33.3%)	-	10 (4.2%)	7 (3.0%)	3 (4.8%)
気管支炎	0	0	-	5 (2.1%)	4 (1.7%)	2 (3.2%)
結膜炎	0	0	-	3 (1.3%)	3 (1.3%)	0
帯状疱疹	0	0	-	8 (3.4%)	7 (3.0%)	1 (1.6%)
大葉性肺炎	0	0	-	3 (1.3%)	3 (1.3%)	0
口腔カンジダ症	0	0	-	6 (2.5%)	6 (2.5%)	0
カンジダ感染	0	0	-	4 (1.7%)	3 (1.3%)	1 (1.6%)
単純ヘルペス	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
感染	0	0	-	3 (1.3%)	3 (1.3%)	0
インフルエンザ	0	0	-	5 (2.1%)	4 (1.7%)	1 (1.6%)
パラインフルエンザウイルス感染	0	0	-	2 (0.8%)	2 (0.8%)	0
咽頭炎	0	0	-	2 (0.8%)	2 (0.8%)	0
鼻炎	0	0	-	2 (0.8%)	2 (0.8%)	0
軟部組織感染	0	0	-	2 (0.8%)	2 (0.8%)	0
水痘	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
蜂巣炎	0	0	-	1 (0.4%)	1 (0.4%)	0
膀胱炎	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
サイトメガロウイルス性脈絡網膜炎	0	0	-	1 (0.4%)	1 (0.4%)	0
医療機器関連感染	0	0	-	1 (0.4%)	1 (0.4%)	0
耳感染	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
胃腸炎	0	0	-	3 (1.3%)	1 (0.4%)	2 (3.2%)

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
ウイルス性胃腸炎	0	0	-	1 (0.4%)	1 (0.4%)	0
性器感染	0	0	-	1 (0.4%)	1 (0.4%)	0
Ｈ１Ｎ１インフルエンザ	0	0	-	1 (0.4%)	1 (0.4%)	0
麦粒腫	0	0	-	1 (0.4%)	1 (0.4%)	0
下気道感染	0	0	-	1 (0.4%)	1 (0.4%)	0
粘膜感染	0	0	-	1 (0.4%)	1 (0.4%)	0
眼部単純ヘルペス	0	0	-	1 (0.4%)	1 (0.4%)	0
口腔真菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
口腔ヘルペス	0	0	-	1 (0.4%)	1 (0.4%)	0
爪囲炎	0	0	-	1 (0.4%)	1 (0.4%)	1 (1.6%)
レンサ球菌性肺炎	0	0	-	1 (0.4%)	1 (0.4%)	0
腎盂腎炎	0	0	-	1 (0.4%)	0	1 (1.6%)
気道感染	0	0	-	1 (0.4%)	0	1 (1.6%)
敗血症	0	0	-	1 (0.4%)	1 (0.4%)	0
レンサ球菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
歯感染	0	0	-	1 (0.4%)	1 (0.4%)	0
ウイルス性上気道感染	0	0	-	1 (0.4%)	0	1 (1.6%)
外陰腟真菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
菌血症	0	0	-	1 (0.4%)	1 (0.4%)	0
真菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
真菌性消化管感染	0	0	-	1 (0.4%)	1 (0.4%)	0
肺感染	0	0	-	1 (0.4%)	1 (0.4%)	0
メタニューモウイルス感染	0	0	-	1 (0.4%)	1 (0.4%)	0
ＲＳウイルス感染	0	0	-	2 (0.8%)	2 (0.8%)	0
細菌性尿路感染	0	0	-	1 (0.4%)	1 (0.4%)	0
ウイルス感染	0	0	-	1 (0.4%)	1 (0.4%)	0
外陰部腟カンジダ症	0	0	-	1 (0.4%)	1 (0.4%)	0
血液およびリンパ系障害	0	0	-	106 (44.7%)	106 (44.7%)	2 (3.2%)
貧血	0	0	-	55 (23.2%)	54 (22.8%)	1 (1.6%)
好中球減少症	0	0	-	38 (16.0%)	38 (16.0%)	0
血小板減少症	0	0	-	44 (18.6%)	44 (18.6%)	1 (1.6%)
白血球減少症	0	0	-	16 (6.8%)	16 (6.8%)	1 (1.6%)
リンパ球減少症	0	0	-	18 (7.6%)	18 (7.6%)	0
ヘモグロビン血症	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
内出血発生の増加傾向	0	0	-	1 (0.4%)	1 (0.4%)	0
汎血球減少症	0	0	-	1 (0.4%)	1 (0.4%)	0
赤血球凝集	0	0	-	1 (0.4%)	1 (0.4%)	0
溶血	0	0	-	3 (1.3%)	3 (1.3%)	0
単球減少症	0	0	-	3 (1.3%)	3 (1.3%)	0
代謝および栄養障害	0	0	-	82 (34.6%)	78 (32.9%)	9 (14.3%)
食欲減退	0	0	-	29 (12.2%)	27 (11.4%)	3 (4.8%)
高カルシウム血症	0	0	-	22 (9.3%)	21 (8.9%)	2 (3.2%)
高血糖	0	0	-	17 (7.2%)	17 (7.2%)	1 (1.6%)
低カリウム血症	0	0	-	16 (6.8%)	14 (5.9%)	3 (4.8%)
低マグネシウム血症	0	0	-	11 (4.6%)	11 (4.6%)	0
低ナトリウム血症	0	0	-	15 (6.3%)	15 (6.3%)	0
高カリウム血症	0	0	-	6 (2.5%)	5 (2.1%)	1 (1.6%)
酵素異常	0	0	-	8 (3.4%)	8 (3.4%)	0
高尿酸血症	0	0	-	6 (2.5%)	5 (2.1%)	1 (1.6%)
低アルブミン血症	0	0	-	8 (3.4%)	8 (3.4%)	0
低カルシウム血症	0	0	-	4 (1.7%)	4 (1.7%)	1 (1.6%)
糖尿病	0	0	-	1 (0.4%)	1 (0.4%)	0
高ナトリウム血症	0	0	-	1 (0.4%)	1 (0.4%)	0
高リン酸塩血症	0	0	-	1 (0.4%)	1 (0.4%)	0
低血糖症	0	0	-	2 (0.8%)	2 (0.8%)	0
栄養障害	0	0	-	1 (0.4%)	1 (0.4%)	0
ビタミンＢ１２欠乏	0	0	-	1 (0.4%)	0	1 (1.6%)
体液貯留	0	0	-	1 (0.4%)	1 (0.4%)	0
低リン酸血症	0	0	-	2 (0.8%)	2 (0.8%)	0
代謝性アシドーシス	0	0	-	1 (0.4%)	1 (0.4%)	0
神経系障害	0	0	-	81 (34.2%)	76 (32.1%)	9 (14.3%)
頭痛	0	0	-	21 (8.9%)	20 (8.4%)	1 (1.6%)
浮動性めまい	0	0	-	22 (9.3%)	21 (8.9%)	2 (3.2%)
末梢性感覚ニューロパチー	0	0	-	14 (5.9%)	14 (5.9%)	1 (1.6%)
感覚鈍麻	0	0	-	7 (3.0%)	5 (2.1%)	2 (3.2%)
傾眠	0	0	-	6 (2.5%)	6 (2.5%)	0
振戦	0	0	-	6 (2.5%)	4 (1.7%)	2 (3.2%)
味覚異常	0	0	-	7 (3.0%)	5 (2.1%)	2 (3.2%)

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
錯感覚	0	0	-	4 (1.7%)	3 (1.3%)	1 (1.6%)
下肢静止不能症候群	0	0	-	2 (0.8%)	2 (0.8%)	0
意識変容状態	0	0	-	1 (0.4%)	1 (0.4%)	0
手根管症候群	0	0	-	1 (0.4%)	0	1 (1.6%)
意識レベルの低下	0	0	-	1 (0.4%)	1 (0.4%)	0
脳症	0	0	-	2 (0.8%)	2 (0.8%)	0
知覚過敏	0	0	-	2 (0.8%)	2 (0.8%)	0
嗜眠	0	0	-	1 (0.4%)	0	1 (1.6%)
記憶障害	0	0	-	1 (0.4%)	1 (0.4%)	0
神経痛	0	0	-	1 (0.4%)	1 (0.4%)	0
嗅覚錯誤	0	0	-	1 (0.4%)	1 (0.4%)	0
脊髄圧迫	0	0	-	1 (0.4%)	1 (0.4%)	0
失神	0	0	-	2 (0.8%)	2 (0.8%)	0
第７脳神経麻痺	0	0	-	1 (0.4%)	1 (0.4%)	0
無感覚	0	0	-	1 (0.4%)	1 (0.4%)	0
坐骨神経痛	0	0	-	1 (0.4%)	1 (0.4%)	0
第６脳神経麻痺	0	0	-	1 (0.4%)	1 (0.4%)	0
皮膚および皮下組織障害	0	0	-	54 (22.8%)	50 (21.1%)	5 (7.9%)
そう痒症	0	0	-	10 (4.2%)	9 (3.8%)	1 (1.6%)
多汗症	0	0	-	6 (2.5%)	6 (2.5%)	0
寝汗	0	0	-	4 (1.7%)	4 (1.7%)	0
発疹	0	0	-	12 (5.1%)	11 (4.6%)	1 (1.6%)
斑状丘疹状皮疹	0	0	-	4 (1.7%)	4 (1.7%)	0
皮膚嚢腫	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
ざ瘡様皮膚炎	0	0	-	2 (0.8%)	2 (0.8%)	0
接触性皮膚炎	0	0	-	2 (0.8%)	2 (0.8%)	0
皮膚乾燥	0	0	-	2 (0.8%)	2 (0.8%)	0
湿疹	0	0	-	2 (0.8%)	2 (0.8%)	0
紅斑	0	0	-	3 (1.3%)	3 (1.3%)	0
点状出血	0	0	-	2 (0.8%)	2 (0.8%)	0
褥瘡性潰瘍	0	0	-	1 (0.4%)	1 (0.4%)	0
薬疹	0	0	-	1 (0.4%)	1 (0.4%)	0
皮脂欠乏性湿疹	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
手掌・足底発赤知覚不全症候群	0	0	-	1 (0.4%)	1 (0.4%)	0
色素沈着障害	0	0	-	1 (0.4%)	1 (0.4%)	0
全身性そう痒症	0	0	-	1 (0.4%)	1 (0.4%)	0
乾癬	0	0	-	1 (0.4%)	0	1 (1.6%)
斑状皮疹	0	0	-	2 (0.8%)	2 (0.8%)	0
丘疹性皮疹	0	0	-	1 (0.4%)	1 (0.4%)	0
皮膚剥脱	0	0	-	1 (0.4%)	1 (0.4%)	0
皮膚色素過剰	0	0	-	1 (0.4%)	1 (0.4%)	0
皮膚潰瘍	0	0	-	1 (0.4%)	1 (0.4%)	0
蕁麻疹	0	0	-	2 (0.8%)	2 (0.8%)	0
脱毛症	0	0	-	1 (0.4%)	1 (0.4%)	0
爪変色	0	0	-	1 (0.4%)	0	1 (1.6%)
血管障害	0	0	-	48 (20.3%)	46 (19.4%)	2 (3.2%)
高血圧	0	0	-	27 (11.4%)	27 (11.4%)	0
低血圧	0	0	-	10 (4.2%)	9 (3.8%)	1 (1.6%)
血腫	0	0	-	5 (2.1%)	5 (2.1%)	0
潮紅	0	0	-	6 (2.5%)	6 (2.5%)	0
深部静脈血栓症	0	0	-	3 (1.3%)	3 (1.3%)	0
ほてり	0	0	-	3 (1.3%)	3 (1.3%)	0
表在性静脈炎	0	0	-	1 (0.4%)	0	1 (1.6%)
レイノー現象	0	0	-	1 (0.4%)	1 (0.4%)	0
四肢静脈血栓症	0	0	-	1 (0.4%)	1 (0.4%)	0
傷害、中毒および処置合併症	0	0	-	32 (13.5%)	28 (11.8%)	4 (6.3%)
挫傷	0	0	-	6 (2.5%)	6 (2.5%)	0
転倒	0	0	-	5 (2.1%)	4 (1.7%)	1 (1.6%)
肋骨骨折	0	0	-	4 (1.7%)	4 (1.7%)	0
上腕骨骨折	0	0	-	2 (0.8%)	2 (0.8%)	0
裂傷	0	0	-	2 (0.8%)	2 (0.8%)	0
腰椎骨折	0	0	-	2 (0.8%)	2 (0.8%)	0
脊椎圧迫骨折	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
骨挫傷	0	0	-	1 (0.4%)	0	1 (1.6%)
擦過傷	0	0	-	1 (0.4%)	1 (0.4%)	0
足骨折	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
骨折	0	0	-	1 (0.4%)	0	1 (1.6%)
肉離れ	0	0	-	1 (0.4%)	1 (0.4%)	0
眼窩周囲挫傷	0	0	-	1 (0.4%)	1 (0.4%)	0
処置による疼痛	0	0	-	1 (0.4%)	1 (0.4%)	0
硬膜下血腫	0	0	-	1 (0.4%)	1 (0.4%)	0
腱断裂	0	0	-	1 (0.4%)	1 (0.4%)	0
輸血反応	0	0	-	1 (0.4%)	1 (0.4%)	0
上肢骨折	0	0	-	1 (0.4%)	1 (0.4%)	0
創傷	0	0	-	1 (0.4%)	0	1 (1.6%)
手首関節骨折	0	0	-	1 (0.4%)	1 (0.4%)	0
四肢外傷性切断	0	0	-	1 (0.4%)	1 (0.4%)	0
精神障害	0	0	-	37 (15.6%)	35 (14.8%)	2 (3.2%)
不安	0	0	-	9 (3.8%)	9 (3.8%)	0
錯乱状態	0	0	-	8 (3.4%)	8 (3.4%)	0
不眠症	0	0	-	11 (4.6%)	10 (4.2%)	1 (1.6%)
激越	0	0	-	4 (1.7%)	4 (1.7%)	0
譫妄	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
うつ病	0	0	-	5 (2.1%)	5 (2.1%)	0
気分変化	0	0	-	2 (0.8%)	2 (0.8%)	0
摂食障害	0	0	-	1 (0.4%)	1 (0.4%)	0
幻覚	0	0	-	1 (0.4%)	1 (0.4%)	0
精神状態変化	0	0	-	2 (0.8%)	2 (0.8%)	0
気分動揺	0	0	-	1 (0.4%)	1 (0.4%)	0
神経過敏	0	0	-	1 (0.4%)	1 (0.4%)	0
腎および尿路障害	1 (33.3%)	1 (33.3%)	-	52 (21.9%)	49 (20.7%)	5 (7.9%)
腎機能障害	0	0	-	20 (8.4%)	19 (8.0%)	2 (3.2%)
排尿困難	0	0	-	4 (1.7%)	3 (1.3%)	1 (1.6%)
頻尿	0	0	-	3 (1.3%)	3 (1.3%)	0
蛋白尿	1 (33.3%)	1 (33.3%)	-	16 (6.8%)	16 (6.8%)	0
尿閉	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
非感染性膀胱炎	0	0	-	1 (0.4%)	1 (0.4%)	0
血尿	0	0	-	3 (1.3%)	3 (1.3%)	0
夜間頻尿	0	0	-	1 (0.4%)	1 (0.4%)	0
腎不全	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
腎静脈血栓症	0	0	-	1 (0.4%)	1 (0.4%)	0
尿失禁	0	0	-	4 (1.7%)	4 (1.7%)	0
尿路閉塞	0	0	-	1 (0.4%)	1 (0.4%)	0
高窒素血症	0	0	-	1 (0.4%)	0	1 (1.6%)
膀胱痙縮	0	0	-	1 (0.4%)	1 (0.4%)	0
尿意切迫	0	0	-	1 (0.4%)	0	1 (1.6%)
急性腎不全	0	0	-	1 (0.4%)	1 (0.4%)	0
臨床検査	0	0	-	37 (15.6%)	37 (15.6%)	1 (1.6%)
体重減少	0	0	-	11 (4.6%)	11 (4.6%)	0
体重増加	0	0	-	5 (2.1%)	5 (2.1%)	0
交差適合試験不適合	0	0	-	3 (1.3%)	3 (1.3%)	0
国際標準比増加	0	0	-	4 (1.7%)	4 (1.7%)	0
血中クレアチンホスホキナーゼ増加	0	0	-	2 (0.8%)	2 (0.8%)	0
血中テストステロン減少	0	0	-	1 (0.4%)	1 (0.4%)	0
心電図異常Q波	0	0	-	1 (0.4%)	1 (0.4%)	0
心電図ＱＴ延長	0	0	-	6 (2.5%)	6 (2.5%)	0
心電図異常Ｔ波	0	0	-	1 (0.4%)	0	1 (1.6%)
酸素飽和度異常	0	0	-	1 (0.4%)	1 (0.4%)	0
尿量減少	0	0	-	1 (0.4%)	1 (0.4%)	0
遊離ヘモグロビン陽性	0	0	-	5 (2.1%)	5 (2.1%)	0
ハプトグロビン減少	0	0	-	1 (0.4%)	1 (0.4%)	0
心拍数増加	0	0	-	1 (0.4%)	1 (0.4%)	0
リンパ球数減少	0	0	-	2 (0.8%)	2 (0.8%)	0
眼障害	0	0	-	24 (10.1%)	23 (9.7%)	1 (1.6%)
霧視	0	0	-	9 (3.8%)	9 (3.8%)	0
眼乾燥	0	0	-	2 (0.8%)	2 (0.8%)	0
眼そう痒症	0	0	-	3 (1.3%)	2 (0.8%)	1 (1.6%)
眼充血	0	0	-	3 (1.3%)	3 (1.3%)	0
白内障	0	0	-	2 (0.8%)	2 (0.8%)	0
結膜出血	0	0	-	1 (0.4%)	1 (0.4%)	0
複視	0	0	-	2 (0.8%)	2 (0.8%)	0
睫毛乱生	0	0	-	1 (0.4%)	1 (0.4%)	0
眼部腫脹	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
眼瞼機能障害	0	0	-	1 (0.4%)	1 (0.4%)	0
眼瞼下垂	0	0	-	1 (0.4%)	1 (0.4%)	0
眼瞼発疹	0	0	-	1 (0.4%)	1 (0.4%)	0
光視症	0	0	-	1 (0.4%)	1 (0.4%)	0
視力障害	0	0	-	1 (0.4%)	1 (0.4%)	0
硝子体浮遊物	0	0	-	1 (0.4%)	1 (0.4%)	0
心臓障害	0	0	-	17 (7.2%)	17 (7.2%)	0
動悸	0	0	-	6 (2.5%)	6 (2.5%)	0
洞性頻脈	0	0	-	3 (1.3%)	3 (1.3%)	0
頻脈	0	0	-	5 (2.1%)	5 (2.1%)	0
狭心症	0	0	-	1 (0.4%)	1 (0.4%)	0
心房粗動	0	0	-	1 (0.4%)	1 (0.4%)	0
徐脈	0	0	-	1 (0.4%)	1 (0.4%)	0
左脚ブロック	0	0	-	1 (0.4%)	1 (0.4%)	0
うっ血性心不全	0	0	-	1 (0.4%)	1 (0.4%)	0
心肺停止	0	0	-	1 (0.4%)	1 (0.4%)	0
心房細動	0	0	-	1 (0.4%)	1 (0.4%)	0
上室性期外収縮	0	0	-	1 (0.4%)	1 (0.4%)	0
肝胆道系障害	0	0	-	13 (5.5%)	13 (5.5%)	0
肝機能異常	0	0	-	10 (4.2%)	10 (4.2%)	0
肝不全	0	0	-	1 (0.4%)	1 (0.4%)	0
高ビリルビン血症	0	0	-	1 (0.4%)	1 (0.4%)	0
黄疸	0	0	-	1 (0.4%)	1 (0.4%)	0
脂肪肝	0	0	-	1 (0.4%)	1 (0.4%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	-	10 (4.2%)	9 (3.8%)	1 (1.6%)
基底細胞癌	0	0	-	3 (1.3%)	3 (1.3%)	0
腫瘍疼痛	0	0	-	2 (0.8%)	2 (0.8%)	0
肛門直腸ヒト乳頭腫ウイルス感染	0	0	-	1 (0.4%)	1 (0.4%)	0
皮膚癌	0	0	-	1 (0.4%)	1 (0.4%)	0
皮膚良性新生物	0	0	-	1 (0.4%)	1 (0.4%)	0
形質細胞性白血病	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE02DPART2OF2: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
皮膚乳頭腫	0	0	-	1 (0.4%)	0	1 (1.6%)
耳および迷路障害	0	0	-	8 (3.4%)	7 (3.0%)	1 (1.6%)
耳痛	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
耳の障害	0	0	-	1 (0.4%)	1 (0.4%)	0
耳鳴	0	0	-	1 (0.4%)	1 (0.4%)	0
回転性めまい	0	0	-	2 (0.8%)	2 (0.8%)	0
耳垢栓塞	0	0	-	1 (0.4%)	1 (0.4%)	0
耳不快感	0	0	-	1 (0.4%)	1 (0.4%)	0
生殖系および乳房障害	1 (33.3%)	1 (33.3%)	-	8 (3.4%)	8 (3.4%)	0
生殖器痛	0	0	-	1 (0.4%)	1 (0.4%)	0
乳頭痛	0	0	-	1 (0.4%)	1 (0.4%)	0
性器浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0
陰茎浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0
腟出血	0	0	-	1 (0.4%)	1 (0.4%)	0
血精液症	0	0	-	1 (0.4%)	1 (0.4%)	0
骨盤痛	0	0	-	1 (0.4%)	1 (0.4%)	0
前立腺炎	1 (33.3%)	1 (33.3%)	-	2 (0.8%)	2 (0.8%)	0
免疫系障害	0	0	-	8 (3.4%)	8 (3.4%)	0
アレルギー性浮腫	0	0	-	1 (0.4%)	1 (0.4%)	0
サイトカイン放出症候群	0	0	-	3 (1.3%)	3 (1.3%)	0
季節性アレルギー	0	0	-	1 (0.4%)	1 (0.4%)	0
過敏症	0	0	-	3 (1.3%)	3 (1.3%)	0
先天性、家族性および遺伝性障害	0	0	-	1 (0.4%)	1 (0.4%)	0
あざ	0	0	-	1 (0.4%)	1 (0.4%)	0

Keys: TEAE = treatment-emergent adverse event.
[a]Includes subjects either treated or experienced any TEAE within the specific window.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects treated within each window as denominator.

[TSFAE02DPART2OF2.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae02d.sas] 16MAR2015, 16:20

表 2.7.4-付録-38 Number of Subjects with Treatment-emergent Adverse Events by System Organ Class, Preferred Term, and Toxicity Grade; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE03A: Number of Subjects with Treatment-emergent Adverse Events by System Organ Class, Preferred Term, and Toxicity Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab 8 mg/kg					Daratumumab 16 mg/kg					All groups				
	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5
Analysis set: All Treated Analysis Population	4					5					9				
Number of subjects with any TEAEs	4 (100.0 %)	3 (75.0%)	0	3 (75.0%)	0	5 (100.0 %)	5 (100.0 %)	2 (40.0%)	3 (60.0%)	0	9 (100.0 %)	8 (88.9%)	2 (22.2%)	6 (66.7%)	0
MedDRA system organ class/preferred term															
感染症および寄生虫症	2 (50.0%)	0	0	0	0	3 (60.0%)	1 (20.0%)	1 (20.0%)	0	0	5 (55.6%)	1 (11.1%)	1 (11.1%)	0	0
鼻咽頭炎	1 (25.0%)	0	0	0	0	1 (20.0%)	0	0	0	0	2 (22.2%)	0	0	0	0
膀胱炎	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
咽頭炎	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
肺炎	0	0	0	0	0	1 (20.0%)	1 (20.0%)	1 (20.0%)	0	0	1 (11.1%)	1 (11.1%)	1 (11.1%)	0	0
上気道感染	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
アデノイド咽頭炎	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
血液およびリンパ系障害	4 (100.0 %)	3 (75.0%)	0	3 (75.0%)	0	5 (100.0 %)	5 (100.0 %)	2 (40.0%)	3 (60.0%)	0	9 (100.0 %)	8 (88.9%)	2 (22.2%)	6 (66.7%)	0
リンパ球減少症	4 (100.0 %)	2 (50.0%)	0	2 (50.0%)	0	5 (100.0 %)	5 (100.0 %)	2 (40.0%)	3 (60.0%)	0	9 (100.0 %)	7 (77.8%)	2 (22.2%)	5 (55.6%)	0
好中球減少症	2 (50.0%)	0	0	0	0	5 (100.0 %)	4 (80.0%)	4 (80.0%)	0	0	7 (77.8%)	4 (44.4%)	4 (44.4%)	0	0
白血球減少症	0	0	0	0	0	3 (60.0%)	3 (60.0%)	3 (60.0%)	0	0	3 (33.3%)	3 (33.3%)	3 (33.3%)	0	0
貧血	1 (25.0%)	1 (25.0%)	1 (25.0%)	0	0	1 (20.0%)	1 (20.0%)	1 (20.0%)	0	0	2 (22.2%)	2 (22.2%)	2 (22.2%)	0	0
血小板減少症	1 (25.0%)	1 (25.0%)	0	1 (25.0%)	0	1 (20.0%)	1 (20.0%)	0	1 (20.0%)	0	2 (22.2%)	2 (22.2%)	0	2 (22.2%)	0
代謝および栄養障害	1 (25.0%)	0	0	0	0	2 (40.0%)	0	0	0	0	3 (33.3%)	0	0	0	0

TSFAE03A: Number of Subjects with Treatment-emergent Adverse Events by System Organ Class, Preferred Term, and Toxicity Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab 8 mg/kg					Daratumumab 16 mg/kg					All groups				
	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5
高カリウム血症	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
低リン酸血症	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
高脂血症	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
神経系障害	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
頭痛	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	0	2 (40.0%)	0	0	0	0	2 (22.2%)	0	0	0	0
低酸素症	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
アレルギー性鼻炎	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
口腔咽頭痛	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
胃腸障害	1 (25.0%)	0	0	0	0	1 (20.0%)	0	0	0	0	2 (22.2%)	0	0	0	0
便秘	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
悪心	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
皮膚および皮下組織障害	2 (50.0%)	0	0	0	0	0	0	0	0	0	2 (22.2%)	0	0	0	0
そう痒症	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
発疹	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	0	1 (20.0%)	1 (20.0%)	1 (20.0%)	0	0	1 (11.1%)	1 (11.1%)	1 (11.1%)	0	0
骨炎	0	0	0	0	0	1 (20.0%)	1 (20.0%)	1 (20.0%)	0	0	1 (11.1%)	1 (11.1%)	1 (11.1%)	0	0
腎および尿路障害	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
排尿困難	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
一般・全身障害および投与部位の状態	1 (25.0%)	0	0	0	0	3 (60.0%)	0	0	0	0	4 (44.4%)	0	0	0	0
発熱	1 (25.0%)	0	0	0	0	3 (60.0%)	0	0	0	0	4 (44.4%)	0	0	0	0

TSFAE03A: Number of Subjects with Treatment-emergent Adverse Events by System Organ Class, Preferred Term, and Toxicity Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab 8 mg/kg					Daratumumab 16 mg/kg					All groups				
	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5	All Grade	Grade 3 or 4	Grade 3	Grade 4	Grade 5
悪寒	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0
臨床検査	1 (25.0%)	0	0	0	0	1 (20.0%)	0	0	0	0	2 (22.2%)	0	0	0	0
Ｃ－反応性蛋白増加	1 (25.0%)	0	0	0	0	0	0	0	0	0	1 (11.1%)	0	0	0	0
体重減少	0	0	0	0	0	1 (20.0%)	0	0	0	0	1 (11.1%)	0	0	0	0

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.
Note: If an AE (PT) was reported more than once in the same subject, only the event with the highest grade was counted.

[TSFAE03A.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae03a.sas] 24MAY2016, 09:56

表 2.7.4-付録-39 Number of Subjects with Treatment-emergent Adverse Events by Time of First Onset by System Organ Class and Preferred Term for Daratumumab 8 mg/kg; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE11: Number of Subjects with Treatment-emergent Adverse Events by Time of First Onset by System Organ Class and Preferred Term for Daratumumab 8 mg/kg; All Treated Analysis Population (Study 54767414MMY1002)

	Total	≤8 Weeks	8 - ≤16 Weeks	16 - ≤24 Weeks	>24 Weeks
Daratumumab 8 mg/kg					
Analysis set: All Treated Analysis Population	4	4	3	3	3
Number of subjects with any TEAEs	4 (100.0%)	4 (100.0%)	0	0	0
Number of subjects with any TEAEs leading to death	0	0	0	0	0
Number of subjects with any serious TEAEs other than death	1 (25.0%)	1 (25.0%)	0	0	0
Number of subjects with any TEAEs leading to study drug discontinuation	0	0	0	0	0
MedDRA system organ class/preferred term					
感染症および寄生虫症	2 (50.0%)	1 (25.0%)	0	1 (33.3%)	0
鼻咽頭炎	1 (25.0%)	0	0	1 (33.3%)	0
上気道感染	1 (25.0%)	1 (25.0%)	0	0	0
血液およびリンパ系障害	4 (100.0%)	4 (100.0%)	0	0	0
リンパ球減少症	4 (100.0%)	4 (100.0%)	0	0	0
好中球減少症	2 (50.0%)	2 (50.0%)	0	0	0
貧血	1 (25.0%)	1 (25.0%)	0	0	0
血小板減少症	1 (25.0%)	1 (25.0%)	0	0	0
代謝および栄養障害	1 (25.0%)	1 (25.0%)	0	0	0
低リン酸血症	1 (25.0%)	1 (25.0%)	0	0	0
胃腸障害	1 (25.0%)	1 (25.0%)	0	0	0
悪心	1 (25.0%)	1 (25.0%)	0	0	0
皮膚および皮下組織障害	2 (50.0%)	1 (25.0%)	1 (33.3%)	0	0
そう痒症	1 (25.0%)	1 (25.0%)	0	0	0
発疹	1 (25.0%)	0	1 (33.3%)	0	0
腎および尿路障害	1 (25.0%)	1 (25.0%)	0	0	0
排尿困難	1 (25.0%)	1 (25.0%)	0	0	0
一般・全身障害および投与部位の状態	1 (25.0%)	1 (25.0%)	0	0	0
発熱	1 (25.0%)	1 (25.0%)	0	0	0
臨床検査	1 (25.0%)	1 (25.0%)	0	0	0
Ｃ－反応性蛋白増加	1 (25.0%)	1 (25.0%)	0	0	0

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.
Note: First-onset AEs (PTs) are tabulated.

[TSFAE11.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae11.sas] 22FEB2016, 11:16

表 2.7.4-付録-40 Number of Subjects with Treatment-emergent Adverse Events by Time of First Onset by System Organ Class and Preferred Term for Daratumumab 16 mg/kg; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE12: Number of Subjects with Treatment-emergent Adverse Events by Time of First Onset by System Organ Class and Preferred Term for Daratumumab 16 mg/kg; All Treated Analysis Population (Study 54767414MMY1002)

	Total	≤8 Weeks	8 - ≤16 Weeks	16 - ≤24 Weeks	>24 Weeks
Daratumumab 16 mg/kg					
Analysis set: All Treated Analysis Population	5	5	3	2	2
Number of subjects with any TEAEs	5 (100.0%)	5 (100.0%)	0	0	0
Number of subjects with any TEAEs leading to death	0	0	0	0	0
Number of subjects with any serious TEAEs other than death	2 (40.0%)	2 (40.0%)	0	0	0
Number of subjects with any TEAEs leading to study drug discontinuation	0	0	0	0	0
MedDRA system organ class/preferred term					
感染症および寄生虫症	3 (60.0%)	2 (40.0%)	1 (33.3%)	1 (50.0%)	0
膀胱炎	1 (20.0%)	0	1 (33.3%)	0	0
鼻咽頭炎	1 (20.0%)	0	0	1 (50.0%)	0
咽頭炎	1 (20.0%)	1 (20.0%)	0	0	0
肺炎	1 (20.0%)	1 (20.0%)	0	0	0
アデノイド咽頭炎	1 (20.0%)	0	1 (33.3%)	0	0
血液およびリンパ系障害	5 (100.0%)	5 (100.0%)	0	0	0
リンパ球減少症	5 (100.0%)	5 (100.0%)	0	0	0
好中球減少症	5 (100.0%)	5 (100.0%)	0	0	0
白血球減少症	3 (60.0%)	3 (60.0%)	0	0	0
貧血	1 (20.0%)	1 (20.0%)	0	0	0
血小板減少症	1 (20.0%)	1 (20.0%)	0	0	0
代謝および栄養障害	2 (40.0%)	1 (20.0%)	0	1 (50.0%)	0
高カリウム血症	1 (20.0%)	1 (20.0%)	0	0	0
高脂血症	1 (20.0%)	0	0	1 (50.0%)	0
神経系障害	1 (20.0%)	1 (20.0%)	0	0	0
頭痛	1 (20.0%)	1 (20.0%)	0	0	0
呼吸器、胸郭および縦隔障害	2 (40.0%)	2 (40.0%)	0	0	0
低酸素症	1 (20.0%)	1 (20.0%)	0	0	0
アレルギー性鼻炎	1 (20.0%)	1 (20.0%)	0	0	0
口腔咽頭痛	1 (20.0%)	1 (20.0%)	0	0	0
胃腸障害	1 (20.0%)	1 (20.0%)	0	0	0
便秘	1 (20.0%)	1 (20.0%)	0	0	0
筋骨格系および結合組織障害	1 (20.0%)	0	1 (33.3%)	0	0
骨炎	1 (20.0%)	0	1 (33.3%)	0	0

TSFAE12: Number of Subjects with Treatment-emergent Adverse Events by Time of First Onset by System Organ Class and Preferred Term for Daratumumab 16 mg/kg; All Treated Analysis Population (Study 54767414MMY1002)

	Total	≤8 Weeks	8 - ≤16 Weeks	16 - ≤24 Weeks	>24 Weeks
一般・全身障害および投与部位の状態	3 (60.0%)	3 (60.0%)	0	0	0
発熱	3 (60.0%)	3 (60.0%)	0	0	0
悪寒	1 (20.0%)	1 (20.0%)	0	0	0
臨床検査	1 (20.0%)	1 (20.0%)	0	0	0
体重減少	1 (20.0%)	1 (20.0%)	0	0	0

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.
Note: First-onset AEs (PTs) are tabulated.

[TSFAE12.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae12.sas] 22FEB2016, 11:17

表 2.7.4-付録-41 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with TEAEs	22 (95.7%)	8 (34.8%)	55 (100.0%)	31 (56.4%)	154 (98.7%)	87 (55.8%)	3 (100.0%)	1 (33.3%)	234 (98.7%)	127 (53.6%)
MedDRA system organ class/Preferred term										
一般・全身障害および投与部位の状態	11 (47.8%)	0	36 (65.5%)	6 (10.9%)	106 (67.9%)	10 (6.4%)	0	0	153 (64.6%)	16 (6.8%)
疲労	2 (8.7%)	0	20 (36.4%)	1 (1.8%)	59 (37.8%)	3 (1.9%)	0	0	81 (34.2%)	4 (1.7%)
発熱	8 (34.8%)	0	20 (36.4%)	1 (1.8%)	29 (18.6%)	2 (1.3%)	0	0	57 (24.1%)	3 (1.3%)
悪寒	0	0	9 (16.4%)	1 (1.8%)	16 (10.3%)	0	0	0	25 (10.5%)	1 (0.4%)
無力症	0	0	3 (5.5%)	0	12 (7.7%)	1 (0.6%)	0	0	15 (6.3%)	1 (0.4%)
末梢性浮腫	1 (4.3%)	0	5 (9.1%)	0	11 (7.1%)	1 (0.6%)	0	0	17 (7.2%)	1 (0.4%)
胸痛	2 (8.7%)	0	1 (1.8%)	1 (1.8%)	9 (5.8%)	0	0	0	12 (5.1%)	1 (0.4%)
疼痛	0	0	2 (3.6%)	0	8 (5.1%)	1 (0.6%)	0	0	10 (4.2%)	1 (0.4%)
インフルエンザ様疾患	3 (13.0%)	0	1 (1.8%)	0	7 (4.5%)	1 (0.6%)	0	0	11 (4.6%)	1 (0.4%)
非心臓性胸痛	0	0	2 (3.6%)	0	6 (3.8%)	0	0	0	8 (3.4%)	0
全身健康状態低下	0	0	1 (1.8%)	1 (1.8%)	5 (3.2%)	1 (0.6%)	0	0	6 (2.5%)	2 (0.8%)
注射部位内出血	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
局所腫脹	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
倦怠感	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
胸部不快感	0	0	3 (5.5%)	0	2 (1.3%)	0	0	0	5 (2.1%)	0
顔面浮腫	0	0	1 (1.8%)	1 (1.8%)	2 (1.3%)	0	0	0	3 (1.3%)	1 (0.4%)
全身性浮腫	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
浮腫	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
腋窩痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
医療機器の問題	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
顔面痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歩行障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
低体温	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
注入部位内出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
注射部位浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
注射部位反応	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
限局性浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腫瘤	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
恥骨上痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
急性期反応	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	8 (34.8%)	1 (4.3%)	32 (58.2%)	1 (1.8%)	95 (60.9%)	8 (5.1%)	2 (66.7%)	0	137 (57.8%)	10 (4.2%)
咳嗽	5 (21.7%)	0	12 (21.8%)	0	31 (19.9%)	0	1 (33.3%)	0	49 (20.7%)	0
鼻閉	0	0	5 (9.1%)	0	25 (16.0%)	0	1 (33.3%)	0	31 (13.1%)	0
呼吸困難	1 (4.3%)	0	11 (20.0%)	0	22 (14.1%)	1 (0.6%)	0	0	34 (14.3%)	1 (0.4%)
口腔咽頭痛	0	0	3 (5.5%)	0	15 (9.6%)	0	0	0	18 (7.6%)	0
アレルギー性鼻炎	1 (4.3%)	0	12 (21.8%)	0	11 (7.1%)	0	0	0	24 (10.1%)	0
咽喉刺激感	0	0	1 (1.8%)	0	10 (6.4%)	0	0	0	11 (4.6%)	0
労作性呼吸困難	0	0	1 (1.8%)	0	8 (5.1%)	0	0	0	9 (3.8%)	0
鼻出血	0	0	2 (3.6%)	0	8 (5.1%)	0	0	0	10 (4.2%)	0
湿性咳嗽	0	0	4 (7.3%)	0	8 (5.1%)	0	0	0	12 (5.1%)	0
喘鳴	0	0	1 (1.8%)	0	6 (3.8%)	0	0	0	7 (3.0%)	0
気管支痙攣	1 (4.3%)	1 (4.3%)	1 (1.8%)	0	5 (3.2%)	2 (1.3%)	1 (33.3%)	0	8 (3.4%)	3 (1.3%)
胸水	0	0	1 (1.8%)	1 (1.8%)	4 (2.6%)	0	0	0	5 (2.1%)	1 (0.4%)
副鼻腔うっ血	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
くしゃみ	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
低酸素症	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
咽喉絞扼感	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
上気道咳症候群	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
呼吸不全	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
急性肺水腫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
アレルギー性咳嗽	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
慢性閉塞性肺疾患	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
発声障害	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
上気道分泌増加	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
喉頭浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
アレルギー性喉頭炎	0	0	3 (5.5%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
鼻部障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
誤嚥性肺炎	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
肺うっ血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
肺塞栓症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
肺水腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
鼻漏	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
喉頭の炎症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
筋骨格系および結合組織障害	6 (26.1%)	1 (4.3%)	30 (54.5%)	5 (9.1%)	89 (57.1%)	12 (7.7%)	1 (33.3%)	0	126 (53.2%)	18 (7.6%)
背部痛	1 (4.3%)	0	8 (14.5%)	3 (5.5%)	33 (21.2%)	3 (1.9%)	1 (33.3%)	0	43 (18.1%)	6 (2.5%)
関節痛	2 (8.7%)	0	5 (9.1%)	0	25 (16.0%)	0	0	0	32 (13.5%)	0
四肢痛	1 (4.3%)	0	1 (1.8%)	0	23 (14.7%)	1 (0.6%)	0	0	25 (10.5%)	1 (0.4%)
筋骨格系胸痛	0	0	5 (9.1%)	0	16 (10.3%)	2 (1.3%)	0	0	21 (8.9%)	2 (0.8%)
骨痛	1 (4.3%)	0	6 (10.9%)	0	14 (9.0%)	1 (0.6%)	0	0	21 (8.9%)	1 (0.4%)
筋骨格痛	0	0	3 (5.5%)	1 (1.8%)	13 (8.3%)	1 (0.6%)	0	0	16 (6.8%)	2 (0.8%)
筋痙縮	0	0	2 (3.6%)	0	10 (6.4%)	0	0	0	12 (5.1%)	0
筋肉痛	0	0	6 (10.9%)	0	6 (3.8%)	0	0	0	12 (5.1%)	0
肢径部痛	0	0	0	0	4 (2.6%)	1 (0.6%)	0	0	4 (1.7%)	1 (0.4%)
頚部痛	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
病的骨折	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
脊椎痛	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
筋力低下	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
骨炎	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
脊柱管狭窄症	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
骨侵食	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
骨病変	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
関節可動域低下	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
四肢不快感	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
運動性低下	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋肉疲労	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋骨格不快感	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
顎骨壊死	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
顎痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腱炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
側腹部痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
脊柱後弯症	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
筋骨格硬直	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
ミオパチー	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
骨壊死	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
骨粗鬆症性骨折	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	9 (39.1%)	0	27 (49.1%)	1 (1.8%)	85 (54.5%)	3 (1.9%)	2 (66.7%)	0	123 (51.9%)	4 (1.7%)
悪心	3 (13.0%)	0	10 (18.2%)	1 (1.8%)	40 (25.6%)	0	0	0	53 (22.4%)	1 (0.4%)
下痢	2 (8.7%)	0	13 (23.6%)	0	24 (15.4%)	0	1 (33.3%)	0	40 (16.9%)	0
便秘	1 (4.3%)	0	6 (10.9%)	0	22 (14.1%)	0	0	0	29 (12.2%)	0
嘔吐	1 (4.3%)	0	8 (14.5%)	1 (1.8%)	20 (12.8%)	0	1 (33.3%)	0	30 (12.7%)	1 (0.4%)
腹痛	2 (8.7%)	0	1 (1.8%)	0	9 (5.8%)	2 (1.3%)	0	0	12 (5.1%)	2 (0.8%)
消化不良	0	0	3 (5.5%)	0	4 (2.6%)	0	0	0	7 (3.0%)	0
口内炎	0	0	3 (5.5%)	0	4 (2.6%)	0	0	0	7 (3.0%)	0
歯痛	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
腹部膨満	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
放屁	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
口の感覚鈍麻	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
腹部不快感	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
上腹部痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
便失禁	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
胃食道逆流性疾患	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
歯肉出血	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
口腔内痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
水疱性出血性口峡炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
大腸炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
憩室	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
嚥下障害	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
胃炎	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
歯肉腫脹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
舌炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
血便排泄	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
痔核	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
大腸閉塞	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
口唇出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
口腔内潰瘍形成	1 (4.3%)	0	0	0	1 (0.6%)	0	0	0	2 (0.8%)	0
口腔粘膜変色	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
膵炎	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
口の錯感覚	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
舌苔	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歯の発育障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歯の障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
アフタ性口内炎	0	0	3 (5.5%)	0	0	0	0	0	3 (1.3%)	0
口内乾燥	1 (4.3%)	0	2 (3.6%)	0	0	0	0	0	3 (1.3%)	0
舌痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
口唇浮腫	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
食道炎	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
感染症および寄生虫症	7 (30.4%)	0	32 (58.2%)	4 (7.3%)	85 (54.5%)	15 (9.6%)	1 (33.3%)	1 (33.3%)	125 (52.7%)	20 (8.4%)
上気道感染	0	0	12 (21.8%)	0	27 (17.3%)	1 (0.6%)	0	0	39 (16.5%)	1 (0.4%)
鼻咽頭炎	2 (8.7%)	0	9 (16.4%)	0	18 (11.5%)	0	1 (33.3%)	0	30 (12.7%)	0
肺炎	1 (4.3%)	0	4 (7.3%)	3 (5.5%)	13 (8.3%)	8 (5.1%)	0	0	18 (7.6%)	11 (4.6%)
副鼻腔炎	1 (4.3%)	0	1 (1.8%)	0	9 (5.8%)	0	0	0	11 (4.6%)	0
尿路感染	0	0	2 (3.6%)	0	7 (4.5%)	0	1 (33.3%)	1 (33.3%)	10 (4.2%)	1 (0.4%)
気管支炎	0	0	0	0	5 (3.2%)	1 (0.6%)	0	0	5 (2.1%)	1 (0.4%)
結膜炎	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
帯状疱疹	1 (4.3%)	0	4 (7.3%)	0	3 (1.9%)	2 (1.3%)	0	0	8 (3.4%)	2 (0.8%)
大葉性肺炎	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
口腔カンジダ症	0	0	3 (5.5%)	0	3 (1.9%)	0	0	0	6 (2.5%)	0
カンジダ感染	0	0	2 (3.6%)	0	2 (1.3%)	0	0	0	4 (1.7%)	0
単純ヘルペス	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
感染	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
インフルエンザ	0	0	3 (5.5%)	0	2 (1.3%)	0	0	0	5 (2.1%)	0
パラインフルエンザウイルス感染	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
咽頭炎	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
鼻炎	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
軟部組織感染	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
水痘	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0

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	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
蜂巣炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
膀胱炎	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
サイトメガロウイルス性脈絡網膜炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
医療機器関連感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
耳感染	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
胃腸炎	1 (4.3%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
ウイルス性胃腸炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
性器感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
麦粒腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
下気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
粘膜感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
眼部単純ヘルペス	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口腔真菌感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口腔ヘルペス	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
爪囲炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
レンサ球菌性肺炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腎盂腎炎	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
敗血症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
レンサ球菌感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歯感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
ウイルス性上気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
外陰腟真菌感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
菌血症	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
真菌感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
真菌性消化管感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
肺感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
メタニューモウイルス感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
ＲＳウイルス感染	0	0	2 (3.6%)	0	0	0	0	0	2 (0.8%)	0
細菌性尿路感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
ウイルス感染	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
外陰部腟カンジダ症	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0

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	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
血液およびリンパ系障害	9 (39.1%)	2 (8.7%)	21 (38.2%)	16 (29.1%)	76 (48.7%)	53 (34.0%)	0	0	106 (44.7%)	71 (30.0%)
貧血	4 (17.4%)	1 (4.3%)	12 (21.8%)	6 (10.9%)	39 (25.0%)	27 (17.3%)	0	0	55 (23.2%)	34 (14.3%)
好中球減少症	1 (4.3%)	1 (4.3%)	3 (5.5%)	1 (1.8%)	34 (21.8%)	19 (12.2%)	0	0	38 (16.0%)	21 (8.9%)
血小板減少症	3 (13.0%)	2 (8.7%)	10 (18.2%)	8 (14.5%)	31 (19.9%)	22 (14.1%)	0	0	44 (18.6%)	32 (13.5%)
白血球減少症	0	0	2 (3.6%)	0	14 (9.0%)	7 (4.5%)	0	0	16 (6.8%)	7 (3.0%)
リンパ球減少症	2 (8.7%)	0	7 (12.7%)	5 (9.1%)	9 (5.8%)	9 (5.8%)	0	0	18 (7.6%)	14 (5.9%)
ヘモグロビン血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
内出血発生の増加傾向	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
汎血球減少症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
赤血球凝集	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
溶血	3 (13.0%)	0	0	0	0	0	0	0	3 (1.3%)	0
単球減少症	3 (13.0%)	0	0	0	0	0	0	0	3 (1.3%)	0
代謝および栄養障害	2 (8.7%)	0	16 (29.1%)	7 (12.7%)	64 (41.0%)	13 (8.3%)	0	0	82 (34.6%)	20 (8.4%)
食欲減退	1 (4.3%)	0	5 (9.1%)	0	23 (14.7%)	1 (0.6%)	0	0	29 (12.2%)	1 (0.4%)
高カルシウム血症	0	0	4 (7.3%)	2 (3.6%)	18 (11.5%)	5 (3.2%)	0	0	22 (9.3%)	7 (3.0%)
高血糖	0	0	4 (7.3%)	1 (1.8%)	13 (8.3%)	4 (2.6%)	0	0	17 (7.2%)	5 (2.1%)
低カリウム血症	0	0	4 (7.3%)	1 (1.8%)	12 (7.7%)	1 (0.6%)	0	0	16 (6.8%)	2 (0.8%)
低マグネシウム血症	0	0	2 (3.6%)	0	9 (5.8%)	0	0	0	11 (4.6%)	0
低ナトリウム血症	1 (4.3%)	0	6 (10.9%)	3 (5.5%)	8 (5.1%)	0	0	0	15 (6.3%)	3 (1.3%)
高カリウム血症	0	0	1 (1.8%)	0	5 (3.2%)	1 (0.6%)	0	0	6 (2.5%)	1 (0.4%)
酵素異常	1 (4.3%)	0	3 (5.5%)	0	4 (2.6%)	0	0	0	8 (3.4%)	0
高尿酸血症	0	0	2 (3.6%)	1 (1.8%)	4 (2.6%)	1 (0.6%)	0	0	6 (2.5%)	2 (0.8%)
低アルブミン血症	0	0	4 (7.3%)	0	4 (2.6%)	0	0	0	8 (3.4%)	0
低カルシウム血症	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
糖尿病	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
高ナトリウム血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
高リン酸塩血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
低血糖症	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
栄養障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
ビタミンＢ１２欠乏	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
体液貯留	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
低リン酸血症	0	0	2 (3.6%)	0	0	0	0	0	2 (0.8%)	0
代謝性アシドーシス	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0

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	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
神経系障害	6 (26.1%)	0	25 (45.5%)	3 (5.5%)	50 (32.1%)	7 (4.5%)	0	0	81 (34.2%)	10 (4.2%)
頭痛	2 (8.7%)	0	4 (7.3%)	0	15 (9.6%)	2 (1.3%)	0	0	21 (8.9%)	2 (0.8%)
浮動性めまい	3 (13.0%)	0	6 (10.9%)	0	13 (8.3%)	0	0	0	22 (9.3%)	0
末梢性感覚ニューロパチー	1 (4.3%)	0	7 (12.7%)	0	6 (3.8%)	0	0	0	14 (5.9%)	0
感覚鈍麻	1 (4.3%)	0	1 (1.8%)	0	5 (3.2%)	0	0	0	7 (3.0%)	0
傾眠	0	0	1 (1.8%)	0	5 (3.2%)	1 (0.6%)	0	0	6 (2.5%)	1 (0.4%)
振戦	0	0	2 (3.6%)	0	4 (2.6%)	0	0	0	6 (2.5%)	0
味覚異常	0	0	4 (7.3%)	0	3 (1.9%)	0	0	0	7 (3.0%)	0
錯感覚	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
下肢静止不能症候群	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
意識変容状態	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手根管症候群	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
意識レベルの低下	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
脳症	0	0	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
知覚過敏	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
嗜眠	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
記憶障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
神経痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
嗅覚錯誤	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脊髄圧迫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
失神	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
第７脳神経麻痺	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
無感覚	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
坐骨神経痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
第６脳神経麻痺	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
皮膚および皮下組織障害	3 (13.0%)	0	16 (29.1%)	0	35 (22.4%)	0	0	0	54 (22.8%)	0
そう痒症	1 (4.3%)	0	4 (7.3%)	0	5 (3.2%)	0	0	0	10 (4.2%)	0
多汗症	0	0	3 (5.5%)	0	3 (1.9%)	0	0	0	6 (2.5%)	0
寝汗	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
発疹	2 (8.7%)	0	7 (12.7%)	0	3 (1.9%)	0	0	0	12 (5.1%)	0
斑状丘疹状皮疹	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
皮膚嚢腫	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
ざ瘡様皮膚炎	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
接触性皮膚炎	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0

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	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
皮膚乾燥	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
湿疹	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
紅斑	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
点状出血	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
褥瘡性潰瘍	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
薬疹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮脂欠乏性湿疹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手掌・足底発赤知覚不全症候群	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
色素沈着障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
全身性そう痒症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
乾癬	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
斑状皮疹	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
丘疹性皮疹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚剥脱	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚色素過剰	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚潰瘍	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
蕁麻疹	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
脱毛症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
爪変色	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
血管障害	5 (21.7%)	0	14 (25.5%)	4 (7.3%)	29 (18.6%)	10 (6.4%)	0	0	48 (20.3%)	14 (5.9%)
高血圧	2 (8.7%)	0	10 (18.2%)	4 (7.3%)	15 (9.6%)	8 (5.1%)	0	0	27 (11.4%)	12 (5.1%)
低血圧	2 (8.7%)	0	1 (1.8%)	0	7 (4.5%)	1 (0.6%)	0	0	10 (4.2%)	1 (0.4%)
血腫	0	0	1 (1.8%)	0	4 (2.6%)	0	0	0	5 (2.1%)	0
潮紅	2 (8.7%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	6 (2.5%)	0
深部静脈血栓症	0	0	1 (1.8%)	0	2 (1.3%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
ほてり	0	0	2 (3.6%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
表在性静脈炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
レイノー現象	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
四肢静脈血栓症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
傷害、中毒および処置合併症	1 (4.3%)	1 (4.3%)	3 (5.5%)	1 (1.8%)	28 (17.9%)	5 (3.2%)	0	0	32 (13.5%)	7 (3.0%)
挫傷	0	0	1 (1.8%)	0	5 (3.2%)	0	0	0	6 (2.5%)	0
転倒	0	0	0	0	5 (3.2%)	1 (0.6%)	0	0	5 (2.1%)	1 (0.4%)
肋骨骨折	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
上腕骨骨折	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
裂傷	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
腰椎骨折	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
脊椎圧迫骨折	1 (4.3%)	1 (4.3%)	0	0	2 (1.3%)	2 (1.3%)	0	0	3 (1.3%)	3 (1.3%)
骨挫傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
擦過傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
足骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
肉離れ	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
眼窩周囲挫傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
処置による疼痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
硬膜下血腫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
腱断裂	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
輸血反応	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
上肢骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
創傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手首関節骨折	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
四肢外傷性切断	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
精神障害	0	0	9 (16.4%)	0	28 (17.9%)	4 (2.6%)	0	0	37 (15.6%)	4 (1.7%)
不安	0	0	0	0	9 (5.8%)	0	0	0	9 (3.8%)	0
錯乱状態	0	0	1 (1.8%)	0	7 (4.5%)	2 (1.3%)	0	0	8 (3.4%)	2 (0.8%)
不眠症	0	0	4 (7.3%)	0	7 (4.5%)	0	0	0	11 (4.6%)	0
激越	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
譫妄	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
うつ病	0	0	2 (3.6%)	0	3 (1.9%)	0	0	0	5 (2.1%)	0
気分変化	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
摂食障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
幻覚	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
精神状態変化	0	0	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
気分動揺	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
神経過敏	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
腎および尿路障害	11 (47.8%)	0	15 (27.3%)	2 (3.6%)	25 (16.0%)	6 (3.8%)	1 (33.3%)	0	52 (21.9%)	8 (3.4%)
腎機能障害	1 (4.3%)	0	8 (14.5%)	1 (1.8%)	11 (7.1%)	2 (1.3%)	0	0	20 (8.4%)	3 (1.3%)
排尿困難	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
頻尿	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
蛋白尿	10 (43.5%)	0	3 (5.5%)	0	2 (1.3%)	1 (0.6%)	1 (33.3%)	0	16 (6.8%)	1 (0.4%)
尿閉	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
非感染性膀胱炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
血尿	0	0	2 (3.6%)	0	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
夜間頻尿	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腎不全	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
腎静脈血栓症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
尿失禁	0	0	3 (5.5%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
尿路閉塞	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
高窒素血症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
膀胱痙縮	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
尿意切迫	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
急性腎不全	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
臨床検査	10 (43.5%)	2 (8.7%)	7 (12.7%)	2 (3.6%)	20 (12.8%)	4 (2.6%)	0	0	37 (15.6%)	8 (3.4%)
体重減少	0	0	4 (7.3%)	0	7 (4.5%)	1 (0.6%)	0	0	11 (4.6%)	1 (0.4%)
体重増加	0	0	1 (1.8%)	0	4 (2.6%)	0	0	0	5 (2.1%)	0
交差適合試験不適合	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
国際標準比増加	0	0	1 (1.8%)	1 (1.8%)	3 (1.9%)	1 (0.6%)	0	0	4 (1.7%)	2 (0.8%)
血中クレアチンホスホキナーゼ増加	1 (4.3%)	1 (4.3%)	0	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
血中テストステロン減少	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図異常Q波	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図ＱＴ延長	5 (21.7%)	1 (4.3%)	0	0	1 (0.6%)	0	0	0	6 (2.5%)	1 (0.4%)
心電図異常Ｔ波	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
酸素飽和度異常	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
尿量減少	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
遊離ヘモグロビン陽性	5 (21.7%)	0	0	0	0	0	0	0	5 (2.1%)	0
ハプトグロビン減少	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
心拍数増加	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
リンパ球数減少	1 (4.3%)	0	1 (1.8%)	1 (1.8%)	0	0	0	0	2 (0.8%)	1 (0.4%)
眼障害	1 (4.3%)	0	10 (18.2%)	1 (1.8%)	13 (8.3%)	0	0	0	24 (10.1%)	1 (0.4%)
霧視	0	0	2 (3.6%)	0	7 (4.5%)	0	0	0	9 (3.8%)	0
眼乾燥	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
眼そう痒症	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
眼充血	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
白内障	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
結膜出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
複視	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
睫毛乱生	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
眼部腫脹	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
眼瞼機能障害	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
眼瞼下垂	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
眼瞼発疹	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
光視症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
視力障害	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
硝子体浮遊物	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
心臓障害	4 (17.4%)	0	2 (3.6%)	0	11 (7.1%)	2 (1.3%)	0	0	17 (7.2%)	2 (0.8%)
動悸	1 (4.3%)	0	0	0	5 (3.2%)	0	0	0	6 (2.5%)	0
洞性頻脈	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
頻脈	2 (8.7%)	0	1 (1.8%)	0	2 (1.3%)	0	0	0	5 (2.1%)	0
狭心症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
心房粗動	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
徐脈	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
左脚ブロック	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
うっ血性心不全	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心肺停止	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心房細動	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
上室性期外収縮	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
肝胆道系障害	1 (4.3%)	1 (4.3%)	4 (7.3%)	0	8 (5.1%)	2 (1.3%)	0	0	13 (5.5%)	3 (1.3%)
肝機能異常	1 (4.3%)	1 (4.3%)	3 (5.5%)	0	6 (3.8%)	1 (0.6%)	0	0	10 (4.2%)	2 (0.8%)
肝不全	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
高ビリルビン血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
黄疸	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脂肪肝	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3%)	0	3 (5.5%)	1 (1.8%)	6 (3.8%)	0	0	0	10 (4.2%)	1 (0.4%)

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
基底細胞癌	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
腫瘍疼痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
肛門直腸ヒト乳頭腫ウイルス感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚癌	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚良性新生物	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
形質細胞性白血病	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
皮膚乳頭腫	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
耳および迷路障害	0	0	3 (5.5%)	0	5 (3.2%)	0	0	0	8 (3.4%)	0
耳痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
耳の障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
耳鳴	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
回転性めまい	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
耳垢栓塞	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
耳不快感	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
生殖系および乳房障害	0	0	3 (5.5%)	1 (1.8%)	4 (2.6%)	0	1 (33.3%)	0	8 (3.4%)	1 (0.4%)
生殖器痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
乳頭痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
性器浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
陰茎浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腟出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
血精液症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
骨盤痛	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
前立腺炎	0	0	1 (1.8%)	0	0	0	1 (33.3%)	0	2 (0.8%)	0
免疫系障害	3 (13.0%)	1 (4.3%)	2 (3.6%)	1 (1.8%)	3 (1.9%)	0	0	0	8 (3.4%)	2 (0.8%)
アレルギー性浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
サイトカイン放出症候群	1 (4.3%)	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	3 (1.3%)	1 (0.4%)
季節性アレルギー	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
過敏症	2 (8.7%)	1 (4.3%)	1 (1.8%)	0	0	0	0	0	3 (1.3%)	1 (0.4%)
先天性、家族性および遺伝性障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
あざ	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02C: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02C.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae02c.sas] 16MAR2015, 12:02

表 2.7.4-付録-42 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with TEAEs	22 (95.7%)	21 (91.3%)	55 (100.0%)	48 (87.3%)	154 (98.7%)	120 (76.9%)	3 (100.0%)	3 (100.0%)	234 (98.7%)	192 (81.0%)
MedDRA system organ class/Preferred term										
一般・全身障害および投与部位の状態	11 (47.8%)	9 (39.1%)	36 (65.5%)	20 (36.4%)	106 (67.9%)	57 (36.5%)	0	0	153 (64.6%)	86 (36.3%)
疲労	2 (8.7%)	2 (8.7%)	20 (36.4%)	11 (20.0%)	59 (37.8%)	30 (19.2%)	0	0	81 (34.2%)	43 (18.1%)
発熱	8 (34.8%)	6 (26.1%)	20 (36.4%)	8 (14.5%)	29 (18.6%)	9 (5.8%)	0	0	57 (24.1%)	23 (9.7%)
悪寒	0	0	9 (16.4%)	7 (12.7%)	16 (10.3%)	13 (8.3%)	0	0	25 (10.5%)	20 (8.4%)
無力症	0	0	3 (5.5%)	0	12 (7.7%)	4 (2.6%)	0	0	15 (6.3%)	4 (1.7%)
末梢性浮腫	1 (4.3%)	0	5 (9.1%)	2 (3.6%)	11 (7.1%)	1 (0.6%)	0	0	17 (7.2%)	3 (1.3%)
胸痛	2 (8.7%)	0	1 (1.8%)	0	9 (5.8%)	2 (1.3%)	0	0	12 (5.1%)	2 (0.8%)
疼痛	0	0	2 (3.6%)	2 (3.6%)	8 (5.1%)	1 (0.6%)	0	0	10 (4.2%)	3 (1.3%)
インフルエンザ様疾患	3 (13.0%)	3 (13.0%)	1 (1.8%)	1 (1.8%)	7 (4.5%)	5 (3.2%)	0	0	11 (4.6%)	9 (3.8%)
非心臓性胸痛	0	0	2 (3.6%)	1 (1.8%)	6 (3.8%)	0	0	0	8 (3.4%)	1 (0.4%)
全身健康状態低下	0	0	1 (1.8%)	0	5 (3.2%)	0	0	0	6 (2.5%)	0
注射部位内出血	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
局所腫脹	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
倦怠感	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
胸部不快感	0	0	3 (5.5%)	2 (3.6%)	2 (1.3%)	2 (1.3%)	0	0	5 (2.1%)	4 (1.7%)
顔面浮腫	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
全身性浮腫	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
浮腫	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
腋窩痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
医療機器の問題	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
顔面痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歩行障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
低体温	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
注入部位内出血	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
注射部位浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
注射部位反応	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
限局性浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腫瘤	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
恥骨上痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
急性期反応	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
呼吸器、胸郭および縦隔障害	8 (34.8%)	4 (17.4%)	32 (58.2%)	26 (47.3%)	95 (60.9%)	61 (39.1%)	2 (66.7%)	2 (66.7%)	137 (57.8%)	93 (39.2%)
咳嗽	5 (21.7%)	1 (4.3%)	12 (21.8%)	7 (12.7%)	31 (19.9%)	15 (9.6%)	1 (33.3%)	1 (33.3%)	49 (20.7%)	24 (10.1%)
鼻閉	0	0	5 (9.1%)	3 (5.5%)	25 (16.0%)	17 (10.9%)	1 (33.3%)	1 (33.3%)	31 (13.1%)	21 (8.9%)
呼吸困難	1 (4.3%)	1 (4.3%)	11 (20.0%)	6 (10.9%)	22 (14.1%)	10 (6.4%)	0	0	34 (14.3%)	17 (7.2%)
口腔咽頭痛	0	0	3 (5.5%)	0	15 (9.6%)	3 (1.9%)	0	0	18 (7.6%)	3 (1.3%)
アレルギー性鼻炎	1 (4.3%)	1 (4.3%)	12 (21.8%)	12 (21.8%)	11 (7.1%)	10 (6.4%)	0	0	24 (10.1%)	23 (9.7%)
咽喉刺激感	0	0	1 (1.8%)	0	10 (6.4%)	9 (5.8%)	0	0	11 (4.6%)	9 (3.8%)
労作性呼吸困難	0	0	1 (1.8%)	0	8 (5.1%)	2 (1.3%)	0	0	9 (3.8%)	2 (0.8%)
鼻出血	0	0	2 (3.6%)	0	8 (5.1%)	0	0	0	10 (4.2%)	0
湿性咳嗽	0	0	4 (7.3%)	1 (1.8%)	8 (5.1%)	2 (1.3%)	0	0	12 (5.1%)	3 (1.3%)
喘鳴	0	0	1 (1.8%)	1 (1.8%)	6 (3.8%)	3 (1.9%)	0	0	7 (3.0%)	4 (1.7%)
気管支痙攣	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	5 (3.2%)	4 (2.6%)	1 (33.3%)	1 (33.3%)	8 (3.4%)	7 (3.0%)
胸水	0	0	1 (1.8%)	0	4 (2.6%)	0	0	0	5 (2.1%)	0
副鼻腔うっ血	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
くしゃみ	0	0	0	0	4 (2.6%)	3 (1.9%)	0	0	4 (1.7%)	3 (1.3%)
低酸素症	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
咽喉絞扼感	0	0	0	0	3 (1.9%)	3 (1.9%)	0	0	3 (1.3%)	3 (1.3%)
上気道咳症候群	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
呼吸不全	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
急性肺水腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
アレルギー性咳嗽	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
慢性閉塞性肺疾患	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
発声障害	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	2 (0.8%)	1 (0.4%)
上気道分泌増加	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
喉頭浮腫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
アレルギー性喉頭炎	0	0	3 (5.5%)	3 (5.5%)	1 (0.6%)	1 (0.6%)	0	0	4 (1.7%)	4 (1.7%)
鼻部障害	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
誤嚥性肺炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
肺うっ血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
肺塞栓症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
肺水腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
鼻漏	0	0	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
喉頭の炎症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
筋骨格系および結合組織障害	6 (26.1%)	0	30 (54.5%)	8 (14.5%)	89 (57.1%)	18 (11.5%)	1 (33.3%)	0	126 (53.2%)	26 (11.0%)
背部痛	1 (4.3%)	0	8 (14.5%)	1 (1.8%)	33 (21.2%)	5 (3.2%)	1 (33.3%)	0	43 (18.1%)	6 (2.5%)
関節痛	2 (8.7%)	0	5 (9.1%)	1 (1.8%)	25 (16.0%)	2 (1.3%)	0	0	32 (13.5%)	3 (1.3%)
四肢痛	1 (4.3%)	0	1 (1.8%)	0	23 (14.7%)	2 (1.3%)	0	0	25 (10.5%)	2 (0.8%)
筋骨格系胸痛	0	0	5 (9.1%)	1 (1.8%)	16 (10.3%)	1 (0.6%)	0	0	21 (8.9%)	2 (0.8%)
骨痛	1 (4.3%)	0	6 (10.9%)	0	14 (9.0%)	2 (1.3%)	0	0	21 (8.9%)	2 (0.8%)
筋骨格痛	0	0	3 (5.5%)	1 (1.8%)	13 (8.3%)	0	0	0	16 (6.8%)	1 (0.4%)
筋痙縮	0	0	2 (3.6%)	1 (1.8%)	10 (6.4%)	5 (3.2%)	0	0	12 (5.1%)	6 (2.5%)
筋肉痛	0	0	6 (10.9%)	2 (3.6%)	6 (3.8%)	2 (1.3%)	0	0	12 (5.1%)	4 (1.7%)
肢径部痛	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
頚部痛	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
病的骨折	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
脊椎痛	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
筋力低下	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
骨炎	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
脊柱管狭窄症	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
骨侵食	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
骨病変	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
関節可動域低下	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
四肢不快感	0	0	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
運動性低下	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋肉疲労	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋骨格不快感	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
顎骨壊死	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
顎痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腱炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
側腹部痛	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
脊柱後弯症	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
筋骨格硬直	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
ミオパチー	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
骨壊死	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
骨粗鬆症性骨折	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
胃腸障害	9 (39.1%)	3 (13.0%)	27 (49.1%)	13 (23.6%)	85 (54.5%)	34 (21.8%)	2 (66.7%)	1 (33.3%)	123 (51.9%)	51 (21.5%)
悪心	3 (13.0%)	2 (8.7%)	10 (18.2%)	4 (7.3%)	40 (25.6%)	22 (14.1%)	0	0	53 (22.4%)	28 (11.8%)
下痢	2 (8.7%)	0	13 (23.6%)	4 (7.3%)	24 (15.4%)	7 (4.5%)	1 (33.3%)	0	40 (16.9%)	11 (4.6%)
便秘	1 (4.3%)	0	6 (10.9%)	1 (1.8%)	22 (14.1%)	7 (4.5%)	0	0	29 (12.2%)	8 (3.4%)
嘔吐	1 (4.3%)	0	8 (14.5%)	6 (10.9%)	20 (12.8%)	11 (7.1%)	1 (33.3%)	1 (33.3%)	30 (12.7%)	18 (7.6%)
腹痛	2 (8.7%)	0	1 (1.8%)	0	9 (5.8%)	0	0	0	12 (5.1%)	0
消化不良	0	0	3 (5.5%)	3 (5.5%)	4 (2.6%)	0	0	0	7 (3.0%)	3 (1.3%)
口内炎	0	0	3 (5.5%)	1 (1.8%)	4 (2.6%)	1 (0.6%)	0	0	7 (3.0%)	2 (0.8%)
歯痛	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
腹部膨満	0	0	1 (1.8%)	0	3 (1.9%)	1 (0.6%)	0	0	4 (1.7%)	1 (0.4%)
放屁	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
口の感覚鈍麻	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
腹部不快感	0	0	1 (1.8%)	0	2 (1.3%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
上腹部痛	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
便失禁	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
胃食道逆流性疾患	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
歯肉出血	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
口腔内痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
水疱性出血性口峡炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
大腸炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
憩室	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
嚥下障害	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
胃炎	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
歯肉腫脹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
舌炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
血便排泄	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
痔核	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
大腸閉塞	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口唇出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口腔内潰瘍形成	1 (4.3%)	0	0	0	1 (0.6%)	0	0	0	2 (0.8%)	0
口腔粘膜変色	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
膵炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口の錯感覚	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
舌苔	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歯の発育障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歯の障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
アフタ性口内炎	0	0	3 (5.5%)	0	0	0	0	0	3 (1.3%)	0
口内乾燥	1 (4.3%)	1 (4.3%)	2 (3.6%)	1 (1.8%)	0	0	0	0	3 (1.3%)	2 (0.8%)
舌痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
口唇浮腫	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
食道炎	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
感染症および寄生虫症	7 (30.4%)	0	32 (58.2%)	8 (14.5%)	85 (54.5%)	22 (14.1%)	1 (33.3%)	1 (33.3%)	125 (52.7%)	31 (13.1%)
上気道感染	0	0	12 (21.8%)	6 (10.9%)	27 (17.3%)	4 (2.6%)	0	0	39 (16.5%)	10 (4.2%)
鼻咽頭炎	2 (8.7%)	0	9 (16.4%)	0	18 (11.5%)	1 (0.6%)	1 (33.3%)	1 (33.3%)	30 (12.7%)	2 (0.8%)
肺炎	1 (4.3%)	0	4 (7.3%)	0	13 (8.3%)	6 (3.8%)	0	0	18 (7.6%)	6 (2.5%)
副鼻腔炎	1 (4.3%)	0	1 (1.8%)	0	9 (5.8%)	3 (1.9%)	0	0	11 (4.6%)	3 (1.3%)
尿路感染	0	0	2 (3.6%)	0	7 (4.5%)	0	1 (33.3%)	0	10 (4.2%)	0
気管支炎	0	0	0	0	5 (3.2%)	0	0	0	5 (2.1%)	0
結膜炎	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
帯状疱疹	1 (4.3%)	0	4 (7.3%)	1 (1.8%)	3 (1.9%)	3 (1.9%)	0	0	8 (3.4%)	4 (1.7%)
大葉性肺炎	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
口腔カンジダ症	0	0	3 (5.5%)	1 (1.8%)	3 (1.9%)	1 (0.6%)	0	0	6 (2.5%)	2 (0.8%)
カンジダ感染	0	0	2 (3.6%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	4 (1.7%)	3 (1.3%)
単純ヘルペス	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
感染	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
インフルエンザ	0	0	3 (5.5%)	0	2 (1.3%)	0	0	0	5 (2.1%)	0
パラインフルエンザウイルス感染	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
咽頭炎	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
鼻炎	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
軟部組織感染	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
水痘	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
蜂巣炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
膀胱炎	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
サイトメガロウイルス性脈絡網膜炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
医療機器関連感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
耳感染	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
胃腸炎	1 (4.3%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
ウイルス性胃腸炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
性器感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
麦粒腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
下気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
粘膜感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
眼部単純ヘルペス	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口腔真菌感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口腔ヘルペス	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
爪囲炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
レンサ球菌性肺炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腎盂腎炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
敗血症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
レンサ球菌感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
歯感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
ウイルス性上気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
外陰腟真菌感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
菌血症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
真菌感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
真菌性消化管感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
肺感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
メタニューモウイルス感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
ＲＳウイルス感染	0	0	2 (3.6%)	0	0	0	0	0	2 (0.8%)	0
細菌性尿路感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
ウイルス感染	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
外陰部腟カンジダ症	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
血液およびリンパ系障害	9 (39.1%)	8 (34.8%)	21 (38.2%)	13 (23.6%)	76 (48.7%)	40 (25.6%)	0	0	106 (44.7%)	61 (25.7%)
貧血	4 (17.4%)	4 (17.4%)	12 (21.8%)	8 (14.5%)	39 (25.0%)	19 (12.2%)	0	0	55 (23.2%)	31 (13.1%)
好中球減少症	1 (4.3%)	1 (4.3%)	3 (5.5%)	1 (1.8%)	34 (21.8%)	17 (10.9%)	0	0	38 (16.0%)	19 (8.0%)
血小板減少症	3 (13.0%)	2 (8.7%)	10 (18.2%)	3 (5.5%)	31 (19.9%)	17 (10.9%)	0	0	44 (18.6%)	22 (9.3%)
白血球減少症	0	0	2 (3.6%)	2 (3.6%)	14 (9.0%)	10 (6.4%)	0	0	16 (6.8%)	12 (5.1%)

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
リンパ球減少症	2 (8.7%)	2 (8.7%)	7 (12.7%)	5 (9.1%)	9 (5.8%)	9 (5.8%)	0	0	18 (7.6%)	16 (6.8%)
ヘモグロビン血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
内出血発生の増加傾向	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
汎血球減少症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
赤血球凝集	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
溶血	3 (13.0%)	3 (13.0%)	0	0	0	0	0	0	3 (1.3%)	3 (1.3%)
単球減少症	3 (13.0%)	3 (13.0%)	0	0	0	0	0	0	3 (1.3%)	3 (1.3%)
代謝および栄養障害	2 (8.7%)	1 (4.3%)	16 (29.1%)	7 (12.7%)	64 (41.0%)	16 (10.3%)	0	0	82 (34.6%)	24 (10.1%)
食欲減退	1 (4.3%)	0	5 (9.1%)	2 (3.6%)	23 (14.7%)	9 (5.8%)	0	0	29 (12.2%)	11 (4.6%)
高カルシウム血症	0	0	4 (7.3%)	0	18 (11.5%)	1 (0.6%)	0	0	22 (9.3%)	1 (0.4%)
高血糖	0	0	4 (7.3%)	2 (3.6%)	13 (8.3%)	1 (0.6%)	0	0	17 (7.2%)	3 (1.3%)
低カリウム血症	0	0	4 (7.3%)	0	12 (7.7%)	3 (1.9%)	0	0	16 (6.8%)	3 (1.3%)
低マグネシウム血症	0	0	2 (3.6%)	0	9 (5.8%)	2 (1.3%)	0	0	11 (4.6%)	2 (0.8%)
低ナトリウム血症	1 (4.3%)	0	6 (10.9%)	2 (3.6%)	8 (5.1%)	3 (1.9%)	0	0	15 (6.3%)	5 (2.1%)
高カリウム血症	0	0	1 (1.8%)	1 (1.8%)	5 (3.2%)	0	0	0	6 (2.5%)	1 (0.4%)
酵素異常	1 (4.3%)	1 (4.3%)	3 (5.5%)	0	4 (2.6%)	1 (0.6%)	0	0	8 (3.4%)	2 (0.8%)
高尿酸血症	0	0	2 (3.6%)	0	4 (2.6%)	0	0	0	6 (2.5%)	0
低アルブミン血症	0	0	4 (7.3%)	0	4 (2.6%)	0	0	0	8 (3.4%)	0
低カルシウム血症	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
糖尿病	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
高ナトリウム血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
高リン酸塩血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
低血糖症	0	0	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
栄養障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
ビタミンＢ１２欠乏	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
体液貯留	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
低リン酸血症	0	0	2 (3.6%)	1 (1.8%)	0	0	0	0	2 (0.8%)	1 (0.4%)
代謝性アシドーシス	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
神経系障害	6 (26.1%)	4 (17.4%)	25 (45.5%)	13 (23.6%)	50 (32.1%)	15 (9.6%)	0	0	81 (34.2%)	32 (13.5%)
頭痛	2 (8.7%)	1 (4.3%)	4 (7.3%)	2 (3.6%)	15 (9.6%)	6 (3.8%)	0	0	21 (8.9%)	9 (3.8%)
浮動性めまい	3 (13.0%)	2 (8.7%)	6 (10.9%)	2 (3.6%)	13 (8.3%)	3 (1.9%)	0	0	22 (9.3%)	7 (3.0%)
末梢性感覚ニューロパチー	1 (4.3%)	1 (4.3%)	7 (12.7%)	4 (7.3%)	6 (3.8%)	2 (1.3%)	0	0	14 (5.9%)	7 (3.0%)
感覚鈍麻	1 (4.3%)	0	1 (1.8%)	0	5 (3.2%)	0	0	0	7 (3.0%)	0
傾眠	0	0	1 (1.8%)	0	5 (3.2%)	0	0	0	6 (2.5%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
振戦	0	0	2 (3.6%)	0	4 (2.6%)	1 (0.6%)	0	0	6 (2.5%)	1 (0.4%)
味覚異常	0	0	4 (7.3%)	4 (7.3%)	3 (1.9%)	2 (1.3%)	0	0	7 (3.0%)	6 (2.5%)
錯感覚	0	0	1 (1.8%)	1 (1.8%)	3 (1.9%)	0	0	0	4 (1.7%)	1 (0.4%)
下肢静止不能症候群	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
意識変容状態	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手根管症候群	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
意識レベルの低下	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脳症	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	2 (0.8%)	1 (0.4%)
知覚過敏	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
嗜眠	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
記憶障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
神経痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
嗅覚錯誤	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脊髄圧迫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
失神	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
第７脳神経麻痺	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
無感覚	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
坐骨神経痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
第６脳神経麻痺	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
皮膚および皮下組織障害	3 (13.0%)	1 (4.3%)	16 (29.1%)	9 (16.4%)	35 (22.4%)	9 (5.8%)	0	0	54 (22.8%)	19 (8.0%)
そう痒症	1 (4.3%)	1 (4.3%)	4 (7.3%)	3 (5.5%)	5 (3.2%)	2 (1.3%)	0	0	10 (4.2%)	6 (2.5%)
多汗症	0	0	3 (5.5%)	2 (3.6%)	3 (1.9%)	1 (0.6%)	0	0	6 (2.5%)	3 (1.3%)
寝汗	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
発疹	2 (8.7%)	1 (4.3%)	7 (12.7%)	4 (7.3%)	3 (1.9%)	0	0	0	12 (5.1%)	5 (2.1%)
斑状丘疹状皮疹	0	0	1 (1.8%)	0	3 (1.9%)	1 (0.6%)	0	0	4 (1.7%)	1 (0.4%)
皮膚嚢腫	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
ざ瘡様皮膚炎	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
接触性皮膚炎	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
皮膚乾燥	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
湿疹	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
紅斑	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
点状出血	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
褥瘡性潰瘍	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
薬疹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
皮脂欠乏性湿疹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手掌・足底発赤知覚不全症候群	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
色素沈着障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
全身性そう痒症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
乾癬	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
斑状皮疹	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
丘疹性皮疹	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚剥脱	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚色素過剰	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚潰瘍	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
蕁麻疹	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
脱毛症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
爪変色	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
血管障害	5 (21.7%)	4 (17.4%)	14 (25.5%)	8 (14.5%)	29 (18.6%)	8 (5.1%)	0	0	48 (20.3%)	20 (8.4%)
高血圧	2 (8.7%)	1 (4.3%)	10 (18.2%)	4 (7.3%)	15 (9.6%)	4 (2.6%)	0	0	27 (11.4%)	9 (3.8%)
低血圧	2 (8.7%)	2 (8.7%)	1 (1.8%)	1 (1.8%)	7 (4.5%)	1 (0.6%)	0	0	10 (4.2%)	4 (1.7%)
血腫	0	0	1 (1.8%)	1 (1.8%)	4 (2.6%)	0	0	0	5 (2.1%)	1 (0.4%)
潮紅	2 (8.7%)	2 (8.7%)	1 (1.8%)	1 (1.8%)	3 (1.9%)	2 (1.3%)	0	0	6 (2.5%)	5 (2.1%)
深部静脈血栓症	0	0	1 (1.8%)	0	2 (1.3%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
ほてり	0	0	2 (3.6%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	2 (0.8%)
表在性静脈炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
レイノー現象	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
四肢静脈血栓症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
傷害、中毒および処置合併症	1 (4.3%)	0	3 (5.5%)	0	28 (17.9%)	0	0	0	32 (13.5%)	0
挫傷	0	0	1 (1.8%)	0	5 (3.2%)	0	0	0	6 (2.5%)	0
転倒	0	0	0	0	5 (3.2%)	0	0	0	5 (2.1%)	0
肋骨骨折	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
上腕骨骨折	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
裂傷	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
腰椎骨折	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
脊椎圧迫骨折	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
骨挫傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
擦過傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
足骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
肉離れ	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
眼窩周囲挫傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
処置による疼痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
硬膜下血腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腱断裂	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
輸血反応	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
上肢骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
創傷	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手首関節骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
四肢外傷性切断	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
精神障害	0	0	9 (16.4%)	0	28 (17.9%)	4 (2.6%)	0	0	37 (15.6%)	4 (1.7%)
不安	0	0	0	0	9 (5.8%)	2 (1.3%)	0	0	9 (3.8%)	2 (0.8%)
錯乱状態	0	0	1 (1.8%)	0	7 (4.5%)	1 (0.6%)	0	0	8 (3.4%)	1 (0.4%)
不眠症	0	0	4 (7.3%)	0	7 (4.5%)	0	0	0	11 (4.6%)	0
激越	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
譫妄	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
うつ病	0	0	2 (3.6%)	0	3 (1.9%)	0	0	0	5 (2.1%)	0
気分変化	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
摂食障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
幻覚	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
精神状態変化	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
気分動揺	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
神経過敏	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
腎および尿路障害	11 (47.8%)	4 (17.4%)	15 (27.3%)	2 (3.6%)	25 (16.0%)	3 (1.9%)	1 (33.3%)	1 (33.3%)	52 (21.9%)	10 (4.2%)
腎機能障害	1 (4.3%)	1 (4.3%)	8 (14.5%)	1 (1.8%)	11 (7.1%)	1 (0.6%)	0	0	20 (8.4%)	3 (1.3%)
排尿困難	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
頻尿	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
蛋白尿	10 (43.5%)	3 (13.0%)	3 (5.5%)	0	2 (1.3%)	0	1 (33.3%)	1 (33.3%)	16 (6.8%)	4 (1.7%)
尿閉	0	0	1 (1.8%)	0	2 (1.3%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
非感染性膀胱炎	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
血尿	0	0	2 (3.6%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
夜間頻尿	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
腎不全	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腎静脈血栓症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
尿失禁	0	0	3 (5.5%)	1 (1.8%)	1 (0.6%)	0	0	0	4 (1.7%)	1 (0.4%)
尿路閉塞	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
高窒素血症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
膀胱痙縮	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
尿意切迫	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
急性腎不全	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
臨床検査	10 (43.5%)	7 (30.4%)	7 (12.7%)	2 (3.6%)	20 (12.8%)	6 (3.8%)	0	0	37 (15.6%)	15 (6.3%)
体重減少	0	0	4 (7.3%)	1 (1.8%)	7 (4.5%)	1 (0.6%)	0	0	11 (4.6%)	2 (0.8%)
体重増加	0	0	1 (1.8%)	0	4 (2.6%)	1 (0.6%)	0	0	5 (2.1%)	1 (0.4%)
交差適合試験不適合	0	0	0	0	3 (1.9%)	3 (1.9%)	0	0	3 (1.3%)	3 (1.3%)
国際標準比増加	0	0	1 (1.8%)	0	3 (1.9%)	0	0	0	4 (1.7%)	0
血中クレアチンホスホキナーゼ増加	1 (4.3%)	1 (4.3%)	0	0	1 (0.6%)	0	0	0	2 (0.8%)	1 (0.4%)
血中テストステロン減少	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図異常Q波	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図ＱＴ延長	5 (21.7%)	3 (13.0%)	0	0	1 (0.6%)	0	0	0	6 (2.5%)	3 (1.3%)
心電図異常Ｔ波	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
酸素飽和度異常	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
尿量減少	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
遊離ヘモグロビン陽性	5 (21.7%)	4 (17.4%)	0	0	0	0	0	0	5 (2.1%)	4 (1.7%)
ハプトグロビン減少	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
心拍数増加	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
リンパ球数減少	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	0	0	0	0	2 (0.8%)	2 (0.8%)
眼障害	1 (4.3%)	0	10 (18.2%)	1 (1.8%)	13 (8.3%)	3 (1.9%)	0	0	24 (10.1%)	4 (1.7%)
霧視	0	0	2 (3.6%)	0	7 (4.5%)	1 (0.6%)	0	0	9 (3.8%)	1 (0.4%)
眼乾燥	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
眼そう痒症	0	0	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
眼充血	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
白内障	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
結膜出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
複視	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
睫毛乱生	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
眼部腫脹	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
眼瞼機能障害	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
眼瞼下垂	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
眼瞼発疹	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
光視症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
視力障害	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
硝子体浮遊物	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
心臓障害	4 (17.4%)	3 (13.0%)	2 (3.6%)	2 (3.6%)	11 (7.1%)	3 (1.9%)	0	0	17 (7.2%)	8 (3.4%)
動悸	1 (4.3%)	1 (4.3%)	0	0	5 (3.2%)	1 (0.6%)	0	0	6 (2.5%)	2 (0.8%)
洞性頻脈	0	0	1 (1.8%)	1 (1.8%)	2 (1.3%)	1 (0.6%)	0	0	3 (1.3%)	2 (0.8%)
頻脈	2 (8.7%)	2 (8.7%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	1 (0.6%)	0	0	5 (2.1%)	4 (1.7%)
狭心症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心房粗動	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
徐脈	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
左脚ブロック	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
うっ血性心不全	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心肺停止	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心房細動	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
上室性期外収縮	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
肝胆道系障害	1 (4.3%)	1 (4.3%)	4 (7.3%)	2 (3.6%)	8 (5.1%)	3 (1.9%)	0	0	13 (5.5%)	6 (2.5%)
肝機能異常	1 (4.3%)	1 (4.3%)	3 (5.5%)	2 (3.6%)	6 (3.8%)	2 (1.3%)	0	0	10 (4.2%)	5 (2.1%)
肝不全	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
高ビリルビン血症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
黄疸	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脂肪肝	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3%)	0	3 (5.5%)	0	6 (3.8%)	0	0	0	10 (4.2%)	0
基底細胞癌	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
腫瘍疼痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
肛門直腸ヒト乳頭腫ウイルス感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚癌	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚良性新生物	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0

TSFAE02A: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
形質細胞性白血病	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
皮膚乳頭腫	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
耳および迷路障害	0	0	3 (5.5%)	0	5 (3.2%)	2 (1.3%)	0	0	8 (3.4%)	2 (0.8%)
耳痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
耳の障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
耳鳴	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
回転性めまい	0	0	1 (1.8%)	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
耳垢栓塞	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
耳不快感	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
生殖系および乳房障害	0	0	3 (5.5%)	0	4 (2.6%)	0	1 (33.3%)	0	8 (3.4%)	0
生殖器痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
乳頭痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
性器浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
陰茎浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腟出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
血精液症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
骨盤痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
前立腺炎	0	0	1 (1.8%)	0	0	0	1 (33.3%)	0	2 (0.8%)	0
免疫系障害	3 (13.0%)	3 (13.0%)	2 (3.6%)	1 (1.8%)	3 (1.9%)	2 (1.3%)	0	0	8 (3.4%)	6 (2.5%)
アレルギー性浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
サイトカイン放出症候群	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	3 (1.3%)
季節性アレルギー	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
過敏症	2 (8.7%)	2 (8.7%)	1 (1.8%)	0	0	0	0	0	3 (1.3%)	2 (0.8%)
先天性、家族性および遺伝性障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
あざ	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-43 Number of Subjects with Treatment-emergent Adverse Events and Drug Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE10: Number of Subjects with Treatment-emergent Adverse Events and Drug Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

	TEAEs			Drug Related TEAEs (Study Drug)[a]		
	8 mg/kg	16 mg/kg	All groups	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9	4	5	9
Number of subjects with any TEAEs	4 (100.0%)	5 (100.0%)	9 (100.0%)	4 (100.0%)	5 (100.0%)	9 (100.0%)
MedDRA system organ class/preferred term						
感染症および寄生虫症	2 (50.0%)	3 (60.0%)	5 (55.6%)	1 (25.0%)	3 (60.0%)	4 (44.4%)
鼻咽頭炎	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	0	0
膀胱炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
咽頭炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
肺炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
上気道感染	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
アデノイド咽頭炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
血液およびリンパ系障害	4 (100.0%)	5 (100.0%)	9 (100.0%)	4 (100.0%)	5 (100.0%)	9 (100.0%)
リンパ球減少症	4 (100.0%)	5 (100.0%)	9 (100.0%)	4 (100.0%)	5 (100.0%)	9 (100.0%)
好中球減少症	2 (50.0%)	5 (100.0%)	7 (77.8%)	0	5 (100.0%)	5 (55.6%)
白血球減少症	0	3 (60.0%)	3 (33.3%)	0	3 (60.0%)	3 (33.3%)
貧血	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	1 (20.0%)	1 (11.1%)
血小板減少症	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	1 (20.0%)	1 (11.1%)
代謝および栄養障害	1 (25.0%)	2 (40.0%)	3 (33.3%)	1 (25.0%)	0	1 (11.1%)
高カリウム血症	0	1 (20.0%)	1 (11.1%)	0	0	0
低リン酸血症	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
高脂血症	0	1 (20.0%)	1 (11.1%)	0	0	0
神経系障害	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
頭痛	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
呼吸器、胸郭および縦隔障害	0	2 (40.0%)	2 (22.2%)	0	1 (20.0%)	1 (11.1%)
低酸素症	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
アレルギー性鼻炎	0	1 (20.0%)	1 (11.1%)	0	0	0
口腔咽頭痛	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
胃腸障害	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	0	0
便秘	0	1 (20.0%)	1 (11.1%)	0	0	0
悪心	1 (25.0%)	0	1 (11.1%)	0	0	0
皮膚および皮下組織障害	2 (50.0%)	0	2 (22.2%)	2 (50.0%)	0	2 (22.2%)
そう痒症	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
発疹	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)

TSFAE10: Number of Subjects with Treatment-emergent Adverse Events and Drug Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

	TEAEs			Drug Related TEAEs (Study Drug)[a]		
	8 mg/kg	16 mg/kg	All groups	8 mg/kg	16 mg/kg	All groups
筋骨格系および結合組織障害	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
骨炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
腎および尿路障害	1 (25.0%)	0	1 (11.1%)	0	0	0
排尿困難	1 (25.0%)	0	1 (11.1%)	0	0	0
一般・全身障害および投与部位の状態	1 (25.0%)	3 (60.0%)	4 (44.4%)	1 (25.0%)	3 (60.0%)	4 (44.4%)
発熱	1 (25.0%)	3 (60.0%)	4 (44.4%)	1 (25.0%)	3 (60.0%)	4 (44.4%)
悪寒	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
臨床検査	1 (25.0%)	1 (20.0%)	2 (22.2%)	1 (25.0%)	0	1 (11.1%)
Ｃ－反応性蛋白増加	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
体重減少	0	1 (20.0%)	1 (11.1%)	0	0	0

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.
[a] Adverse events whose causal relationship to the investigational medication were judged as ("possible", "probable", or "very likely") by the investigator.

[TSFAE10.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae10.sas] 22FEB2016, 11:16

表 2.7.4-付録-44 List of Deaths; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

LSFDTH_JST01_3004: List of Deaths; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Site ID	Enrollement No.	Age (years)/ Sex/Race/Country	Date of First Dose	Date of Last Dose (Study Day)	Death Date (Study Day of Death)	Cause of Death
Vd	AU00144	610001	63/M/White/Aus	20OCT2014	27MAR2015 (159)	22OCT2015 (368)	Progressive Disease
		610021	66/M/White/Aus	09MAR2015	21APR2015 (44)	25DEC2015 (292)	Progressive Disease
	AU00151	610039	60/M/White/Aus	02JUN2015	13JUN2015 (12)	14JUL2015 (43)	Adverse Event
	BR00293	550014	69/M/White/Bra	29JUN2015	03DEC2015 (158)	26DEC2015 (181)	Progressive Disease
		550015	75/M/Black Or African American/Bra	29JUN2015	21AUG2015 (54)	16SEP2015 (80)	Adverse Event
	CZ00128	420016	69/F/White/Cze	21APR2015	21JUL2015 (92)	24AUG2015 (126)	Progressive Disease
	DE00466	490013	75/M/White/Deu	13FEB2015	10MAR2015 (26)	12APR2015 (59)	Progressive Disease
	DE00474	490006	74/F/White/Deu	19JAN2015	09FEB2015 (22)	17APR2015 (89)	Progressive Disease
	ES00352	340002	58/M/White/Esp	24SEP2014	06JAN2015 (105)	28SEP2015 (370)	Other: Brain Stroke
	ES12018	340031	79/F/White/Esp	07JUL2015	21NOV2015 (138)	28NOV2015 (145)	Adverse Event
	ES12025	340022	71/M/White/Esp	14APR2015	08AUG2015 (117)	25SEP2015 (165)	Progressive Disease
		340028	83/M/White/Esp	05JUN2015	15JUN2015 (11)	17JUN2015 (13)	Adverse Event
	ES90250	340033	85/M/White/Esp	28JUL2015	08AUG2015 (12)	13SEP2015 (48)	Adverse Event
	HU90018	360008	80/F/White/Hun	19JAN2015	14MAY2015 (116)	28SEP2015 (253)	Progressive Disease
		360017	66/F/White/Hun	26FEB2015	08MAY2015 (72)	03JUN2015 (98)	Adverse Event
	IT00356	390022	72/F/White/Ita	05JUN2015	15JUN2015 (11)	30JUL2015 (56)	Progressive Disease
	IT00357	390052	69/M/White/Ita	17JUL2015	18AUG2015 (33)	11OCT2015 (87)	Progressive Disease
	IT12032	390003	73/M/White/Ita	23MAR2015	29MAY2015 (68)	30JUN2015 (100)	Progressive Disease
		390010	77/M/White/Ita	03APR2015	18AUG2015 (138)	30OCT2015 (211)	Progressive Disease
		390021	67/M/White/Ita	01JUN2015	28AUG2015 (89)	18NOV2015 (171)	Progressive Disease
	IT90256	390043	72/M/White/Ita	01JUL2015	01DEC2015 (154)	20DEC2015 (173)	Progressive Disease
	KR90291	820005	54/M/Asian/Kor	10MAR2015	13JUN2015 (96)	10NOV2015 (246)	Progressive Disease
	NL00151	310019	56/M/White/Nld	26MAY2015	29SEP2015 (127)	28NOV2015 (187)	Progressive Disease
	NL00154	310016	68/M/White/Nld	19MAY2015	12AUG2015 (86)	22AUG2015 (96)	Adverse Event
	PL00211	480009	65/M/White/Pol	18MAY2015	16JUN2015 (30)	03NOV2015 (170)	Progressive Disease
	RU00267	700023	46/M/White/Rus	27MAY2015	17JUL2015 (52)	19JUL2015 (54)	Adverse Event
		700038	69/F/White/Rus	10AUG2015	10SEP2015 (32)	13SEP2015 (35)	Adverse Event
	RU00385	700007	54/M/White/Rus	03MAR2015	05APR2015 (34)	28APR2015 (57)	Progressive Disease
	RU90443	700035	57/M/White/Rus	13JUL2015	17SEP2015 (67)	18SEP2015 (68)	Adverse Event
	TR00053	900001	62/F/White/Tur	26SEP2014	03MAR2015 (159)	10OCT2015 (380)	Other: Respiratory Arrest During Anesthesia Procedure
	TR00059	900023	54/M/White/Tur	17APR2015	16MAY2015 (30)	06DEC2015 (234)	Progressive Disease
	UA00157	380042	72/M/White/Ukr	02JUN2015	19NOV2015 (171)	27NOV2015 (179)	Adverse Event
	UA90176	380019	56/F/White/Ukr	05MAR2015	19JUN2015 (107)	20JUN2015 (108)	Adverse Event
		380024	58/M/White/Ukr	24MAR2015	29AUG2015 (159)	23NOV2015 (245)	Other: No Detailed Information Is Available At The Present Time
	UA90216	380058	37/M/White/Ukr	03JUL2015	14JUL2015 (12)	19AUG2015 (48)	Progressive Disease
DVd	AU00143	610037	44/M/White/Aus	12MAY2015	23MAY2015 (12)	21NOV2015 (194)	Progressive Disease
	AU00144	610009	53/M/Native Hawaiian Or Other Pacific Islander/Aus	01DEC2014	10JAN2015 (41)	07APR2015 (128)	Progressive Disease
		610025	67/M/White/Aus	13APR2015	24APR2015 (12)	18MAY2015 (36)	Adverse Event
	DE00463	490044	68/F/White/Deu	21JUL2015	09JAN2016 (173)	11JAN2016 (175)	Adverse Event

LSFDTH_JST01_3004: List of Deaths; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Site ID	Enrollement No.	Age (years)/ Sex/Race/Country	Date of First Dose	Date of Last Dose (Study Day)	Death Date (Study Day of Death)	Cause of Death
	DE00475	490039	52/M/White/Deu	17JUL2015	25JUL2015 (9)	17AUG2015 (32)	Adverse Event
	ES12026	340015	71/F/White/Esp	16FEB2015	27FEB2015 (12)	01MAR2015 (14)	Adverse Event
	HU90018	360010	68/F/White/Hun	28JAN2015	02JUL2015 (156)	09OCT2015 (255)	Progressive Disease
		360014	52/M/White/Hun	11FEB2015	02MAY2015 (81)	20OCT2015 (252)	Other: Patient Had Progressive Myeloma, Fell And Fatal Intracranial Bleeding Developed
	IT00259	390044	69/F/White/Ita	16JUL2015	06OCT2015 (83)	19DEC2015 (157)	Adverse Event
	IT12032	390038	67/F/White/Ita	07JUL2015	04AUG2015 (29)	10OCT2015 (96)	Other: U
	KR90164	820010	61/M/Asian/Kor	07MAY2015	18MAY2015 (12)	29JUL2015 (84)	Progressive Disease
	KR90291	820020	63/M/Asian/Kor	07JUL2015	21JUL2015 (15)	11SEP2015 (67)	Progressive Disease
	MX00214	520005	68/F/Other/Mex	05OCT2015	24DEC2015 (81)	31DEC2015 (88)	Adverse Event
	NL00149	310008	79/M/White/Nld	29DEC2014	13JUL2015 (197)	10DEC2015 (347)	Progressive Disease
	NL00150	310006	62/M/White/Nld	16DEC2014	07JUL2015 (204)	28JUL2015 (225)	Progressive Disease
	PL00200	480004	61/F/White/Pol	24APR2015	06NOV2015 (197)	08DEC2015 (229)	Other: Telephone Information From The Family That The Patient On 08 Dec 2015 Died While Sleeping At Home.
		480027	62/M/White/Pol	26JUN2015	29SEP2015 (96)	10JAN2016 (199)	Other: In The Hospital Due To Sepsis
	RU00183	700003	69/M/White/Rus	03MAR2015	27MAR2015 (25)	06APR2015 (35)	Adverse Event
		700020	58/M/White/Rus	21APR2015	22APR2015 (2)	29APR2015 (9)	Adverse Event
	RU00386	700017	53/F/White/Rus	08APR2015	26SEP2015 (172)	11OCT2015 (187)	Adverse Event
	SE00069	460006	77/F/White/Swe	09DEC2014	30DEC2014 (22)	12FEB2015 (66)	Adverse Event
	SE90044	460014	67/M/White/Swe	04MAY2015	13JUL2015 (71)	28NOV2015 (209)	Other: Infection
	TR00053	900028	61/M/White/Tur	18MAY2015	01JUN2015 (15)	12JUN2015 (26)	Adverse Event
	UA90173	380018	66/M/White/Ukr	10MAR2015	20MAY2015 (72)	10JUN2015 (93)	Progressive Disease
	UA90216	380063	55/F/White/Ukr	07SEP2015	10SEP2015 (4)	12SEP2015 (6)	Adverse Event
	UA90218	380007	66/M/White/Ukr	03FEB2015	18APR2015 (75)	28APR2015 (85)	Adverse Event

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone

LSFDTH_JST01_3003: List of Deaths; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Site ID	Enrollement No.	Age (years)/ Sex/Race/Country	Date of First Dose	Date of Last Dose (Study Day)	Death Date (Study Day of Death)	Cause of Death
Rd	AU00154	610003	81/M/White/Aus	22AUG2014	10DEC2015 (476)	11FEB2016 (539)	Other: Multiple Myelomna And Multiple Organ Failure
	BE00103	320009	67/M/White/Bel	27NOV2014	07MAY2015 (162)	16AUG2015 (263)	Progressive Disease
	BE00106	320010	75/F/White/Bel	20JAN2015	25MAY2015 (126)	08JUN2015 (140)	Adverse Event
		320013	71/F/White/Bel	23JAN2015	12JUN2015 (141)	02JAN2016 (345)	Other: Euthanasia
	CA00098	101020	76/M/White/Can	20DEC2014	27APR2015 (129)	27MAY2015 (159)	Progressive Disease
		101022	66/F/White/Can	12JAN2015	24JUN2015 (164)	17NOV2015 (310)	Progressive Disease
	CA00102	101009	72/F/White/Can	05NOV2014	13NOV2014 (9)	19NOV2014 (15)	Adverse Event
	CA00109	101019	51/F/White/Can	18DEC2014	12MAR2015 (85)	14MAY2015 (148)	Progressive Disease
	DE00428	490016	73/F/White/Deu	05FEB2015	13APR2015 (68)	14JUL2015 (160)	Progressive Disease
	DK00051	450013	58/M/White/Dnk	27JAN2015	17FEB2015 (22)	27JUN2015 (152)	Progressive Disease
	ES00349	340002	66/M/White/Esp	01JUL2014	06FEB2015 (221)	07MAR2016 (616)	Adverse Event
		340009	67/M/White/Esp	17JUL2014	05NOV2014 (112)	21NOV2014 (128)	Adverse Event
		340021	60/F/White/Esp	06OCT2014	22DEC2014 (78)	09FEB2015 (127)	Progressive Disease
		340025	44/M/White/Esp	21OCT2014	11MAR2015 (142)	04AUG2015 (288)	Progressive Disease
		340043	73/M/White/Esp	20JAN2015	14OCT2015 (268)	23OCT2015 (277)	Adverse Event
	ES00350	340056	70/F/White/Esp	19FEB2015	13JUL2015 (145)	06JAN2016 (322)	Progressive Disease
	FR01346	330003	74/M/Not Reported/Fra	03JUL2014	24JUL2014 (22)	13MAY2015 (315)	Progressive Disease
		330019	67/M/Not Reported/Fra	14OCT2014	19AUG2015 (310)	03DEC2015 (416)	Other: Acute Hepatitis Due To Pomalidomide
	FR01350	330013	56/M/Not Reported/Fra	09SEP2014	30SEP2014 (22)	06OCT2015 (393)	Progressive Disease
	FR01447	330034	71/M/Not Reported/Fra	01DEC2014	10NOV2015 (345)	12DEC2015 (377)	Other: Psoas Hematoma Not Related To Sutdy Treatment That Started After Start Of Subsequent Therapy
	GB00355	440047	78/M/Black Or African American/Gbr	03FEB2015	18MAY2015 (105)	28NOV2015 (299)	Progressive Disease
	GB00358	440003	71/M/Unknown/Gbr	03SEP2014	08APR2015 (218)	22AUG2015 (354)	Other: As Per Death Certficate: 1. Multi-Organ Failure 2. Community Acquired Pneumonia 3. Multiple Myeloma
		440018	43/M/Not Reported/Gbr	28OCT2014	19NOV2014 (23)	09DEC2014 (43)	Progressive Disease
	GB00361	440050	80/F/White/Gbr	10FEB2015	05MAY2015 (85)	29JAN2016 (354)	Adverse Event
	GB00371	440016	78/M/White/Gbr	03NOV2014	26JAN2015 (85)	15MAR2015 (133)	Adverse Event
		440017	70/M/White/Gbr	03NOV2014	17NOV2014 (15)	29NOV2014 (27)	Adverse Event
	GR90041	300002	63/M/White/Grc	29DEC2014	30AUG2015 (245)	02SEP2015 (248)	Adverse Event
	IL00062	972005	54/F/White/Isr	12NOV2014	25JUN2015 (226)	22FEB2016 (468)	Progressive Disease
	IL00066	972016	62/F/White/Isr	17DEC2014	03JAN2015 (18)	10JAN2015 (25)	Adverse Event
	IL00067	972038	54/M/White/Isr	02FEB2015	24FEB2015 (23)	05MAR2015 (32)	Adverse Event
	JP91211	810005	69/M/Asian/Jpn	08APR2015	17SEP2015 (163)	30JAN2016 (298)	Other: Sepsis Shock
	JP91216	810024	59/M/Asian/Jpn	19MAY2015	07SEP2015 (112)	27SEP2015 (132)	Progressive Disease
		810031	69/F/Asian/Jpn	04JUN2015	19AUG2015 (77)	06NOV2015 (156)	Other: Multiple Myeloma
	KR00119	820037	68/F/Asian/Kor	30JAN2015	11AUG2015 (194)	01OCT2015 (245)	Progressive Disease

LSFDTH_JST01_3003: List of Deaths; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Site ID	Enrollement No.	Age (years)/ Sex/Race/Country	Date of First Dose	Date of Last Dose (Study Day)	Death Date (Study Day of Death)	Cause of Death
	KR00120	820020	60/F/Asian/Kor	27NOV2014	16MAR2015 (110)	21SEP2015 (299)	Progressive Disease
	PL00200	480018	64/F/White/Pol	23JAN2015	30AUG2015 (220)	30AUG2015 (220)	Adverse Event
	PL00202	480005	68/M/White/Pol	18DEC2014	22MAR2015 (95)	17JAN2016 (396)	Progressive Disease
	PL00206	480038	51/F/White/Pol	10MAR2015	15SEP2015 (190)	05OCT2015 (210)	Adverse Event
	RU00183	700040	56/M/White/Rus	17FEB2015	26FEB2015 (10)	02MAR2015 (14)	Adverse Event
		700049	47/F/White/Rus	24FEB2015	09MAY2015 (75)	29MAY2015 (95)	Progressive Disease
	RU00264	700029	57/M/White/Rus	29DEC2014	06JUL2015 (190)	11FEB2016 (410)	Progressive Disease
	TW00056	886010	58/M/Asian/Twn	20NOV2014	12MAR2015 (113)	29DEC2015 (405)	Progressive Disease
		886017	78/M/Asian/Twn	18DEC2014	24DEC2014 (7)	04JAN2015 (18)	Adverse Event
		886025	65/F/Asian/Twn	09FEB2015	17MAY2015 (98)	21JUN2015 (133)	Adverse Event
	US12160	100047	61/F/White/Usa	20MAR2015	10APR2015 (22)	14AUG2015 (148)	Progressive Disease
DRd	BE00105	320007	69/M/White/Bel	17NOV2014	28DEC2015 (407)	04FEB2016 (445)	Progressive Disease
	CA00098	101002	67/M/White/Can	15AUG2014	21NOV2014 (99)	04DEC2014 (112)	Adverse Event
		101035	74/M/White/Can	06FEB2015	01JUN2015 (116)	26AUG2015 (202)	Progressive Disease
	CA00100	101033	74/M/White/Can	29JAN2015	14MAY2015 (106)	22JUN2015 (145)	Progressive Disease
	DE00422	490011	69/M/White/Deu	16DEC2014	24MAR2015 (99)	31MAR2015 (106)	Adverse Event
	DE00426	490015	67/M/White/Deu	05FEB2015	08JUL2015 (154)	17JAN2016 (347)	Progressive Disease
	DK00050	450006	71/M/White/Dnk	23DEC2014	12FEB2015 (52)	12MAR2015 (80)	Adverse Event
	ES00349	340005	71/M/White/Esp	07JUL2014	26AUG2014 (51)	28AUG2014 (53)	Adverse Event
		340012	74/M/White/Esp	01AUG2014	25APR2015 (268)	17SEP2015 (413)	Progressive Disease
		340017	66/F/White/Esp	10SEP2014	01JUL2015 (295)	30JUL2015 (324)	Adverse Event
		340038	65/F/White/Esp	05JAN2015	23SEP2015 (262)	04NOV2015 (304)	Progressive Disease
	ES00444	340058	56/M/White/Esp	26FEB2015	17MAR2015 (20)	27MAR2015 (30)	Adverse Event
	ES12017	340010	72/M/White/Esp	01AUG2014	26JAN2015 (179)	22MAR2015 (234)	Adverse Event
	FR01346	330050	50/M/Not Reported/Fra	27JAN2015	12JUN2015 (137)	26NOV2015 (304)	Adverse Event
	FR01348	330041	67/M/Not Reported/Fra	09JAN2015	02SEP2015 (237)	02MAR2016 (419)	Progressive Disease
	GR90041	300001	64/F/White/Grc	22DEC2014	18JUL2015 (209)	31AUG2015 (253)	Progressive Disease
	IL00047	972015	62/M/White/Isr	27NOV2014	05JUN2015 (191)	08OCT2015 (316)	Progressive Disease
	IL00066	972003	55/M/White/Isr	14OCT2014	26FEB2015 (136)	16NOV2015 (399)	Progressive Disease
	IL00067	972018	63/M/White/Isr	15DEC2014	01MAR2015 (77)	03MAR2015 (79)	Adverse Event
	KR00119	820023	64/M/Asian/Kor	18DEC2014	21JUL2015 (216)	09SEP2015 (266)	Progressive Disease
	KR00121	820013	71/M/Asian/Kor	05NOV2014	04FEB2016 (457)	06FEB2016 (459)	Adverse Event
	KR00122	820015	54/F/Asian/Kor	06NOV2014	11MAY2015 (187)	05FEB2016 (457)	Progressive Disease
	KR00124	820002	73/M/Asian/Kor	23SEP2014	18MAR2015 (177)	27MAR2015 (186)	Adverse Event
		820032	54/F/Asian/Kor	19JAN2015	04MAR2015 (45)	22MAY2015 (124)	Other: Pneumonia
	RU00192	700020	75/F/White/Rus	11DEC2014	25FEB2015 (77)	02MAR2015 (82)	Adverse Event
	RU00204	700026	70/F/White/Rus	25DEC2014	09JAN2015 (16)	15JAN2015 (22)	Adverse Event
	RU00264	700030	62/M/White/Rus	30DEC2014	17MAR2015 (78)	01APR2015 (93)	Progressive Disease
	TW00052	886026	34/M/Asian/Twn	13FEB2015	03SEP2015 (203)	27FEB2016 (380)	Other: Septic Shock
	US01325	100016	70/M/White/Usa	28OCT2014	05JAN2015 (70)	24OCT2015 (362)	Progressive Disease
	US02108	100017	50/M/White/Usa	30OCT2014	26FEB2015 (120)	23AUG2015 (298)	Progressive Disease

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

LSFDTH-JST01_503: List of Subjects Who Died During the Study; All Treated Analysis Set (Study GEN503)

Treatment Group	Site ID	Enrollment No.	Age (years) /Sex/Race/ Country	Date of First Dose	Date of Last Dose (Study Day)	Death Date (Study Day of Death)	Cause of Death
16 mg/kg Dara + Len/Dex	DK01	503045	41/M/WHITE/DNK	2014-08-13	2014-10-09 (58)	2015-01-15 (156)	DISEASE PROGRESSION
	IT01	503016	62/F/WHITE/ITA	2014-03-18	2015-02-12 (332)	2015-03-05 (353)	ADVERSE EVENT
	UK01	503041	52/M/WHITE/GBR	2014-07-22	2014-07-22 (1)	2015-04-18 (271)	DISEASE PROGRESSION
	UK02	503011	56/M/WHITE/GBR	2013-09-25	2013-12-20 (87)	2014-01-23 (121)	DISEASE PROGRESSION

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LSFDTH-JST01_1001: List of Deaths; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race/Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day)	Cause of Death
VD + Dara (16 mg/kg)	ES00349-100024	63/M/White/Spain	2014-06-30	2014-10-21 (114)	2015-01-03 (188)	OTHER - SEPTIC SHOCK DUE TO ESCHERICHIA COLI
	ES00351-100028	70/F/White/Spain	2014-07-15	2015-04-22 (282)	2015-11-01 (475)	PROGRESSIVE DISEASE
	ES00352-100026	82/M/White/Spain	2014-07-02	2015-01-13 (196)	2015-08-26 (421)	OTHER - PANCOLITIS
Pom-dex + Dara (16 mg/kg)	FR01347-100116	65/M/White/France	2015-05-12	2015-09-09 (121)	2015-10-11 (153)	PROGRESSIVE DISEASE
	FR01348-100165	59/M/Not Reported/France	2015-08-26	2015-10-08 (44)	2015-10-13 (49)	PROGRESSIVE DISEASE
	FR01350-100137	58/M/White/France	2015-06-17	2015-09-23 (99)	2015-10-04 (110)	ADVERSE EVENT
	FR01350-100144	61/F/White/France	2015-06-25	2015-06-26 (2)	2015-07-01 (7)	ADVERSE EVENT
	US01028-100011	64/F/White/United States	2014-04-16	2015-01-25 (285)	2015-08-04 (476)	PROGRESSIVE DISEASE
	US01029-100006	68/M/White/United States	2014-04-15	2014-06-16 (63)	2015-02-11 (303)	PROGRESSIVE DISEASE
	US01029-100013	59/M/White/United States	2014-04-22	2014-06-29 (69)	2014-08-08 (109)	PROGRESSIVE DISEASE
	US01029-100034	42/M/Black or African American/United States	2014-11-03	2014-11-25 (23)	2015-02-19 (109)	PROGRESSIVE DISEASE
	US10973-100049	62/F/White/United States	2014-12-10	2015-02-10 (63)	2015-04-21 (133)	PROGRESSIVE DISEASE
	US10973-100090	51/M/White/United States	2015-02-10	2015-03-04 (23)	2015-05-02 (82)	PROGRESSIVE DISEASE
	US10973-100092	68/M/White/United States	2015-02-19	2015-02-25 (7)	2015-03-21 (31)	ADVERSE EVENT
	US10974-100040	59/M/White/United States	2014-10-30	2015-05-30 (213)	2015-09-02 (308)	PROGRESSIVE DISEASE
	US10974-100073	67/M/White/United States	2015-01-13	2015-03-11 (58)	2015-08-18 (218)	PROGRESSIVE DISEASE
	US10974-100079	71/F/White/United States	2015-02-10	2016-01-28 (353)	2016-03-04 (389)	PROGRESSIVE DISEASE
	US10974-100107	55/M/White/United States	2015-04-21	2015-10-21 (184)	2016-01-09 (264)	PROGRESSIVE DISEASE
	US10974-100169	71/M/White/United States	2015-09-08	2015-09-10 (3)	2015-11-16 (70)	PROGRESSIVE DISEASE
	US10975-100054	64/F/Black or African American/United States	2015-01-07	2015-05-20 (134)	2016-02-16 (406)	PROGRESSIVE DISEASE
	US10975-100057	69/F/White/United States	2015-01-08	2015-05-01 (114)	2015-06-30 (174)	PROGRESSIVE DISEASE
	US10975-100065	78/M/White/United States	2015-01-15	2015-01-15 (1)	2015-05-26 (132)	ADVERSE EVENT
	US10975-100075	68/M/White/United States	2015-01-22	2015-02-23 (33)	2015-03-29 (67)	ADVERSE EVENT

LSFDTH-JST01_1001: List of Deaths; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race/Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day)	Cause of Death
	US10975-100094	74/F/White/United States	2015-02-18	2015-02-19 (2)	2015-04-11 (53)	ADVERSE EVENT
	US10975-100109	61/F/White/United States	2015-04-22	2015-05-21 (30)	2015-05-24 (33)	ADVERSE EVENT
	US10977-100076	46/M/White/United States	2015-01-22	2015-06-04 (134)	2015-07-17 (177)	OTHER - THE SUBJECT WAS NO LONGER A PATIENT AT CITY OF HOPE AT THE TIME OF DEATH. SPECIFIC CAUSE OF DEATH IS UNKNOWN.
	US10977-100155	64/F/Black or African American/United States	2015-08-24	2015-09-18 (26)	2015-11-06 (75)	PROGRESSIVE DISEASE
	US10978-100053	51/M/Black or African American/United States	2015-01-07	2015-04-24 (108)	2016-01-24 (383)	PROGRESSIVE DISEASE
	US10978-100064	59/F/Black or African American/United States	2015-01-14	2015-05-13 (120)	2015-06-19 (157)	PROGRESSIVE DISEASE
	US10978-100124	62/M/White/United States	2015-05-14	2015-05-22 (9)	2015-05-25 (12)	ADVERSE EVENT
	US10978-100127	73/M/White/United States	2015-05-15	2015-05-15 (1)	2015-05-31 (17)	PROGRESSIVE DISEASE

Keys:D-Vd = daratumumab-bortezomib-dexamethasone; D-VTd= daratumumab-bortezomib-thalidomide-dexamethasone; D-VMP = daratumumab-bortezomib-melphalan-prednisone; D-Pom-dex = daratumumab-pomalidomide-dexamethasone.

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表 2.7.4-付録-45 Number of Subjects with 1 or More Treatment-emergent Adverse Events With Outcome Death by Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE16: Number of Subjects with 1 or More Treatment-emergent Adverse Events With Outcome Death by Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004					MMY3003+GEN503					MMY1001		
	Vd		DVd			Rd		DRd			DPd		
	Total n(%)	Related to Other	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to Other	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
Analysis set: safety	237		243			281		318			103		
Total number of subjects with TEAE with outcome death	14 (5.9%)	2 (0.8%)	13 (5.3%)	3 (1.2%)	5 (2.1%)	15 (5.3%)	1 (0.4%)	12 (3.8%)	3 (0.9%)	7 (2.2%)	7 (6.8%)	0	1 (1.0%)
MedDRA system organ class/Preferred term													
感染症および寄生虫症	4 (1.7%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	0	7 (2.2%)	2 (0.6%)	5 (1.6%)	2 (1.9%)	0	1 (1.0%)
敗血症性ショック	1 (0.4%)	0	0	0	0	1 (0.4%)	0	3 (0.9%)	1 (0.3%)	1 (0.3%)	0	0	0
肺炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	2 (0.6%)	0	2 (0.6%)	0	0	0
細菌性肺炎	0	0	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
ウイルス性肺炎	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
進行性多巣性白質脳症	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	0	1 (1.0%)
肺敗血症	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
敗血症	0	0	0	0	0	1 (0.4%)	0	0	0	0	1 (1.0%)	0	0
気管気管支炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0
心臓障害	1 (0.4%)	0	3 (1.2%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0	0	0	0	0
心肺不全	0	0	0	0	0	0	0	1 (0.3%)	0	0	0	0	0
急性冠動脈症候群	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
心停止	1 (0.4%)	0	1 (0.4%)	0	0	1 (0.4%)	0	0	0	0	0	0	0
心原性ショック	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
一般・全身障害および投与部位の状態	4 (1.7%)	0	1 (0.4%)	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (1.0%)	0	0
多臓器不全	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
状態悪化	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0
全身健康状態低下	3 (1.3%)	0	1 (0.4%)	0	0	0	0	0	0	0	1 (1.0%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0	0	2 (0.7%)	0	1 (0.3%)	0	1 (0.3%)	0	0	0

TSFAE16: Number of Subjects with 1 or More Treatment-emergent Adverse Events With Outcome Death by Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004					MMY3003+GEN503					MMY1001		
	Vd		DVd			Rd		DRd			DPd		
	Total n(%)	Related to Other	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to Other	Total n(%)	Related to DARA	Related to Other	Total n(%)	Related to DARA	Related to Other
急性単球性白血病	0	0	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
肺腺癌	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0
腎および尿路障害	1 (0.4%)	0	0	0	0	4 (1.4%)	1 (0.4%)	1 (0.3%)	0	0	0	0	0
急性腎不全	0	0	0	0	0	3 (1.1%)	1 (0.4%)	1 (0.3%)	0	0	0	0	0
骨髄腫円柱腎症	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0
腎不全	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	2 (0.8%)	0	3 (1.2%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	1 (0.3%)	0	0	3 (2.9%)	0	0
肺水腫	1 (0.4%)	0	0	0	0	1 (0.4%)	0	1 (0.3%)	0	0	0	0	0
急性呼吸不全	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0
間質性肺疾患	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	0	0
器質化肺炎	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
胸水	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	0	0
肺塞栓症	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0
呼吸不全	0	0	2 (0.8%)	0	0	0	0	0	0	0	1 (1.0%)	0	0
胃腸障害	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0	0
十二指腸潰瘍	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0	0
代謝および栄養障害	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0
低ナトリウム血症	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0
神経系障害	1 (0.4%)	0	3 (1.2%)	0	1 (0.4%)	2 (0.7%)	0	0	0	0	1 (1.0%)	0	0
脳出血	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0
脳梗塞	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
脳血管発作	1 (0.4%)	0	0	0	0	0	0	0	0	0	1 (1.0%)	0	0
虚血性脳卒中	0	0	2 (0.8%)	0	1 (0.4%)	0	0	0	0	0	0	0	0
神経系障害	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-46 List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

LSFDTH01: List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Subject ID	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total Len/Vel (mg) Pom Dose (mg/m2)	Study Day ofLast Len/Vel/Pom Dose	Total Dex Dose (mg)	Study Day of Last DEX Dose	Primary Cause of Death	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to DARA
Vd	54767414MMY3004-310016	22AUG2015 (96)	.	.	19.787632	85	600	86	ADVERSE EVENT	全身健康状態低下 [WORSENING OF CONDITIONING]	NOT RELATED
	54767414MMY3004-340028	17JUN2015 (13)	.	.	5.2996298	11	140	11	ADVERSE EVENT	敗血症性ショック [SEPTIC SHOCK]	NOT RELATED
	54767414MMY3004-340031	28NOV2015 (145)	.	.	30.619447	137	1000	138	ADVERSE EVENT	気管気管支炎 [ACUTE TRACHEOBRONCHITIS]	NOT RELATED
	54767414MMY3004-340033	13SEP2015 (48)	.	.	5.0498791	11	160	12	ADVERSE EVENT	肺炎 [PNEUMONIA]	NOT RELATED
	54767414MMY3004-360017	03JUN2015 (98)	.	.	18.088091	68	560	72	ADVERSE EVENT	心停止 [CARDIAC ARREST]	NOT RELATED
	54767414MMY3004-380019	20JUN2015 (108)	.	.	27.354032	106	840	107	ADVERSE EVENT	肺塞栓症 [PULMONARY EMBOLISM]	NOT RELATED
	54767414MMY3004-380042	27NOV2015 (179)	.	.	33.358033	170	1080	171	ADVERSE EVENT	状態悪化 [WORSENING OF CONDITDON]	NOT RELATED
	54767414MMY3004-390043	20DEC2015 (173)	.	.	30.681301	153	1120	154	PROGRESSIVE DISEASE	全身健康状態低下 [WORSENING OF GENERAL CONDITION]	NOT RELATED
	54767414MMY3004-550014	26DEC2015 (181)	.	.	24.967447	142	820	158	PROGRESSIVE DISEASE	低ナトリウム血症 [HYPONATREMIA]	NOT RELATED
	54767414MMY3004-550015	16SEP2015 (80)	.	.	14.543897	53	480	54	ADVERSE EVENT	肺炎 [PNEUMONIA]	NOT RELATED
	54767414MMY3004-700007	28APR2015 (57)	.	.	4.9594419	11	323.7	34	PROGRESSIVE DISEASE	全身健康状態低下 [GENERAL DETERIORATION OF CONDITION]	NOT RELATED
	54767414MMY3004-700023	19JUL2015 (54)	.	.	11.519146	48	400	52	ADVERSE EVENT	肺水腫 [PULMONARY EDEMA]	NOT RELATED

LSFDTH01: List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Subject ID	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total Len/Vel (mg) Pom Dose (mg/m2)	Study Day ofLast Len/Vel/Pom Dose	Total Dex Dose (mg)	Study Day of Last DEX Dose	Primary Cause of Death	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to DARA
	54767414MMY3004-700035	18SEP2015 (68)	.	.	15.588872	67	440	65	ADVERSE EVENT	脳血管発作 [ACUTE CEREBROVASCULAR ACCIDENT]	NOT RELATED
	54767414MMY3004-700038	13SEP2015 (35)	.	.	10.236509	32	300	32	ADVERSE EVENT	骨髄腫円柱腎症 [MYELOMA NEPHROPATHY]	NOT RELATED
DVd	54767414MMY3004-310006	28JUL2015 (225)	10	193	21.210924	203	640	204	PROGRESSIVE DISEASE	肺敗血症 [PNEUMOSEPSIS]	DOUBTFUL
	54767414MMY3004-340015	01MAR2015 (14)	2	8	5.159922	11	160	12	ADVERSE EVENT	脳梗塞 [CEREBRAL INFARCT]	NOT RELATED
	54767414MMY3004-380007	28APR2015 (85)	10	64	19.913026	71	640	75	ADVERSE EVENT	器質化肺炎 [BILATERAL FIBRINOUS PNEUMONIA]	POSSIBLE
	54767414MMY3004-380063	12SEP2015 (6)	1	1	1.3057308	1	60	4	ADVERSE EVENT	急性冠動脈症候群 [ACUTE CORONARY SYNDROM]	POSSIBLE
	54767414MMY3004-460006	12FEB2015 (66)	4	21	6.0502101	21	200	22	ADVERSE EVENT	肺炎 [PNEUMONIA]	POSSIBLE
	54767414MMY3004-490039	17AUG2015 (32)	2	8	3.8387746	8	120	9	ADVERSE EVENT	心原性ショック [CARDIAC SHOCK]	NOT RELATED
	54767414MMY3004-490044	11JAN2016 (175)	14	169	37.101388	172	1200	173	ADVERSE EVENT	虚血性脳卒中 [ISCHAEMIC STROKE]	NOT RELATED
	54767414MMY3004-520005	31DEC2015 (88)	10	75	20.208918	81	380	75	ADVERSE EVENT	呼吸不全 [RESPIRATORY INSUFFICIENCY]	NOT RELATED
	54767414MMY3004-610025	18MAY2015 (36)	2	9	4.8720421	12	160	12	ADVERSE EVENT	十二指腸潰瘍 [DUODENAL ULCER]	NOT RELATED
	54767414MMY3004-700003	06APR2015 (35)	3	22	6.6332496	25	200	25	ADVERSE EVENT	呼吸不全 [RESPIRATORY FAILURE DUE TO DISEASE PROGRESSION]	NOT RELATED

LSFDTH01: List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Subject ID	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total Len/Vel (mg) Pom Dose (mg/m2)	Study Day ofLast Len/Vel/Pom Dose	Total Dex Dose (mg)	Study Day of Last DEX Dose	Primary Cause of Death	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to DARA
	54767414MMY3004-700017	11OCT2015 (187)	14	161	42.275367	171	1280	172	ADVERSE EVENT	全身健康状態低下 [GENERAL DETERIORATION OF CONDITION]	NOT RELATED
	54767414MMY3004-700020	29APR2015 (9)	1	1	1.2943856	1	40	2	ADVERSE EVENT	虚血性脳卒中 [LEFT-SIDE ISCHEMIC STROKE]	NOT RELATED
	54767414MMY3004-900028	12JUN2015 (26)	3	15	5.2147325	11	160	12	ADVERSE EVENT	心停止 [CARDIAC ARREST]	NOT RELATED
Rd	54767414MMY3003-101009	19NOV2014 (15)	.	.	90	9	40	1	ADVERSE EVENT	腎不全 [RENAL FAILURE]	NOT RELATED
	54767414MMY3003-300002	02SEP2015 (248)	.	.	4700	245	1400	243	ADVERSE EVENT	敗血症性ショック [SEPTIC SHOCK]	NOT RELATED
	54767414MMY3003-320010	08JUN2015 (140)	.	.	1485	126	640	126	ADVERSE EVENT	神経系障害 [GENERAL WEAKNESS DUE TO NEUROLOGICAL SYNDROME]	NOT RELATED
	54767414MMY3003-340009	21NOV2014 (128)	.	.	1680	90	560	112	ADVERSE EVENT	肺腺癌 [PULMONARY ADENOCARCINOMA]	NOT RELATED
	54767414MMY3003-340043	23OCT2015 (277)	.	.	4800	268	1480	262	ADVERSE EVENT	脳出血 [MASSIVE CEREBRAL HEMORRHAGE]	NOT RELATED
	54767414MMY3003-440017	29NOV2014 (27)	.	.	.	.	120	15	ADVERSE EVENT	肺炎 [PNEUMONIA]	NOT RELATED
	54767414MMY3003-450013	27JUN2015 (152)	.	.	525	21	160	22	PROGRESSIVE DISEASE	形質細胞性白血病 [PLASMA CELL LEUKEMIA]	NOT RELATED
	54767414MMY3003-480018	30AUG2015 (220)	.	.	3455	220	1200	217	ADVERSE EVENT	心停止 [CARDIAC ARREST]	NOT RELATED
	54767414MMY3003-480038	05OCT2015 (210)	.	.	3675	189	1120	190	ADVERSE EVENT	肺水腫 [PULMONARY OEDEMA]	NOT RELATED

LSFDTH01: List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Subject ID	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total Len/Vel (mg) Pom Dose (mg/m2)	Study Day ofLast Len/Vel/Pom Dose	Total Dex Dose (mg)	Study Day of Last DEX Dose	Primary Cause of Death	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to DARA
	54767414MMY3003-700040	02MAR2015 (14)	.	.	250	10	80	8	ADVERSE EVENT	急性呼吸不全 [ACUTE RESPIRATORY FAILURE]	NOT RELATED
	54767414MMY3003-700049	29MAY2015 (95)	.	.	885	75	360	71	PROGRESSIVE DISEASE	急性腎不全 [ACUTE RENAL FAILURE]	NOT RELATED
	54767414MMY3003-810024	27SEP2015 (132)	.	.	340	112	520	107	PROGRESSIVE DISEASE	急性腎不全 [ACUTE KIDNEY INJURY]	NOT RELATED
	54767414MMY3003-886017	04JAN2015 (18)	.	.	70	7	20	1	ADVERSE EVENT	敗血症 [SEPSIS]	NOT RELATED
	54767414MMY3003-972016	10JAN2015 (25)	.	.	450	18	120	14	ADVERSE EVENT	肺炎 [PNEUMONIA]	NOT RELATED
	54767414MMY3003-972038	05MAR2015 (32)	.	.	400	16	160	23	ADVERSE EVENT	急性腎不全 [ACUTE RENAL FAILURE]	NOT RELATED
DRd	54767414MMY3003-101002	04DEC2014 (112)	12	99	1925	98	280	99	ADVERSE EVENT	急性単球性白血病 [ACUTE MONOBLASTIC LEUKEMIA]	NOT RELATED
	54767414MMY3003-340005	28AUG2014 (53)	8	50	1050	49	320	51	ADVERSE EVENT	敗血症性ショック [SEPTIC SHOCK]	DOUBTFUL
	54767414MMY3003-340058	27MAR2015 (30)	3	15	500	20	120	16	ADVERSE EVENT	敗血症性ショック [SEPTIC SHOCK]	DOUBTFUL
	54767414MMY3003-450006	12MAR2015 (80)	8	51	1050	49	320	52	ADVERSE EVENT	肺炎 [PNEUMONIA]	NOT RELATED
	54767414MMY3003-490011	31MAR2015 (106)	12	99	1575	84	480	99	ADVERSE EVENT	敗血症性ショック [SEPTIC SHOCK]	POSSIBLE
	54767414MMY3003-700020	02MAR2015 (82)	10	71	680	77	440	72	ADVERSE EVENT	細菌性肺炎 [BILATERAL BACTERIAL PNEUMONIA]	NOT RELATED
	54767414MMY3003-700026	15JAN2015 (22)	2	15	375	15	120	16	ADVERSE EVENT	心肺不全 [ACUTE CARDIOPULMONARY FAILURE]	NOT RELATED

LSFDTH01: List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Subject ID	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total Len/Vel (mg) Pom Dose (mg/m2)	Study Day ofLast Len/Vel/Pom Dose	Total Dex Dose (mg)	Study Day of Last DEX Dose	Primary Cause of Death	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to DARA
	54767414MMY3003-700030	01APR2015 (93)	10	71	895	78	480	78	PROGRESSIVE DISEASE	肺水腫 [PULMONARY EDEMA]	NOT RELATED
	54767414MMY3003-820002	27MAR2015 (186)	17	168	1395	177	520	175	ADVERSE EVENT	肺炎 [INFECTIOUS PNEUMONITIS]	NOT RELATED
	54767414MMY3003-820013	06FEB2016 (459)	27	449	8625	457	2640	456	ADVERSE EVENT	多臓器不全 [MULTIPLE ORGAN FAILURE]	POSSIBLE
	54767414MMY3003-972018	03MAR2015 (79)	9	73	335	77	400	74	ADVERSE EVENT	急性腎不全 [ACUTE RENAL FAILURE]	NOT RELATED
	JNJ54767414GEN503-IT01001	05MAR2015 (353)	23	331	5580	331	1907.5047	338	ADVERSE EVENT	ウイルス性肺炎 [VIRAL PNEUMONIA]	POSSIBLE/PROBABLE
DPd	54767414MMY1001-100092	21MAR2015 (31)	1	1	28	7	20	1	ADVERSE EVENT	進行性多巣性白質脳症 [PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY]	NOT RELATED
	54767414MMY1001-100109	24MAY2015 (33)	5	30	87	30	180	30	ADVERSE EVENT	呼吸不全 [RESPIRATORY FAILURE]	NOT RELATED
	54767414MMY1001-100124	25MAY2015 (12)	2	9	.	.	40	9	ADVERSE EVENT	敗血症 [SEPSIS]	NOT RELATED
	54767414MMY1001-100127	31MAY2015 (17)	1	1	.	.	20	1	PROGRESSIVE DISEASE	全身健康状態低下 [GENERAL DETERIORATION OF HEALTH STATUS]	NOT RELATED
	54767414MMY1001-100137	04OCT2015 (110)	9	85	284	99	480	92	ADVERSE EVENT	間質性肺疾患 [PULMONARY BILATERAL INTERSTITIAL SYNDROME]	NOT RELATED
	54767414MMY1001-100144	01JUL2015 (7)	1	1	4	1	40	2	ADVERSE EVENT	脳血管発作 [CEREBRAL STROKE]	DOUBTFUL

LSFDTH01: List of subjects who died due to Treatment-emergent Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Subject ID	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total Len/Vel (mg) Pom Dose (mg/m2)	Study Day ofLast Len/Vel/Pom Dose	Total Dex Dose (mg)	Study Day of Last DEX Dose	Primary Cause of Death	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to DARA
	54767414MMY1001-100165	13OCT2015 (49)	5	43	71	34	200	44	PROGRESSIVE DISEASE	胸水 [PLEURAL EFFUSION]	NOT RELATED

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.

表 2.7.4-付録-47 Listing of Deaths; Safety Analysis Set (Study 54767414MMY1005)

LSFDTH01: Listing of Deaths; Safety Analysis Set (Study 54767414MMY1005)

Treatment Group	Subject ID	Age(years)/Sex	Death Date (Study Day of Death)	Total No. of DARA Infusions	Study Day of Last DARA Infusion	Total No. of BORT Infusions	Study Day of Last BORT Infusion	Total DEX Dose (mg)	Study Day of Last DEX Dose	Adverse Event (MedDRA Preferred Term [Verbatim])	Related to		
											DARA	BORT	DEX
No Data to Report													

Keys: Vd = bortezomib-dexamethasone; Dara = daratumumab, Bort = bortezomib, Dex = dexamethasone.

[LSFDTH01.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\LSFDTH01.SAS] 28SEP2016, 04:02

表 2.7.4-付録-48 Summary of Death and Cause of Death; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

TSFDTH01_3003: Summary of Death and Cause of Death; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: intent-to-treat	15	44	283	21	52	286	36	96	569
Total number of subject who died during study	3 (20.0%)	8 (18.2%)	45 (15.9%)	0	6 (11.5%)	30 (10.5%)	3 (8.3%)	14 (14.6%)	75 (13.2%)
Primary cause of death									
Adverse event	0	2 (4.5%)	16 (5.7%)	0	2 (3.8%)	13 (4.5%)	0	4 (4.2%)	29 (5.1%)
At least one related[c]	0	0	0	0	2 (3.8%)	6 (2.1%)	0	2 (2.1%)	6 (1.1%)
AE(s) unrelated	0	2 (4.5%)	15 (5.3%)	0	0	7 (2.4%)	0	2 (2.1%)	22 (3.9%)
Progressive disease	1 (6.7%)	4 (9.1%)	22 (7.8%)	0	2 (3.8%)	15 (5.2%)	1 (2.8%)	6 (6.3%)	37 (6.5%)
Other	2 (13.3%)	2 (4.5%)	7 (2.5%)	0	2 (3.8%)	2 (0.7%)	2 (5.6%)	4 (4.2%)	9 (1.6%)
Total number of subjects who died within 30 days of last study treatment dose	1 (6.7%)	2 (4.5%)	16 (5.7%)	0	2 (3.8%)	12 (4.2%)	1 (2.8%)	4 (4.2%)	28 (4.9%)
Primary cause of death									
Adverse event	0	1 (2.3%)	12 (4.2%)	0	2 (3.8%)	11 (3.8%)	0	3 (3.1%)	23 (4.0%)
At least one related[c]	0	0	0	0	2 (3.8%)	6 (2.1%)	0	2 (2.1%)	6 (1.1%)
AE(s) unrelated	0	1 (2.3%)	12 (4.2%)	0	0	5 (1.7%)	0	1 (1.0%)	17 (3.0%)
Progressive disease	1 (6.7%)	1 (2.3%)	4 (1.4%)	0	0	1 (0.3%)	1 (2.8%)	1 (1.0%)	5 (0.9%)
Total number of subjects who died within 60 days of first study treatment dose	0	1 (2.3%)	7 (2.5%)	0	0	3 (1.0%)	0	1 (1.0%)	10 (1.8%)
Primary cause of death									
Adverse event	0	1 (2.3%)	6 (2.1%)	0	0	3 (1.0%)	0	1 (1.0%)	9 (1.6%)
AE(s) unrelated	0	1 (2.3%)	6 (2.1%)	0	0	3 (1.0%)	0	1 (1.0%)	9 (1.6%)
Progressive disease	0	0	1 (0.4%)	0	0	0	0	0	1 (0.2%)

TSFDTH01_3003: Summary of Death and Cause of Death; Intent-to-Treat Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			Total n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
[c] Includes adverse events that were related to at least 1 of the 3 study treatment: lenalidomide, dexamethasone, or daratumumab.

表 2.7.4-付録-49 Number of Subjects With 1 or More Treatment-emergent Adverse Events with Outcome Death by MedDRA Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

TSFAE16_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events with Outcome Death by MedDRA Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Total	Related to LEN	Related to DEX	Total	Related to DARA	Related to LEN	Related to DEX
Total[a]							
Analysis set: safety	281			283			
Total number of subjects with TEAE with outcome death	15 (5.3%)	1 (0.4%)	0	11 (3.9%)	2 (0.7%)	4 (1.4%)	4 (1.4%)
Preferred term							
敗血症性ショック	1 (0.4%)	0	0	3 (1.1%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肺炎	2 (0.7%)	0	0	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
急性腎不全	3 (1.1%)	1 (0.4%)	0	1 (0.4%)	0	0	0
急性単球性白血病	0	0	0	1 (0.4%)	0	1 (0.4%)	0
心肺不全	0	0	0	1 (0.4%)	0	0	0
多臓器不全	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細菌性肺炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
肺水腫	1 (0.4%)	0	0	1 (0.4%)	0	0	0
急性呼吸不全	1 (0.4%)	0	0	0	0	0	0
心停止	1 (0.4%)	0	0	0	0	0	0
脳出血	1 (0.4%)	0	0	0	0	0	0
肺腺癌	1 (0.4%)	0	0	0	0	0	0
神経系障害	1 (0.4%)	0	0	0	0	0	0
形質細胞性白血病	1 (0.4%)	0	0	0	0	0	0
腎不全	1 (0.4%)	0	0	0	0	0	0
敗血症	1 (0.4%)	0	0	0	0	0	0
Japanese							
Analysis set: safety	15			20			
Total number of subjects with TEAE with outcome death	1 (6.7%)	1 (6.7%)	0	0	0	0	0

TSFAE16_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events with Outcome Death by MedDRA Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Total	Related to LEN	Related to DEX	Total	Related to DARA	Related to LEN	Related to DEX
Preferred term							
敗血症性ショック	0	0	0	0	0	0	0
肺炎	0	0	0	0	0	0	0
急性腎不全	1 (6.7%)	1 (6.7%)	0	0	0	0	0
急性単球性白血病	0	0	0	0	0	0	0
心肺不全	0	0	0	0	0	0	0
多臓器不全	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0	0
急性呼吸不全	0	0	0	0	0	0	0
心停止	0	0	0	0	0	0	0
脳出血	0	0	0	0	0	0	0
肺腺癌	0	0	0	0	0	0	0
神経系障害	0	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0	0
腎不全	0	0	0	0	0	0	0
敗血症	0	0	0	0	0	0	0
East Asian[b]							
Analysis set: safety	44			51			
Total number of subjects with TEAE with outcome death	2 (4.5%)	1 (2.3%)	0	2 (3.9%)	1 (2.0%)	2 (3.9%)	1 (2.0%)
Preferred term							
敗血症性ショック	0	0	0	0	0	0	0
肺炎	0	0	0	1 (2.0%)	0	1 (2.0%)	0
急性腎不全	1 (2.3%)	1 (2.3%)	0	0	0	0	0
急性単球性白血病	0	0	0	0	0	0	0
心肺不全	0	0	0	0	0	0	0
多臓器不全	0	0	0	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
細菌性肺炎	0	0	0	0	0	0	0

TSFAE16_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events with Outcome Death by MedDRA Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)			
	Total	Related to LEN	Related to DEX	Total	Related to DARA	Related to LEN	Related to DEX
肺水腫	0	0	0	0	0	0	0
急性呼吸不全	0	0	0	0	0	0	0
心停止	0	0	0	0	0	0	0
脳出血	0	0	0	0	0	0	0
肺腺癌	0	0	0	0	0	0	0
神経系障害	0	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0	0
腎不全	0	0	0	0	0	0	0
敗血症	1 (2.3%)	0	0	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE16_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE16_3003.SAS] 30JUN2016, 21:49

表 2.7.4-付録-50 List of Deaths; All Treated Analysis Set (Studies: MMY2002 and GEN501)

LSFDTH-JST01_2002: List of Deaths; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day of Death)	Cause of Death
8 mg/kg	US10766	100023	67/F/WHITE/USA	2013-11-12	2014-02-04 (85)	2014-05-08 (178)	PROGRESSIVE DISEASE
	US10771	100002	66/F/WHITE/USA	2013-10-08	2013-11-05 (29)	2014-05-30 (235)	PROGRESSIVE DISEASE
		100004	57/M/WHITE/USA	2013-10-29	2014-01-22 (86)	2014-11-21 (389)	PROGRESSIVE DISEASE
	US10782	100005	62/M/WHITE/USA	2013-10-29	2013-11-26 (29)	2014-06-24 (239)	PROGRESSIVE DISEASE
		100014	52/F/WHITE/USA	2013-11-05	2013-12-03 (29)	2014-05-14 (191)	PROGRESSIVE DISEASE
	US10785	100039	55/M/WHITE/USA	2013-12-03	2013-12-04 (2)	2014-03-26 (114)	OTHER: CARDIAC DEATH
8 mg/kg-16 mg/kg	ES00349	100037	62/M/WHITE/ESP	2013-11-26	2014-07-15 (232)	2014-10-27 (336)	OTHER: SUBDURAL HEMATOMA
16 mg/kg	CA00096	100054	78/M/WHITE/CAN	2014-02-21	2014-03-10 (18)	2014-04-03 (42)	ADVERSE EVENT
		100057	59/M/WHITE/CAN	2014-03-12	2014-05-21 (71)	2014-06-17 (98)	PROGRESSIVE DISEASE
		100088	61/M/WHITE/CAN	2014-03-27	2014-05-15 (50)	2014-06-05 (71)	PROGRESSIVE DISEASE
	CA00097	100100	53/M/WHITE/CAN	2014-04-04	2014-04-17 (14)	2014-07-25 (113)	PROGRESSIVE DISEASE
		100101	59/M/WHITE/CAN	2014-04-10	2014-06-05 (57)	2014-06-12 (64)	PROGRESSIVE DISEASE
		100152	73/F/WHITE/CAN	2014-05-13	2014-08-06 (86)	2014-12-31 (233)	PROGRESSIVE DISEASE
	CA00098	100040	63/F/WHITE/CAN	2014-02-19	2014-03-05 (15)	2014-03-15 (25)	PROGRESSIVE DISEASE
		100043	67/M/WHITE/CAN	2014-02-20	2014-04-16 (56)	2014-08-09 (171)	PROGRESSIVE DISEASE
		100044	57/F/WHITE/CAN	2014-02-20	2014-03-13 (22)	2014-04-05 (45)	PROGRESSIVE DISEASE
	CA00104	100121	58/F/WHITE/CAN	2014-04-17	2014-07-24 (99)	2014-10-17 (184)	PROGRESSIVE DISEASE
	ES00349	100087	72/F/WHITE/ESP	2014-04-01	2014-05-20 (50)	2014-05-27 (57)	PROGRESSIVE DISEASE
		100125	63/F/WHITE/ESP	2014-04-15	2014-04-22 (8)	2014-04-28 (14)	PROGRESSIVE DISEASE
	ES00350	100109	64/F/WHITE/ESP	2014-04-10	2014-10-06 (180)	2014-11-24 (229)	PROGRESSIVE DISEASE
	ES00352	100084	80/F/WHITE/ESP	2014-04-09	2014-04-09 (1)	2014-05-06 (28)	ADVERSE EVENT
	US10550	100141	62/M/WHITE/USA	2014-04-25	2014-04-25 (1)	2014-06-05 (42)	PROGRESSIVE DISEASE
	US10554	100074	73/M/WHITE/USA	2014-03-25	2014-05-13 (50)	2014-07-20 (118)	PROGRESSIVE DISEASE
		100080	71/F/WHITE/USA	2014-03-26	2014-04-29 (35)	2014-05-13 (49)	PROGRESSIVE DISEASE
	US10555	100059	59/M/WHITE/USA	2014-02-20	2014-03-27 (36)	2014-04-05 (45)	PROGRESSIVE DISEASE
		100117	57/F/WHITE/USA	2014-03-28	2014-04-18 (22)	2014-05-17 (51)	PROGRESSIVE DISEASE
	US10765	100072	66/F/WHITE/USA	2014-03-24	2014-05-19 (57)	2014-10-08 (199)	PROGRESSIVE DISEASE
	US10767	100096	76/F/WHITE/USA	2014-03-26	2014-06-23 (90)	2014-12-12 (262)	PROGRESSIVE DISEASE
	US10768	100124	64/F/WHITE/USA	2014-04-08	2014-04-22 (15)	2014-10-07 (183)	PROGRESSIVE DISEASE
	US10769	100083	59/F/BLACK OR AFRICAN AMERICAN/USA	2014-04-07	2014-05-19 (43)	2014-10-25 (202)	PROGRESSIVE DISEASE
	US10771	100001	50/F/BLACK OR AFRICAN AMERICAN/USA	2013-10-09	2013-10-24 (16)	2014-08-19 (315)	PROGRESSIVE DISEASE
	US10774	100024	76/M/WHITE/USA	2013-11-12	2014-02-03 (84)	2015-01-01 (416)	PROGRESSIVE DISEASE
	US10782	100065	74/M/NOT REPORTED/USA	2014-03-04	2014-08-19 (169)	2014-10-06 (217)	PROGRESSIVE DISEASE
	US10785	100008	60/M/WHITE/USA	2013-10-28	2013-11-25 (29)	2014-01-29 (94)	PROGRESSIVE DISEASE
		100020	69/M/WHITE/USA	2013-11-11	2013-12-09 (29)	2014-09-19 (313)	PROGRESSIVE DISEASE
	US10796	100078	47/M/WHITE/USA	2014-04-01	2014-05-06 (36)	2014-11-17 (231)	PROGRESSIVE DISEASE

LSFDTH-JST01_2002: List of Deaths; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day of Death)	Cause of Death
		100140	58/F/WHITE/USA	2014-04-11	2014-10-22 (195)	2014-12-30 (264)	PROGRESSIVE DISEASE
		100142	71/M/WHITE/USA	2014-04-21	2014-05-28 (38)	2014-10-18 (181)	PROGRESSIVE DISEASE

LSFDTH-JST01_501P1: List of Deaths; All Treated Analysis Set (Study GEN501 Part1)

Dose Level	Site ID	Enrollment No.	Age (years)/ Sex/ Race/ Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day of Death)	Cause of Death
0.005 mg/kg	DK01	501001	67/M/WHITE/DNK	2008-03-26	2008-03-27 (2)	2008-06-11 (78)	PROGRESSIVE DISEASE
16 mg/kg	DK02	501029	51/M/WHITE/DNK	2012-02-13	2012-02-14 (2)	2012-04-09 (57)	PROGRESSIVE DISEASE

LSFDTH-JST01_501P2: List of Deaths; All Treated Analysis Set (Study GEN501 Part2)

Dose Level	Site ID	Enrollment No.	Age (years)/ Sex/ Race/ Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day of Death)	Cause of Death
SCHEDULE A - 8 mg/kg	50123	501213	73/M//NLD	2013-02-12	2013-07-30 (169)	2014-10-26 (622)	OTHER: LIVER METASTASES ADENOCARCINOMA (PRIMARY TUMOR UNKNOWN)
	50124	501206	60/M/WHITE/SWE	2013-01-08	2013-03-20 (72)	2014-10-14 (645)	DISEASE PROGRESSION
SCHEDULE B - 8 mg/kg	50122	501223	67/M/WHITE/DNK	2013-06-17	2013-08-26 (71)	2013-10-09 (115)	DISEASE PROGRESSION
	50123	501217	53/F//NLD	2013-05-13	2013-08-09 (89)	2014-04-04 (327)	DISEASE PROGRESSION
SCHEDULE C - 8 mg/kg	50122	501226	72/F/WHITE/DNK	2013-07-11	2013-10-09 (91)	2014-02-16 (221)	OTHER: S. AUREOUS PNEUMONIA - PATIENT REFUSED FURTHER TREATMENT FOR THIS
	50123	501227	65/M//NLD	2013-07-25	2013-09-05 (43)	2014-05-03 (283)	DISEASE PROGRESSION
	50125	501225	54/M/WHITE/USA	2013-07-03	2014-02-19 (232)	2014-11-11 (497)	OTHER: NOT KNOWN
		501228	48/M/WHITE/USA	2013-07-24	2013-08-08 (16)	2013-08-21 (29)	DISEASE PROGRESSION
SCHEDULE D - 16 mg/kg	50121	501240	50/M/OTHER/DNK	2013-10-28	2013-10-28 (1)	2014-01-26 (91)	DISEASE PROGRESSION
	50123	501238	66/F//NLD	2013-10-29	2013-11-19 (22)	2014-08-26 (302)	OTHER: UNKNOWN
	50124	501241	50/M/WHITE/SWE	2013-11-07	2014-04-01 (146)	2014-05-06 (181)	DISEASE PROGRESSION
	50125	501245	59/M/WHITE/USA	2013-12-20	2014-01-10 (22)	2014-09-10 (265)	OTHER: NOT KNOWN
SCHEDULE E - 16 mg/kg	50121	501264	67/M/WHITE/DNK	2014-05-27	2014-07-09 (44)	2014-12-27 (215)	DISEASE PROGRESSION
	50122	501268	61/F/WHITE/DNK	2014-05-27	2014-07-29 (64)	2014-11-04 (162)	DISEASE PROGRESSION
	50124	501255	71/M/WHITE/SWE	2014-04-15	2014-05-13 (29)	2014-06-07 (54)	DISEASE PROGRESSION
	50125	501262	61/M/WHITE/USA	2014-05-09	2014-06-02 (25)	2014-06-14 (37)	ADVERSE EVENT

LSFDTH-JST01_501P2: List of Deaths; All Treated Analysis Set (Study GEN501 Part2)

Dose Level	Site ID	Enrollment No.	Age (years)/ Sex/ Race/ Country	Date of First Dose	Date of Last Dose (Study Day)	Date of Death (Study Day of Death)	Cause of Death
SCHEDULE A - 8 mg/kg	50123	501213	73/M//NLD	2013-02-12	2013-07-30 (169)	2014-10-26 (622)	OTHER: LIVER METASTASES ADENOCARCINOMA (PRIMARY TUMOR UNKNOWN)
	50124	501206	60/M/WHITE/SWE	2013-01-08	2013-03-20 (72)	2014-10-14 (645)	DISEASE PROGRESSION
SCHEDULE B - 8 mg/kg	50122	501223	67/M/WHITE/DNK	2013-06-17	2013-08-26 (71)	2013-10-09 (115)	DISEASE PROGRESSION
	50123	501217	53/F//NLD	2013-05-13	2013-08-09 (89)	2014-04-04 (327)	DISEASE PROGRESSION
SCHEDULE C - 8 mg/kg	50122	501226	72/F/WHITE/DNK	2013-07-11	2013-10-09 (91)	2014-02-16 (221)	OTHER: S. AUREOUS PNEUMONIA - PATIENT REFUSED FURTHER TREATMENT FOR THIS
	50123	501227	65/M//NLD	2013-07-25	2013-09-05 (43)	2014-05-03 (283)	DISEASE PROGRESSION
	50125	501225	54/M/WHITE/USA	2013-07-03	2014-02-19 (232)	2014-11-11 (497)	OTHER: NOT KNOWN
		501228	48/M/WHITE/USA	2013-07-24	2013-08-08 (16)	2013-08-21 (29)	DISEASE PROGRESSION
SCHEDULE D - 16 mg/kg	50121	501240	50/M/OTHER/DNK	2013-10-28	2013-10-28 (1)	2014-01-26 (91)	DISEASE PROGRESSION
	50123	501238	66/F//NLD	2013-10-29	2013-11-19 (22)	2014-08-26 (302)	OTHER: UNKNOWN
	50124	501241	50/M/WHITE/SWE	2013-11-07	2014-04-01 (146)	2014-05-06 (181)	DISEASE PROGRESSION
	50125	501245	59/M/WHITE/USA	2013-12-20	2014-01-10 (22)	2014-09-10 (265)	OTHER: NOT KNOWN
SCHEDULE E - 16 mg/kg	50121	501264	67/M/WHITE/DNK	2014-05-27	2014-07-09 (44)	2014-12-27 (215)	DISEASE PROGRESSION
	50122	501268	61/F/WHITE/DNK	2014-05-27	2014-07-29 (64)	2014-11-04 (162)	DISEASE PROGRESSION
	50124	501255	71/M/WHITE/SWE	2014-04-15	2014-05-13 (29)	2014-06-07 (54)	DISEASE PROGRESSION
	50125	501262	61/M/WHITE/USA	2014-05-09	2014-06-02 (25)	2014-06-14 (37)	ADVERSE EVENT

表 2.7.4-付録-51 Listing of Grade 5 Treatment-emergent Adverse Events; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

LSFAE02: Listing of Grade 5 Treatment-emergent Adverse Events; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

Study ID	Dose Level	Site ID	Enrollment No.	AE Onset Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	MedDRA Preferred Term	Serious?	Infusion Related Reaction?	Relationship to Study Drug	Action Taken	Outcome
GEN501 Part 1	<=4 mg/kg	DK01	501001	2008-04-02 (8)	2	7	腹痛	Y	N	NOT RELATED	DOSE NOT CHANGED	FATAL
GEN501 Part 2	16 mg/kg	50125	501262	2014-06-08 (31)	2	7	肺炎	Y	N	NOT RELATED	DRUG WITHDRAWN	FATAL
MMY2002	16 mg/kg	CA00096	100054	2014-04-03 (42)	3	25	心肺停止	Y	N	NOT RELATED	NOT APPLICABLE	FATAL
			100057	2014-06-11 (92)	10	22	全身健康状態低下	Y	N	NOT RELATED	NOT APPLICABLE	FATAL
		CA00097	100101	2014-06-12 (64)	9	8	呼吸不全	Y	N	NOT RELATED	NOT APPLICABLE	FATAL
		CA00098	100040	2014-03-08 (18)	3	4	全身健康状態低下	Y	N	NOT RELATED	DOSE NOT CHANGED	FATAL
		ES00349	100087	2014-05-27 (57)	8	8	高カルシウム血症	Y	N	NOT RELATED	NOT APPLICABLE	FATAL
			100125	2014-04-28 (14)	2	7	全身健康状態低下	Y	N	NOT RELATED	DOSE NOT CHANGED	FATAL
		ES00352	100084	2014-05-06 (28)	1	28	全身健康状態低下	Y	N	NOT RELATED	DRUG WITHDRAWN	FATAL
		US10554	100080	2014-05-13 (49)	6	15	全身健康状態低下	Y	N	NOT RELATED	NOT APPLICABLE	FATAL
		US10555	100059	2014-04-05 (45)	6	10	肝不全	Y	N	NOT RELATED	NOT APPLICABLE	FATAL

Note: Adverse events were coded using MedDRA Version 17.0 and CTCAE version 4.03 for toxicity grades.
For adverse events with onset date same as infusion date but missing onset time (hour and minute), they were considered after the infusion.

[LSFAE02.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\lsfae02.sas] 14APR2015, 09:46

表 2.7.4-付録-52 Listing of Adverse Events Leading to Death; All Treated Analysis Population (Study 54767414MMY1002)

LSFAE02: Listing of Adverse Events Leading to Death; All Treated Analysis Population (Study 54767414MMY1002)

Treatment Group	Subject ID	Sex/ Age	Race	Reported Term	Preferred Term[a]	TEAE	Onset Date/ (Study Day)	Outcome Date/ (Study Day)	Duration[b]	Outcome	Toxicity Grade	Action Taken	Causality	Serious Event	DLT Evaluated?

No Data to Report

[a] Adverse Events are coded using MedDRA 18.0.
[b] Calculated as the number of days between Onset Date and Outcome Date when outcome is Recovered or Recovering.

[LSFAE02.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\lsfae02.sas] 22FEB2016, 11:19

表 2.7.4-付録-53 Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with serious TEAE	80 (33.8%)	102 (42.0%)	118 (42.0%)	156 (49.1%)	50 (48.5%)
MedDRA system organ class/Preferred term					
感染症および寄生虫症	43 (18.1%)	48 (19.8%)	64 (22.8%)	94 (29.6%)	21 (20.4%)
肺炎	22 (9.3%)	19 (7.8%)	24 (8.5%)	24 (7.5%)	7 (6.8%)
インフルエンザ	2 (0.8%)	0	4 (1.4%)	8 (2.5%)	1 (1.0%)
下気道感染	2 (0.8%)	2 (0.8%)	3 (1.1%)	7 (2.2%)	0
気管支炎	1 (0.4%)	5 (2.1%)	4 (1.4%)	6 (1.9%)	0
気道感染	1 (0.4%)	0	2 (0.7%)	5 (1.6%)	0
尿路感染	1 (0.4%)	0	1 (0.4%)	5 (1.6%)	1 (1.0%)
胃腸炎	3 (1.3%)	2 (0.8%)	1 (0.4%)	3 (0.9%)	0
感染	0	0	3 (1.1%)	3 (0.9%)	0
インフルエンザ性肺炎	0	0	0	3 (0.9%)	0
敗血症性ショック	1 (0.4%)	0	1 (0.4%)	3 (0.9%)	0
虫垂炎	0	0	1 (0.4%)	2 (0.6%)	0
気管支肺炎	1 (0.4%)	3 (1.2%)	0	2 (0.6%)	0
ウイルス性胃腸炎	0	0	1 (0.4%)	2 (0.6%)	0
大葉性肺炎	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	0
細菌性肺炎	0	0	1 (0.4%)	2 (0.6%)	0
ＲＳウイルス感染	0	1 (0.4%)	0	2 (0.6%)	0
敗血症	2 (0.8%)	2 (0.8%)	5 (1.8%)	2 (0.6%)	4 (3.9%)
上気道感染	2 (0.8%)	4 (1.6%)	5 (1.8%)	2 (0.6%)	1 (1.0%)
急性副鼻腔炎	0	0	0	1 (0.3%)	0
細菌感染	1 (0.4%)	0	0	1 (0.3%)	0
細気管支炎	0	0	0	1 (0.3%)	0
細菌性気管支炎	0	0	0	1 (0.3%)	0
カンジダ感染	0	0	0	1 (0.3%)	0
蜂巣炎	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
サイトメガロウイルス感染	0	0	0	1 (0.3%)	0
喉頭蓋炎	0	0	0	1 (0.3%)	0
大腸菌性菌血症	0	0	0	1 (0.3%)	0
硬膜外膿瘍	0	0	0	1 (0.3%)	0
歯肉炎	0	0	0	1 (0.3%)	0
Ｈ１Ｎ１インフルエンザ	0	0	0	1 (0.3%)	0
感染性脊椎炎	0	0	0	1 (0.3%)	0
リステリア性敗血症	0	0	0	1 (0.3%)	0
肺感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (1.0%)
鼻膿瘍	0	0	0	1 (0.3%)	0
好中球減少性敗血症	0	0	0	1 (0.3%)	0
口腔真菌感染	0	0	0	1 (0.3%)	0
パラインフルエンザウイルス感染	0	0	1 (0.4%)	1 (0.3%)	1 (1.0%)
耳下腺炎	0	0	0	1 (0.3%)	0
眼窩周囲蜂巣炎	0	0	0	1 (0.3%)	0
ヘモフィルス性肺炎	0	0	0	1 (0.3%)	0
クレブシエラ菌性肺炎	0	0	0	1 (0.3%)	0
レジオネラ菌性肺炎	0	0	1 (0.4%)	1 (0.3%)	0
レンサ球菌性肺炎	0	0	0	1 (0.3%)	0
ウイルス性肺炎	0	0	0	1 (0.3%)	0
ウイルス性気道感染	0	0	0	1 (0.3%)	0
サルモネラ性菌血症	0	0	0	1 (0.3%)	0

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
皮膚感染	0	0	0	1 (0.3%)	0
軟部組織感染	0	0	0	1 (0.3%)	0
扁桃炎	0	0	0	1 (0.3%)	0
細菌性上気道感染	0	0	0	1 (0.3%)	0
子宮膿瘍	0	0	0	1 (0.3%)	0
ウイルス感染	0	0	1 (0.4%)	1 (0.3%)	0
肛門膿瘍	0	0	1 (0.4%)	0	0
脳膿瘍	1 (0.4%)	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (1.0%)
クロストリジウム・ディフィシレ感染	0	0	2 (0.7%)	0	0
憩室炎	0	0	0	0	1 (1.0%)
感染性小腸結腸炎	0	0	1 (0.4%)	0	0
精巣上体炎	1 (0.4%)	0	0	0	0
丹毒	0	0	1 (0.4%)	0	0
真菌性食道炎	0	1 (0.4%)	0	0	0
壊疽	1 (0.4%)	0	0	0	0
消化管感染	0	0	1 (0.4%)	0	0
ヘモフィルス感染	0	0	1 (0.4%)	0	0
帯状疱疹	2 (0.8%)	1 (0.4%)	0	0	0
真菌性角膜炎	0	0	1 (0.4%)	0	0
乳腺炎	0	0	0	0	1 (1.0%)
メタニューモウイルス感染	0	1 (0.4%)	0	0	0
壊死性筋膜炎	0	0	1 (0.4%)	0	0
ノカルジア症	1 (0.4%)	0	0	0	0
眼部単純ヘルペス	1 (0.4%)	0	0	0	0
骨髄炎	0	0	2 (0.7%)	0	0
腹膜炎	0	1 (0.4%)	0	0	0
咽頭炎	0	0	1 (0.4%)	0	0
ニューモシスチス・イロベチイ肺炎	0	1 (0.4%)	0	0	0
サイトメガロウイルス性肺炎	0	2 (0.8%)	0	0	0
肺炎球菌性肺炎	0	1 (0.4%)	0	0	0
進行性多巣性白質脳症	0	0	0	0	1 (1.0%)
シュードモナス性敗血症	0	0	0	0	1 (1.0%)
肺敗血症	0	2 (0.8%)	0	0	0
肺結核	0	0	1 (0.4%)	0	0
腎盂腎炎	0	1 (0.4%)	0	0	0
急性腎盂腎炎	0	0	1 (0.4%)	0	0
慢性腎盂腎炎	1 (0.4%)	0	0	0	0
ライノウイルス感染	0	1 (0.4%)	0	0	0
副鼻腔炎	0	1 (0.4%)	0	0	0
脊髄感染	0	0	0	0	1 (1.0%)
気管気管支炎	1 (0.4%)	0	0	0	0
尿路性敗血症	0	0	1 (0.4%)	0	0
水痘帯状疱疹ウイルス感染	0	0	1 (0.4%)	0	0
血液およびリンパ系障害	2 (0.8%)	15 (6.2%)	11 (3.9%)	21 (6.6%)	8 (7.8%)
発熱性好中球減少症	0	2 (0.8%)	4 (1.4%)	12 (3.8%)	4 (3.9%)
好中球減少症	0	2 (0.8%)	0	5 (1.6%)	1 (1.0%)
貧血	1 (0.4%)	8 (3.3%)	2 (0.7%)	3 (0.9%)	3 (2.9%)
血小板減少症	1 (0.4%)	6 (2.5%)	1 (0.4%)	1 (0.3%)	2 (1.9%)
骨髄機能不全	0	0	1 (0.4%)	0	0
過粘稠度症候群	0	0	1 (0.4%)	0	1 (1.0%)
リンパ節症	0	0	1 (0.4%)	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	0	0	1 (0.4%)	0	0
呼吸器、胸郭および縦隔障害	7 (3.0%)	15 (6.2%)	14 (5.0%)	17 (5.3%)	11 (10.7%)

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
肺塞栓症	2 (0.8%)	1 (0.4%)	8 (2.8%)	8 (2.5%)	0
呼吸困難	0	0	1 (0.4%)	2 (0.6%)	3 (2.9%)
肺水腫	1 (0.4%)	0	1 (0.4%)	2 (0.6%)	0
呼吸不全	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
急性肺水腫	0	0	0	1 (0.3%)	0
低酸素症	0	0	0	1 (0.3%)	2 (1.9%)
喉頭浮腫	0	1 (0.4%)	0	1 (0.3%)	0
肺臓炎	0	0	0	1 (0.3%)	1 (1.0%)
肺石灰化	0	0	0	1 (0.3%)	0
急性呼吸不全	0	0	1 (0.4%)	0	0
喘息	0	1 (0.4%)	0	0	1 (1.0%)
気管支反応性亢進	0	0	0	0	1 (1.0%)
気管支肺症	0	0	0	0	1 (1.0%)
気管支痙攣	0	0	1 (0.4%)	0	0
慢性閉塞性肺疾患	1 (0.4%)	1 (0.4%)	0	0	1 (1.0%)
鼻出血	0	2 (0.8%)	0	0	0
胸水症	0	1 (0.4%)	0	0	0
過換気	0	1 (0.4%)	0	0	0
間質性肺疾患	0	0	1 (0.4%)	0	2 (1.9%)
肺障害	0	0	1 (0.4%)	0	0
器質化肺炎	0	1 (0.4%)	0	0	0
口腔咽頭腫脹	0	1 (0.4%)	0	0	0
胸水	0	2 (0.8%)	0	0	1 (1.0%)
誤嚥性肺炎	0	1 (0.4%)	0	0	0
気胸	0	0	1 (0.4%)	0	0
肺胞出血	1 (0.4%)	0	0	0	0
肺動脈血栓症	0	1 (0.4%)	0	0	0
肺出血	0	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	12 (5.1%)	9 (3.7%)	8 (2.8%)	16 (5.0%)	4 (3.9%)
発熱	4 (1.7%)	4 (1.6%)	4 (1.4%)	10 (3.1%)	0
全身健康状態低下	3 (1.3%)	1 (0.4%)	0	2 (0.6%)	2 (1.9%)
無力症	3 (1.3%)	0	0	1 (0.3%)	0
胸部不快感	0	0	0	1 (0.3%)	0
歩行障害	0	0	0	1 (0.3%)	0
多臓器不全	0	0	0	1 (0.3%)	0
非心臓性胸痛	0	0	1 (0.4%)	1 (0.3%)	0
疼痛	0	1 (0.4%)	2 (0.7%)	1 (0.3%)	0
全身性炎症反応症候群	0	0	0	1 (0.3%)	0
状態悪化	3 (1.3%)	0	0	0	0
疲労	0	2 (0.8%)	1 (0.4%)	0	1 (1.0%)
全身性浮腫	0	0	1 (0.4%)	0	0
インフルエンザ様疾患	1 (0.4%)	0	0	0	0
末梢性浮腫	0	1 (0.4%)	0	0	1 (1.0%)
胃腸障害	8 (3.4%)	13 (5.3%)	11 (3.9%)	13 (4.1%)	5 (4.9%)
下痢	0	4 (1.6%)	6 (2.1%)	6 (1.9%)	1 (1.0%)
憩室穿孔	0	1 (0.4%)	0	2 (0.6%)	0
悪心	0	0	0	2 (0.6%)	0
大腸炎	0	0	1 (0.4%)	1 (0.3%)	0
便秘	3 (1.3%)	0	0	1 (0.3%)	0
出血性胃腸管血管異形成	0	0	0	1 (0.3%)	0
胃腸障害	0	0	0	1 (0.3%)	0
鼠径ヘルニア	0	0	0	1 (0.3%)	0
嘔吐	0	0	1 (0.4%)	1 (0.3%)	0
腹痛	3 (1.3%)	0	0	0	2 (1.9%)
上腹部痛	0	1 (0.4%)	0	0	0
十二指腸潰瘍	0	1 (0.4%)	0	0	0

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
糞塊	1 (0.4%)	0	0	0	0
胃炎	0	1 (0.4%)	0	0	0
吐血	0	0	1 (0.4%)	0	0
嵌頓臍ヘルニア	1 (0.4%)	0	0	0	0
腸閉塞	0	1 (0.4%)	1 (0.4%)	0	0
下部消化管出血	0	0	1 (0.4%)	0	0
メレナ	0	1 (0.4%)	0	0	0
食道炎	0	0	1 (0.4%)	0	0
急性膵炎	0	1 (0.4%)	0	0	0
慢性膵炎	0	1 (0.4%)	0	0	0
小腸閉塞	0	1 (0.4%)	0	0	2 (1.9%)
筋骨格系および結合組織障害	8 (3.4%)	8 (3.3%)	12 (4.3%)	10 (3.1%)	4 (3.9%)
背部痛	2 (0.8%)	1 (0.4%)	5 (1.8%)	3 (0.9%)	0
骨痛	1 (0.4%)	2 (0.8%)	0	2 (0.6%)	2 (1.9%)
側腹部痛	0	1 (0.4%)	0	1 (0.3%)	0
椎間板突出	0	0	0	1 (0.3%)	0
筋骨格痛	0	0	1 (0.4%)	1 (0.3%)	0
骨壊死	0	0	0	1 (0.3%)	0
四肢痛	2 (0.8%)	0	0	1 (0.3%)	0
関節痛	0	1 (0.4%)	0	0	0
筋力低下	0	0	1 (0.4%)	0	2 (1.9%)
筋骨格系胸痛	0	1 (0.4%)	0	0	0
頚部痛	1 (0.4%)	0	0	0	0
顎骨壊死	1 (0.4%)	0	2 (0.7%)	0	0
病的骨折	0	2 (0.8%)	1 (0.4%)	0	0
脊柱管狭窄症	0	0	2 (0.7%)	0	0
脊椎痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
心臓障害	5 (2.1%)	12 (4.9%)	9 (3.2%)	9 (2.8%)	2 (1.9%)
心房細動	0	5 (2.1%)	2 (0.7%)	2 (0.6%)	1 (1.0%)
急性冠動脈症候群	0	1 (0.4%)	0	1 (0.3%)	0
狭心症	0	0	0	1 (0.3%)	0
心房粗動	0	0	0	1 (0.3%)	0
心アミロイドーシス	0	0	0	1 (0.3%)	0
うっ血性心不全	1 (0.4%)	2 (0.8%)	0	1 (0.3%)	2 (1.9%)
心肺不全	0	0	0	1 (0.3%)	0
心筋梗塞	2 (0.8%)	0	1 (0.4%)	1 (0.3%)	0
洞性不整脈	0	0	0	1 (0.3%)	0
急性心筋梗塞	0	1 (0.4%)	3 (1.1%)	0	0
上室性不整脈	0	1 (0.4%)	0	0	0
心停止	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
心不全	0	1 (0.4%)	0	0	0
心原性ショック	1 (0.4%)	1 (0.4%)	0	0	0
心膜炎	0	0	1 (0.4%)	0	0
上室性頻脈	0	0	1 (0.4%)	0	0
心室性期外収縮	1 (0.4%)	0	0	0	0
神経系障害	5 (2.1%)	9 (3.7%)	13 (4.6%)	9 (2.8%)	5 (4.9%)
失神	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
脳梗塞	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
脳血管発作	1 (0.4%)	0	0	1 (0.3%)	1 (1.0%)
認知障害	0	0	0	1 (0.3%)	0
失神寸前の状態	0	0	0	1 (0.3%)	1 (1.0%)
痙攣発作	0	0	0	1 (0.3%)	0
一過性脳虚血発作	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
三叉神経障害	0	0	0	1 (0.3%)	0
失語症	0	0	1 (0.4%)	0	0
頚動脈硬化症	0	0	1 (0.4%)	0	0

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
脳出血	0	0	1 (0.4%)	0	0
塞栓性脳卒中	0	1 (0.4%)	0	0	0
頭痛	0	1 (0.4%)	0	0	0
感覚鈍麻	0	0	0	0	1 (1.0%)
肋間神経痛	0	0	1 (0.4%)	0	0
虚血性脳卒中	0	2 (0.8%)	1 (0.4%)	0	0
意識消失	0	0	1 (0.4%)	0	1 (1.0%)
不全単麻痺	1 (0.4%)	0	0	0	0
神経系障害	0	0	1 (0.4%)	0	0
末梢性感覚ニューロパチー	0	0	1 (0.4%)	0	0
根症候群	0	1 (0.4%)	0	0	0
下肢静止不能症候群	1 (0.4%)	0	0	0	0
傾眠	0	0	1 (0.4%)	0	0
脊髄圧迫	0	0	0	0	1 (1.0%)
第７脳神経麻痺	0	0	1 (0.4%)	0	0
第６脳神経麻痺	0	1 (0.4%)	0	0	0
傷害、中毒および処置合併症	5 (2.1%)	7 (2.9%)	8 (2.8%)	8 (2.5%)	7 (6.8%)
圧迫骨折	0	0	0	1 (0.3%)	0
足骨折	0	0	0	1 (0.3%)	0
手骨折	0	0	0	1 (0.3%)	0
股関節部骨折	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0
腓骨神経損傷	0	0	0	1 (0.3%)	0
肋骨骨折	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
脊椎圧迫骨折	0	0	0	1 (0.3%)	1 (1.0%)
脊椎骨折	0	1 (0.4%)	0	1 (0.3%)	0
挫傷	1 (0.4%)	0	0	0	0
転倒	0	0	1 (0.4%)	0	4 (3.9%)
大腿骨頚部骨折	0	0	1 (0.4%)	0	0
大腿骨骨折	0	2 (0.8%)	0	0	2 (1.9%)
上腕骨骨折	0	2 (0.8%)	1 (0.4%)	0	1 (1.0%)
関節脱臼	0	0	1 (0.4%)	0	0
骨盤骨折	0	0	1 (0.4%)	0	1 (1.0%)
橈骨骨折	0	0	1 (0.4%)	0	0
硬膜下血腫	1 (0.4%)	0	1 (0.4%)	0	0
胸椎骨折	1 (0.4%)	0	0	0	0
上肢骨折	0	1 (0.4%)	0	0	0
代謝および栄養障害	7 (3.0%)	6 (2.5%)	3 (1.1%)	6 (1.9%)	2 (1.9%)
高カルシウム血症	0	2 (0.8%)	1 (0.4%)	2 (0.6%)	1 (1.0%)
脱水	2 (0.8%)	1 (0.4%)	0	1 (0.3%)	1 (1.0%)
電解質失調	0	0	0	1 (0.3%)	0
高血糖	2 (0.8%)	2 (0.8%)	0	1 (0.3%)	0
低カルシウム血症	0	0	0	1 (0.3%)	0
食欲減退	0	0	1 (0.4%)	0	0
痛風	0	0	1 (0.4%)	0	0
低血糖症	1 (0.4%)	0	0	0	0
低ナトリウム血症	2 (0.8%)	0	0	0	0
代謝性アシドーシス	1 (0.4%)	1 (0.4%)	0	0	0
腫瘍崩壊症候群	0	1 (0.4%)	0	0	0
腎および尿路障害	4 (1.7%)	6 (2.5%)	12 (4.3%)	6 (1.9%)	2 (1.9%)
急性腎不全	1 (0.4%)	3 (1.2%)	8 (2.8%)	3 (0.9%)	2 (1.9%)
高窒素血症	0	0	1 (0.4%)	1 (0.3%)	0
腎不全	0	0	3 (1.1%)	1 (0.3%)	0
尿道出血	0	0	0	1 (0.3%)	0
慢性腎臓病	1 (0.4%)	1 (0.4%)	0	0	0
血尿	0	1 (0.4%)	0	0	0
骨髄腫円柱腎症	1 (0.4%)	0	0	0	0

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
腎機能障害	0	1 (0.4%)	0	0	0
尿閉	1 (0.4%)	0	0	0	0
血管障害	2 (0.8%)	3 (1.2%)	3 (1.1%)	6 (1.9%)	1 (1.0%)
塞栓症	0	0	0	1 (0.3%)	0
出血性梗塞	0	0	0	1 (0.3%)	0
高血圧	0	1 (0.4%)	0	1 (0.3%)	0
低血圧	0	0	0	1 (0.3%)	0
起立性低血圧	2 (0.8%)	0	0	1 (0.3%)	0
末梢動脈狭窄	0	0	0	1 (0.3%)	0
大動脈解離	0	0	0	0	1 (1.0%)
深部静脈血栓症	0	0	1 (0.4%)	0	0
高血圧クリーゼ	0	1 (0.4%)	0	0	0
末梢動脈瘤	0	1 (0.4%)	0	0	0
静脈炎	0	0	1 (0.4%)	0	0
静脈閉塞	0	0	1 (0.4%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	6 (2.5%)	8 (2.8%)	5 (1.6%)	0
急性単球性白血病	0	0	0	1 (0.3%)	0
胃腺癌	0	0	0	1 (0.3%)	0
ボーエン病	0	0	0	1 (0.3%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.3%)	0
形質細胞性白血病	0	0	2 (0.7%)	1 (0.3%)	0
結腸腺癌	0	1 (0.4%)	0	0	0
肛門直腸の良性新生物	0	0	1 (0.4%)	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0
乳癌	0	1 (0.4%)	0	0	0
再発乳癌	1 (0.4%)	0	0	0	0
胃腸管腺腫	0	1 (0.4%)	0	0	0
脂肪肉腫	0	1 (0.4%)	0	0	0
肺腺癌	0	0	1 (0.4%)	0	0
形質細胞腫	0	1 (0.4%)	0	0	0
前立腺癌	0	0	1 (0.4%)	0	0
直腸腺癌	0	0	1 (0.4%)	0	0
扁平上皮癌	0	0	1 (0.4%)	0	0
皮膚有棘細胞癌	0	1 (0.4%)	0	0	0
移行上皮癌	0	1 (0.4%)	0	0	0
臨床検査	0	2 (0.8%)	2 (0.7%)	3 (0.9%)	0
Ａ型インフルエンザウイルス検査陽性	0	0	0	1 (0.3%)	0
国際標準比増加	0	0	0	1 (0.3%)	0
トロポニン増加	0	0	0	1 (0.3%)	0
アラニンアミノトランスフェラーゼ増加	0	1 (0.4%)	0	0	0
体温上昇	0	0	1 (0.4%)	0	0
診断法	0	0	1 (0.4%)	0	0
心電図ＱＴ間隔異常	0	1 (0.4%)	0	0	0
γ－グルタミルトランスフェラーゼ増加	0	1 (0.4%)	0	0	0
眼障害	0	1 (0.4%)	0	2 (0.6%)	1 (1.0%)
白内障	0	0	0	1 (0.3%)	0
後嚢破裂	0	0	0	1 (0.3%)	0
複視	0	1 (0.4%)	0	0	0
霧視	0	0	0	0	1 (1.0%)
内分泌障害	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	0
ステロイド離脱症候群	0	0	0	1 (0.3%)	0
副腎機能不全	1 (0.4%)	0	0	0	0

TSFAE05A: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
甲状腺機能亢進症	0	1 (0.4%)	0	0	0
精神障害	1 (0.4%)	2 (0.8%)	2 (0.7%)	1 (0.3%)	0
うつ病	1 (0.4%)	0	0	1 (0.3%)	0
錯乱状態	0	1 (0.4%)	1 (0.4%)	0	0
抑うつ気分	0	1 (0.4%)	0	0	0
抑うつ症状	0	0	1 (0.4%)	0	0
生殖系および乳房障害	0	0	0	1 (0.3%)	0
前立腺腫大	0	0	0	1 (0.3%)	0
皮膚および皮下組織障害	0	0	0	1 (0.3%)	0
全身性皮疹	0	0	0	1 (0.3%)	0
丘疹性皮疹	0	0	0	1 (0.3%)	0
肝胆道系障害	0	0	2 (0.7%)	0	0
胆管結石	0	0	1 (0.4%)	0	0
肝障害	0	0	1 (0.4%)	0	0
免疫系障害	0	0	0	0	1 (1.0%)
サイトカイン放出症候群	0	0	0	0	1 (1.0%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE05A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE05A.SAS] 01JUN2016, 10:38

表 2.7.4-付録-54 List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
Vd	100003	40/M/White/ USA		上気道感染 [UPPER RESPIRATORY INFECTION]	20/7	Yes	3	NR	DO	Poss.	NA	DI	DNC	RECOVERED /RESOLVED	NA
	100009	84/M/White/ USA		インフルエンザ [INFLUENZA A]	39/8	Yes	3	NR	Poss.	Prob.	NA	DR	DI	RECOVERED /RESOLVED	NA
	100020	80/M/White/ USA		便秘 [CONSTIPATION]	49/48	Yes	2	NR	Poss.	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				尿閉 [URINARY RETENTION]	57/71	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				無力症 [WEAKNESS]	91/2	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	100044	81/M/Unknown/ USA		肺炎 [BILATERAL PNEUMONIA]	37/14	Yes	3	NR	DO	Poss.	NA	DI	DI	RECOVERED /RESOLVED	No
	310007	69/M/Not Reported/ NLD		慢性閉塞性肺疾患 [EXACERBATION COPD]	151/2	Yes	3	NR	DO	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	310011	71/M/White/ NLD		腹痛 [ABDOMINAL PAIN]	28/4	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
	310016	68/M/White/ NLD		気道感染 [RESPIRATORY TRACT INFECTION]	17/9	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
				気道感染 [RESPIRATORY TRACT INFECTION]	28/4	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
				四肢痛 [PAIN LEFT LEG]	84/3	Yes	3	NR	NR	NR	NA	DW	DW	RECOVERED /RESOLVED	No
				不全単麻痺 [PARESIS LEFT LEG]	84/3	Yes	3	NR	NR	NR	NA	DW	DW	RECOVERED /RESOLVED	No
				全身健康状態低下 [WORSENING OF CONDITIONING]	96/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	310021	69/M/White/ NLD		糞塊 [COPROSTASIS]	119/2	Yes	2	NR	Poss.	Poss.	NA	DR	DNC	RECOVERED /RESOLVED	NA
	310027	67/F/White/ NLD		便秘 [OBSTIPATION]	16/2	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
				骨痛 [INCREASED SKELETAL PAIN]	102/12	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	NA
	310029	70/M/White/ NLD		胃腸炎 [GASTROENTERITIS]	161/3	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	340002	58/M/White/ ESP		硬膜下血腫 [SUBDURAL HEMATOMA IN SKULL]	115/14	Yes	3	NR	Poss.	NR	NA	DW	DW	RECOVERED /RESOLVED	NA
	340005	81/F/White/ ESP		嵌頓臍ヘルニア [ENCARCERATED UMBILICAL HERNIA]	27/6	Yes	4	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
	340006	48/M/White/ ESP		肺炎 [PNEUMONY]	49/9	Yes	3	NR	Prob.	Prob.	NA	DI	DI	RECOVERED /RESOLVED	NA
	340008	67/F/White/ ESP		呼吸不全 [RESPIRATORY INSUFFICIENCY]	31/3	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				発熱 [FEVER WITHOUT FOCUS]	99/4	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
	340009	70/F/White/ ESP		肺炎 [PNEUMONIA]	39/13	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED WITH SEQUELAE	NA
	340010	71/F/White/ ESP		顎骨壊死 [OVERINFECTED OSTEONECROSIS JAW]	65/3	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	NA
				股関節部骨折 [HIP FRACTURE]	165/23	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	340012	77/F/White/ ESP		下気道感染 [LOWER RESPIRATORY TRACT INFECTION]	62/9	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				尿路感染 [URINARY TRACT INFECTION]	62/9	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
	340013	80/F/White/ ESP		下気道感染 [LOW RESPIRATORY TRACT INFECTION]	107/5	Yes	2	NR	Poss.	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
				肺塞栓症 [PULMONARY EMBOLISM]	200/33	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
	340022	71/M/White/ ESP		敗血症 [SEPSIS]	28/10	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
				細菌感染 [BACTERIAL INFECTIOUS PROCESS]	50/8	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				代謝性アシドーシス [METABOLIC ACIDOSIS]	80/23	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				慢性腎臓病 [RENAL INSUFFICIENCY CHRONIC]	120/11	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	No
				腹痛 [ABDOMINAL PAIN]	141/4	Yes	2	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	340026	66/M/White/ ESP		肋骨骨折 [RIB FRACTURE]	19/7	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				胃腸炎 [ACUTE GASTROENTERITIS]	74/1	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
				起立性低血圧 [ORTHOSTATIC HYPOTENSION]	74/1	Yes	3	NR	Poss.	Poss.	NA	DW	DW	RECOVERED /RESOLVED	NA
	340028	83/M/White/ ESP		敗血症性ショック [SEPTIC SHOCK]	12/2	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	340031	79/F/White/ ESP		肺炎 [PNEUMONIA]	88/8	Yes	3	NR	Prob.	Prob.	NA	DR	DI	RECOVERED /RESOLVED	No
				気管気管支炎 [ACUTE TRACHEOBRONCHITIS]	140/5	Yes	4	NR	NR	Poss.	NA	NA	NA	RECOVERED /RESOLVED	No
				気管気管支炎 [ACUTE TRACHEOBRONCHITIS]	145/1	Yes	5	NR	NR	Poss.	DNC	DNC	DNC	FATAL	NA
	340033	85/M/White/ ESP		肺炎 [PNEUMONIA]	13/35	Yes	3	NR	Poss.	Poss.	NA	DW	DW	NOT RECOVERED /NOT RESOLVED	No
				肺炎 [PNEUMONIA]	48/1	Yes	5	NR	Poss.	Poss.	NA	NA	NA	FATAL	No
	360012	46/F/White/ HUN		肺炎 [PNEUMONIA]	15/11	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	360017	66/F/White/ HUN		胃腸炎 [GASTROENTERITIS]	74/	Yes	3	NR	DO	Poss.	NA	DI	DI	NOT RECOVERED /NOT RESOLVED	NA
				呼吸不全 [RESPIRATORY FAILURE]	76/	Yes	4	NR	NR	Poss.	NA	NA	NA	UNKNOWN	NA
				心停止 [CARDIAC ARREST]	98/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	360021	64/M/White/ HUN		大葉性肺炎 [LOBULAR PNEUMONIA RIGHT SIDE]	12/14	Yes	2	NR	NR	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
				高血糖 [HYPERGLYCAEMIA]	38/5	Yes	2	NR	NR	VL	NA	DNC	DNC	RECOVERED /RESOLVED	NA

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	360030	83/M/White/ HUN		脱水 [DEHYDRATION]	21/5	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				うつ病 [DEPRESSION]	60/21	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED WITH SEQUELAE	NA
	380011	45/M/White/ UKR		肺炎 [PNEUMONIA]	151/5	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
	380016	54/M/White/ UKR		肺炎 [PNEUMONIA]	6/10	Yes	3	NR	NR	Poss.	NA	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	NA
	380019	56/F/White/ UKR		肺塞栓症 [PULMONARY EMBOLISM]	108/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	380021	56/F/White/ UKR		肺炎 [PNEUMONIA]	43/16	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
	380030	65/M/White/ UKR		慢性腎盂腎炎 [EXACERBATION OF CHRONIC PYELONEPHRITIS]	141/6	Yes	3	NR	NR	NR	NA	DI	NA	RECOVERED /RESOLVED	NA
	380042	72/M/White/ UKR		精巣上体炎 [LEFT-SIDED ORHIEPIDIDIMIT]	69/23	Yes	3	NR	DO	DO	NA	DI	DI	RECOVERED /RESOLVED	NA
				肺炎 [HOSPITAL DOUBLE PNEUMONIA]	79/13	Yes	4	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				状態悪化 [WORSENING OF CONDITDON]	179/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	380050	66/M/White/ UKR		副腎機能不全 [ADRENAL INSUFFICIENCY]	15/2	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				肺炎 [RIGHT-SIDED PNEUMONIA]	16/	Yes	3	NR	NR	NR	NA	DI	DI	NOT RECOVERED /NOT RESOLVED	NA
	390004	75/F/White/ ITA		下肢静止不能症候群 [RESTLESS LEGS SYNDROME]	15/25	Yes	3	NR	Poss.	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
	390010	77/M/White/ ITA		肺炎 [PNEUMONIA]	91/16	Yes	3	NR	NR	VL	NA	DI	DR	RECOVERED /RESOLVED	NA
	390018	60/F/Not Reported/ ITA		脳膿瘍 [BRAIN ABSCESSES]	141/35	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
				ノカルジア症 [SUSPECTED PULMONARY NOCARDIOSIS]	141/35	Yes	3	NR	NR	NR	NA	DW	DW	RECOVERED /RESOLVED	NA

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	390043	72/M/White/ ITA		無力症 [STRONG ASTHENIA]	160/4	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED WITH SEQUELAE	NA
				状態悪化 [WORSENING GENERAL CONDITION]	160/13	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED WITH SEQUELAE	NA
				全身健康状態低下 [WORSENING OF GENERAL CONDITION]	173/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	390045	74/M/White/ ITA		失神 [FAINTING]	9/12	Yes	1	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				発熱 [FEVER]	176/16	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	390047	57/F/White/ ITA		背部痛 [DORSAL PAIN]	19/12	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	No
	420001	66/M/White/ CZE		心室性期外収縮 [FREQUENT VENTRICULAR EXTRASYSTOLIA]	34/6	Yes	3	NR	Poss.	NR	NA	DR	DR	RECOVERED /RESOLVED	NA
	420005	68/M/White/ CZE		背部痛 [BACK PAIN]	11/17	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	420013	78/M/White/ CZE		壊疽 [GANGRENE OF THE RIGHT LOWER LIMB]	43/	Yes	4	NR	NR	NR	NA	DW	DW	NOT RECOVERED /NOT RESOLVED	NA
	420015	67/F/White/ CZE		気管支肺炎 [BRONCHOPNEUMONIA - RIGHT]	165/14	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	420016	69/F/White/ CZE		低ナトリウム血症 [HYPONATREMIA]	77/11	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				状態悪化 [WORSENING OVERAL CONDITION DUE TO MULTIPLE MYELOMA]	112/9	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	460015	66/M/White/ SWE		便秘 [CONSTIPATION]	28/3	Yes	2	NR	Poss.	NR	NA	DNC	DI	RECOVERED /RESOLVED	No
	460016	73/F/White/ SWE		再発乳癌 [BREAST CANCER RELAPSE]	113/	Yes	3	NR	NR	NR	NA	DI	DI	NOT RECOVERED /NOT RESOLVED	NA

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	460018	80/M/White/ SWE		帯状疱疹 [HERPES ZOSTER INFECTION]	60/10	Yes	2	NR	VL	Prob.	NA	DI	DI	RECOVERED /RESOLVED	No
	480022	61/M/White/ POL		発熱 [FEVER]	130/35	Yes	2	NR	Poss.	Poss.	NA	NA	NA	RECOVERED /RESOLVED	No
	480025	65/M/White/ POL		胸椎骨折 [FRACTURE OF VERTEBRAE (TH3-7)]	77/10	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				気管支炎 [ACUTE BRONCHITIS]	145/20	Yes	3	NR	Poss.	Prob.	NA	DI	DI	RECOVERED /RESOLVED	NA
	480029	53/M/White/ POL		血小板減少症 [THROMBOCYTOPENIA]	35/9	Yes	4	NR	Poss.	NR	NA	DR	DNC	RECOVERED /RESOLVED	NA
	480036	70/M/White/ POL		貧血 [ANEMIA]	43/3	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	490006	74/F/White/ DEU		心筋梗塞 [MYOCARDIAL INFARCTION]	25/31	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	490007	64/F/White/ DEU		インフルエンザ [INFLUENZA]	29/16	Yes	3	NR	Poss.	Poss.	NA	DI	DNC	RECOVERED /RESOLVED	NA
	490013	75/M/White/ DEU		挫傷 [PELVIS CONTUSION]	9/3	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				肺炎 [PNEUMONIA]	11/49	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	490019	77/F/White/ DEU		眼部単純ヘルペス [HERPES SIMPLEX VIRUS-ASSOCIATED KERATITIS]	151/	Yes	2	NR	VL	NR	NA	DNC	DNC	NOT RECOVERED /NOT RESOLVED	NA
				脊椎痛 [PAIN LOWER SPINE]	171/8	Yes	2	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	490022	67/M/White/ DEU		肺炎 [PNEUMONIA]	42/16	Yes	3	NR	DO	DO	NA	DI	DI	RECOVERED /RESOLVED	NA
				肺炎 [PNEUMONIA]	73/13	Yes	3	NR	DO	DO	NA	NA	NA	RECOVERED /RESOLVED	NA
	550006	58/F/White/ BRA		肺炎 [PNEUMONIA]	10/8	Yes	3	NR	NR	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
				発熱 [FEVER]	174/2	Yes	3	NR	NR	Poss.	NA	NA	NA	RECOVERED /RESOLVED	NA
				発熱 [FEVER]	178/56	Yes	2	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	550009	63/M/White/ BRA		頚部痛 [NECK PAIN]	192/9	Yes	1	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	550014	69/M/White/ BRA		低ナトリウム血症 [HYPONATREMIA]	172/9	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED /NOT RESOLVED	NA
				低ナトリウム血症 [HYPONATREMIA]	181/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	550015	75/M/Black Or African American/ BRA		肺炎 [PNEUMONIA]	56/24	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
				肺炎 [PNEUMONIA]	80/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	610001	63/M/White/ AUS		敗血症 [SEPTICAEMIA]	43/5	Yes	3	NR	Prob.	Prob.	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				肺炎 [PNEUMONIA]	100/5	Yes	4	NR	Poss.	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
				敗血症 [SEPSIS]	100/5	Yes	4	NR	Poss.	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	610006	69/F/Asian/ AUS		うっ血性心不全 [CONGESTIVE HEART FAILURE]	64/3	Yes	3	NR	NR	VL	NA	DI	DI	RECOVERED /RESOLVED	NA
	610039	60/M/White/ AUS		心筋梗塞 [MYOCARDIAL INFARCTION]	23/20	Yes	4	NR	NR	NR	NA	DW	DW	RECOVERED /RESOLVED WITH SEQUELAE	No
				心原性ショック [CARDIOGENIC SHOCK]	26/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED /NOT RESOLVED	NA
				肺感染 [LUNG INFECTION (SERRATIA SP.)]	26/	Yes	3	NR	NR	NR	NA	NA	NA	NOT RECOVERED /NOT RESOLVED	No
				急性腎不全 [ACUTE KIDNEY INJURY]	27/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED /NOT RESOLVED	NA
	610041	61/M/Asian/ AUS		帯状疱疹 [SHINGLES]	45/	Yes	3	NR	Prob.	NR	NA	DNC	DNC	NOT RECOVERED /NOT RESOLVED	No
				上気道感染 [UPPER RESPIRATORY INFECTION]	118/5	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	610042	49/M/White/ AUS		インフルエンザ様疾患 [FLU-LIKE SYMPTOMS]	80/2	Yes	1	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	610050	81/M/Not Reported/ AUS		脱水 [DEHYDRATION]	69/1	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
				失神 [SYNCOPE]	69/1	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
				起立性低血圧 [POSTURAL HYPOTENSION]	71/8	Yes	3	NR	VL	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	700007	54/M/White/ RUS		全身健康状態低下 [GENERAL DETERIORATION OF CONDITION]	57/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	700023	46/M/White/ RUS		肺水腫 [PULMONARY EDEMA]	52/3	Yes	4	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
				肺水腫 [PULMONARY EDEMA]	54/	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	700035	57/M/White/ RUS		脳血管発作 [ACUTE CEREBROVASCULAR ACCIDENT]	68/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	No
	700038	69/F/White/ RUS		骨髄腫円柱腎症 [MYELOMA NEPHROPATHY]	35/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	820001	62/M/Asian/ KOR		肺炎 [PNEUMONIA]	53/19	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
	820002	77/M/Asian/ KOR		高血糖 [HYPERGLYCEMIA]	36/15	Yes	3	NR	NR	Poss.	NA	DNC	DR	RECOVERED /RESOLVED	NA
				低血糖症 [HYPOGLYCEMIA]	54/6	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	820005	54/M/Asian/ KOR		肺炎 [PNEUMONIA]	36/31	Yes	3	NR	NR	Poss.	NA	DR	DI	RECOVERED /RESOLVED	NA
	820013	56/M/Asian/ KOR		腹痛 [ABDOMINAL PAIN]	42/4	Yes	2	NR	DO	NR	NA	NA	NA	RECOVERED /RESOLVED	No
				無力症 [GENERAL WEAKNESS]	53/6	Yes	2	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	820017	60/M/Asian/ KOR		四肢痛 [LEFT LEG PAIN]	105/12	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	900014	58/M/White/ TUR		肺炎 [PNEUMONIA]	111/13	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED /RESOLVED	NA
	900018	59/M/White/ TUR		肺炎 [PNEUMONIA]	34/10	Yes	3	NR	Poss.	Poss.	NA	DR	DI	RECOVERED /RESOLVED	NA

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	900020	47/F/White/ TUR		肺炎 [PNEUMONIA]	4/29	Yes	4	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED /RESOLVED	NA
	900023	54/M/White/ TUR		肺胞出血 [ALVEOLAR HEMORRAGE]	36/63	Yes	1	NR	NR	NR	NA	DI	DI	RECOVERED /RESOLVED	NA
DVd	100011	68/M/Black Or African American/ USA	16.30 mg/kg	貧血 [ANEMIA]	21/31	Yes	3	NR	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
			16.30 mg/kg	疲労 [FATIGUE]	24/29	Yes	3	NR	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	100026	66/F/Black Or African American/ USA	15.56 mg/kg	疼痛 [INTRACTABLE PAIN]	125/16	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	100036	59/M/Black Or African American/ USA	15.27 mg/kg	急性腎不全 [ACUTE RENAL FAILURE]	64/7	Yes	3	DO	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			16.51 mg/kg	一過性脳虚血発作 [TRANSIENT ISCHEMIC ATTACK]	174/4	Yes	2	Poss.	Poss.	Poss.	DNC	DI	DI	RECOVERED /RESOLVED	No
	310003	65/M/White/ NLD	16.03 mg/kg	肺敗血症 [PNEUMOSEPSIS]	14/15	Yes	4	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	310006	62/M/White/ NLD	16.42 mg/kg	病的骨折 [PATHOLOGICAL FRACTURE HUMERUS RIGHT SIDE]	35/36	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			16.42 mg/kg	病的骨折 [PATHOLOGICAL FRACTURE OF FEMUR RIGHT]	35/36	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			15.97 mg/kg	肺炎 [PNEUMONIA]	209/17	Yes	3	Poss.	Poss.	Poss.	DW	DW	DW	NOT RECOVERED /NOT RESOLVED	No
			15.97 mg/kg	肺敗血症 [PNEUMOSEPSIS]	225/1	Yes	5	DO	DO	DO	NA	NA	NA	FATAL	No
	310017	63/F/Not Reported/ NLD	16.00 mg/kg	過換気 [HYPERVENTILATION]	79/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	310024	82/M/White/ NLD	15.93 mg/kg	発熱 [DRUG FEVER]	2/2	Yes	2	Prob.	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	Yes
			15.93 mg/kg	敗血症 [SEPSIS]	112/46	Yes	3	Poss.	DO	Poss.	DW	DW	DW	RECOVERED /RESOLVED	No

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Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	340015	71/F/White/ ESP	15.90 mg/kg	脳梗塞 [CEREBRAL INFARCT]	13/1	Yes	4	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED /NOT RESOLVED	No
			15.90 mg/kg	誤嚥性肺炎 [BRONCHOASPIRATION PNEUMONIA]	13/	Yes	4	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED /NOT RESOLVED	NA
			15.90 mg/kg	脳梗塞 [CEREBRAL INFARCT]	14/1	Yes	5	NR	NR	NR	DW	DW	DW	FATAL	No
	340016	70/M/White/ ESP	16.00 mg/kg	肺塞栓症 [PULMONARY THROMBOEMBOLISM]	77/185	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	下気道感染 [LOWER RESPIRATORY INFECTION]	313/3	Yes	2	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
	340019	84/M/White/ ESP	16.00 mg/kg	肺炎 [NEUMONIA]	21/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	340030	71/M/White/ ESP	16.00 mg/kg	腸閉塞 [INTESTINAL OCCLUSION]	54/7	Yes	3	NR	Poss.	NR	DI	DNC	DNC	RECOVERED /RESOLVED	No
	360003	64/M/White/ HUN	16.00 mg/kg	胃腸管腺腫 [ADENOMA VILLOSUM COLI]	176/8	Yes	3	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
			16.00 mg/kg	メレナ [MELAENA]	192/5	Yes	3	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
			16.00 mg/kg	結腸腺癌 [ADENOCARCINOMA MUCINOSUM COLON]	196/	Yes	3	NR	NR	NR	DNC	NA	NA	NOT RECOVERED /NOT RESOLVED	No
	360009	70/M/White/ HUN	16.03 mg/kg	気管支炎 [ACUTE BRONCHITIS]	29/12	Yes	3	Poss.	DO	Prob.	DI	DI	DI	RECOVERED /RESOLVED	No
			16.03 mg/kg	うっ血性心不全 [WORSENING OF CONGESTIVE HEART FAILURE]	40/4	Yes	3	NR	Poss.	Poss.	NA	NA	NA	RECOVERED /RESOLVED WITH SEQUELAE	No
	360010	68/F/White/ HUN	16.00 mg/kg	大腿骨骨折 [PERTROCHANTER FRACTURE OF LEFT FEMUR]	70/12	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	上腕骨骨折 [FRACTURE OF LEFT HUMERUS]	134/8	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED /RESOLVED	No
	360014	52/M/White/ HUN	16.03 mg/kg	副鼻腔炎 [SINUSITIS MAXILLARIS]	44/9	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
			16.03 mg/kg	発熱 [FEVER OF UNKNOWN ORIGIN]	54/6	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No

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Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	380007	66/M/White/ UKR	16.00 mg/kg	肺炎 [PNEUMONIA]	74/12	Yes	3	Poss.	Poss.	NR	DW	DW	DW	RECOVERED /RESOLVED	No
			16.00 mg/kg	器質化肺炎 [BILATERAL FIBRINOUS PNEUMONIA]	85/1	Yes	5	Poss.	Poss.	NR	NA	NA	NA	FATAL	No
	380014	51/F/White/ UKR	15.81 mg/kg	肺炎 [PNEUMONIA]	60/9	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	380018	66/M/White/ UKR	15.56 mg/kg	根症候群 [RADICULAR SYNDROME]	11/18	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	貧血 [ANEMIA]	14/15	Yes	3	NR	NR	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	14/9	Yes	3	NR	NR	NR	DI	DNC	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	17/20	Yes	4	NR	NR	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	肺炎 [PNEUMONIA]	17/20	Yes	3	DO	NR	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	好中球減少症 [NEUTROPENIA]	22/15	Yes	4	NR	NR	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	貧血 [ANEMIA]	36/8	Yes	3	NR	NR	NR	DI	DNC	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	貧血 [ANEMIA]	49/35	Yes	3	NR	NR	NR	NA	DI	DNC	RECOVERED /RESOLVED	No
			15.56 mg/kg	肺炎 [PNEUMONIA]	52/32	Yes	4	NR	NR	NR	NA	DI	DNC	RECOVERED /RESOLVED	No
	380026	46/F/White/ UKR	16.00 mg/kg	気管支炎 [OBSTRUCTIVE BRONCHITIS]	106/5	Yes	2	DO	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	380032	73/F/White/ UKR	16.03 mg/kg	腎盂腎炎 [PYELONEPHRITIS]	112/3	Yes	3	DO	DO	Poss.	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	380040	66/M/White/ UKR	16.00 mg/kg	肺炎 [BILATERAL MULTISEGMENTAL PNEUMONIA]	29/13	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	380056	66/M/White/ UKR	16.00 mg/kg	肺炎 [RIGHT SIDE PNEUMONIA]	28/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No

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Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	380061	55/F/White/ UKR	15.43 mg/kg	気管支炎 [ODSTRUCTIVE BRONCHITIS]	42/6	Yes	2	DO	Prob.	Prob.	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	380063	55/F/White/ UKR	16.00 mg/kg	肺動脈血栓症 [SUSPECTED THROMBOEMBOLISM OF PULMONARY ARTERY]	4/	Yes	4	Poss.	Poss.	Poss.	DNC	DI	DI	NOT RECOVERED /NOT RESOLVED	No
			16.00 mg/kg	急性冠動脈症候群 [ACUTE CORONARY SYNDROM]	5/1	Yes	4	Poss.	Poss.	Poss.	DNC	DNC	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
			16.00 mg/kg	急性冠動脈症候群 [ACUTE CORONARY SYNDROM]	6/1	Yes	5	Poss.	Poss.	Poss.	DW	DW	DW	FATAL	No
	390002	75/M/White/ ITA	16.69 mg/kg	サイトメガロウイルス性肺炎 [CMV PNEUMONIA]	64/10	Yes	3	DO	NR	VL	DI	DI	DI	RECOVERED /RESOLVED	No
	390005	77/F/White/ ITA	15.74 mg/kg	錯乱状態 [CONFUSIONAL STATE TRANSITORY]	61/5	Yes	3	NR	DO	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.74 mg/kg	錯乱状態 [CONFUSIONAL STATE TRANSITORY]	123/4	Yes	3	DO	DO	DO	DNC	DNC	DNC	RECOVERED /RESOLVED	U
	390016	62/F/White/ ITA	16.00 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	57/3	Yes	4	Poss.	Poss.	NR	DI	DR	DI	RECOVERED /RESOLVED	No
	390024	75/M/White/ ITA	15.77 mg/kg	心房細動 [ATRIAL FIBRILLATION]	44/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.77 mg/kg	心房細動 [ATRIAL FIBRILLATION]	87/11	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	心房細動 [ATRIAL FIBRILLATION]	154/23	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	390028	61/F/White/ ITA	16.00 mg/kg	貧血 [ANEMIA]	2/3	Yes	3	NR	Poss.	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	心不全 [HEART FAILURE]	127/29	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
			16.00 mg/kg	心電図ＱＴ間隔異常 [QT CHANGES NOS]	127/29	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	390036	64/M/White/ ITA	16.00 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	14/2	Yes	4	Prob.	VL	NR	DNC	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			16.00 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	28/2	Yes	4	Prob.	VL	NR	DNC	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
			16.00 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	35/2	Yes	4	Prob.	VL	NR	DNC	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
	390044	69/F/White/ ITA	16.00 mg/kg	上室性不整脈 [ATRIAL PAROXISTIC ARRYTHMIA]	46/20	Yes	2	NR	NR	DO	DI	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	胃腸炎 [GASTROENTERITIS]	86/29	Yes	1	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	390049	78/M/White/ ITA	16.23 mg/kg	肺炎 [PNEUMONIA]	54/20	Yes	3	NR	NR	VL	DI	DI	DR	RECOVERED /RESOLVED	No
			16.46 mg/kg	肺炎 [PNEUMONIA]	142/15	Yes	3	NR	NR	VL	DI	DI	DI	RECOVERED /RESOLVED	No
	390050	68/M/White/ ITA	15.84 mg/kg	肋骨骨折 [MULTIPLE RIBS FRACTURES]	84/1	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			15.84 mg/kg	皮膚有棘細胞癌 [SPINOCELLULAR CARCINOMA]	101/35	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	420002	52/M/White/ CZE	16.00 mg/kg	肺炎 [PNEUMONIA]	19/21	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	420006	72/F/White/ CZE	16.00 mg/kg	心房細動 [TACHYFIBRILLATION - ATRIAL FIBRILATION PAROXYSMUS]	169/5	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	420009	63/M/White/ CZE	16.00 mg/kg	脱水 [PRAECOLLAPS (DEHYDRATION)]	15/3	Yes	3	NR	NR	NR	DI	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	肺炎 [PNEUMONIA]	81/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	脱水 [COLLAPSE (DEHYDRATION)]	117/4	Yes	3	NR	DO	DO	DNC	DNC	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	脱水 [COLLAPSE (DEHYDRATION)]	126/5	Yes	3	NR	Poss.	Poss.	DI	DR	DI	RECOVERED /RESOLVED	No
	420011	61/F/White/ CZE	16.91 mg/kg	高血糖 [HYPERGLYCEMIA]	57/1	Yes	4	NR	NR	Poss.	DNC	DNC	DI	RECOVERED /RESOLVED	No
	420026	68/F/White/ CZE	16.00 mg/kg	肺炎 [PNEUMONIA BILATERAL]	99/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	420028	50/F/White/ CZE	16.00 mg/kg	アラニンアミノトランスフェラーゼ増加 [ALANINE AMINOTRANSFERASE INCREASED]	8/2	Yes	3	NR	Poss.	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	γ－グルタミルトランスフェラーゼ増加 [GLUTAMYLTRANSFERASE INCREASED]	8/2	Yes	3	NR	Poss.	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
	420030	52/M/White/ CZE	16.00 mg/kg	帯状疱疹 [HERPES ZOSTER]	44/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	420036	83/F/White/ CZE	16.00 mg/kg	気管支炎 [BRONCHITIS ACUTE]	53/9	Yes	3	NR	NR	Prob.	DI	DI	DI	RECOVERED /RESOLVED	No
	460002	69/F/White/ SWE	16.00 mg/kg	発熱 [FEVER]	147/11	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	460004	72/F/White/ SWE	16.00 mg/kg	上気道感染 [UPPER RESPIRATORY INFECTION]	61/13	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	460006	77/F/White/ SWE	16.00 mg/kg	骨痛 [SKELLET PAIN]	4/3	Yes	3	DO	DO	DO	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	骨痛 [SKELETT PAIN]	7/4	Yes	3	DO	DO	DO	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	上腕骨骨折 [HUMERUSFRACHTUR]	19/48	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	貧血 [LOW HEMOGLOBIN]	21/46	Yes	3	DO	Prob.	DO	DNC	DNC	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	肺炎 [PNEUMONI]	53/14	Yes	4	Poss.	Poss.	Poss.	DW	DW	DW	RECOVERED /RESOLVED	No
			16.00 mg/kg	胸水症 [HYDROTHORAX]	53/14	Yes	4	Poss.	Poss.	NR	DW	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	肺炎 [PNEUMONIA]	66/1	Yes	5	Poss.	Poss.	Poss.	NA	DW	DW	FATAL	No
	460009	43/M/White/ SWE	16.00 mg/kg	肺炎球菌性肺炎 [PNEUMOCOCC PNEUMONIA]	171/4	Yes	3	Poss.	Poss.	Poss.	DI	NA	NA	RECOVERED /RESOLVED	No
			16.00 mg/kg	敗血症 [SEPTIKEMIA]	171/4	Yes	4	Poss.	Poss.	Poss.	DI	NA	NA	RECOVERED /RESOLVED	No
	460014	67/M/White/ SWE	16.10 mg/kg	肺炎 [PNEUMONIA]	14/4	Yes	3	NR	NR	Poss.	DI	DNC	DNC	RECOVERED /RESOLVED	No
			14.44 mg/kg	発熱 [FEVER]	29/17	Yes	3	NR	NR	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
			16.39 mg/kg	失神 [SYNCOPE]	60/1	Yes	3	DO	DO	DO	DNC	DNC	DNC	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	460019	79/M/White/ SWE	16.00 mg/kg	筋骨格系胸痛 [MUSCLE PAIN IN CHEST]	124/2	Yes	2	DO	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	480001	63/F/White/ POL	16.00 mg/kg	脊椎痛 [PAIN IN THE LUMBER PART OF VERTEBRAL COLUMN]	141/	Yes	3	NR	NR	NR	DW	DW	DW	NOT RECOVERED /NOT RESOLVED	No
	480004	61/F/White/ POL	15.62 mg/kg	貧血 [ANEMIA]	106/4	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.47 mg/kg	上肢骨折 [ARM FRACTURE REQUIRING AMPUTATION]	132/8	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	480013	71/M/White/ POL	16.13 mg/kg	貧血 [ANAEMIA]	36/22	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			16.13 mg/kg	血尿 [HAEMATURIA]	37/21	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			17.25 mg/kg	移行上皮癌 [CARCINOMA UROTHELIALE (PREVIOUSLY REPORTED BLADDER TUMOR URINARY)]	58/	Yes	3	NR	NR	NR	DW	DW	DW	NOT RECOVERED /NOT RESOLVED	No
			17.25 mg/kg	真菌性食道炎 [FUNGAL ESOPHAGITIS]	73/4	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	480019	59/M/White/ POL	16.00 mg/kg	憩室穿孔 [SIGMOID DIVERTICULUM PERFORATION]	168/7	Yes	4	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	腹膜炎 [PERITONITIS]	168/7	Yes	4	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	480024	56/F/White/ POL	14.93 mg/kg	肺炎 [PNEUMONIA]	147/9	Yes	4	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	480034	67/M/White/ POL	16.83 mg/kg	心房細動 [ATRIAL FIBRILLATION]	1/4	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	480037	52/M/White/ POL	16.00 mg/kg	病的骨折 [PATHOLOGICAL FRACTURE OF VERTEBRAE]	64/3	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	背部痛 [BACK PAIN]	92/3	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	490001	70/F/White/ DEU	16.00 mg/kg	高血圧 [HYPERTENSION]	1/1	Yes	3	VL	NR	Poss.	DI	DNC	DNC	RECOVERED /RESOLVED	Yes
	490002	73/M/White/ DEU	17.07 mg/kg	口腔咽頭腫脹 [OROPHARYNEAL SWELLING]	1/1	Yes	3	VL	NR	NR	DI	DNC	DNC	RECOVERED /RESOLVED	Yes

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			15.90 mg/kg	複視 [DIPLOPIC VISION]	41/8	Yes	3	NR	Prob.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	490012	64/F/White/ DEU	16.26 mg/kg	上気道感染 [UPPER RESPERATORY INFECTION]	115/4	Yes	2	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	NA
	490023	76/M/White/ DEU	16.67 mg/kg	甲状腺機能亢進症 [HYPERTHYREOSIS]	188/4	Yes	2	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
			16.44 mg/kg	塞栓性脳卒中 [EMBOLIC CEREBRAL INSULT]	199/14	Yes	3	NR	NR	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	490025	73/F/White/ DEU	15.66 mg/kg	急性腎不全 [ACUTE KIDNEY INJURY]	53/5	Yes	3	NR	NR	NR	DI	DI	DNC	RECOVERED /RESOLVED	No
	490028	65/M/White/ DEU	16.36 mg/kg	第６脳神経麻痺 [ADUCENS NERVE PALSY RIGHT SIDE]	67/12	Yes	2	NR	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	U
	490039	52/M/White/ DEU	16.36 mg/kg	高カルシウム血症 [HYPERCALCEMIA]	18/6	Yes	2	NR	VL	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.36 mg/kg	腎機能障害 [CREATININE ELEVATION/RENAAL FUNCTION IMPAIRMENT]	20/3	Yes	1	NR	VL	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.36 mg/kg	鼻出血 [EPISTAXIS]	20/	Yes	3	Poss.	VL	NR	DNC	NA	NA	NOT RECOVERED /NOT RESOLVED	No
			16.36 mg/kg	肺出血 [PULMONARY BLEEDING]	29/	Yes	4	NR	NR	NR	DI	DI	DI	NOT RECOVERED /NOT RESOLVED	No
			16.36 mg/kg	心原性ショック [CARDIAC SHOCK]	31/	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	U
	490044	68/F/White/ DEU	14.76 mg/kg	虚血性脳卒中 [ISCHAEMIC STROKE]	175/1	Yes	5	NR	Poss.	NR	DW	DW	DW	FATAL	No
	520005	68/F/Other/ MEX	16.03 mg/kg	肺炎 [COMMUNITY ACQUIRED PNEUMONIA]	82/6	Yes	4	NR	Poss.	NR	DNC	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
			16.03 mg/kg	心房細動 [ATRIAL FIBRILATION]	87/2	Yes	4	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			16.03 mg/kg	うっ血性心不全 [CONGESTIVE HEART FAILURE]	87/2	Yes	4	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
			16.03 mg/kg	呼吸不全 [RESPIRATORY INSUFFICIENCY]	88/1	Yes	5	NR	NR	NR	DW	DW	DW	FATAL	No
	550003	66/F/Other/ BRA	16.00 mg/kg	胃腸炎 [ACUTE GASTROENTEROCOLITIS]	54/18	Yes	3	DO	NR	NR	DW	DI	DI	RECOVERED /RESOLVED	No
	550022	71/M/White/ BRA	15.93 mg/kg	高血圧クリーゼ [HYPERTENSION CRISIS]	16/3	Yes	4	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	610009	53/M/Native Hawaiian Or Other Pacific Islander/ AUS	16.00 mg/kg	形質細胞腫 [PLASMACYTOMA (RIGHT RENAL MASS)]	2/	Yes	3	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED /NOT RESOLVED	No
			16.00 mg/kg	血小板減少症 [PLATELET COUNT DECREASED]	15/	Yes	3	Prob.	Poss.	NR	DI	DI	DNC	NOT RECOVERED /NOT RESOLVED	No
			16.50 mg/kg	腫瘍崩壊症候群 [TUMOUR LYSIS SYNDROME]	33/2	Yes	3	VL	Prob.	Prob.	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.50 mg/kg	側腹部痛 [RIGHT FLANK PAIN]	37/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.50 mg/kg	形質細胞腫 [PLASMACYTOMA (NEOPLASM)]	40/	Yes	3	NR	NR	NR	NA	DNC	DNC	NOT RECOVERED /NOT RESOLVED	No
	610016	63/M/White/ AUS	16.69 mg/kg	関節痛 [SEVER LEFT HIP PAIN]	113/15	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			17.70 mg/kg	肺炎 [PNEUMONIA]	153/16	Yes	3	NR	NR	VL	DI	DI	DR	RECOVERED /RESOLVED	No
	610017	59/F/White/ AUS	15.84 mg/kg	ライノウイルス感染 [RHINOVIRUS]	132/4	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.74 mg/kg	メタニューモウイルス感染 [HUMAN METAPNEUMOVIRUS]	154/12	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED /RESOLVED	No
			15.74 mg/kg	喘息 [ASTHMA EXACERBATION]	154/12	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED /RESOLVED	No
	610025	67/M/White/ AUS	16.07 mg/kg	急性腎不全 [ACUTE KIDNEY INJURY]	8/5	Yes	2	Poss.	Poss.	Poss.	DNC	DNC	DNC	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			16.07 mg/kg	十二指腸潰瘍 [DUODENAL ULCER]	13/23	Yes	4	NR	NR	Prob.	DW	DW	DW	RECOVERED /RESOLVED WITH SEQUELAE	No
			16.07 mg/kg	十二指腸潰瘍 [DUODENAL ULCER]	36/1	Yes	5	NR	NR	Prob.	DNC	DNC	DNC	FATAL	No
	610026	72/M/White/ AUS	16.00 mg/kg	末梢動脈瘤 [VASCULAR DISORDER: LEFT INTERIOR ILIAC ARTERY ANEURYSM]	12/43	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.98 mg/kg	鼻出血 [EPISTAXIS]	103/2	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	610031	70/F/White/ AUS	16.00 mg/kg	ＲＳウイルス感染 [RESPIRATORY SYNCYTIAL VIRUS INFECTION]	10/15	Yes	3	Prob.	Prob.	Prob.	DI	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	頭痛 [HEADACHE]	31/3	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	抑うつ気分 [PSYCHIATRIC DISORDERS - OTHER - LOW MOOD]	40/6	Yes	4	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			15.77 mg/kg	骨痛 [HIP BONE PAIN]	93/31	Yes	3	NR	NR	NR	DNC	DI	DNC	RECOVERED /RESOLVED	No
			14.88 mg/kg	骨痛 [HIP BONE PAIN]	135/10	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	股関節部骨折 [FRACTURED RIGHT HIP]	162/12	Yes	3	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
			14.79 mg/kg	末梢性浮腫 [OEDEMA LOWER LIMBS]	224/4	Yes	3	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
			14.79 mg/kg	蜂巣炎 [CELLULITIS LEFT LOWER LEG]	224/4	Yes	2	NR	NR	NR	DNC	NA	NA	RECOVERED /RESOLVED	No
	610037	44/M/White/ AUS	16.00 mg/kg	上腹部痛 [RIGHT UPPER QUADRANT PAIN]	4/3	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	胸水 [BILATERAL PLEURAL EFFUSION]	4/	Yes	2	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED /NOT RESOLVED	No
			16.00 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	8/37	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
	610044	71/M/White/ AUS	15.91 mg/kg	ニューモシスチス・イロベチイ肺炎 [PNEUMOCYSTIS JIROVECII PNUEMONIA]	2/5	Yes	3	NR	NR	NR	DNC	DI	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
	610048	66/F/White/ AUS	15.45 mg/kg	下気道感染 [LOWER RESPIRATORY TRACT INFECTION]	44/6	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	610049	71/M/White/ AUS	16.15 mg/kg	肺感染 [SUSPECTED LUNG INFECTION]	72/12	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	610052	78/M/White/ AUS	15.58 mg/kg	下痢 [DIARRHOEA]	12/3	Yes	3	Poss.	Poss.	NR	DNC	DNC	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
			15.66 mg/kg	急性心筋梗塞 [NON ST ELEVATION MYOCARDIAL INFARCTION]	26/20	Yes	3	NR	NR	NR	DW	DW	DW	RECOVERED /RESOLVED	No
	610054	74/F/White/ AUS	16.75 mg/kg	下痢 [DIARRHEA]	26/18	Yes	3	NR	VL	NR	DNC	DI	DNC	RECOVERED /RESOLVED WITH SEQUELAE	No
	610056	68/M/White/ AUS	16.21 mg/kg	肺炎 [PNEUMONIA]	141/2	Yes	3	DO	DO	Prob.	DNC	DNC	DNC	RECOVERED /RESOLVED	NA
	700002	62/F/White/ RUS	16.34 mg/kg	急性膵炎 [ACUTE PANCREATITIS]	64/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED WITH SEQUELAE	No
	700003	69/M/White/ RUS	16.00 mg/kg	慢性閉塞性肺疾患 [EXACERBATION OF CHRONIC OBSTRUCTIVE LUNG DISEASE]	8/2	Yes	4	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	呼吸不全 [RESPIRATORY FAILURE DUE TO DISEASE PROGRESSION]	34/2	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
			16.00 mg/kg	呼吸不全 [RESPIRATORY FAILURE DUE TO DISEASE PROGRESSION]	35/	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	700004	65/F/White/ RUS	16.13 mg/kg	小腸閉塞 [ACUTE ILEAL OBSTRUCTION]	69/2	Yes	4	DO	Poss.	DO	DNC	DI	DI	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			16.13 mg/kg	心房細動 [ATRIAL FIBRILLATION]	72/1	Yes	4	DO	Poss.	DO	DNC	DR	DNC	RECOVERED /RESOLVED	No
	700017	53/F/White/ RUS	15.97 mg/kg	脊椎骨折 [FRACTURE OF THE SECOND SPINAL BONE]	169/	Yes	3	NR	NR	NR	DW	DW	DW	WITH SEQUELAE	No
			15.97 mg/kg	全身健康状態低下 [GENERAL DETERIORATION OF CONDITION]	187/1	Yes	5	NR	NR	NR	NA	NA	NA	NOT RECOVERED /NOT RESOLVED	No
	700019	71/M/White/ RUS	16.00 mg/kg	脂肪肉腫 [LIPISARCOMA OF RIGHT KIDNEY]	172/67	Yes	2	DO	NR	NR	DNC	NA	NA	FATAL	No
	700020	58/M/White/ RUS	16.00 mg/kg	気管支肺炎 [ACUTE SUBTOTAL RIGHT-SIDE BRONCHOPNEUMONIA]	2/	Yes	3	NR	NR	NR	DNC	DW	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	虚血性脳卒中 [LEFT-SIDE ISCHEMIC STROKE]	4/6	Yes	3	NR	NR	NR	DW	DW	DW	WITH SEQUELAE	No
			16.00 mg/kg	虚血性脳卒中 [LEFT-SIDE ISCHEMIC STROKE]	9/	Yes	5	NR	NR	NR	NA	NA	NA	NOT RECOVERED /NOT RESOLVED	No
	700022	54/F/White/ RUS	16.00 mg/kg	慢性腎臓病 [CHRONIC KIDNEY FAILURE]	17/48	Yes	4	NR	NR	NR	DNC	DNC	DNC	FATAL	No
			16.00 mg/kg	大腿骨骨折 [RIGHT SUBTROCHANTERIC FRACTURE]	50/	Yes	1	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	700028	61/F/White/ RUS	16.03 mg/kg	乳癌 [LEFT BREAST CANCER]	32/8	Yes	3	NR	NR	NR	DI	DI	DI	NOT RECOVERED /NOT RESOLVED	No
	700032	59/F/White/ RUS	0.40 mg/kg	慢性膵炎 [CHRONIC PANCREATITIS EXACERBATION]	125/9	Yes	3	NR	NR	NR	NA	DNC	DI	RECOVERED /RESOLVED	No
	820003	66/M/Asian/ KOR	16.00 mg/kg	気管支炎 [BRONCHIAL INFECTION]	61/19	Yes	3	NR	NR	NR	DW	DI	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	気管支肺炎 [BRONCHOPNEUMONIA]	92/	Yes	3	NR	NR	NR	NA	DW	DW	RECOVERING/RESOLVING	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			16.00 mg/kg	好中球減少症 [NEUTROPENIA]	104/4	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	820007	61/M/Asian/ KOR	16.00 mg/kg	上気道感染 [UPPER RESPIRATORY INFECTION]	162/18	Yes	3	NR	NR	NR	DI	DNC	DNC	RECOVERED /RESOLVED	No
	820009	57/F/Asian/ KOR	15.85 mg/kg	気管支肺炎 [BRONCHO PNEUMONIA]	130/27	Yes	2	Prob.	Prob.	Prob.	DNC	DI	DNC	RECOVERED /RESOLVED	No
	820010	61/M/Asian/ KOR	16.00 mg/kg	胸水 [PLERAL EFFUSION]	16/53	Yes	2	NR	NR	NR	DI	DNC	DNC	RECOVERED /RESOLVED	No
	820014	48/M/Asian/ KOR	16.15 mg/kg	上気道感染 [UPPER RESPIRATORY INFECTION]	17/10	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
	820016	71/M/Asian/ KOR	16.74 mg/kg	肺炎 [PNEUMONIA]	32/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			16.74 mg/kg	高血糖 [HYPERGLYCEMIA]	51/9	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED /RESOLVED	No
			15.80 mg/kg	代謝性アシドーシス [METABOLIC ACIDOSIS]	141/9	Yes	3	DO	NR	NR	DW	DW	DW	RECOVERED /RESOLVED	No
	820020	63/M/Asian/ KOR	15.65 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	22/2	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	900003	46/M/White/ TUR	16.00 mg/kg	胃炎 [GASTRITIS]	115/8	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	高カルシウム血症 [HYPERCALCEMIC]	313/55	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED /RESOLVED	No
	900019	59/M/White/ TUR	16.00 mg/kg	サイトメガロウイルス性肺炎 [CMV PNEUMONIA]	22/20	Yes	3	VL	VL	VL	DI	DR	DI	RECOVERED /RESOLVED	No
	900022	46/M/White/ TUR	1.60 mg/kg	喉頭浮腫 [LARYNGEAL EDEMA]	1/	Yes	3	VL	NR	NR	DW	DW	DW	NOT RECOVERED /NOT RESOLVED	Yes
	900024	54/M/White/ TUR	16.00 mg/kg	血小板減少症 [TROMBOSTOPENIA]	15/18	Yes	4	DO	Poss.	NR	DI	DR	DI	RECOVERED /RESOLVED	No
			16.00 mg/kg	血小板減少症 [TROMBOCYTOPENIA]	81/4	Yes	4	NR	Poss.	NR	DNC	DR	DI	RECOVERED /RESOLVED	No
	900026	69/M/White/ TUR	16.00 mg/kg	貧血 [ANEMIA]	49/3	Yes	2	DO	Poss.	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No
	900028	61/M/White/ TUR	16.00 mg/kg	心停止 [CARDIAC ARREST]	26/1	Yes	5	NR	NR	NR	DW	DW	DW	FATAL	No
	900035	55/F/White/ TUR	16.00 mg/kg	下痢 [DIARRHEA]	88/13	Yes	4	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED /RESOLVED	No
	900038	56/M/White/ TUR	16.00 mg/kg	貧血 [ANEMIA]	2/4	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED /RESOLVED	No

LSFAE_JST02_3004: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3004)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
			16.00 mg/kg	疲労 [FATIGUE]	11/3	Yes	3	Poss.	Poss.	Poss.	DNC	DNC	DNC	RECOVERED /RESOLVED	No
			16.00 mg/kg	肺炎 [PNEUMONIA]	172/11	Yes	3	Poss.	Poss.	Poss.	DNC	DNC	DNC	RECOVERED /RESOLVED	NA
			16.00 mg/kg	下痢 [DIARRHEA]	186/19	Yes	3	NR	Poss.	NR	DNC	DI	DNC	RECOVERED /RESOLVED	NA

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone
Keys: AE = adverse event.
[a] Keys: NR = Not Related, DO = Doubtful, Poss. = Possible, Prob. = Probable, VL = Very Likely.
[b] Keys: DI = Drug Interrupted, DNC = Dose Not Changed, DR = Dose Reduced, DW = Drug Withdrawn, NA = Not Applicable, UN = Unknown.
[c] Keys: Dara = daratumumab, Bort = bortezomib, Dex = dexamethasone.
Note: Adverse events are coded using MedDRA Version 18.0.

[LSFAE_JST02_3004.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\LSFAE_JST02_3004.SAS] 30JUN2016, 10:00

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
Rd	100004	65/F/White/ Usa		下部消化管出血 [LOWER GASTROINTESTINAL HEMORRHAGE]	337/4	Yes	2	NR	DO	DO	NA	DI	DI	RECOVERED/ RESOLVED	No
	100014	67/F/White/ Usa		末梢性感覚ニューロパチー [SENSORY NEUROPATHY]	126/1	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				感染性小腸結腸炎 [ENTEROCOLITIS INFECTIOUS]	134/10	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	100018	80/F/White/ Usa		血栓性血小板減少性紫斑病 [THROMBOTIC THROMBOCYTOPENIA PURPURA]	127/11	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				急性心筋梗塞 [NON-ST ELEVATED MYOCARDIAL INFACTION]	127/26	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	No
	100022	77/M/Black Or African American/ Usa		細菌性肺炎 [BACTERIAL PNEUMONIA]	46/20	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				気管支痙攣 [BRONCHOSPAM]	99/69	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				クロストリジウム・ディフィシレ感染 [C DIFFICILE INFECTION]	333/9	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				急性腎不全 [ACUTE KIDNEY INJURY]	333/9	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				大腿骨頚部骨折 [FEMORAL NECK FRACTURE]	341/9	Yes	3	NR	NR	NR	NA	DNC	DI	RECOVERED/ RESOLVED	NA
	100041	70/F/Black Or African American/ Usa		急性腎不全 [ACUTE KIDNEY INJURE]	22/4	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				クロストリジウム・ディフィシレ感染 [CLOSTRIDIUM DIFFICILE INFECTION]	23/7	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				肺炎 [LUNG INFECTION (PNEUMONIA)]	23/3	Yes	2	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				失神 [SYNCOPE]	268/1	Yes	3	NR	DO	NR	NA	DI	DNC	RECOVERED/ RESOLVED	No
	101009	72/F/White/ Can		腎不全 [RENAL FAILURE]	3/12	Yes	3	NR	NR	NR	NA	DW	DW	RECOVERED/ RESOLVED	NA
				腎不全 [RENAL FAILURE]	15/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	101014	80/M/White/ Can		筋力低下 [GENERAL MUSCLE WEAKNESS]	301/2	Yes	3	NR	Poss.	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				失語症 [EXPRESSIVE ASPHAGIA]	301/2	Yes	3	NR	Poss.	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				肺炎 [PNEUMONIA]	417/5	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				敗血症 [SEPSIS]	417/5	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	101020	76/M/White/ Can		肺炎 [PNEUMONIA]	107/6	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				下痢 [DIARRHEA]	129/4	Yes	3	NR	DO	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	101031	56/M/White/ Can		肺塞栓症 [PULMONARY EMBOLISM]	18/54	Yes	4	NR	Prob.	Prob.	NA	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	101032	75/M/White/ Can		上気道感染 [UPPER RESPIRATORY INFECTION]	11/13	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	101040	58/M/White/ Can		急性心筋梗塞 [NON ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION]	247/5	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	No
				下痢 [DIARRHEA]	273/8	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				大葉性肺炎 [LEFT LOWER LOBE PNEUMONIA]	277/3	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				急性腎不全 [ACUTE RENAL FAILURE]	277/5	Yes	1	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
	300002	63/M/White/ Grc		敗血症性ショック [SEPTIC SHOCK]	246/3	Yes	4	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				敗血症性ショック [SEPTIC SHOCK]	248/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	No
	300011	53/F/White/ Grc		深部静脈血栓症 [DEEP VEIN THROMBOSIS OF LEFT LOWER LIMB]	217/8	Yes	2	NR	Poss.	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				肺塞栓症 [PULMONARY EMBOLISM]	285/7	Yes	3	NR	Poss.	NR	NA	DW	DW	RECOVERED/ RESOLVED	NA
				深部静脈血栓症 [DEEP VEIN TROMBOSIS OF LEFT LOWER LIMB]	285/7	Yes	2	NR	Poss.	NR	NA	DW	DW	RECOVERED/ RESOLVED	NA
	310004	75/M/White/ Nld		肺炎 [PNEUMONIA]	69/3	Yes	3	NR	VL	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
				肺塞栓症 [LUNG EMBOLISM]	69/3	Yes	3	NR	VL	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	320008	64/M/White/ Bel		発熱性好中球減少症 [NEUTROPENIC FEVER]	8/11	Yes	3	NR	VL	NR	NA	DNC	DI	RECOVERED/ RESOLVED	NA
				血小板減少症 [PLATELET COUNT LOW]	8/1	Yes	4	NR	Poss.	NR	NA	DW	DW	RECOVERED/ RESOLVED	NA
	320009	67/M/White/ Bel		消化管感染 [GASTROINTESTINAL INFECTION]	8/7	Yes	3	NR	NR	NR	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				心房細動 [ATRIAL FIBRILLATION]	44/9	Yes	3	NR	Poss.	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				上気道感染 [UPPER RESPIRATORY INFECTION]	44/9	Yes	3	NR	NR	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				リンパ節症 [LYMPH NODE MASS AXILLARY RIGHT]	162/	Yes	3	NR	NR	NR	NA	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	NA
	320010	75/F/White/ Bel		神経系障害 [GENERAL WEAKNESS DUE TO NEUROLOGICAL SYNDROME]	140/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	320013	71/F/White/ Bel		ウイルス感染 [VIRAL INFECTION]	8/6	Yes	2	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	320016	67/F/White/ Bel		膀胱移行上皮癌 [TRANSITIONAL CELL CARCINOMA OF THE BLADDER]	217/	Yes	3	NR	DO	NR	NA	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	NA
	330001	76/M/Not Reported/ Fra		肺塞栓症 [PULMONARY EMBOLISM]	146/16	Yes	3	NR	Prob.	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				脊椎痛 [SPINAL PAIN]	357/12	Yes	3	NR	NR	Poss.	NA	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	No
				背部痛 [LUMBAR PAIN (L4)]	406/3	Yes	3	NR	NR	NR	NA	DI	DNC	RECOVERED/ RESOLVED	No
	330013	56/M/Not Reported/ Fra		下痢 [DIARRHEA]	17/5	Yes	3	NR	Poss.	Poss.	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	330027	75/F/Not Reported/ Fra		背部痛 [LUMBAR PAIN]	159/27	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED WITH SEQUELAE	NA

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
				抑うつ症状 [DEPRESSIVE SYNDROME]	159/27	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				骨盤骨折 [FISSURE OF PELVIS]	311/31	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	330029	63/F/Not Reported/ Fra		肺炎 [PNEUMONIA (UN-IDENTIFIED)]	233/4	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	330032	62/M/Not Reported/ Fra		直腸腺癌 [RECTAL ADENOCARNINOMA]	429/	Yes	3	NR	DO	NR	NA	DW	DW	NOT RECOVERED/ NOT RESOLVED	NA
	330038	74/M/Not Reported/ Fra		背部痛 [HOSPITALIZATION FOR BACK PAIN]	13/18	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	330046	69/M/White/ Fra		鉄芽球性貧血 [IDIOPATHIC SIDEROBLASTIC ANEMIA]	114/	Yes	3	NR	Poss.	NR	NA	DW	DW	NOT RECOVERED/ NOT RESOLVED	NA
				敗血症 [SEPSIS]	151/8	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	NA
	330048	71/M/Not Reported/ Fra		ヘモフィルス感染 [INFLUENZA LUNG INFECTION]	10/16	Yes	3	NR	NR	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
				虚血性脳卒中 [ISCHEMIC STROKE]	15/12	Yes	4	NR	DO	NR	NA	DNC	DNC	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	330059	87/F/Not Reported/ Fra		静脈炎 [PHLEBITIS ON POSTERIOR TIBIAL AND PERONEAL LEFT VEINS]	30/22	Yes	3	NR	VL	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				診断法 [DIAGNOSTIC EVALUATIONS]	77/15	Yes	1	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	330060	54/F/Not Reported/ Fra		肺障害 [PNEUMOPATHY]	120/3	Yes	3	NR	VL	VL	NA	DI	DI	RECOVERED/ RESOLVED	NA
	330063	63/F/Not Reported/ Fra		橈骨骨折 [FRACTURE AT THE TOP OF THE LEFT RADIUS]	162/3	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	330067	79/F/Not Reported/ Fra		肺炎 [FEBRILE PNEUMONIA]	12/10	Yes	2	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
				丹毒 [ERYSIPELAS]	89/10	Yes	3	NR	Prob.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				壊死性筋膜炎 [LEFT THIGH NECROTIZING FACIITIS]	145/43	Yes	4	NR	VL	VL	NA	DW	DW	RECOVERED/ RESOLVED WITH SEQUELAE	No
	340008	58/M/White/ Esp		大腸炎 [INFLAMATORY COLLITIS]	61/13	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	340009	67/M/White/ Esp		肺腺癌 [PULMONARY ADENOCARCINOMA]	77/52	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				肺腺癌 [PULMONARY ADENOCARCINOMA]	128/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	340011	58/M/Other/ Esp		顎骨壊死 [JAW NECROSIS]	174/3	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				肺炎 [PNEUMONIA]	593/	Yes	4	NR	DO	DO	NA	DI	DI	RECOVERING /RESOLVING	NA
	340013	51/F/White/ Esp		水痘帯状疱疹ウイルス感染 [VVZ INFECTION]	359/8	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
	340023	63/F/White/ Esp		咽頭炎 [PHARYNGEAL INFECTION]	179/3	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	340031	66/F/White/ Esp		胆管結石 [CHOLEDOCHOLITHIASIS]	236/13	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				肺炎 [LEFT BASAL PNEUMONIA]	272/12	Yes	2	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	No
	340039	63/M/White/ Esp		呼吸不全 [UPPER RESPIRATORY TRACT FAILURE]	5/5	Yes	3	NR	DO	DO	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				貧血 [ANEMIA]	165/19	Yes	3	NR	Prob.	DO	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	340043	73/M/White/ Esp		発熱性好中球減少症 [NEUTROPENIC FEVER]	244/3	Yes	3	NR	VL	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
				硬膜下血腫 [SUBDURAL HEMATOMA]	271/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	No
				脳出血 [MASSIVE CEREBRAL HEMORRHAGE]	276/2	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	No

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Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	340047	66/M/White/ Esp		肺塞栓症 [PULMONARY EMBOLISM]	47/4	Yes	2	NR	Prob.	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				下痢 [DIARRHEA]	376/5	Yes	1	NR	Poss.	DO	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	340049	70/F/White/ Esp		発熱性好中球減少症 [FEBRILE NEUTROPENIA]	390/3	Yes	3	NR	Prob.	Prob.	NA	DI	DI	RECOVERED/ RESOLVED	NA
				インフルエンザ [INFLUENZA B VIRUS INFECTION]	390/4	Yes	2	NR	Prob.	Prob.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	340055	68/M/White/ Esp		気道感染 [RESPIRATORY INFECTION]	65/2	Yes	3	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	440005	68/F/White/ Gbr		扁平上皮癌 [SECONDARY PRIMARY MALIGNANCY OF SQUAMOUS CELL CARCINOMA]	320/12	Yes	3	NR	Poss.	DO	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	440006	62/M/White/ Gbr		肺炎 [PNEUMONIA]	15/15	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				虫垂炎 [NECROTIC APPENDIX]	266/29	Yes	4	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				腸閉塞 [SUB ACUTE INTESTINAL OBSTRUCTION]	274/21	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				肺炎 [PNEUMONIA]	276/19	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	NA
				腸閉塞 [INCOMPLETE BOWEL OBSTRUCTION]	296/7	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				腸閉塞 [SUBACUTE BOWEL OBSTRUCTION]	309/5	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				胃腸炎 [GASTROENTERITIS]	391/6	Yes	2	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
				上気道感染 [UPPER RESPIRATORY TRACT INFECTION]	391/6	Yes	2	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	440015	66/F/White/ Gbr		下気道感染 [LOWER RESPIRATORY TRACT INFECTION]	48/2	Yes	3	NR	Poss.	DO	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				肺炎 [PNEUMONIA]	122/18	Yes	3	NR	Poss.	DO	NA	DI	DI	RECOVERED/ RESOLVED	NA
				下気道感染 [CHEST INFECTION]	202/4	Yes	3	NR	Prob.	VL	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	440016	78/M/White/ Gbr		インフルエンザ [INFLUENZA A]	57/1	Yes	1	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA

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Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
				急性腎不全 [ACUTE KIDNEY INJURY]	99/34	Yes	4	NR	Prob.	NR	NA	DW	DI	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	440017	70/M/White/ Gbr		肺炎 [PNEUMONIA]	18/9	Yes	4	NR	NR	NR	NA	DW	DW	RECOVERED/ RESOLVED WITH SEQUELAE	NA
				肺炎 [PNEUMONIA]	27/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	440018	43/M/Not Reported/ Gbr		上気道感染 [UPPER RESPIRATORY INFECTION]	26/	Yes	2	NR	NR	NR	NA	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	NA
				形質細胞性白血病 [PLASMA CELL LEUKEMIA]	27/16	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED WITH SEQUELAE	No
				過粘稠度症候群 [HYPERVISCOSITY]	32/2	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	NA
	440029	56/M/Other/ Gbr		ウイルス性胃腸炎 [VIRAL GASTROENTERITIS]	327/4	Yes	3	NR	DO	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	440039	69/F/Not Reported/ Gbr		急性腎不全 [ACUTE KIDNEY INJURY]	344/8	Yes	2	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	NA
	440041	57/F/Asian/ Gbr		上腕骨骨折 [FRACTURED HUMEROUS]	128/5	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	No
	440045	70/M/White/ Gbr		関節脱臼 [DISPLACED OLECRANON]	351/2	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
	440050	80/F/White/ Gbr		貧血 [ANAEMIA]	67/	Yes	3	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	NA
				腎不全 [RENAL FAILURE]	72/282	Yes	4	NR	Poss.	NR	NA	DW	DW	RECOVERED/ RESOLVED	No
	440053	56/M/White/ Gbr		体温上昇 [BODY TEMPERATURE INCREASED]	7/5	Yes	2	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				発熱 [FEVER]	149/4	Yes	1	NR	Prob.	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	440056	67/M/White/ Gbr		下気道感染 [CHEST INFECTION]	335/14	Yes	3	NR	DO	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
				嘔吐 [VOMITING]	359/3	Yes	3	NR	DO	NR	NA	DI	NA	RECOVERED/ RESOLVED	NA
				吐血 [HAEMATESIS]	369/2	Yes	3	NR	DO	NR	NA	DI	NA	RECOVERED/ RESOLVED	No
	440057	74/F/White/ Gbr		痛風 [GOUT]	188/9	Yes	2	NR	Prob.	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED WITH SEQUELAE	No
				下気道感染 [ACUTE LOWER RESPIRATORY INFECTION]	262/7	Yes	3	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	440058	69/M/White/ Gbr		肺炎 [PNEUMONIA]	76/12	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	450005	59/M/White/ Dnk		敗血症 [SEPSIS, UNSPECIFIED]	411/3	Yes	3	NR	NR	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	450007	73/M/White/ Dnk		上気道感染 [UPPER RESPIRATORY INFECTION]	5/3	Yes	3	NR	NR	Poss.	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				気管支炎 [BRONCHIAL INFECTION]	18/17	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				肺塞栓症 [PULMONARY EMBOLISM]	47/8	Yes	3	NR	VL	NR	NA	DW	DW	RECOVERED/ RESOLVED	NA
	450010	72/M/White/ Dnk		肺塞栓症 [PULMONARY EMBOLISM]	393/1	Yes	3	NR	VL	NR	NA	DW	DW	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	450013	58/M/White/ Dnk		形質細胞性白血病 [PLASMA CELL LEUKEMIA]	38/115	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
				発熱 [FEVER]	39/4	Yes	3	NR	NR	DO	NA	NA	NA	RECOVERED/ RESOLVED	No
	450015	64/M/White/ Dnk		肺感染 [LUNG INFECTION]	49/16	Yes	3	NR	Prob.	Prob.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	450018	71/F/White/ Dnk		インフルエンザ [INFLUENZA]	337/5	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	460009	70/M/White/ Swe		心膜炎 [PERICARDITIS]	54/6	Yes	3	NR	Poss.	DO	NA	DI	DI	RECOVERED/ RESOLVED	NA
				感染 [INFECTION OF UNKNOWN ORIGION]	54/21	Yes	3	NR	Poss.	DO	NA	DW	DW	RECOVERED/ RESOLVED	NA
				心膜炎 [PERICARDITIS]	68/7	Yes	3	NR	Poss.	DO	NA	DW	DW	RECOVERED/ RESOLVED	NA
	460010	62/F/White/ Swe		インフルエンザ [INFLUENZA]	101/5	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	460013	63/M/White/ Swe		肺炎 [PNEUMONIA]	263/6	Yes	3	NR	DO	DO	NA	DI	DI	RECOVERED/ RESOLVED	NA
	460031	65/M/White/ Swe		発熱性好中球減少症 [FEBRILE NEUTROPENIA]	38/13	Yes	4	NR	VL	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				敗血症 [SEPSIS]	245/12	Yes	4	NR	DO	DO	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				心房細動 [ATRIAL FIBRILLATION]	328/3	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	480005	68/M/White/ Pol		下痢 [DIARRHEA]	80/8	Yes	3	NR	Poss.	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	480007	72/M/White/ Pol		心筋梗塞 [MYOCARDIAL INFARCTION]	36/9	Yes	3	NR	DO	DO	NA	DI	DI	RECOVERED/ RESOLVED	NA
	480016	66/F/White/ Pol		上室性頻脈 [SUPRAVENTRICULAR TACHYCARDIA]	340/4	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	480018	64/F/White/ Pol		心停止 [CARDIAC ARREST]	220/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	480019	61/M/White/ Pol		意識消失 [LOSS OF CONSCIOUSNESS]	47/3	Yes	1	NR	VL	DO	NA	DI	DI	RECOVERED/ RESOLVED	NA
				前立腺癌 [PROSTATE ADENOCARCINOMA]	309/	Yes	3	NR	Prob.	DO	NA	DW	DW	RECOVERING /RESOLVING	No
	480021	73/F/White/ Pol		静脈閉塞 [LEFT FEMORAL VEIN OCCLUSION]	100/5	Yes	2	NR	DO	DO	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	480033	67/F/White/ Pol		肛門直腸の良性新生物 [BENIGN TUMOUR (OF THE ANUS AND RECTAL CANAL)]	106/8	Yes	1	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				股関節部骨折 [LEFT HIP FRACTURE]	365/6	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	No
	480035	56/F/White/ Pol		尿路性敗血症 [SEPSIS -INFECTION OF THE URINARY TRACT]	72/12	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	480038	51/F/White/ Pol		感染 [UNSPECIFIED INFECTION-]	182/	Yes	3	NR	NR	NR	NA	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
				間質性肺疾患 [INTERSTITIAL PNEUMONIA]	197/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
				骨髄機能不全 [BONE MARROW APLASIA]	198/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	NA
				肝障害 [INFILTRATION IN THE LIVER (UNSPECIFIED)]	206/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	NA
				肺水腫 [PULMONARY OEDEMA]	210/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	490010	63/F/White/ Deu		発熱 [FEVER OF UNKNOWN ORIGIN]	193/3	Yes	1	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	No
	490012	60/F/White/ Deu		疼痛 [BODY PAIN]	291/4	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	490028	57/M/White/ Deu		急性心筋梗塞 [NON-ST-ELEVATED MYOCARDIAL INFARCIATION]	45/4	Yes	3	NR	Poss.	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
				肋間神経痛 [INTERCOSTAL NEURALGIA]	69/7	Yes	3	NR	Poss.	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	No
	610002	65/M/White/ Aus		真菌性角膜炎 [FUSARIUM KERATITIS RIGHT EYE]	386/25	Yes	4	NR	NR	Poss.	NA	DNC	DW	RECOVERED/ RESOLVED WITH SEQUELAE	No
	610003	81/M/White/ Aus		転倒 [FALL]	13/6	Yes	3	NR	DO	DO	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				肺炎 [PNEUMONIA]	34/10	Yes	3	NR	NR	DO	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				発熱 [FEVER]	45/10	Yes	1	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				発熱 [FEVER]	57/4	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				発熱 [FEBRILE]	441/7	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				脊柱管狭窄症 [SPINAL CANAL STENOSIS]	467/	Yes	3	NR	Prob.	Poss.	NA	DW	DW	NOT RECOVERED/ NOT RESOLVED	NA
	610007	66/M/White/ Aus		脳梗塞 [MIDDLE CEREBRAL ARTERY INFARCTION]	20/2	Yes	3	NR	Poss.	DO	NA	DW	DW	RECOVERED/ RESOLVED	NA

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	610008	69/M/White/ Aus		頚動脈硬化症 [MINIMAL ATHEROMA IN THE INTERNAL CAROTID ARTERIES BILATERALLY REQUIRING STENTING]	303/30	Yes	1	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	No
				肺炎 [PNEUMONIA]	336/12	Yes	3	NR	DO	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	610009	58/F/White/ Aus		肺塞栓症 [PULMONARY EMBOLISM]	209/71	Yes	3	NR	Poss.	DO	NA	DI	DNC	RECOVERED/ RESOLVED	No
	610017	63/M/White/ Aus		高カルシウム血症 [HYPERCALCEMIA]	8/3	Yes	4	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	610022	79/M/White/ Aus		パラインフルエンザウイルス感染 [PARAINFLUENZA 3]	296/22	Yes	3	NR	Poss.	Poss.	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	700032	63/M/White/ Rus		肺炎 [PNEUMONIA]	112/16	Yes	3	NR	NR	NR	NA	DNC	DR	RECOVERED/ RESOLVED	NA
	700035	62/M/White/ Rus		肺炎 [PNEUMONIA]	238/16	Yes	3	NR	Poss.	Poss.	NA	DI	DI	RECOVERED/ RESOLVED	NA
	700040	56/M/White/ Rus		気胸 [RIGHT-SIDE PNEUMOTHORAX]	9/2	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				急性呼吸不全 [ACUTE RESPIRATORY FAILURE]	11/4	Yes	4	NR	NR	NR	NA	DI	DW	RECOVERED/ RESOLVED	NA
				急性呼吸不全 [ACUTE RESPIRATORY FAILURE]	14/1	Yes	5	NR	NR	NR	NA	DW	NA	FATAL	NA
	700045	63/F/White/ Rus		肺炎 [PNEUMONIA]	33/14	Yes	3	NR	Poss.	Poss.	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	700049	47/F/White/ Rus		急性腎不全 [ACUTE RENAL FAILURE]	78/18	Yes	3	NR	NR	NR	NA	DW	DW	RECOVERED/ RESOLVED	NA
				急性腎不全 [ACUTE RENAL FAILURE]	95/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	NA
	810005	69/M/Asian/ Jpn		第 7 脳神経麻痺 [LEFT FACIAL NERVE PARALYSIS]	21/44	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	810024	59/M/Asian/ Jpn		急性腎不全 [ACUTE KIDNEY INJURY]	3/130	Yes	4	NR	Prob.	DO	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				傾眠 [SOMNOLENCE]	125/	Yes	3	NR	NR	NR	NA	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	NA
				急性腎不全 [ACUTE KIDNEY INJURY]	132/1	Yes	5	NR	Prob.	DO	NA	NA	NA	FATAL	NA

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	810042	50/M/Asian/ Jpn		肺炎 [PNEUMONIA]	193/7	Yes	3	NR	Prob.	Prob.	NA	DNC	DNC	RECOVERED/ RESOLVED	No
	820005	66/M/Asian/ Kor		筋骨格痛 [SHOULDER PAIN AGGRAVATION]	22/2	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				肺炎 [PNEUMONIA]	125/22	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				食道炎 [ESOPHAGITIS]	147/20	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	820008	44/F/Asian/ Kor		背部痛 [BACK PAIN AGGRAVATION]	15/5	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	820021	62/F/Asian/ Kor		急性腎盂腎炎 [ACUTE PYELONEPHRITIS]	161/15	Yes	3	NR	DO	DO	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	820025	67/F/Asian/ Kor		気管支炎 [BRONCHITIS]	61/25	Yes	2	NR	DO	DO	NA	DI	DI	RECOVERED/ RESOLVED	NA
	820036	69/M/Asian/ Kor		肺炎 [PNEUMONIA]	369/37	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	820037	68/F/Asian/ Kor		疲労 [FATIGUE]	193/10	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				疼痛 [PAIN(GENERALACHE)]	193/10	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				疲労 [FATIGUE]	208/	Yes	2	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	NA
				高窒素血症 [AZOTEMIA]	208/	Yes	1	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	NA
	820038	60/M/Asian/ Kor		肺結核 [PULMONARY TUBERCULOSIS]	115/57	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	820040	64/M/Asian/ Kor		脊柱管狭窄症 [SPINAL STENOSIS]	137/36	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	886001	72/M/Asian/ Twn		顎骨壊死 [#12 -BRONJ]	362/4	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	No
	886002	59/F/Asian/ Twn		食欲減退 [POOR APPETITE]	11/37	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				下痢 [WATERY DIARRHEA]	15/33	Yes	3	NR	DO	NR	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				骨髄炎 [OSTEOMYELITIS-LEFT]	305/6	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
				骨髄炎 [OSTEOMYELITIS-RIGHT]	305/6	Yes	3	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	No
	886008	54/M/Asian/ Twn		骨髄炎 [OSTEOMYELITIS, JAW]	36/5	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				肛門膿瘍 [RIGHT PERIANAL ABSCESS]	53/6	Yes	3	NR	Poss.	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	886013	85/M/Asian/ Twn		一過性脳虚血発作 [TRANSIENT ISCHEMIC ATTACK]	160/6	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	886017	78/M/Asian/ Twn		敗血症 [SEPSIS]	7/12	Yes	4	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	NA
				敗血症 [SEPSIS]	18/1	Yes	5	NR	NR	NR	NA	DW	DW	FATAL	NA
	886020	54/M/Asian/ Twn		肺炎 [PNEUMONIA]	193/33	Yes	2	NR	NR	NR	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	886025	65/F/Asian/ Twn		尿路感染 [URINARY TRACT INFECTION]	8/13	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	972002	61/F/White/ Isr		レジオネラ菌性肺炎 [LEGIONALA PNEUMONIA]	320/39	Yes	4	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	972004	79/M/White/ Isr		病的骨折 [PATHOLOGIC FRACTURE]	7/3	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				蜂巣炎 [BILATERAL CELLULITIS OF LOWER LIMB]	29/15	Yes	3	NR	NR	Poss.	NA	DNC	DI	RECOVERED/ RESOLVED	NA
				非心臓性胸痛 [NON CARDIAC UNCPECIFIED CHEST PAIN]	135/3	Yes	2	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				呼吸困難 [DYSPNEA]	161/9	Yes	2	NR	NR	Poss.	NA	DNC	DI	RECOVERED/ RESOLVED	NA
	972013	75/M/White/ Isr		全身性浮腫 [ANASARCA]	184/99	Yes	2	NR	Prob.	Prob.	NA	DR	DNC	RECOVERED/ RESOLVED	NA
	972016	62/F/White/ Isr		肺炎 [PNEUMONIA]	18/4	Yes	3	NR	DO	NR	NA	DW	DI	RECOVERED/ RESOLVED WITH SEQUELAE	NA
				肺炎 [PNEUMONIA]	21/4	Yes	4	NR	DO	NR	NA	NA	DW	RECOVERED/ RESOLVED WITH SEQUELAE	NA
				肺炎 [PNEUMONIA]	25/1	Yes	5	NR	DO	NR	NA	NA	NA	FATAL	NA

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	972032	78/M/White/ Isr		気管支炎 [BRONCHITIS]	74/26	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
	972038	54/M/White/ Isr		背部痛 [BACK PAIN]	3/6	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
				錯乱状態 [SEVERE CONFUSION]	18/	Yes	4	NR	NR	NR	NA	DI	DNC	NOT RECOVERED/ NOT RESOLVED	NA
				急性腎不全 [ACUTE RENAL FAILURE]	23/9	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED WITH SEQUELAE	NA
				急性腎不全 [ACUTE RENAL FAILURE]	32/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	972042	63/M/White/ Isr		感染 [GENERAL INFECTION OF UNK ORIGIN]	41/3	Yes	3	NR	Poss.	Poss.	NA	DI	DNC	RECOVERED/ RESOLVED	NA
				気管支炎 [BRONCHITIS]	210/4	Yes	3	NR	VL	NR	NA	DI	DNC	RECOVERED/ RESOLVED	NA
	972048	66/F/White/ Isr		腎不全 [RENAL FAILURE]	230/	Yes	4	NR	NR	NR	NA	NA	NA	NOT RECOVERED/ NOT RESOLVED	NA
	972053	59/M/White/ Isr		気道感染 [RESPIRATORY INFECTION]	27/7	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
				肺炎 [PNEUMONIA]	55/7	Yes	3	NR	NR	NR	NA	DNC	DNC	RECOVERED/ RESOLVED	NA
DRd	100006	82/F/White/ Usa	16 mg/kg	蜂巣炎 [LEFT HAND CELLULITIS]	164/4	Yes	3	DO	DO	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	大葉性肺炎 [RIGHT MIDDLE LOBE PNEUMONIA/LUNG INFECTION]	164/4	Yes	3	Poss.	Prob.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	100007	59/M/White/ Usa	15.21 mg/kg	心筋梗塞 [ACUTE ANTERIOR MYOCARDIAL INFARCTION]	241/5	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	100016	70/M/White/ Usa	16 mg/kg	インフルエンザ性肺炎 [INFLUENZA A PNEUMONIA]	56/4	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
	100037	73/M/Black Or African American/ Usa	16.21 mg/kg	椎間板突出 [BULGING DISC DISEASE]	27/3	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.21 mg/kg	椎間板突出 [BULGING DISC DISEASE]	30/5	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			15.86 mg/kg	敗血症 [SEPTICEMIA]	70/48	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.81 mg/kg	硬膜外膿瘍 [EPIDURAL ABSCESS]	128/52	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
	100043	62/M/White/ Usa	16.42 mg/kg	痙攣発作 [SEIZURE]	240/3	Yes	2	DO	DO	DO	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.65 mg/kg	痙攣発作 [RECURRENT SEIZURE]	289/2	Yes	2	DO	DO	DO	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	100049	57/F/Black Or African American/ Usa	16.16 mg/kg	レジオネラ菌性肺炎 [LEGIONELLA PNEUMONIA]	238/3	Yes	3	Prob.	DO	Poss.	DI	DI	DNC	RECOVERED/ RESOLVED	No
	100050	73/M/White/ Usa	16.21 mg/kg	腎不全 [RENALE FAILURE]	20/3	Yes	3	DO	Poss.	DO	DW	DW	DW	RECOVERED/ RESOLVED	No
			16.21 mg/kg	全身性皮疹 [WORSENING RASH COVERING BODY]	20/32	Yes	3	Poss.	Poss.	NR	DW	DW	DW	RECOVERED/ RESOLVED	No
			16.21 mg/kg	丘疹性皮疹 [WORSENING RASH WITH PAPULAR LESIONS]	30/22	Yes	3	Poss.	NR	Prob.	NA	NA	NA	RECOVERED/ RESOLVED	No
	100051	54/F/White/ Usa	16.3 mg/kg	下痢 [DIARRHEA]	80/5	Yes	3	Poss.	Poss.	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.3 mg/kg	失神 [VASOVAGAL SYNCOPE]	82/1	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	101001	62/F/White/ Can	16 mg/kg	肺塞栓症 [PROVOKED PULMONARY EMBOLISM]	37/3	Yes	3	NR	Poss.	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	101002	67/M/White/ Can	16 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	88/4	Yes	3	NR	VL	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	104/	Yes	3	NR	VL	Poss.	NA	DI	NA	NOT RECOVERED/ NOT RESOLVED	No
			16 mg/kg	急性単球性白血病 [ACUTE MONOBLASTIC LEUKEMIA]	106/6	Yes	4	NR	Prob.	NR	DW	DW	DW	RECOVERED/ RESOLVED WITH SEQUELAE	No
			16 mg/kg	急性単球性白血病 [ACUTE MONOBLASTIC LEUKEMIA]	112/1	Yes	5	NR	Prob.	NR	NA	NA	NA	FATAL	No
	101005	52/M/White/ Can	16.07 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	78/6	Yes	3	NR	Prob.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	101008	66/M/White/ Can	16 mg/kg	肺炎 [PNEUMONIA]	240/11	Yes	3	NR	Poss.	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	101012	73/F/White/ Can	16.23 mg/kg	呼吸不全 [RESPIRATORY FAILURE]	8/6	Yes	4	NR	NR	NR	DW	DNC	DNC	RECOVERED/ RESOLVED	No
			16.23 mg/kg	うっ血性心不全 [CONGESTIVE HEART FAILURE]	57/7	Yes	3	NR	NR	NR	NA	DI	DNC	RECOVERED/ RESOLVED WITH SEQUELAE	No
			16.23 mg/kg	肺水腫 [PULMONARY EDEMA RELATED CONGESTIVE HEART FAILURE]	106/6	Yes	3	NR	NR	NR	NA	DR	DR	RECOVERED/ RESOLVED WITH SEQUELAE	No
			16.23 mg/kg	肺水腫 [PULMONARY EDEMA]	162/7	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
			16.23 mg/kg	急性肺水腫 [ACUTE PULMONARY EDEMA]	204/6	Yes	3	NR	NR	NR	NA	DI	DNC	RECOVERED/ RESOLVED	No
			16.23 mg/kg	気管支炎 [BRONCHIAL INFECTION]	383/6	Yes	2	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	NA
	101015	74/M/White/ Can	15.76 mg/kg	気管支肺炎 [BRONCHOPNEUMONIA]	148/8	Yes	3	DO	Poss.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	101016	70/F/White/ Can	16 mg/kg	尿路感染 [URINARY TRACT INFECTION]	152/16	Yes	3	NR	NR	NR	DI	NA	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	足骨折 [FRACTURE OF METATARSALS ON RIGHT FOOT]	424/5	Yes	3	NR	NR	NR	DI	NA	DI	RECOVERED/ RESOLVED	No
	101018	73/M/White/ Can	16 mg/kg	出血性胃腸管血管異形成 [LOWER GI BLEED SECONDARY TO ANGIODYSPLASIA]	151/5	Yes	3	NR	NR	NR	DI	DI	DNC	RECOVERED/ RESOLVED	NA
			16 mg/kg	肺炎 [PNEUMONIA]	214/10	Yes	3	NR	NR	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	101033	74/M/White/ Can	15.95 mg/kg	前立腺腫大 [ENLARGED PROSTATE]	97/	Yes	4	DO	NR	NR	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
			15.95 mg/kg	呼吸困難 [SHORTNESS OF BREATH]	97/49	Yes	4	DO	Poss.	DO	DI	DR	DNC	RECOVERED/ RESOLVED	No
	101037	64/M/White/ Can	16.04 mg/kg	軟部組織感染 [INFECTION SOFT TISSUE UNDER CHIN AREA]	141/28	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	300001	64/F/White/ Grc	16 mg/kg	気道感染 [RESPIRATORY INFECTION]	210/11	Yes	3	NR	NR	NR	NA	DI	DI	RECOVERED/ RESOLVED	No
	300005	89/M/White/ Grc	16 mg/kg	気管支炎 [ACUTE BRONCHITIS]	81/5	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	300006	63/F/White/ Grc	16 mg/kg	肺塞栓症 [PULMONARY EMBOLISM]	57/8	Yes	3	DO	Poss.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	気道感染 [FEBRILE RESPIRATORY INFECTION]	60/5	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.76 mg/kg	気道感染 [FEBRILE RESPIRATORY INFECTION]	167/20	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.76 mg/kg	脊椎圧迫骨折 [CONSTRICTIVE FRACTURE THORASIC OF LUMBAR SPINE]	179/249	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	320001	65/M/White/ Bel	16.02 mg/kg	発熱性好中球減少症 [NEUTROPENIC FEVER]	131/5	Yes	4	NR	VL	NR	DNC	DI	DI	RECOVERED/ RESOLVED	No
	320003	71/F/White/ Bel	16 mg/kg	憩室穿孔 [PERFORED DIVERTICULITIS]	10/17	Yes	4	DO	DO	Prob.	DW	DW	DW	RECOVERED/ RESOLVED	No
	320004	68/M/White/ Bel	15.83 mg/kg	末梢動脈狭窄 [STENOSIS LEG A. FEMORALIS SUPERIOR LEFT]	466/32	Yes	4	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	NA
	320006	65/M/White/ Bel	15.47 mg/kg	インフルエンザ [INFLUENZA]	78/9	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.85 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	398/13	Yes	3	NR	Prob.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	320007	69/M/White/ Bel	16 mg/kg	国際標準比増加 [INR INCREASED]	58/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.45 mg/kg	発熱 [FEVER]	391/13	Yes	1	Poss.	Poss.	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.45 mg/kg	国際標準比増加 [INR INCREASED]	401/3	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.45 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	404/15	Yes	3	NR	Prob.	NR	DNC	DNC	DI	RECOVERED/ RESOLVED	No
	320014	48/F/White/ Bel	16 mg/kg	骨痛 [INCREASED BONE PAIN]	146/12	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			15.94 mg/kg	感染性脊椎炎 [SPONDYLITIS WITH SALMONELLA]	220/16	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	320017	73/M/White/ Bel	16.24 mg/kg	手骨折 [FRACTURE MIDDLE FINGER RIGHT HAND (AFTER BICYCLE ACCIDENT)]	164/1	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.41 mg/kg	敗血症 [SEPSIS]	392/8	Yes	4	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	320023	34/M/Other/ Bel	15.93 mg/kg	気道感染 [RESPIRATORY TRACT INFECTION]	350/5	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	330005	64/M/Not Reported/ Fra	16.03 mg/kg	大腸炎 [SIGMOIDITIS]	328/9	Yes	3	NR	Prob.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.99 mg/kg	心房粗動 [ATRIAL FLUTTER]	571/9	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.99 mg/kg	急性腎不全 [ACUTE RENAL INSUFICIENCY]	586/3	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.99 mg/kg	急性冠動脈症候群 [ACUTE CORONARIAN SYNDROM]	595/6	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	330006	65/F/Not Reported/ Fra	15.8 mg/kg	カンジダ感染 [URINARY AND STOOLS CANDIDA INFECTION]	4/17	Yes	1	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.25 mg/kg	うつ病 [DEPRESSION WORSENING]	542/56	Yes	3	DO	Prob.	DO	DI	DW	DW	RECOVERED/ RESOLVED	No
	330014	59/F/White/ Fra	16.55 mg/kg	肺炎 [BILATERAL HYPOXIC PNEUMONIA]	513/11	Yes	3	NR	NR	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	330041	67/M/Not Reported/ Fra	16.52 mg/kg	レンサ球菌性肺炎 [STREPTOCOCCUS PNEUMONIA]	236/11	Yes	3	NR	NR	NR	NA	DI	NA	RECOVERED/ RESOLVED	No
	330050	50/M/Not Reported/ Fra	15.82 mg/kg	形質細胞性白血病 [PLASMA CELL LEUKEMIA]	141/3	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED WITH SEQUELAE	NA
	330061	84/M/Not Reported/ Fra	15.78 mg/kg	腓骨神経損傷 [MECHANICAL COMPRESSION OF PERONEAL NERVE]	50/	Yes	1	NR	NR	NR	DI	DI	DI	NOT RECOVERED/ NOT RESOLVED	No
			16.17 mg/kg	一過性脳虚血発作 [TRANSIENT ISCHEMIC ATTACK]	93/21	Yes	1	DO	DO	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	330062	68/F/Not Reported/ Fra	16.5 mg/kg	全身健康状態低下 [DETERIORATION OF HEALTH STATUS]	138/4	Yes	3	Poss.	Poss.	Poss.	DW	DW	DW	RECOVERED/ RESOLVED WITH SEQUELAE	No
			16.5 mg/kg	肺塞栓症 [PULMONARY EMBOLISM]	140/2	Yes	3	NR	Poss.	NR	NA	NA	NA	RECOVERED/ RESOLVED WITH SEQUELAE	No
	330065	42/M/Not Reported/ Fra	16.37 mg/kg	筋骨格痛 [FEBRILE ARTHROMYALGIA]	5/6	Yes	3	Prob.	DO	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	Yes

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	340005	71/M/White/ Esp	16 mg/kg	敗血症性ショック [SEPTIC SHOCK]	53/1	Yes	5	DO	NR	NR	DW	DW	DW	FATAL	No
	340006	72/M/White/ Esp	16 mg/kg	急性副鼻腔炎 [BILATERAL ACUTE MAXILLARY SINUSITIS]	376/7	Yes	2	NR	DO	DO	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			16.09 mg/kg	下痢 [DIARRHEA]	519/6	Yes	2	DO	Poss.	DO	NA	NA	NA	RECOVERED/ RESOLVED	No
			16.09 mg/kg	歩行障害 [GAIT INSTABILITY]	519/44	Yes	3	DO	DO	DO	NA	NA	NA	RECOVERED/ RESOLVED	No
			16.09 mg/kg	全身健康状態低下 [DECLINE IN GENERAL CONDITION]	519/6	Yes	3	DO	DO	DO	DW	DW	DW	RECOVERED/ RESOLVED	No
			16.09 mg/kg	眼窩周囲蜂巣炎 [PERIORBITAL CELLULITIS]	547/16	Yes	3	Poss.	Poss.	Poss.	NA	NA	NA	RECOVERED/ RESOLVED	No
	340010	72/M/White/ Esp	16.2 mg/kg	発熱性好中球減少症 [FEBRIL NEUTROPENIA]	180/11	Yes	4	NR	Poss.	Poss.	DNC	DI	DI	RECOVERED/ RESOLVED	No
	340012	74/M/White/ Esp	16 mg/kg	発熱性好中球減少症 [NEUTROPENIC FEVER]	282/5	Yes	4	NR	Poss.	NR	NA	NA	NA	RECOVERED/ RESOLVED	No
	340026	69/M/White/ Esp	16 mg/kg	細菌性肺炎 [BACTERIAL PNEUMONIAE]	15/15	Yes	2	Prob.	DO	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.81 mg/kg	細菌性気管支炎 [ACUTE BACTERIAL BRONCHITIS]	75/11	Yes	2	Prob.	Prob.	NR	DW	DW	DW	RECOVERED/ RESOLVED	No
			15.81 mg/kg	心房細動 [ATRIAL FIBRILATION]	91/3	Yes	2	NR	NR	DO	NA	NA	NA	RECOVERED/ RESOLVED	No
	340033	64/F/White/ Esp	15.85 mg/kg	心アミロイドーシス [CARDIAC AMYLOIDOSIS]	90/21	Yes	2	NR	NR	NR	DI	DR	DI	RECOVERED/ RESOLVED	No
			16.2 mg/kg	気管支炎 [ACUTE BRONCHITIS]	157/5	Yes	2	NR	DO	DO	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.07 mg/kg	血小板減少症 [THROMBOCYTOPENIA]	292/48	Yes	4	NR	VL	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.07 mg/kg	下痢 [DIARRHEA]	292/28	Yes	2	DO	Poss.	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.07 mg/kg	脱水 [DEHYDRATATION]	292/28	Yes	2	DO	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.07 mg/kg	子宮膿瘍 [UTERINE ABSCESS]	303/17	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	340035	66/F/White/ Esp	16.59 mg/kg	耳下腺炎 [PAROTITIS]	72/13	Yes	2	NR	NR	NR	DNC	DI	DI	RECOVERED/ RESOLVED	No
	340037	59/F/White/ Esp	16.27 mg/kg	リステリア性敗血症 [SEPSIS BY LISTERIA]	336/4	Yes	3	DO	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.55 mg/kg	低カルシウム血症 [HYPOCALCEMIA]	366/11	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No

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Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	340038	65/F/White/ Esp	16 mg/kg	肺炎 [PNEUMONIA]	13/13	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	インフルエンザ [INFLUENZA INFECTION]	23/18	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	呼吸不全 [RESPIRATORY FAILURE]	33/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	インフルエンザ [INFLUENZA A INFECTION]	61/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	肺炎 [PNEUMONIA]	61/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			17.54 mg/kg	発熱 [FEVER]	122/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	尿路感染 [URINE INFECION]	162/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	四肢痛 [ARM'S PAIN]	162/2	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	発熱性好中球減少症 [FEBRIL NEUTROPENIA]	199/6	Yes	4	NR	Prob.	NR	DI	DI	DI	RECOVERED/ RESOLVED	NA
			16 mg/kg	疼痛 [GENERAL PAIN]	263/22	Yes	3	NR	NR	NR	DW	DW	DW	RECOVERED/ RESOLVED	No
			16 mg/kg	高カルシウム血症 [HYPERCALCEMIA]	263/22	Yes	3	NR	NR	NR	DW	DW	DW	RECOVERED/ RESOLVED	No
	340040	41/M/White/ Esp	16.22 mg/kg	三叉神経障害 [TRIGEMINAL NERVE DISORDER]	412/8	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.22 mg/kg	ウイルス性気道感染 [RESPIRATORY INFECTION BY INFLUENZA A VIRUS]	417/3	Yes	1	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	340051	48/M/White/ Esp	16 mg/kg	インフルエンザ [INFLUENZA B INFECTION]	20/7	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
	340054	59/M/White/ Esp	16.02 mg/kg	気道感染 [FEVER (RESPIRATORY INFECTION)]	200/5	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.98 mg/kg	気道感染 [RESPIRATORY INFECTION]	369/10	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	340058	56/M/White/ Esp	16 mg/kg	敗血症性ショック [SEPTIC SHOCK]	20/10	Yes	4	DO	DO	DO	DW	DW	DW	RECOVERED/ RESOLVED	No
			16 mg/kg	敗血症性ショック [SEPTIC SHOCK]	30/1	Yes	5	DO	DO	DO	NA	NA	NA	FATAL	No
	440007	49/M/Asian/ Gbr	15.98 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	22/8	Yes	3	Poss.	Prob.	DO	DI	DNC	DI	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	440014	66/F/White/ Gbr	15.97 mg/kg	インフルエンザ [INFLUENZA]	57/7	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.67 mg/kg	Ｈ１Ｎ１インフルエンザ [H1N1 INFLUENZA]	478/30	Yes	4	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	440021	69/M/White/ Gbr	16 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	84/8	Yes	3	Poss.	Prob.	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.48 mg/kg	下気道感染 [CHEST INFECTION]	154/12	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.48 mg/kg	鼻膿瘍 [NASAL ABSCESS]	158/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.62 mg/kg	肺炎 [PNEUMONIA]	347/32	Yes	3	NR	Poss.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	440023	76/M/White/ Gbr	16.85 mg/kg	下気道感染 [CHEST INFECTION]	125/22	Yes	2	Prob.	Prob.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	440025	64/M/Not Reported/ Gbr	15.78 mg/kg	下気道感染 [LOWER RESPIRATORY TRACT INFECTION]	404/25	Yes	2	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	440027	66/M/Not Reported/ Gbr	16.05 mg/kg	インフルエンザ [INFLUENZA B VIRUS TEST POSITIVE]	83/47	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.04 mg/kg	肺炎 [RIGHT MIDDLE ZONE PNEUMONIA]	284/28	Yes	2	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.04 mg/kg	ウイルス性胃腸炎 [VIRAL GASTEROENTRITIS]	293/19	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	440033	75/M/Unknown/ Gbr	15.96 mg/kg	背部痛 [BACK PAIN]	14/23	Yes	3	NR	NR	NR	DNC	DNC	DI	RECOVERED/ RESOLVED	No
			15.95 mg/kg	悪心 [NAUSEA]	39/19	Yes	1	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.95 mg/kg	嘔吐 [VOMITING]	39/19	Yes	1	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.95 mg/kg	急性腎不全 [ACUTE KIDNEY INJURY]	56/10	Yes	2	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.99 mg/kg	急性腎不全 [ACUTE KIDNEY INJURY]	412/	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERING /RESOLVING	No
			16.99 mg/kg	好中球減少性敗血症 [SUSPECTED NEUTROPENIC SEPSIS]	438/	Yes	3	NR	NR	NR	DI	DI	DI	NOT RECOVERED/ NOT RESOLVED	No
	440035	65/M/White/ Gbr	16.15 mg/kg	起立性低血圧 [POSTURAL HYPOTENSION]	160/3	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			15.96 mg/kg	肺炎 [PNEUMONIA]	297/18	Yes	3	Poss.	Prob.	DO	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.64 mg/kg	尿路感染 [URINARY TRACT INFECTION]	297/18	Yes	3	Poss.	Prob.	DO	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	440038	61/M/White/ Gbr	16.33 mg/kg	下気道感染 [LOWER RESPIRATORY TRACT INFECTION (WITH FEVER)]	81/6	Yes	4	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	440043	62/F/White/ Gbr	15.83 mg/kg	ウイルス性胃腸炎 [VIRAL GASTROENTERITIS]	243/4	Yes	3	DO	DO	DO	DNC	DI	DI	RECOVERED/ RESOLVED	No
	440046	68/M/White/ Gbr	15.97 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	18/4	Yes	3	NR	Poss.	Prob.	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.97 mg/kg	ヘモフィルス性肺炎 [HAEMOPHILUS INFLUENZA TYPE B PNEUMONIA]	18/7	Yes	3	NR	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	U
	440048	76/M/White/ Gbr	16.59 mg/kg	下気道感染 [CHEST INFECTION]	128/3	Yes	3	NR	DO	Poss.	DI	DNC	DI	RECOVERED/ RESOLVED	No
	440054	70/M/White/ Gbr	15.19 mg/kg	下気道感染 [CHEST INFECTION]	22/4	Yes	3	DO	DO	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.19 mg/kg	下気道感染 [CHEST INFECTION]	293/3	Yes	3	DO	Poss.	VL	DI	DI	DI	RECOVERED/ RESOLVED	No
	440059	71/M/White/ Gbr	16.8 mg/kg	下気道感染 [LOWER RESPIRATORY TRACT INFECTION]	271/	Yes	3	NR	Poss.	Poss.	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
			16.8 mg/kg	呼吸困難 [DYSPNOEA]	271/	Yes	3	NR	Poss.	Poss.	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
	450001	67/F/White/ Dnk	16 mg/kg	肺感染 [PULMONARY INFECTION]	12/13	Yes	3	NR	NR	Poss.	DI	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	発熱 [FEBRILIA]	219/2	Yes	1	Prob.	Prob.	Prob.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	発熱 [FEVER]	373/2	Yes	1	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	450004	67/M/White/ Dnk	16 mg/kg	感染 [INFECTION WITH UNKNOWN ORIGIN]	52/6	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	肺塞栓症 [EMBOLIA PULMONIS]	196/65	Yes	3	NR	VL	NR	DNC	DI	DI	RECOVERED/ RESOLVED	No
	450006	71/M/White/ Dnk	16 mg/kg	肺炎 [PNEUMONIA]	54/8	Yes	3	NR	NR	Poss.	DW	DW	DW	RECOVERED/ RESOLVED	No

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								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			16 mg/kg	肺炎 [PNEUMONIA]	61/20	Yes	4	NR	NR	Poss.	NA	NA	NA	RECOVERED/ RESOLVED	No
			16 mg/kg	肺炎 [PNEUMONIA]	80/1	Yes	5	NR	NR	Poss.	NA	NA	NA	FATAL	No
	450012	77/F/White/ Dnk	16 mg/kg	上気道感染 [UPPER RESPIRATORY INFECTION]	270/10	Yes	2	Poss.	DO	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	上気道感染 [UPPER RESPIRATORY INFECTION]	340/5	Yes	3	NR	NR	NR	DNC	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	失神寸前の状態 [LIPOTHYMIA]	370/7	Yes	3	NR	Poss.	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	450014	75/M/White/ Dnk	16 mg/kg	肺炎 [PNEUMONIA]	20/132	Yes	4	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
	450020	68/F/White/ Dnk	16 mg/kg	感染 [INFECTION UNKNOWN CASUSE AND LOCATION]	193/7	Yes	3	NR	Poss.	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	450021	73/F/White/ Dnk	16 mg/kg	便秘 [CONSTIPATION]	92/7	Yes	3	DO	Prob.	DO	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.63 mg/kg	発熱 [FEVER WITHOUT KNOWN ORIGIN]	220/8	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.63 mg/kg	発熱 [FEVER]	323/4	Yes	2	DO	DO	DO	DNC	DI	DI	RECOVERED/ RESOLVED	No
	460001	68/M/White/ Swe	15.78 mg/kg	後嚢破裂 [POSTERIOR CAPSULE RUPTURE]	554/2	Yes	3	NR	NR	NR	DI	NA	DI	RECOVERED/ RESOLVED	No
	460005	72/M/White/ Swe	16.36 mg/kg	股関節部骨折 [HIP FRACTURE]	536/	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERING /RESOLVING	No
	460008	73/M/White/ Swe	16 mg/kg	インフルエンザ性肺炎 [INFLUENZA PNEUMONITIS]	155/21	Yes	2	DO	DO	Poss.	DI	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	No
			16 mg/kg	皮膚感染 [SKIN INFECTION]	295/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	肺炎 [PNEUMONIA]	307/10	Yes	3	DO	DO	DO	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	460012	70/M/White/ Swe	15.45 mg/kg	非心臓性胸痛 [NON-CARDIAC CHEST PAIN]	22/2	Yes	2	Poss.	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	狭心症 [CHEST PAIN - CARDIAC]	167/3	Yes	3	DO	Poss.	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
	460016	58/M/White/ Swe	16 mg/kg	肺炎 [PNEUMONIA]	70/11	Yes	3	Poss.	Poss.	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
	460027	53/F/White/ Swe	15.79 mg/kg	インフルエンザ [INFLUENZA A]	319/15	Yes	2	DO	DO	DO	DNC	DI	DI	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			15.79 mg/kg	肺炎 [PNEUMONIA]	323/11	Yes	2	DO	DO	DO	DNC	DI	DI	RECOVERED/ RESOLVED	No
	460029	55/F/White/ Swe	16.65 mg/kg	扁桃炎 [TONSILLITIS]	146/2	Yes	3	DO	Poss.	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	460030	64/F/White/ Swe	16.02 mg/kg	ＲＳウイルス感染 [FEVER DUE TO RESPIRATORY SYNCYTIALVIRUS]	23/6	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	480001	59/F/White/ Pol	15.54 mg/kg	気管支肺炎 [BILATERAL BRONCHIAL PNEUMONIA]	154/8	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.2 mg/kg	肺炎 [PNEUMONIA]	183/28	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	480003	48/M/White/ Pol	16 mg/kg	下痢 [DIARRHOEA]	302/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	気管支炎 [BRONCHITIS]	313/11	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	480004	58/M/White/ Pol	16 mg/kg	失神 [ORTHOSTATIC COLLAPSE]	9/4	Yes	3	DO	DO	VL	DI	DI	DI	RECOVERED/ RESOLVED	No
	480012	61/F/White/ Pol	16 mg/kg	憩室穿孔 [PERFORATION OF SIGMOID DIVERTICULUM]	192/11	Yes	3	DO	DO	VL	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	胃腸障害 [SURGICAL CLOSURE OF STOMY]	377/10	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	480025	66/M/White/ Pol	16 mg/kg	口腔真菌感染 [ORAL MYCOSIS]	295/12	Yes	3	Prob.	Prob.	VL	DI	DI	DI	RECOVERED/ RESOLVED	No
	480030	68/M/White/ Pol	16 mg/kg	電解質失調 [ELECTROLYTE IMBALANCE]	6/4	Yes	4	NR	NR	NR	DI	DNC	DNC	RECOVERED/ RESOLVED	No
	480037	73/M/White/ Pol	16.42 mg/kg	肺石灰化 [CALCIFICATION OF THE LEFT LUNG - 3 SEGMENT]	36/7	Yes	1	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	480040	67/F/White/ Pol	16 mg/kg	歯肉炎 [GINGIVITIS]	151/8	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	気管支炎 [BRONCHITIS]	337/4	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	490002	64/M/White/ Deu	15.87 mg/kg	トロポニン増加 [INCREASE OF TROPONIN]	421/2	Yes	1	Poss.	Poss.	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	490011	69/M/White/ Deu	16.67 mg/kg	敗血症性ショック [SEPTIC SHOCK]	106/1	Yes	5	Poss.	Poss.	Poss.	DW	DW	DW	FATAL	No
	490013	71/M/White/ Deu	16 mg/kg	尿道出血 [HEMORRHAGIC LESION OF THE URETHRAL MUCOSA (SYMPTOM: MACROHEMATURIA)]	256/6	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	490014	55/M/White/ Deu	16 mg/kg	高血糖 [HYPERGLYCEMIA]	25/4	Yes	4	NR	NR	VL	DI	DI	DR	RECOVERED/ RESOLVED	No
			17.73 mg/kg	クレブシエラ菌性肺炎 [KLEBSIELLA PNEUMONIA]	43/12	Yes	3	NR	NR	VL	DI	DI	DI	RECOVERED/ RESOLVED	No
	490019	71/F/White/ Deu	16 mg/kg	細菌性上気道感染 [BACTERIAL INFECTION PULMONARY/UPPER RESPIRATORY]	12/16	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	肋骨骨折 [FRACTURED RIB AFTER FALLING DOWN A CLEAR ICED STAIR]	323/2	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	490021	80/F/White/ Deu	15.86 mg/kg	洞性不整脈 [SINUS TACHYARRHYTMIA]	295/48	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	490022	71/M/White/ Deu	16 mg/kg	出血性梗塞 [RIGHT SIDE HAEMORRHAGIC INFARCT IN POSTERIOR AREA]	69/26	Yes	3	NR	Poss.	DO	NA	NA	NA	RECOVERED/ RESOLVED	No
	490023	62/F/White/ Deu	16.1 mg/kg	肺塞栓症 [PULMONARY EMBOLISM]	66/20	Yes	2	Poss.	Prob.	Poss.	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	490025	78/M/White/ Deu	15.79 mg/kg	肺炎 [PNEUMONIA]	71/28	Yes	3	Prob.	VL	VL	DW	DW	DW	RECOVERED/ RESOLVED	No
	610006	64/F/White/ Aus	15.94 mg/kg	下痢 [DIARRHEA]	169/6	Yes	2	DO	DO	NR	DI	DI	DNC	RECOVERED/ RESOLVED	U
			15.94 mg/kg	悪心 [WORSENNG NAUSEA]	169/4	Yes	3	NR	Poss.	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			16.5 mg/kg	インフルエンザ [INFLUENZA B]	284/7	Yes	3	NR	DO	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	610010	60/M/White/ Aus	15.96 mg/kg	気道感染 [RESPIRATORY INFECTION]	75/33	Yes	3	Poss.	Poss.	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	610012	53/M/White/ Aus	15.7 mg/kg	インフルエンザ [INFLUENZA B VIRUS INFECTION]	227/5	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
			15.7 mg/kg	骨痛 [BONE PAIN (PRESUMED SECONDARY TO COUHGING)]	232/7	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	610014	68/M/White/ Aus	15.26 mg/kg	ＲＳウイルス感染 [RESPIRATORY SYNCYTIAL VIRUS]	157/8	Yes	3	DO	DO	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
			14.91 mg/kg	肺炎 [PNEUMONIA]	391/13	Yes	4	Poss.	Poss.	Poss.	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	610016	74/F/White/ Aus	16.08 mg/kg	肺炎 [PNEUMONIA]	155/15	Yes	4	NR	Poss.	Poss.	DNC	DNC	DI	RECOVERED/ RESOLVED	No
	610023	64/M/White/ Aus	15.46 mg/kg	胸部不快感 [CHEST DISCOMFORT NON CARDIAC BUT NO ACTUAL DIAGNOSIS]	1/1	Yes	1	Poss.	NR	NR	DI	DI	DNC	RECOVERED/ RESOLVED	Yes

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			15.46 mg/kg	高血圧 [DRUG INFUSION REACTION TO DARA TO HYPERTENSION(IRR)]	1/3	Yes	1	VL	NR	NR	DI	NA	DNC	RECOVERED/ RESOLVED	Yes
			16.68 mg/kg	発熱 [FEBRILE EVENT]	154/10	Yes	2	DO	DO	NR	DI	DNC	DNC	RECOVERED/ RESOLVED	No
			14.96 mg/kg	貧血 [ANEAMIA]	223/28	Yes	2	NR	VL	DO	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	700004	53/F/White/ Rus	16 mg/kg	肺炎 [PNEUMONIA]	29/15	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No
	700013	51/F/White/ Rus	16 mg/kg	虫垂炎 [APPENDICITIS]	75/11	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	700020	75/F/White/ Rus	15.51 mg/kg	細菌性肺炎 [BILATERAL BACTERIAL PNEUMONIA]	77/5	Yes	4	Poss.	NR	Poss.	DNC	DW	DW	RECOVERED/ RESOLVED	No
			15.51 mg/kg	細菌性肺炎 [BILATERAL BACTERIAL PNEUMONIA]	81/2	Yes	5	NR	NR	Poss.	DW	NA	NA	FATAL	No
	700026	70/F/White/ Rus	16 mg/kg	全身性炎症反応症候群 [SYSTEMIC INFLAMMATORY RESPONSE SYNDROME]	18/	Yes	4	DO	Poss.	DO	DNC	DI	DNC	NOT RECOVERED/ NOT RESOLVED	No
			16 mg/kg	心肺不全 [ACUTE CARDIOPULMONARY FAILURE]	22/1	Yes	5	NR	NR	NR	DW	DW	DW	FATAL	NA
	700030	62/M/White/ Rus	16 mg/kg	貧血 [ANEMIA]	71/	Yes	3	NR	Poss.	DO	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
			16 mg/kg	肺水腫 [PULMONARY EDEMA]	92/1	Yes	4	NR	NR	NR	NA	NA	NA	RECOVERED/ RESOLVED	No
			16 mg/kg	肺水腫 [PULMONARY EDEMA]	92/2	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	700034	60/M/White/ Rus	16 mg/kg	肺炎 [BILATERAL PNEUMONIA]	13/24	Yes	3	NR	Poss.	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	700043	69/M/White/ Rus	16 mg/kg	肺塞栓症 [TROMBOEMBOLIC EVENT (PULMONARY EMBOLISM)]	292/14	Yes	3	NR	Prob.	Prob.	DNC	DI	DI	RECOVERED/ RESOLVED WITH SEQUELAE	No
	700048	36/F/White/ Rus	16 mg/kg	虫垂炎 [APPENDICITIS]	239/29	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	700050	76/F/White/ Rus	16 mg/kg	肺炎 [PNEUMONIA IN RIGHT LUNG]	87/26	Yes	3	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	810003	45/M/Asian/ Jpn	16.11 mg/kg	塞栓症 [THROMBOEMBOLIC EVENT]	44/20	Yes	2	NR	Prob.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			16.11 mg/kg	塞栓症 [THROMBOEMBOLIC EVENT]	63/6	Yes	1	NR	Prob.	Poss.	DNC	DR	DNC	RECOVERED/ RESOLVED	No
	810011	73/F/Asian/ Jpn	15.43 mg/kg	ボーエン病 [WORSENING OF BOWEN DISEASE(RIGHT LOWER THIGH)]	179/47	Yes	1	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	810015	72/M/Asian/ Jpn	16.81 mg/kg	脳梗塞 [CEREBRAL INFARCTION]	81/	Yes	4	NR	NR	NR	DW	DW	DW	NOT RECOVERED/ NOT RESOLVED	No
	810016	74/M/Asian/ Jpn	16.86 mg/kg	肺炎 [PHEUMONIA]	200/51	Yes	3	DO	NR	Prob.	DW	DW	DW	RECOVERED/ RESOLVED	No
	810018	73/F/Asian/ Jpn	15.72 mg/kg	肺炎 [PNEUMONIA]	185/9	Yes	3	NR	DO	DO	DNC	DI	DI	RECOVERED/ RESOLVED	No
	810020	60/M/Asian/ Jpn	16 mg/kg	細菌感染 [BACTERIAL INFECTION]	14/15	Yes	3	Prob.	Prob.	Prob.	DI	DI	DI	RECOVERED/ RESOLVED	No
			16.63 mg/kg	低酸素症 [HYPOXIA]	61/10	Yes	1	Prob.	Prob.	Prob.	DNC	DI	DI	RECOVERED/ RESOLVED	No
	810037	68/F/Asian/ Jpn	17.44 mg/kg	サイトメガロウイルス感染 [CYTOMEGALOVIRUS INFECTION]	77/31	Yes	3	Poss.	Poss.	Prob.	DI	DI	DI	RECOVERED/ RESOLVED	No
			17.44 mg/kg	エプスタイン・バーウイルス関連リンパ増殖性障害 [EBV-POSITIVE LYMPHOPROLIFERATIVE DISORDER]	91/	Yes	3	Prob.	Prob.	Prob.	DW	DW	DW	NOT RECOVERED/ NOT RESOLVED	No
	820002	73/M/Asian/ Kor	15.93 mg/kg	好中球減少症 [NEUTROPHIL COUNT DECREASED]	15/2	Yes	3	NR	Poss.	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.93 mg/kg	好中球減少症 [NEUTROPHIL COUNT DECREASED]	17/2	Yes	4	NR	Poss.	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.93 mg/kg	好中球減少症 [NEUTROPHIL COUNT DECREASED]	19/2	Yes	3	NR	Poss.	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.96 mg/kg	低血圧 [HYPOTENSION]	57/1	Yes	3	Poss.	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	Yes
			17.74 mg/kg	圧迫骨折 [AGGRAVATED OF MULTIPLE COMPRESSION FRACTURE]	154/	Yes	2	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
			15.96 mg/kg	肺炎 [INFECTIOUS PNEUMONITIS]	178/9	Yes	4	NR	Poss.	NR	DW	DW	DW	RECOVERED/ RESOLVED	No
			15.96 mg/kg	肺炎 [INFECTIOUS PNEUMONITIS]	186/1	Yes	5	NR	Poss.	NR	NA	NA	NA	FATAL	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
	820013	71/M/Asian/ Kor	16 mg/kg	多臓器不全 [MULTIPLE ORGAN FAILURE]	459/1	Yes	5	Poss.	Poss.	Poss.	DW	DW	DW	FATAL	No
	820014	62/F/Asian/ Kor	15.07 mg/kg	肺臓炎 [PNEUMONITIS]	139/15	Yes	2	Poss.	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	820019	70/F/Asian/ Kor	15.87 mg/kg	白内障 [CATARACT(OU)]	385/8	Yes	3	NR	NR	Poss.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	820022	55/F/Asian/ Kor	15.83 mg/kg	発熱 [FEVER]	266/2	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	820023	64/M/Asian/ Kor	16.24 mg/kg	高カルシウム血症 [HYPERCALCEMIA]	219/4	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16.24 mg/kg	高窒素血症 [AZOTEMIA]	219/4	Yes	2	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	820032	54/F/Asian/ Kor	15.6 mg/kg	好中球減少症 [NEUTROPHIL COUNT DECREASED]	42/2	Yes	4	NR	Poss.	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
			15.6 mg/kg	側腹部痛 [BOTH FLANK PAIN]	42/	Yes	3	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
	886003	77/M/Asian/ Twn	17.13 mg/kg	大葉性肺炎 [PNEUMONIA-LEFT LOWER LOBE]	157/16	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	886016	63/M/Asian/ Twn	15.38 mg/kg	サルモネラ性菌血症 [GRAM NEGATIVE BACILLI BACTEREMIA-SALMONELLA]	150/10	Yes	3	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
	886023	64/F/Asian/ Twn	15.9 mg/kg	発熱 [FEVER]	311/6	Yes	3	Poss.	Poss.	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	886027	57/M/Asian/ Twn	16.03 mg/kg	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	46/6	Yes	3	VL	VL	VL	DNC	DI	DI	RECOVERED/ RESOLVED	No
	972001	66/M/White/ Isr	16 mg/kg	喉頭蓋炎 [SUPRAGLOTITIS]	35/11	Yes	4	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	肺炎 [PNEUMONIA]	223/13	Yes	3	Prob.	Prob.	Prob.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	細気管支炎 [BRONCHIOLITIS]	402/3	Yes	3	NR	NR	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	972010	49/M/White/ Isr	16 mg/kg	インフルエンザ性肺炎 [PNEUMONIA WITH INFLUENZA]	96/4	Yes	3	Poss.	Poss.	Poss.	DI	DNC	DNC	RECOVERED/ RESOLVED	No
	972011	70/M/White/ Isr	16 mg/kg	心房細動 [ATRIAL FIBRILLATION]	140/73	Yes	2	NR	NR	NR	DNC	DNC	DI	RECOVERED/ RESOLVED	No
	972012	76/F/White/ Isr	16 mg/kg	パラインフルエンザウイルス感染 [PARAINFLUENZA VIRUS INFECTION]	39/7	Yes	3	DO	DO	DO	DI	DI	DI	RECOVERED/ RESOLVED	No

LSFAE_JST02_3003: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY3003)

Treatment Group	Subject ID	Age (years)/ Sex/Race/ Country	Onset Dose (dose unit)	Adverse Event (MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
								Dara[c]	Len[c]	Dex[c]	Dara[c]	Len[c]	Dex[c]		
			16 mg/kg	大腸菌性菌血症 [E.COLI BACTEREMIA]	223/4	Yes	3	Prob.	Prob.	Prob.	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
			16 mg/kg	無力症 [WEAKNESS]	294/5	Yes	3	NR	Poss.	NR	DNC	DNC	DNC	RECOVERED/ RESOLVED	No
	972017	77/M/White/ Isr	16 mg/kg	認知障害 [COGNAITIVE AND FUNCTIONAL DECLINE]	180/12	Yes	3	NR	NR	NR	DW	DW	DW	RECOVERED/ RESOLVED WITH SEQUELAE	No
	972018	63/M/White/ Isr	16 mg/kg	発熱 [FEVER]	2/17	Yes	2	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No
			16 mg/kg	背部痛 [BACK PAIN]	66/	Yes	3	NR	NR	NR	DNC	DNC	DNC	NOT RECOVERED/ NOT RESOLVED	No
			16 mg/kg	急性腎不全 [ACUTE RENAL FAILURE]	79/1	Yes	5	NR	NR	NR	NA	NA	NA	FATAL	No
	972033	69/M/White/ Isr	16 mg/kg	胃腸炎 [GASTROENTERITIS]	153/7	Yes	3	DO	Poss.	Poss.	DI	DI	DI	RECOVERED/ RESOLVED	No
	972034	52/M/White/ Isr	16 mg/kg	肺塞栓症 [PULMONARY EMBOLISM]	6/4	Yes	3	NR	VL	NR	DNC	DI	DNC	RECOVERED/ RESOLVED	No
	972052	77/M/White/ Isr	16 mg/kg	鼠径ヘルニア [RIGHT INGUINAL HERNIA]	157/1	Yes	1	NR	NR	NR	DI	DI	DI	RECOVERED/ RESOLVED	No

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: AE = adverse event; SAE = Serious adverse event.
[a] Keys: NR = Not Related, DO = Doubtful, Poss. = Possible, Prob. = Probable, VL = Very Likely.
[b] Keys: DI = Drug Interrupted, DNC = Dose Not Changed, DR = Dose Reduced, DW = Drug Withdrawn, NA = Not Applicable, UN = Unknown.
[c] Keys: Dara = daratumumab, Len = lenalidomide, Dex = dexamethasone.
Note: Adverse events are coded using MedDRA Version 18.0.

LSFAE-JST02_503: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN503)

Treatment Group	Site ID	Enrollment No.	Age (years) /Sex/Race/ Country	AE Onset Date and Time	AE End Date and Time	AE Duration (days)	Reported Term /MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious
2 mg/kg Dara + Len/Dex	DK01	503003	69/M/WHITE/DNK	2013-04-16T12:00	2013-05-06T10:11	21	ARTERIAL RETINAL THROMBOSIS./網膜動脈血栓症	3	DARA: INTERRUPTED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2013-06-07T08:00	2013-06-18T08:00	12	COMMON COLD/鼻咽頭炎	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
	UK02	503002	48/M/WHITE/GBR	2014-01-02	2014-01-03	2	CHEST INFECTION/下気道感染	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2014-09-17	2014-09-18	2	CEREBRAL INFARCT/脳梗塞	3	DARA: INTERRUPTED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
4 mg/kg Dara + Len/Dex	DK01	503005	65/F/WHITE/DNK	2013-09-16T22:44	2013-09-17T02:05	2	ABDOMINAL PAIN/腹痛	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED WITH SEQUELAE	Y
				2014-10-18	2014-10-29	12	FRACTURA PELVIS/骨盤骨折	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2014-12-17T11:00	2014-12-22T15:34	6	BRONCHIAL INFECTION/気管支炎	3	DARA: NOT CHANGED LEN: INTERRUPTED DEX: NOT CHANGED	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
				2015-03-15T22:51	2015-04-01T10:34	18	DIARRHOEA/下痢	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
	UK02	503004	62/M/WHITE/GBR	2013-03-22	2013-04-08	18	POSTERIOR VITREOUS DETACHMENT/硝子体剥離	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2015-05-15	2015-05-16	2	SYNCOPE/失神	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: POSSIBLE/PROBABLE LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
8 mg/kg Dara + Len/Dex	DK02	503008	49/M/WHITE/DNK	2014-09-23T10:15	2014-09-23T12:00	1	ATRIAL FIBRILLATION, PAROXYSMAL/心房細動	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2015-06-11	2015-06-30	20	DIARRHEA/下痢	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED	Y

LSFAE-JST02_503: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN503)

Treatment Group	Site ID	Enrollment No.	Age (years) /Sex/Race/ Country	AE Onset Date and Time	AE End Date and Time	AE Duration (days)	Reported Term /MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious
	NL01	503012	50/M/WHITE/NLD	2015-01-10	2015-01-12	3	PNEUMONIA/肺炎	3	DARA: NOT CHANGED LEN: INTERRUPTED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
16 mg/kg Dara + Len/Dex	DK01	503013	70/F/WHITE/DNK	2013-12-07T10:00	2013-12-11T10:30	5	STEROID WITHDRAWAL SYMPTOMS/ステロイド離脱症候群	3	DARA: INTERRUPTED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: NOT RELATED LEN: NOT RELATED DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
				2014-02-14T15:40	2014-02-25T14:15	12	ANEMIA/貧血	1	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2014-08-25T13:28	2014-09-07T00:00	14	URINARY TRACT INFECTION/尿路感染	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
		503014	70/M/WHITE/DNK	2014-11-11T11:21	2014-11-14T11:56	4	FEVER/発熱	1	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
		503030	60/M/WHITE/DNK	2014-10-24T00:00	2014-11-02T00:00	10	URINARY TRACT INFECTION/尿路感染	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
		503032	50/F/WHITE/DNK	2014-10-27T23:01	2014-11-04T14:29	9	VIRUS INFECTION/ウイルス感染	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2015-02-02T00:50	2015-02-03T17:15	2	UPPER RESPIRATORY INFECTION/上気道感染	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2015-03-09T23:08	2015-03-10T15:25	2	INFLUENZA A, TEST POSITIVE./A型インフルエンザウイルス検査陽性	2	DARA: NOT CHANGED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: NOT RELATED LEN: NOT RELATED DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
	DK02	503034	58/M/WHITE/DNK	2014-06-27			PULMONARY EMBOLISM/肺塞栓症	3	DARA: NOT CHANGED LEN: INTERRUPTED DEX: NOT CHANGED	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y
				2014-07-07T09:16	2014-07-14T11:15	8	NEUTROPENIA/好中球減少症	3	DARA: NOT CHANGED LEN: NOT APPLICABLE DEX: NOT CHANGED	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
	FR01	503010	76/F/WHITE/FRA	2014-01-16			LUMBAR PAIN/背部痛	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y

LSFAE-JST02_503: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN503)

Treatment Group	Site ID	Enroll-ment No.	Age (years) /Sex/Race/ Country	AE Onset Date and Time	AE End Date and Time	AE Duration (days)	Reported Term /MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Ser-ious
		503042	64/M/WHITE/FRA	2014-11-28			GASTRIC ADENOCARCINOMA/胃腺癌	4	DARA: WITHDRAWN LEN: WITHDRAWN DEX: WITHDRAWN	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y
	FR03	503019	62/M/WHITE/FRA	2014-06-06	2014-07-25	50	OSTEONECROSIS OF THE FEMORAL HEAD/骨壊死	3	DARA: INTERRUPTED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
				2014-10-23	2014-10-31	9	SERIOUS BRONCHITIS/気管支炎	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
		503022	73/F/WHITE/FRA	2014-08-21	2014-08-27	7	DIARRHOEA/下痢	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
				2014-11-26	2014-11-27	2	GASTROENTERITIS/胃腸炎	2	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
	IT01	503016	62/F/WHITE/ITA	2015-02-26	2015-03-04	7	VIRAL PNEUMONIA/ウイルス性肺炎	4	DARA: WITHDRAWN LEN: INTERRUPTED DEX: INTERRUPTED	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
				2015-03-05	2015-03-05	1	VIRAL PNEUMONIA/ウイルス性肺炎	5	DARA: WITHDRAWN LEN: WITHDRAWN DEX: WITHDRAWN	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: POSSIBLE/PROBABLE	FATAL	Y
		503037	50/M/WHITE/ITA	2014-07-02	2014-07-14	13	FEVER/発熱	1	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
	NL01	503031	56/M/WHITE/NLD	2014-09-21	2014-10-06	16	WORSENING OF ACUTE GASTROENTERITIS/胃腸炎	3	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
		503039	59/M/WHITE/NLD	2015-07-23T23:10	2015-07-27	5	STROKE/脳血管発作	2	DARA: WITHDRAWN LEN: WITHDRAWN DEX: WITHDRAWN	DARA: NOT RELATED LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED WITH SEQUELAE	Y

LSFAE-JST02_503: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN503)

Treatment Group	Site ID	Enrollment No.	Age (years) /Sex/Race/ Country	AE Onset Date and Time	AE End Date and Time	AE Duration (days)	Reported Term /MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious
	UK01	503040	46/M/WHITE/GBR	2015-09-18T15:00	2015-09-25T17:45	8	SUSPECTED INFECTION/感染	1	DARA: NOT CHANGED LEN: NOT CHANGED DEX: NOT CHANGED	DARA: NOT RELATED LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
		503041	52/M/WHITE/GBR	2014-07-22T14:15	2014-07-22T15:30	1	SAE LARYNGEAL OEDEMA (IRR)/喉頭浮腫	3	DARA: WITHDRAWN LEN: WITHDRAWN DEX: WITHDRAWN	DARA: POSSIBLE/PROBABLE LEN: NOT RELATED DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
	UK02	503028	69/M/WHITE/GBR	2015-08-11			SPINAL FRACTURE/脊椎骨折	3	DARA: INTERRUPTED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: NOT RELATED LEN: NOT RELATED DEX: POSSIBLE/PROBABLE	NOT RECOVERED/ NOT RESOLVED	Y
	US01	503029	69/M/WHITE/USA	2014-10-14T10:32	2014-10-27T07:17	14	NEUTROPENIA/好中球減少症	4	DARA: INTERRUPTED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED	Y
		503044	67/F/WHITE/USA	2014-09-12	2014-09-15	4	PNEUMONIA/肺炎	3	DARA: INTERRUPTED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: POSSIBLE/PROBABLE	RECOVERED/ RESOLVED	Y
				2014-10-23T07:52	2014-11-05T08:14	14	NEUTROPENIA/好中球減少症	3	DARA: INTERRUPTED LEN: INTERRUPTED DEX: INTERRUPTED	DARA: POSSIBLE/PROBABLE LEN: POSSIBLE/PROBABLE DEX: NOT RELATED	RECOVERED/ RESOLVED	Y

Note: Adverse events are reported using MedDRA version 18.0.

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
VD + Dara (16 mg/kg)	ES00351-100028	70/F/White/Spain	2015-04-22(282)/16.17 (mg/kg)	2015-04-23(283)	2	高血糖 [HYPERGLYCEMIA]	代謝および栄養障害	4	DARA: NOT RELATED DEX: VERY LIKELY BOR: NOT RELATED	No	DARA: NOT CHANGED DEX: WITHDRAWN BOR: NOT CHANGED	RECOVERED/RESOLVED
	ES00352-100029	82/F/White/Spain	2014-10-02(78)/16 (mg/kg)	2014-10-11(87)	10	軟部組織感染 [SOFT TISSUE INFECTION IN RIGHT LEG]	感染症および寄生虫症	3	DARA: NOT RELATED DEX: NOT RELATED BOR: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED BOR: INTERRUPTED	RECOVERED/RESOLVED
			2014-10-18(94)/16 (mg/kg)	2014-10-26(102)	9	肺炎 [RIGHT PNEUMONY]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE BOR: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED BOR: INTERRUPTED	RECOVERED/RESOLVED
			2014-10-18(94)/16 (mg/kg)	2014-10-26(102)	9	腎前性腎不全 [RENAL INSUFFICIENCY PRE-RENAL]	腎および尿路障害	2	DARA: NOT RELATED DEX: NOT RELATED BOR: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED BOR: INTERRUPTED	RECOVERED/RESOLVED
			2014-10-25(101)/16 (mg/kg)	2014-11-05(112)	12	下痢 [DIARRHEA BY CANDIDA]	胃腸障害	2	DARA: NOT RELATED DEX: NOT RELATED BOR: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED BOR: INTERRUPTED	RECOVERED/RESOLVED
			2015-08-25(405)/16 (mg/kg)	2015-09-07(418)	14	呼吸不全 [PARTIAL RESPIRATORY FAILURE]	呼吸器、胸郭および縦隔障害	3	DARA: NOT RELATED DEX: NOT RELATED BOR: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE BOR: NOT APPLICABLE	RECOVERED/RESOLVED
	FR01350-100018	50/F/Black or African American/France	2014-08-13(87)/15.09 (mg/kg)	2014-12-14(210)	124	臨床検査干渉 [INTERFERENCE WITH LABORATORY TEST FOR BLOOD TYPING]	臨床検査	1	DARA: PROBABLE DEX: NOT RELATED BOR: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE BOR: NOT APPLICABLE	RECOVERED/RESOLVED
VMP + Dara (16 mg/kg)	ES12018-100043	78/F/White/Spain	2014-11-30(13)/15.58 (mg/kg)	2014-12-01(14)	2	心不全 [CARDIAC INSUFFICIENCY]	心臓障害	3	DARA: NOT RELATED MEL: NOT RELATED PRE: NOT RELATED BOR: PROBABLE	No	DARA: INTERRUPTED MEL: NOT CHANGED PRE: NOT CHANGED BOR: REDUCED	RECOVERED/RESOLVED
Pom-dex + Dara (16 mg/kg)	FR01347-100103	38/M/Black or African American/France	2015-06-05(46)/16.11 (mg/kg)	2015-06-05(46)	1	意識消失 [LOST OF CONSCIOUNESS]	神経系障害	1	DARA: DOUBTFUL DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
			2015-11-02(196)/15.89 (mg/kg)	2015-11-04(198)	3	骨痛 [WORSENING OF BONE PAIN]	筋骨格系および結合組織障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2016-02-14(300)/15.91 (mg/kg)	2016-03-09(324)	25	脊髄圧迫 [MEDULLARY COMPRESSION ON T1]	神経系障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	FR01347-100116	65/M/White/France	2015-09-22(134)/15.41 (mg/kg)	2015-09-28(140)	7	全身健康状態低下 [DETERIORATION OF THE GENERAL STATUS]	一般・全身障害および投与部位の状態	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	RECOVERED/RESOLVED
	FR01347-100119	64/M/White/France	2015-05-13(1)/16.3 (mg/kg)	2015-05-13(1)	1	腹痛 [ABDOMINAL PAIN]	胃腸障害	1	DARA: VERY LIKELY DEX: NOT RELATED POM: NOT RELATED	Yes	DARA: INTERRUPTED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-05-13(1)/16.3 (mg/kg)	2015-05-13(1)	1	呼吸困難 [DYSPNEA]	呼吸器、胸郭および縦隔障害	2	DARA: VERY LIKELY DEX: NOT RELATED POM: NOT RELATED	Yes	DARA: INTERRUPTED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-05-13(1)/16.3 (mg/kg)	2015-05-13(1)	1	低酸素症 [HYPOXEMIA]	呼吸器、胸郭および縦隔障害	2	DARA: VERY LIKELY DEX: NOT RELATED POM: NOT RELATED	Yes	DARA: INTERRUPTED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	FR01347-100136	35/F/Not Reported/France	2015-06-20(6)/15.31 (mg/kg)	2015-06-25(11)	6	パラインフルエンザウイルス感染 [NOSOCOMIAL PULMONARY DISEASE (PARAINFLUENZAE VIRUS 3)]	感染症および寄生虫症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	FR01347-100164	68/M/White/France	2016-02-01(161)/15.96 (mg/kg)	2016-02-16(176)	16	インフルエンザ [RESPIRATORY DISTRESS DUE TO INFLUENZA VIRUS INFECTION]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	FR01347-100167	66/F/White/France	2016-02-01(148)/15.61 (mg/kg)			骨痛 [WORSENING OF BONE PAIN]	筋骨格系および結合組織障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	NOT RECOVERED/NOT RESOLVED

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
	FR01347-100173	61/M/ White/ France	2016-02-25(148)/16.2 (mg/kg)	2016-03-07(159)	12	敗血症 [SEPTICEMIA]	感染症および寄生虫症	4	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	FR01348-100165	59/M/Not Reported/France	2015-09-29(35)/16 (mg/kg)			呼吸困難 [DYSPNEA]	呼吸器、胸郭および縦隔障害	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: INTERRUPTED	NOT RECOVERED/NOT RESOLVED
			2015-09-29(35)/16 (mg/kg)	2015-10-12(48)	14	胸水 [PLEURAL EFFUSION]	呼吸器、胸郭および縦隔障害	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED
			2015-10-13(49)/16 (mg/kg)	2015-10-13(49)	1	胸水 [PLEURAL EFFUSION]	呼吸器、胸郭および縦隔障害	5	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	FATAL
	FR01349-100123	59/M/ White/ France	2016-02-02(246)/16.39 (mg/kg)	2016-02-15(259)	14	間質性肺疾患 [BILATERAL INTERSTITIAL PNEUMOPATHY]	呼吸器、胸郭および縦隔障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	FR01350-100137	58/M/ White/ France	2015-06-18(2)/16.15 (mg/kg)	2015-06-21(5)	4	急性腎不全 [ACUTE KIDNEY INJURY]	腎および尿路障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-07-27(41)/15.97 (mg/kg)	2015-08-12(57)	17	気管支肺症 [BRONCHOPNEUMOPATHY]	呼吸器、胸郭および縦隔障害	3	DARA: POSSIBLE DEX: PROBABLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-09-23(99)/15.76 (mg/kg)	2015-10-03(109)	11	間質性肺疾患 [PULMONARY BILATERAL INTERSTITIAL SYNDROME]	呼吸器、胸郭および縦隔障害	4	DARA: DOUBTFUL DEX: DOUBTFUL POM: POSSIBLE	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED
			2015-10-04(110)/15.76 (mg/kg)	2015-10-04(110)	1	間質性肺疾患 [PULMONARY BILATERAL INTERSTITIAL SYNDROME]	呼吸器、胸郭および縦隔障害	5	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	FATAL

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
	FR01350-100144	61/F/White/France	2015-06-26(2)/16 (mg/kg)	2015-06-27(3)	2	血小板減少症 [THROMBOPENIA]	血液およびリンパ系障害	4	DARA: DOUBTFUL DEX: NOT RELATED POM: DOUBTFUL	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT APPLICABLE	RECOVERED/RESOLVED
			2015-06-26(2)/16 (mg/kg)	2015-06-29(5)	4	貧血 [ANEMIA]	血液およびリンパ系障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT APPLICABLE	RECOVERED/RESOLVED
			2015-06-30(6)/16 (mg/kg)	2015-07-01(7)	2	脳血管発作 [CEREBRAL STROKE]	神経系障害	5	DARA: DOUBTFUL DEX: NOT RELATED POM: DOUBTFUL	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	FATAL
	FR01350-100145	55/F/White/France	2015-09-23(87)/16 (mg/kg)	2015-10-14(108)	22	脊髄感染 [EPIDURITIS]	感染症および寄生虫症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US01028-100011	64/F/White/United States	2014-06-09(55)/16 (mg/kg)	2014-06-18(64)	10	肺炎 [INFECTIOUS PNEUMONIA]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE POM: VERY LIKELY	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED WITH SEQUELAE
	US01029-100034	42/M/Black or African American/United States	2014-12-03(31)/17.19 (mg/kg)			過粘稠度症候群 [HYPERVISCOSITY IN THE SETTING OF DISEASE PROGRESSION]	血液およびリンパ系障害	2	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: INTERRUPTED POM: NOT APPLICABLE	NOT RECOVERED/NOT RESOLVED
	US01030-100041	86/M/White/United States	2015-04-10(156)/14.84 (mg/kg)	2015-04-16(162)	7	上腕骨骨折 [FRACTURE OF HUMERUS]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-06-12(219)/16 (mg/kg)	2015-06-13(220)	2	疲労 [FATIGUE]	一般・全身障害および投与部位の状態	3	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US01030-100074	79/M/White/United States	2016-01-21(372)/16 (mg/kg)			大動脈解離 [AORTIC DISSECTION]	血管障害	4	DARA: NOT RELATED DEX: POSSIBLE POM: PROBABLE	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	NOT RECOVERED/NOT RESOLVED

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	US10973-100049	62/F/White/United States	2015-01-19(41)/16.48 (mg/kg)	2015-01-26(48)	8	肺炎 [PNEUMONIA]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10973-100068	70/M/White/United States	2015-03-08(48)/16.1 (mg/kg)	2015-03-13(53)	6	肺炎 [PNEUMONIA]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2016-02-06(383)/14.71 (mg/kg)	2016-02-07(384)	2	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	血液およびリンパ系障害	3	DARA: POSSIBLE DEX: NOT RELATED POM: PROBABLE	No	DARA: NOT CHANGED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2016-02-21(398)/14.71 (mg/kg)			心房細動 [ATRIAL FIBRILLATION]	心臓障害	3	DARA: DOUBTFUL DEX: DOUBTFUL POM: DOUBTFUL	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERING/RESOLVING
			2016-02-21(398)/14.71 (mg/kg)			うっ血性心不全 [CONGESTIVE HEART FAILURE]	心臓障害	3	DARA: DOUBTFUL DEX: POSSIBLE POM: POSSIBLE	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERING/RESOLVING
			2016-02-22(399)/14.71 (mg/kg)	2016-03-08(414)	16	蜂巣炎 [CELLULITIS (SKIN INFECTION)]	感染症および寄生虫症	3	DARA: DOUBTFUL DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2016-02-22(399)/14.71 (mg/kg)	2016-03-08(414)	16	肺臓炎 [PNEUMONITIS]	呼吸器、胸郭および縦隔障害	2	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US10973-100092	68/M/White/United States	2015-02-26(8)/16.03 (mg/kg)	2015-03-16(26)	19	進行性多巣性白質脳症 [PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY]	感染症および寄生虫症	3	DARA: NOT RELATED DEX: POSSIBLE POM: DOUBTFUL	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED
			2015-03-16(26)/16.03 (mg/kg)	2015-03-21(31)	6	進行性多巣性白質脳症 [PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY]	感染症および寄生虫症	4	DARA: NOT RELATED DEX: POSSIBLE POM: DOUBTFUL	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	NOT RECOVERED/NOT RESOLVED

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			2015-03-21(31)/16.03 (mg/kg)	2015-03-21(31)	1	進行性多巣性白質脳症 [PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY]	感染症および寄生虫症	5	DARA: NOT RELATED DEX: POSSIBLE POM: DOUBTFUL	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	FATAL
	US10973-100097	67/F/White/United States	2015-04-07(13)/16 (mg/kg)			肺炎 [PNEUMONIA]	感染症および寄生虫症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERING/RESOLVING
	US10974-100079	71/F/White/United States	2015-04-23(73)/15.08 (mg/kg)	2015-04-26(76)	4	気管支反応性亢進 [REACTIVE AIRWAYS DISEASE]	呼吸器、胸郭および縦隔障害	3	DARA: POSSIBLE DEX: DOUBTFUL POM: POSSIBLE	No	DARA: INTERRUPTED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US10974-100088	53/F/White/United States	2015-03-05(31)/15.64 (mg/kg)	2015-03-10(36)	6	乳腺炎 [BREAST INFECTION]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED
	US10974-100114	55/M/White/United States	2015-09-09(140)/16.14 (mg/kg)	2015-09-11(142)	3	うっ血性心不全 [CONGESTIVE HEART FAILURE]	心臓障害	3	DARA: DOUBTFUL DEX: PROBABLE POM: DOUBTFUL	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-11-30(222)/15.7 (mg/kg)	2015-12-02(224)	3	慢性閉塞性肺疾患 [CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION]	呼吸器、胸郭および縦隔障害	3	DARA: DOUBTFUL DEX: DOUBTFUL POM: DOUBTFUL	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: INTERRUPTED	RECOVERED/RESOLVED
			2016-01-31(284)/15.95 (mg/kg)	2016-02-02(286)	3	小腸閉塞 [SMALL INTESTINAL OBSTRUCTION]	胃腸障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US10974-100154	63/M/White/United States	2015-08-27(38)/17 (mg/kg)	2015-09-05(47)	10	敗血症 [SEPSIS]	感染症および寄生虫症	4	DARA: DOUBTFUL DEX: POSSIBLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: REDUCED	RECOVERED/RESOLVED
			2015-09-11(53)/16.27 (mg/kg)	2015-09-12(54)	2	脱水 [DEHYDRATION]	代謝および栄養障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-10-28(100)/16.27 (mg/kg)	2015-11-07(110)	11	下痢 [DIARRHEA]	胃腸障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED

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	US10974-100160	70/M/ White/ United States	2015-09-03(24)/15.54 (mg/kg)	2015-09-06(27)	4	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	血液およびリンパ系障害	3	DARA: DOUBTFUL DEX: POSSIBLE POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: REDUCED	RECOVERED/RESOLVED
	US10974-100169	71/M/ White/ United States	2015-09-12(5)/16.89 (mg/kg)	2015-10-01(24)	20	尿路感染 [URINARY TRACT INFECTION]	感染症および寄生虫症	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED
	US10974-100172	72/M/ White/ United States	2015-12-24(99)/15.67 (mg/kg)	2015-12-25(100)	2	肺感染 [LUNG INFECTION]	感染症および寄生虫症	3	DARA: PROBABLE DEX: PROBABLE POM: PROBABLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: REDUCED	RECOVERED/RESOLVED
	US10975-100054	64/F/Black or African American/United States	2015-05-24(138)/16.34 (mg/kg)			感覚鈍麻 [LEFT FACIAL NUMBNESS]	神経系障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	NOT RECOVERED/NOT RESOLVED
	US10975-100057	69/F/White/United States	2015-01-23(16)/15.84 (mg/kg)	2015-01-26(19)	4	小腸閉塞 [SMALL BOWEL OBSTRUCTION]	胃腸障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: REDUCED	RECOVERED/RESOLVED
	US10975-100065	78/M/ White/ United States	2015-01-15(1)/0.21 (mg/kg)	2015-01-16(2)	2	低酸素症 [HYPOXIA]	呼吸器、胸郭および縦隔障害	3	DARA: PROBABLE DEX: NOT RELATED POM: NOT RELATED	Yes	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED
	US10975-100075	68/M/ White/ United States	2015-02-24(34)/16.95 (mg/kg)			転倒 [FALL]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: INTERRUPTED	NOT RECOVERED/NOT RESOLVED
	US10975-100094	74/F/White/United States	2015-02-20(3)/16.11 (mg/kg)	2015-03-26(37)	35	呼吸困難 [SHORTNESS OF BREATH]	呼吸器、胸郭および縦隔障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	RECOVERED/RESOLVED

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	US10975-100109	61/F/White/United States	2015-05-24(33)/16.27 (mg/kg)	2015-05-24(33)	1	呼吸不全 [RESPIRATORY FAILURE]	呼吸器、胸郭および縦隔障害	5	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	FATAL
	US10975-100147	54/F/White/United States	2015-07-17(10)/15.83 (mg/kg)	2015-07-27(20)	11	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	血液およびリンパ系障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10976-100110	83/M/White/United States	2015-05-05(21)/15.62 (mg/kg)	2015-05-28(44)	24	シュードモナス性敗血症 [PSEUDOMONAL SEPSIS]	感染症および寄生虫症	3	DARA: DOUBTFUL DEX: DOUBTFUL POM: PROBABLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-07-07(84)/15.62 (mg/kg)	2015-07-11(88)	5	憩室炎 [SIGMOID DIVERTICULITIS]	感染症および寄生虫症	4	DARA: POSSIBLE DEX: NOT RELATED POM: PROBABLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: NOT APPLICABLE	RECOVERED/RESOLVED
	US10976-100126	70/F/White/United States	2015-07-23(59)/16.13 (mg/kg)	2015-08-01(68)	10	急性腎不全 [ACUTE RENAL FAILURE]	腎および尿路障害	2	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	RECOVERED/RESOLVED
	US10976-100138	72/M/Black or African American/United States	2015-07-07(22)/15.84 (mg/kg)			骨盤骨折 [PELVIC FRACTURES]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERING/RESOLVING
			2015-10(108)/16.71 (mg/kg)	2015-11-06(144)	37	敗血症 [SEPSIS]	感染症および寄生虫症	4	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10976-100148	58/M/White/United States	2015-06-25(1)/17.38 (mg/kg)	2015-06-26(2)	2	サイトカイン放出症候群 [CYTOKINE RELEASE SYNDROME]	免疫系障害	2	DARA: PROBABLE DEX: NOT RELATED POM: NOT RELATED	Yes	DARA: INTERRUPTED DEX: NOT CHANGED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-07-07(13)/17.38 (mg/kg)	2015-07-08(14)	2	高カルシウム血症 [WORSENING HYPERCALCEMIA]	代謝および栄養障害	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED

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	US10977-100076	46/M/White/United States	2015-02-09(19)/16.23 (mg/kg)	2015-02-10(20)	2	発熱性好中球減少症 [FEBRILE NEUTROPENIA]	血液およびリンパ系障害	3	DARA: POSSIBLE DEX: NOT RELATED POM: POSSIBLE	No	DARA: INTERRUPTED DEX: NOT CHANGED POM: REDUCED	RECOVERED/RESOLVED
			2015-06-16(146)/17.37 (mg/kg)	2015-06-17(147)	2	失神寸前の状態 [PRESYNCOPE]	神経系障害	2	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	RECOVERED/RESOLVED
			2015-06-16(146)/17.37 (mg/kg)	2015-06-19(149)	4	霧視 [BLURRED VISION]	眼障害	2	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	RECOVERED/RESOLVED
	US10977-100132	70/M/White/United States	2015-08-02(55)/15.91 (mg/kg)	2015-08-02(55)	1	転倒 [FALL]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10977-100135	75/F/White/United States	2015-09-23(98)/15.75 (mg/kg)	2015-09-27(102)	5	上気道感染 [UPPER RESPIRATORY INFECTION]	感染症および寄生虫症	3	DARA: POSSIBLE DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: INTERRUPTED POM: REDUCED	RECOVERED/RESOLVED
			2015-10-09(114)/15.75 (mg/kg)	2015-10-13(118)	5	筋力低下 [GENERALIZED MUSCLE WEAKNESS]	筋骨格系および結合組織障害	3	DARA: NOT RELATED DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-10-09(114)/15.75 (mg/kg)	2015-10-13(118)	5	末梢性浮腫 [EDEMA LIMBS]	一般・全身障害および投与部位の状態	2	DARA: NOT RELATED DEX: POSSIBLE POM: POSSIBLE	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US10977-100155	64/F/Black or African American/United States	2015-09-02(10)/15.97 (mg/kg)	2015-09-16(24)	15	脊椎圧迫骨折 [CORD COMPRESSION FRACTURE T11]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
			2015-09-25(33)/16 (mg/kg)			筋力低下 [LOWER EXTREMITY WEAKNESS]	筋骨格系および結合組織障害	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: NOT CHANGED POM: NOT CHANGED	NOT RECOVERED/NOT RESOLVED
			2015-09-25(33)/16 (mg/kg)			脊椎圧迫骨折 [UNSTABLE COMPRESSION FRACTURE T11]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	NOT RECOVERED/NOT RESOLVED
			2015-09-25(33)/16 (mg/kg)	2015-09-25(33)	1	転倒 [FALL]	傷害、中毒および処置合併症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US10978-100053	51/M/Black or African American/United States	2015-03-27(80)/16 (mg/kg)	2015-03-27(80)	1	転倒 [FALL]	傷害、中毒および処置合併症	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-03-27(80)/16 (mg/kg)	2015-03-28(81)	2	大腿骨骨折 [FRACTURE (RIGHT FEMUR)]	傷害、中毒および処置合併症	2	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-04-27(111)/15.54 (mg/kg)	2015-04-30(114)	4	貧血 [ANEMIA]	血液およびリンパ系障害	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE
			2015-05-03(117)/15.54 (mg/kg)			肺炎 [PNEUMONIA]	感染症および寄生虫症	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERING/RESOLVING

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
	US10978-100064	59/F/Black or African American/United States	2015-03-09(55)/16 (mg/kg)	2015-03-11(57)	3	大腿骨骨折 [RIGHT FEMUR FRACTURE]	傷害、中毒および処置合併症	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10978-100124	62/M/White/United States	2015-05-24(11)/15.74 (mg/kg)	2015-05-25(12)	2	敗血症 [SEPSIS]	感染症および寄生虫症	5	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: WITHDRAWN DEX: WITHDRAWN POM: WITHDRAWN	FATAL
	US10978-100127	73/M/White/United States	2015-05-18(4)/15.96 (mg/kg)			肺炎 [PNEUMONIA]	感染症および寄生虫症	3	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: INTERRUPTED	NOT RECOVERED/NOT RESOLVED
			2015-05-31(17)/15.96 (mg/kg)	2015-05-31(17)	1	全身健康状態低下 [GENERAL DETERIORATION OF HEALTH STATUS]	一般・全身障害および投与部位の状態	5	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT APPLICABLE DEX: NOT APPLICABLE POM: NOT APPLICABLE	FATAL
	US10978-100128	72/M/White/United States	2015-07-27(61)/16.54 (mg/kg)	2015-08-02(67)	7	肺炎 [PNEUMONIA]	感染症および寄生虫症	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10978-100131	74/F/White/United States	2016-01-11(217)/16.22 (mg/kg)	2016-01-20(226)	10	喘息 [ASTHMATIC BRONCHITIS]	呼吸器、胸郭および縦隔障害	4	DARA: NOT RELATED DEX: NOT RELATED POM: NOT RELATED	No	DARA: NOT CHANGED DEX: NOT CHANGED POM: NOT CHANGED	RECOVERED/RESOLVED
	US10978-100133	74/F/White/United States	2015-09-22(111)/15.75 (mg/kg)	2015-09-24(113)	3	クロストリジウム・ディフィシレ大腸炎 [DIARRHEA (C. DIFF)]	感染症および寄生虫症	3	DARA: DOUBTFUL DEX: NOT RELATED POM: NOT RELATED	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
	US10978-100176	40/M/White/United States	2015-10-27(13)/15.34 (mg/kg)	2015-10-29(15)	3	貧血 [ANEMIA]	血液およびリンパ系障害	1	DARA: NOT RELATED DEX: DOUBTFUL POM: POSSIBLE	No	DARA: INTERRUPTED DEX: NOT CHANGED POM: INTERRUPTED	RECOVERED/RESOLVED

LSFAE-JST02_1001: List of Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1001)

Treatment Regimen	Subject ID	Age (years)/ Sex/Race /Country	Adverse Event Onset Date (Study Day)/ Onset Dose (unit)	Adverse Event End Date (Study Day)	AE Duration (days)	Adverse Event Preferred Term [Verbatim]	Adverse Event Body System	Toxicity Grade	Relation	Was This an Infusion Reaction Associated with Dara?	Action Taken	Outcome
			2015-10-27(13)/15.89 (mg/kg)	2015-10-29(15)	3	好中球減少症 [NEUTROPENIA]	血液およびリンパ系障害	4	DARA: NOT RELATED DEX: DOUBTFUL POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-10-27(13)/15.89 (mg/kg)	2015-10-29(15)	3	失神 [SYNCOPE]	神経系障害	3	DARA: NOT RELATED DEX: DOUBTFUL POM: DOUBTFUL	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: NOT CHANGED	RECOVERED/RESOLVED
			2015-10-27(13)/15.89 (mg/kg)	2015-10-29(15)	3	血小板減少症 [THROMBOCYTOPENIA]	血液およびリンパ系障害	4	DARA: NOT RELATED DEX: DOUBTFUL POM: POSSIBLE	No	DARA: INTERRUPTED DEX: INTERRUPTED POM: INTERRUPTED	RECOVERED/RESOLVED
			2015-11-11(28)/15.89 (mg/kg)	2015-11-17(34)	7	腹痛 [ABDOMINAL PAIN]	胃腸障害	4	DARA: NOT RELATED DEX: DOUBTFUL POM: DOUBTFUL	No	DARA: INTERRUPTED DEX: NOT CHANGED POM: INTERRUPTED	RECOVERED/RESOLVED

Keys:D-Vd = daratumumab-bortezomib-dexamethasone; D-VTd= daratumumab-bortezomib-thalidomide-dexamethasone; D-VMP = daratumumab-bortezomib-melphalan-prednisone; D-Pom-dex = daratumumab-pomalidomide-dexamethasone.
Keys: DARA=daratumumab; BOR =bortezomib; DEX=dexamethasone; THA=thalidomide; MEL=melphalan; PRE=prednisone; POM=pomalidomide.
Adverse events are reported using MedDRA Version 18.0.

表 2.7.4-付録-55 Number of Subjects with Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE04: Number of Subjects with Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: Safety	8
Total number of subjects with serious TEAE	3 (37.5%)
MedDRA system organ class/Preferred term	
感染症および寄生虫症	2 (25.0%)
帯状疱疹	1 (12.5%)
鼻咽頭炎	1 (12.5%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)
前立腺癌	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE04.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE04.SAS] 28SEP2016, 04:13

表 2.7.4-付録-56 Listing of Subjects with Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1005)

LSFAE05: Listing of Subjects with Treatment-emergent Serious Adverse Events; Safety Analysis Set (Study 54767414MMY1005)

Treatment Group	Subject ID	Age(years)/ Sex/Race	Adverse Event(MedDRA Preferred Term [Verbatim])	Study Day of AE Onset/AE Duration (days)	SAE?	Toxicity Grade	Relationship to[a]			Action Taken with[b]			Outcome	Was This an Infusion Reaction Associated with Dara?
							Dara[c]	Bort[c]	Dex[c]	Dara[c]	Bort[c]	Dex[c]		
Vd + Daratumumab (16 mg/kg)	JP10001-810102	73/F/Asian	帯状疱疹 [HERPES ZOSTER]	83/10	Yes	3	Prob	Prob	Prob	DI	DI	DI	RECOVERED/ RESOLVED	No
	JP10002-810201	80/M/Asian	鼻咽頭炎 [INFECTION(COMMON COLD)]	53/5	Yes	3	Poss	Poss	Poss	DI	DI	DI	RECOVERED/ RESOLVED	No
	JP10003-810301	71/M/Asian	前立腺癌 [PROSTATE CANCER]	103/	Yes	3	DO	DO	DO	DW	DW	DW	NOT RECOVERED/ NOT RESOLVED	No

Key: Vd = bortezomib-dexamethasone.
[a] Keys: NR = Not Related, DO = Doubtful, Poss. = Possible, Prob. = Probable, VL = Very Likely.
[b] Keys: DI = Drug Interrupted, DNC = Dose Not Changed, DR = Dose Reduced, DW = Drug withdrawn, NA = Not Applicable, UN = Unknown.
[c] Keys: Dara = daratumumab, Bort = bortezomib, Dex = dexamethasone.
Note: Adverse events are coded using MedDRA version 18.0.

[LSFAE05.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\LSFAE05.SAS] 28SEP2016, 04:01

表 2.7.4-付録-57 Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283
Total number of subjects with serious TEAE	3 (20.0%)	18 (40.9%)	118 (42.0%)	7 (35.0%)	18 (35.3%)	138 (48.8%)
MedDRA system organ class/Preferred term						
感染症および寄生虫症	1 (6.7%)	11 (25.0%)	64 (22.8%)	4 (20.0%)	7 (13.7%)	85 (30.0%)
肺炎	1 (6.7%)	4 (9.1%)	24 (8.5%)	2 (10.0%)	3 (5.9%)	23 (8.1%)
インフルエンザ	0	0	4 (1.4%)	0	0	8 (2.8%)
下気道感染	0	0	3 (1.1%)	0	0	7 (2.5%)
気管支炎	0	1 (2.3%)	4 (1.4%)	0	0	5 (1.8%)
気道感染	0	0	2 (0.7%)	0	0	5 (1.8%)
インフルエンザ性肺炎	0	0	0	0	0	3 (1.1%)
敗血症性ショック	0	0	1 (0.4%)	0	0	3 (1.1%)
尿路感染	0	1 (2.3%)	1 (0.4%)	0	0	3 (1.1%)
虫垂炎	0	0	1 (0.4%)	0	0	2 (0.7%)
気管支肺炎	0	0	0	0	0	2 (0.7%)
ウイルス性胃腸炎	0	0	1 (0.4%)	0	0	2 (0.7%)
感染	0	0	3 (1.1%)	0	0	2 (0.7%)
大葉性肺炎	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)
細菌性肺炎	0	0	1 (0.4%)	0	0	2 (0.7%)
ＲＳウイルス感染	0	0	0	0	0	2 (0.7%)
敗血症	0	1 (2.3%)	5 (1.8%)	0	0	2 (0.7%)
急性副鼻腔炎	0	0	0	0	0	1 (0.4%)
細菌感染	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
細気管支炎	0	0	0	0	0	1 (0.4%)
細菌性気管支炎	0	0	0	0	0	1 (0.4%)
カンジダ感染	0	0	0	0	0	1 (0.4%)
蜂巣炎	0	0	1 (0.4%)	0	0	1 (0.4%)
サイトメガロウイルス感染	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
喉頭蓋炎	0	0	0	0	0	1 (0.4%)
大腸菌性菌血症	0	0	0	0	0	1 (0.4%)

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
硬膜外膿瘍	0	0	0	0	0	1 (0.4%)
胃腸炎	0	0	1 (0.4%)	0	0	1 (0.4%)
歯肉炎	0	0	0	0	0	1 (0.4%)
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	1 (0.4%)
感染性脊椎炎	0	0	0	0	0	1 (0.4%)
リステリア性敗血症	0	0	0	0	0	1 (0.4%)
肺感染	0	0	1 (0.4%)	0	0	1 (0.4%)
鼻膿瘍	0	0	0	0	0	1 (0.4%)
好中球減少性敗血症	0	0	0	0	0	1 (0.4%)
口腔真菌感染	0	0	0	0	0	1 (0.4%)
パラインフルエンザウイルス感染	0	0	1 (0.4%)	0	0	1 (0.4%)
耳下腺炎	0	0	0	0	0	1 (0.4%)
眼窩周囲蜂巣炎	0	0	0	0	0	1 (0.4%)
ヘモフィルス性肺炎	0	0	0	0	0	1 (0.4%)
クレブシエラ菌性肺炎	0	0	0	0	0	1 (0.4%)
レジオネラ菌性肺炎	0	0	1 (0.4%)	0	0	1 (0.4%)
レンサ球菌性肺炎	0	0	0	0	0	1 (0.4%)
ウイルス性気道感染	0	0	0	0	0	1 (0.4%)
サルモネラ性菌血症	0	0	0	0	1 (2.0%)	1 (0.4%)
皮膚感染	0	0	0	0	0	1 (0.4%)
軟部組織感染	0	0	0	0	0	1 (0.4%)
扁桃炎	0	0	0	0	0	1 (0.4%)
上気道感染	0	0	5 (1.8%)	0	0	1 (0.4%)
細菌性上気道感染	0	0	0	0	0	1 (0.4%)
子宮膿瘍	0	0	0	0	0	1 (0.4%)
肛門膿瘍	0	1 (2.3%)	1 (0.4%)	0	0	0
クロストリジウム・ディフィシレ感染	0	0	2 (0.7%)	0	0	0
感染性小腸結腸炎	0	0	1 (0.4%)	0	0	0
丹毒	0	0	1 (0.4%)	0	0	0
消化管感染	0	0	1 (0.4%)	0	0	0
ヘモフィルス感染	0	0	1 (0.4%)	0	0	0
真菌性角膜炎	0	0	1 (0.4%)	0	0	0
壊死性筋膜炎	0	0	1 (0.4%)	0	0	0
骨髄炎	0	2 (4.5%)	2 (0.7%)	0	0	0

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
咽頭炎	0	0	1 (0.4%)	0	0	0
肺結核	0	1 (2.3%)	1 (0.4%)	0	0	0
急性腎盂腎炎	0	1 (2.3%)	1 (0.4%)	0	0	0
尿路性敗血症	0	0	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	0	0	1 (0.4%)	0	0	0
ウイルス感染	0	0	1 (0.4%)	0	0	0
血液およびリンパ系障害	0	0	11 (3.9%)	0	3 (5.9%)	17 (6.0%)
発熱性好中球減少症	0	0	4 (1.4%)	0	1 (2.0%)	12 (4.2%)
貧血	0	0	2 (0.7%)	0	0	2 (0.7%)
好中球減少症	0	0	0	0	2 (3.9%)	2 (0.7%)
血小板減少症	0	0	1 (0.4%)	0	0	1 (0.4%)
骨髄機能不全	0	0	1 (0.4%)	0	0	0
過粘稠度症候群	0	0	1 (0.4%)	0	0	0
リンパ節症	0	0	1 (0.4%)	0	0	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0	0
血栓性血小板減少性紫斑病	0	0	1 (0.4%)	0	0	0
呼吸器、胸郭および縦隔障害	0	0	14 (5.0%)	1 (5.0%)	2 (3.9%)	15 (5.3%)
肺塞栓症	0	0	8 (2.8%)	0	0	7 (2.5%)
呼吸困難	0	0	1 (0.4%)	0	0	2 (0.7%)
肺水腫	0	0	1 (0.4%)	0	0	2 (0.7%)
呼吸不全	0	0	1 (0.4%)	0	0	2 (0.7%)
急性肺水腫	0	0	0	0	0	1 (0.4%)
低酸素症	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
肺臓炎	0	0	0	0	1 (2.0%)	1 (0.4%)
肺石灰化	0	0	0	0	0	1 (0.4%)
急性呼吸不全	0	0	1 (0.4%)	0	0	0
気管支痙攣	0	0	1 (0.4%)	0	0	0
間質性肺疾患	0	0	1 (0.4%)	0	0	0
肺障害	0	0	1 (0.4%)	0	0	0
気胸	0	0	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	0	1 (2.3%)	8 (2.8%)	0	3 (5.9%)	14 (4.9%)
発熱	0	0	4 (1.4%)	0	2 (3.9%)	8 (2.8%)
全身健康状態低下	0	0	0	0	0	2 (0.7%)
無力症	0	0	0	0	0	1 (0.4%)

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
胸部不快感	0	0	0	0	0	1 (0.4%)
歩行障害	0	0	0	0	0	1 (0.4%)
多臓器不全	0	0	0	0	1 (2.0%)	1 (0.4%)
非心臓性胸痛	0	0	1 (0.4%)	0	0	1 (0.4%)
疼痛	0	1 (2.3%)	2 (0.7%)	0	0	1 (0.4%)
全身性炎症反応症候群	0	0	0	0	0	1 (0.4%)
疲労	0	1 (2.3%)	1 (0.4%)	0	0	0
全身性浮腫	0	0	1 (0.4%)	0	0	0
胃腸障害	0	2 (4.5%)	11 (3.9%)	0	0	12 (4.2%)
下痢	0	1 (2.3%)	6 (2.1%)	0	0	5 (1.8%)
憩室穿孔	0	0	0	0	0	2 (0.7%)
悪心	0	0	0	0	0	2 (0.7%)
大腸炎	0	0	1 (0.4%)	0	0	1 (0.4%)
便秘	0	0	0	0	0	1 (0.4%)
出血性胃腸管血管異形成	0	0	0	0	0	1 (0.4%)
胃腸障害	0	0	0	0	0	1 (0.4%)
鼠径ヘルニア	0	0	0	0	0	1 (0.4%)
嘔吐	0	0	1 (0.4%)	0	0	1 (0.4%)
吐血	0	0	1 (0.4%)	0	0	0
腸閉塞	0	0	1 (0.4%)	0	0	0
下部消化管出血	0	0	1 (0.4%)	0	0	0
食道炎	0	1 (2.3%)	1 (0.4%)	0	0	0
心臓障害	0	0	9 (3.2%)	0	0	9 (3.2%)
心房細動	0	0	2 (0.7%)	0	0	2 (0.7%)
急性冠動脈症候群	0	0	0	0	0	1 (0.4%)
狭心症	0	0	0	0	0	1 (0.4%)
心房粗動	0	0	0	0	0	1 (0.4%)
心アミロイドーシス	0	0	0	0	0	1 (0.4%)
うっ血性心不全	0	0	0	0	0	1 (0.4%)
心肺不全	0	0	0	0	0	1 (0.4%)
心筋梗塞	0	0	1 (0.4%)	0	0	1 (0.4%)
洞性不整脈	0	0	0	0	0	1 (0.4%)
急性心筋梗塞	0	0	3 (1.1%)	0	0	0
心停止	0	0	1 (0.4%)	0	0	0

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
心膜炎	0	0	1 (0.4%)	0	0	0
上室性頻脈	0	0	1 (0.4%)	0	0	0
筋骨格系および結合組織障害	0	4 (9.1%)	12 (4.3%)	0	1 (2.0%)	8 (2.8%)
背部痛	0	1 (2.3%)	5 (1.8%)	0	0	2 (0.7%)
骨痛	0	0	0	0	0	2 (0.7%)
側腹部痛	0	0	0	0	1 (2.0%)	1 (0.4%)
椎間板突出	0	0	0	0	0	1 (0.4%)
筋骨格痛	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
四肢痛	0	0	0	0	0	1 (0.4%)
筋力低下	0	0	1 (0.4%)	0	0	0
顎骨壊死	0	1 (2.3%)	2 (0.7%)	0	0	0
病的骨折	0	0	1 (0.4%)	0	0	0
脊柱管狭窄症	0	1 (2.3%)	2 (0.7%)	0	0	0
脊椎痛	0	0	1 (0.4%)	0	0	0
神経系障害	2 (13.3%)	3 (6.8%)	13 (4.6%)	1 (5.0%)	1 (2.0%)	8 (2.8%)
失神	0	0	1 (0.4%)	0	0	2 (0.7%)
脳梗塞	0	0	1 (0.4%)	1 (5.0%)	1 (2.0%)	1 (0.4%)
認知障害	0	0	0	0	0	1 (0.4%)
失神寸前の状態	0	0	0	0	0	1 (0.4%)
痙攣発作	0	0	0	0	0	1 (0.4%)
一過性脳虚血発作	0	1 (2.3%)	1 (0.4%)	0	0	1 (0.4%)
三叉神経障害	0	0	0	0	0	1 (0.4%)
失語症	0	0	1 (0.4%)	0	0	0
頚動脈硬化症	0	0	1 (0.4%)	0	0	0
脳出血	0	0	1 (0.4%)	0	0	0
肋間神経痛	0	0	1 (0.4%)	0	0	0
虚血性脳卒中	0	0	1 (0.4%)	0	0	0
意識消失	0	0	1 (0.4%)	0	0	0
神経系障害	0	0	1 (0.4%)	0	0	0
末梢性感覚ニューロパチー	0	0	1 (0.4%)	0	0	0
傾眠	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
第７脳神経麻痺	1 (6.7%)	1 (2.3%)	1 (0.4%)	0	0	0
傷害、中毒および処置合併症	0	0	8 (2.8%)	0	1 (2.0%)	7 (2.5%)
圧迫骨折	0	0	0	0	1 (2.0%)	1 (0.4%)

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
足骨折	0	0	0	0	0	1 (0.4%)
手骨折	0	0	0	0	0	1 (0.4%)
股関節部骨折	0	0	1 (0.4%)	0	0	1 (0.4%)
腓骨神経損傷	0	0	0	0	0	1 (0.4%)
肋骨骨折	0	0	0	0	0	1 (0.4%)
脊椎圧迫骨折	0	0	0	0	0	1 (0.4%)
転倒	0	0	1 (0.4%)	0	0	0
大腿骨頚部骨折	0	0	1 (0.4%)	0	0	0
上腕骨骨折	0	0	1 (0.4%)	0	0	0
関節脱臼	0	0	1 (0.4%)	0	0	0
骨盤骨折	0	0	1 (0.4%)	0	0	0
橈骨骨折	0	0	1 (0.4%)	0	0	0
硬膜下血腫	0	0	1 (0.4%)	0	0	0
代謝および栄養障害	0	1 (2.3%)	3 (1.1%)	0	1 (2.0%)	6 (2.1%)
高カルシウム血症	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.7%)
脱水	0	0	0	0	0	1 (0.4%)
電解質失調	0	0	0	0	0	1 (0.4%)
高血糖	0	0	0	0	0	1 (0.4%)
低カルシウム血症	0	0	0	0	0	1 (0.4%)
食欲減退	0	1 (2.3%)	1 (0.4%)	0	0	0
痛風	0	0	1 (0.4%)	0	0	0
腎および尿路障害	1 (6.7%)	2 (4.5%)	12 (4.3%)	0	1 (2.0%)	6 (2.1%)
急性腎不全	1 (6.7%)	1 (2.3%)	8 (2.8%)	0	0	3 (1.1%)
高窒素血症	0	1 (2.3%)	1 (0.4%)	0	1 (2.0%)	1 (0.4%)
腎不全	0	0	3 (1.1%)	0	0	1 (0.4%)
尿道出血	0	0	0	0	0	1 (0.4%)
血管障害	0	0	3 (1.1%)	1 (5.0%)	2 (3.9%)	6 (2.1%)
塞栓症	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
出血性梗塞	0	0	0	0	0	1 (0.4%)
高血圧	0	0	0	0	0	1 (0.4%)
低血圧	0	0	0	0	1 (2.0%)	1 (0.4%)
起立性低血圧	0	0	0	0	0	1 (0.4%)
末梢動脈狭窄	0	0	0	0	0	1 (0.4%)
深部静脈血栓症	0	0	1 (0.4%)	0	0	0

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
静脈炎	0	0	1 (0.4%)	0	0	0
静脈閉塞	0	0	1 (0.4%)	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	8 (2.8%)	2 (10.0%)	2 (3.9%)	4 (1.4%)
急性単球性白血病	0	0	0	0	0	1 (0.4%)
ボーエン病	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (5.0%)	1 (2.0%)	1 (0.4%)
形質細胞性白血病	0	0	2 (0.7%)	0	0	1 (0.4%)
肛門直腸の良性新生物	0	0	1 (0.4%)	0	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0	0
肺腺癌	0	0	1 (0.4%)	0	0	0
前立腺癌	0	0	1 (0.4%)	0	0	0
直腸腺癌	0	0	1 (0.4%)	0	0	0
扁平上皮癌	0	0	1 (0.4%)	0	0	0
眼障害	0	0	0	0	1 (2.0%)	2 (0.7%)
白内障	0	0	0	0	1 (2.0%)	1 (0.4%)
後嚢破裂	0	0	0	0	0	1 (0.4%)
臨床検査	0	0	2 (0.7%)	0	0	2 (0.7%)
国際標準比増加	0	0	0	0	0	1 (0.4%)
トロポニン増加	0	0	0	0	0	1 (0.4%)
体温上昇	0	0	1 (0.4%)	0	0	0
診断法	0	0	1 (0.4%)	0	0	0
精神障害	0	0	2 (0.7%)	0	0	1 (0.4%)
うつ病	0	0	0	0	0	1 (0.4%)
錯乱状態	0	0	1 (0.4%)	0	0	0
抑うつ症状	0	0	1 (0.4%)	0	0	0
生殖系および乳房障害	0	0	0	0	0	1 (0.4%)
前立腺腫大	0	0	0	0	0	1 (0.4%)
皮膚および皮下組織障害	0	0	0	0	0	1 (0.4%)
全身性皮疹	0	0	0	0	0	1 (0.4%)
丘疹性皮疹	0	0	0	0	0	1 (0.4%)
肝胆道系障害	0	0	2 (0.7%)	0	0	0
胆管結石	0	0	1 (0.4%)	0	0	0

TSFAE05A_3003: Number of Subjects With 1 or More Treatment-emergent Serious Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
肝障害	0	0	1 (0.4%)	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE05A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE05A_3003.SAS] 30JUN2016, 21:42

表 2.7.4-付録-58 Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE04: Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Total number of subjects with serious TEAEs	7 (30.4%)	20 (36.4%)	50 (32.1%)	2 (66.7%)	79 (33.3%)
MedDRA system organ class/Preferred term					
感染症および寄生虫症	0	6 (10.9%)	19 (12.2%)	1 (33.3%)	26 (11.0%)
肺炎	0	3 (5.5%)	9 (5.8%)	0	12 (5.1%)
帯状疱疹	0	0	2 (1.3%)	0	2 (0.8%)
大葉性肺炎	0	0	2 (1.3%)	0	2 (0.8%)
水痘	0	0	2 (1.3%)	0	2 (0.8%)
気管支炎	0	0	1 (0.6%)	0	1 (0.4%)
Ｈ１Ｎ１インフルエンザ	0	0	1 (0.6%)	0	1 (0.4%)
パラインフルエンザウイルス感染	0	0	1 (0.6%)	0	1 (0.4%)
レンサ球菌性肺炎	0	0	1 (0.6%)	0	1 (0.4%)
腎盂腎炎	0	0	1 (0.6%)	0	1 (0.4%)
敗血症	0	0	1 (0.6%)	0	1 (0.4%)
軟部組織感染	0	0	1 (0.6%)	0	1 (0.4%)
上気道感染	0	0	1 (0.6%)	0	1 (0.4%)
菌血症	0	1 (1.8%)	0	0	1 (0.4%)
インフルエンザ	0	1 (1.8%)	0	0	1 (0.4%)
メタニューモウイルス感染	0	1 (1.8%)	0	0	1 (0.4%)
ＲＳウイルス感染	0	1 (1.8%)	0	0	1 (0.4%)
尿路感染	0	0	0	1 (33.3%)	1 (0.4%)
一般・全身障害および投与部位の状態	1 (4.3%)	4 (7.3%)	13 (8.3%)	0	18 (7.6%)
全身健康状態低下	0	1 (1.8%)	5 (3.2%)	0	6 (2.5%)
発熱	1 (4.3%)	2 (3.6%)	5 (3.2%)	0	8 (3.4%)
無力症	0	0	1 (0.6%)	0	1 (0.4%)
疲労	0	0	1 (0.6%)	0	1 (0.4%)
末梢性浮腫	0	0	1 (0.6%)	0	1 (0.4%)
胸痛	0	1 (1.8%)	0	0	1 (0.4%)
代謝および栄養障害	0	1 (1.8%)	6 (3.8%)	0	7 (3.0%)
高カルシウム血症	0	0	4 (2.6%)	0	4 (1.7%)
高カリウム血症	0	0	1 (0.6%)	0	1 (0.4%)
低カリウム血症	0	0	1 (0.6%)	0	1 (0.4%)
低マグネシウム血症	0	0	1 (0.6%)	0	1 (0.4%)
高尿酸血症	0	1 (1.8%)	0	0	1 (0.4%)
筋骨格系および結合組織障害	0	2 (3.6%)	6 (3.8%)	0	8 (3.4%)
筋骨格系胸痛	0	0	2 (1.3%)	0	2 (0.8%)
背部痛	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
骨痛	0	0	1 (0.6%)	0	1 (0.4%)
病的骨折	0	0	1 (0.6%)	0	1 (0.4%)
脊柱管狭窄症	0	0	1 (0.6%)	0	1 (0.4%)
脊椎痛	0	0	1 (0.6%)	0	1 (0.4%)
骨粗鬆症性骨折	0	1 (1.8%)	0	0	1 (0.4%)
胃腸障害	1 (4.3%)	1 (1.8%)	5 (3.2%)	0	7 (3.0%)
腹痛	1 (4.3%)	0	1 (0.6%)	0	2 (0.8%)
便失禁	0	0	1 (0.6%)	0	1 (0.4%)
大腸閉塞	0	0	1 (0.6%)	0	1 (0.4%)
悪心	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
膵炎	0	0	1 (0.6%)	0	1 (0.4%)
嘔吐	0	1 (1.8%)	0	0	1 (0.4%)
臨床検査	1 (4.3%)	1 (1.8%)	4 (2.6%)	0	6 (2.5%)
交差適合試験不適合	0	0	3 (1.9%)	0	3 (1.3%)

TSFAE04: Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
酸素飽和度異常	0	0	1 (0.6%)	0	1 (0.4%)
遊離ヘモグロビン陽性	1 (4.3%)	0	0	0	1 (0.4%)
国際標準比増加	0	1 (1.8%)	0	0	1 (0.4%)
呼吸器、胸郭および縦隔障害	1 (4.3%)	1 (1.8%)	4 (2.6%)	1 (33.3%)	7 (3.0%)
急性肺水腫	0	0	1 (0.6%)	0	1 (0.4%)
胸水	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
誤嚥性肺炎	0	0	1 (0.6%)	0	1 (0.4%)
呼吸不全	0	0	1 (0.6%)	0	1 (0.4%)
気管支痙攣	1 (4.3%)	0	0	1 (33.3%)	2 (0.8%)
血液およびリンパ系障害	1 (4.3%)	3 (5.5%)	3 (1.9%)	0	7 (3.0%)
貧血	1 (4.3%)	1 (1.8%)	2 (1.3%)	0	4 (1.7%)
好中球減少症	0	0	1 (0.6%)	0	1 (0.4%)
血小板減少症	1 (4.3%)	2 (3.6%)	1 (0.6%)	0	4 (1.7%)
心臓障害	1 (4.3%)	0	3 (1.9%)	0	4 (1.7%)
心房粗動	0	0	1 (0.6%)	0	1 (0.4%)
うっ血性心不全	0	0	1 (0.6%)	0	1 (0.4%)
心肺停止	0	0	1 (0.6%)	0	1 (0.4%)
心房細動	1 (4.3%)	0	0	0	1 (0.4%)
傷害、中毒および処置合併症	1 (4.3%)	1 (1.8%)	3 (1.9%)	0	5 (2.1%)
脊椎圧迫骨折	1 (4.3%)	0	2 (1.3%)	0	3 (1.3%)
硬膜下血腫	0	0	1 (0.6%)	0	1 (0.4%)
四肢外傷性切断	0	1 (1.8%)	0	0	1 (0.4%)
神経系障害	0	2 (3.6%)	3 (1.9%)	0	5 (2.1%)
頭痛	0	0	2 (1.3%)	0	2 (0.8%)
脊髄圧迫	0	0	1 (0.6%)	0	1 (0.4%)
振戦	0	0	1 (0.6%)	0	1 (0.4%)
失神	0	1 (1.8%)	0	0	1 (0.4%)
第６脳神経麻痺	0	1 (1.8%)	0	0	1 (0.4%)
腎および尿路障害	0	4 (7.3%)	3 (1.9%)	0	7 (3.0%)
血尿	0	0	1 (0.6%)	0	1 (0.4%)
腎機能障害	0	2 (3.6%)	1 (0.6%)	0	3 (1.3%)
尿路閉塞	0	0	1 (0.6%)	0	1 (0.4%)
急性腎不全	0	1 (1.8%)	0	0	1 (0.4%)
尿閉	0	1 (1.8%)	0	0	1 (0.4%)
精神障害	0	0	2 (1.3%)	0	2 (0.8%)
錯乱状態	0	0	1 (0.6%)	0	1 (0.4%)
譫妄	0	0	1 (0.6%)	0	1 (0.4%)
血管障害	0	0	2 (1.3%)	0	2 (0.8%)
深部静脈血栓症	0	0	1 (0.6%)	0	1 (0.4%)
低血圧	0	0	1 (0.6%)	0	1 (0.4%)
肝胆道系障害	1 (4.3%)	0	1 (0.6%)	0	2 (0.8%)
肝不全	0	0	1 (0.6%)	0	1 (0.4%)
肝機能異常	1 (4.3%)	0	0	0	1 (0.4%)
免疫系障害	1 (4.3%)	0	0	0	1 (0.4%)
サイトカイン放出症候群	1 (4.3%)	0	0	0	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (1.8%)	0	0	1 (0.4%)
形質細胞性白血病	0	1 (1.8%)	0	0	1 (0.4%)
生殖系および乳房障害	0	1 (1.8%)	0	0	1 (0.4%)
骨盤痛	0	1 (1.8%)	0	0	1 (0.4%)

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
[TSFAE04.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae04.sas] 16MAR2015, 12:04

表 2.7.4-付録-59 List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Studies: MMY2002 and GEN501)

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Onset Date (Study Day)	Number of DARA Infusions Before AE Onset	Days Since Last DARA Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious	Infusion Related Reaction
8 mg/kg	US10766	100034	72/M/WHITE/USA	570(mg)/2013-11-23 (4)	1	4	2013-11-29 (10)/7	URINARY RETENTION/尿閉	2	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				570(mg)/2013-12-28 (39)	2	11		WORSENING BACK PAIN/背部痛	3	DOSE NOT CHANGED	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
	US10782	100005	62/M/WHITE/USA	151.308(mg)/2013-11-26 (29)	2	1		PLASMA CELL LEUKEMIA/形質細胞性白血病	3	DRUG WITHDRAWN	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				992(mg)/2013-11-07 (10)	1	10	2013-12-12 (45)/36	PLEURAL EFFUSION/胸水	3	DOSE NOT CHANGED	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
		100014	52/F/WHITE/USA	528(mg)/2013-12-13 (39)	2	11		GENERAL DETERIORATION/全身健康状態低下	4	NOT APPLICABLE	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				528(mg)/2013-12-30 (56)	2	28	2013-12-30 (56)/1	HYPERURICEMIA/高尿酸血症	4	NOT APPLICABLE	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				528(mg)/2013-12-30 (56)	2	28	2014-02-04 (92)/37	ACUTE RENAL IMPAIRMENT/腎機能障害	1	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				568(mg)/2013-11-21 (17)	1	17	2013-11-28 (24)/8	NAUSEA/悪心	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				568(mg)/2013-11-21 (17)	1	17	2013-11-28 (24)/8	VOMITING/嘔吐	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				568(mg)/2013-11-21 (17)	1	17	2013-11-29 (25)/9	ACUTE RENAL IMPAIRMENT/腎機能障害	1	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
	US10785	100007	75/M/WHITE/USA	661(mg)/2013-11-05 (8)	1	8	2013-11-06 (9)/2	SYNCOPE/失神	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
		100010	70/M/WHITE/USA	545(mg)/2013-12-11 (38)	2	10		ACUTE RENAL FAILURE/急性腎不全	3	NOT APPLICABLE	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
		100039	55/M/WHITE/USA	610(mg)/2013-12-07 (5)	1	5	2013-12-17 (15)/11	PELVIC PAIN/骨盤痛	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Onset Date (Study Day)	Number of DARA Infusions Before AE Onset	Days Since Last DARA Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious	Infusion Related Reaction
16 mg/kg	CA00096	100051	31/M/WHITE/CAN	1232(mg)/2014-03-31 (34)	5	6	2014-04-01 (35)/2	THROMBOCYTOPENIA/血小板減少症	4	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014-04-07 (41)	6	6	2014-04-10 (44)/4	THROMBOCYTOPENIA/血小板減少症	4	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014-04-08 (42)	6	7	2014-04-13 (47)/6	HYPERCALCEMIA/高カルシウム血症	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014-04-21 (55)	8	6	2014-04-23 (57)/3	THROMBOCYTOPENIA/血小板減少症	4	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014-04-21 (55)	8	6	2014-05-02 (66)/12	ANEMIA/貧血	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				1424(mg)/2014-03-17 (20)	3	6	2014-03-31 (34)/15	STREPTOCOCCUS PNEUMONIAE/レンサ球菌性肺炎	2	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
		100054	78/M/WHITE/CAN	1488(mg)/2014-03-16 (24)	3	7		INFLUENZA A VIRUS (RNA) HEMAGGLUTININ (SUBTYPE H1N1)/Ｈ１Ｎ１インフルエンザ	3	DRUG WITHDRAWN	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				1488(mg)/2014-04-03 (42)	3	25	2014-04-03 (42)/1	CARDIOVASCULAR RESPIRATORY ARREST/心肺停止	5	NOT APPLICABLE	NOT RELATED	FATAL	Y	N
		100057	59/M/WHITE/CAN	1632(mg)/2014-05-25 (75)	10	5	2014-05-30 (80)/6	BRONCHITIS/気管支炎	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				1632(mg)/2014-06-11 (92)	10	22		DELIRIUM/譫妄	4	NOT APPLICABLE	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				1632(mg)/2014-06-11 (92)	10	22		SEVERE DETERIORATION IN HEALTH/全身健康状態低下	5	NOT APPLICABLE	NOT RELATED	FATAL	Y	N
		100088	61/M/WHITE/CAN	1200(mg)/2014-04-15 (20)	3	6		HYPERCALCEMIA/高カルシウム血症	4	DRUG INTERRUPTED	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Onset Date (Study Day)	Number of DARA Infusions Before AE Onset	Days Since Last DARA Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious	Infusion Related Reaction
	CA00097	100101	59/M/WHITE/CAN	1136(mg)/2014-06-11 (63)	9	7		UPPER BACK PAIN/背部痛	3	NOT APPLICABLE	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				1136(mg)/2014-06-12 (64)	9	8		RESPIRATORY FAILURE RELATED TO MYELOMA/呼吸不全	5	NOT APPLICABLE	NOT RELATED	FATAL	Y	N
	CA00098	100040	63/F/WHITE/CAN	757(mg)/2014-03-01 (11)	2	4		PLEURAL EFFUSION/胸水	2	DOSE NOT CHANGED	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				757(mg)/2014-03-08 (18)	3	4		GENERAL HEALTH DETERIORATION/全身健康状態低下	5	DOSE NOT CHANGED	NOT RELATED	FATAL	Y	N
		100046	65/F/ASIAN/CAN	814(mg)/2014-08-03 (164)	15	24	2014-08-11 (172)/9	FATIGUE DUE TO DISEASE PROGRESSION/疲労	3	NOT APPLICABLE	NOT RELATED	RECOVERED/ RESOLVED	Y	N
	CA00104	100095	61/F/WHITE/CAN	1248(mg)/2014-11-25 (237)	17	41	2014-11-29 (241)/5	PYELONEPHRITIS/腎盂腎炎	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
		100121	58/F/WHITE/CAN	746(mg)/2014-08-05 (111)	11	13	2014-08-12 (118)/8	PANCREATITIS/膵炎	3	NOT APPLICABLE	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
				784(mg)/2014-06-20 (65)	9	9		SOFT TISSUE INFECTION/軟部組織感染	3	DRUG INTERRUPTED	NOT RELATED	RECOVERING /RESOLVING	Y	N
	ES00349	100087	72/F/WHITE/ESP	736(mg)/2014-05-27 (57)	8	8		HYPERCALCEMY/高カルシウム血症	5	NOT APPLICABLE	NOT RELATED	FATAL	Y	N
		100125	63/F/WHITE/ESP	880(mg)/2014-04-28 (14)	2	7		GENERAL HEALTH DETERIORATION/全身健康状態低下	5	DOSE NOT CHANGED	NOT RELATED	FATAL	Y	N
	ES00350	100109	64/F/WHITE/ESP	592(mg)/2014-09-13 (157)	14	9	2014-09-19 (163)/7	VARICELLA/水痘	2	NOT APPLICABLE	POSSIBLE	RECOVERED/ RESOLVED	Y	N
	ES00351	100031	58/M/WHITE/ESP	1000(mg)/2014-01-26 (69)	9	13	2014-01-31 (74)/6	PNEUMONIA/肺炎	2	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	Y	N

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Onset Date (Study Day)	Number of DARA Infusions Before AE Onset	Days Since Last DARA Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious	Infusion Related Reaction
	ES00352	100084	80/F/WHITE/ESP	110.3536(mg)/ 2014-04-09 (1)	1	1	2014-04-30 (22)/22	NEUMONIA BY ASPIRATION/誤嚥性肺炎	3	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				110.3536(mg)/ 2014-05-06 (28)	1	28		GENERAL DETERIORATION/全身健康状態低下	5	DRUG WITHDRAWN	NOT RELATED	FATAL	Y	N
	US10550	100112	65/M/WHITE/USA	1216(mg)/2014 -06-21 (80)	10	10	2014-06-30 (89)/10	PNEUMONIA-BILATERAL/肺炎	3	DRUG INTERRUPTED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014 -08-22 (142)	14	9	2014-08-29 (149)/8	SEPSIS/敗血症	4	DRUG INTERRUPTED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014 -08-23 (143)	14	10	2014-08-29 (149)/7	ANEMIA-INTERMITTENT/貧血	3	DOSE NOT CHANGED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014 -08-23 (143)	14	10	2014-08-29 (149)/7	FLASH PULMOMARY EDEMA/急性肺水腫	3	NOT APPLICABLE	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
				1232(mg)/2014 -09-12 (163)	15	2	2014-09-16 (167)/5	SEPSIS/敗血症	3	DOSE NOT CHANGED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
				1248(mg)/2014 -08-04 (124)	13	5	2014-08-08 (128)/5	PNEUMONIA- RIGHT LOWER LOBE/大葉性肺炎	3	DOSE NOT CHANGED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
		100141	62/M/WHITE/USA	1306(mg)/2014 -05-01 (7)	1	7		PNEUMONIA/肺炎	3	DRUG INTERRUPTED	POSSIBLE	RECOVERING /RESOLVING	Y	N
				1306(mg)/2014 -05-01 (7)	1	7	2014-05-01 (7)/1	OXYGEN DESATURATION OF 89%/酸素飽和度異常	3	DRUG INTERRUPTED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
				1306(mg)/2014 -05-02 (8)	1	8		BILATERAL SUBDURAL HEMATOMA/硬膜下血腫	3	DRUG INTERRUPTED	DOUBTFUL	RECOVERING /RESOLVING	Y	N
		100147	70/F/WHITE/USA	960(mg)/2014-06-04 (42)	6	7	2014-06-13 (51)/10	HEADACHE- RIGHT SIDE/頭痛	3	DRUG INTERRUPTED	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
				960(mg)/2014-06-04 (42)	6	7	2014-06-19 (57)/16	WORSENED CHRONIC PAIN-RIBS/筋骨格系胸痛	3	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	Y	N

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

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				960(mg)/2014-06-04 (42)	6	7	2014-06-19 (57)/16	WORSENED CHRONIC PAIN-SPINE/脊椎痛	3	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				960(mg)/2014-06-18 (56)	7	7	2014-06-26 (64)/9	FECAL INCONTINENCE/便失禁	1	DOSE NOT CHANGED	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
				960(mg)/2014-06-18 (56)	7	7	2014-06-26 (64)/9	TREMORS/振戦	2	DOSE NOT CHANGED	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
				960(mg)/2014-06-18 (56)	7	7	2014-06-26 (64)/9	WEAKNESS/無力症	3	DOSE NOT CHANGED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
		100148	70/F/ASIAN/USA	992(mg)/2014-04-26 (2)	1	2	2014-04-27 (3)/2	PAINLESS HEMATURIA/血尿	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
	US10554	100074	73/M/WHITE/USA	1488(mg)/2014-05-17 (54)	8	5	2014-05-23 (60)/7	RIGHT LOWER LOBE PNEUMONIA/大葉性肺炎	3	NOT APPLICABLE	POSSIBLE	RECOVERED/ RESOLVED	Y	N
				1488(mg)/2014-05-24 (61)	8	12	2014-05-29 (66)/6	PARAINFLUENZA 3 INFECTION/パラインフルエンザウイルス感染	3	NOT APPLICABLE	POSSIBLE	RECOVERED/ RESOLVED	Y	N
		100080	71/F/WHITE/USA	816(mg)/2014-05-13 (49)	6	15	2014-05-13 (49)/1	PHYSICAL HEALTH DETERIORATION/全身健康状態低下	5	NOT APPLICABLE	NOT RELATED	FATAL	Y	N
	US10555	100059	59/M/WHITE/USA	784(mg)/2014-04-05 (45)	6	10		HEPATIC FAILURE/肝不全	5	NOT APPLICABLE	NOT RELATED	FATAL	Y	N
	US10764	100079	55/F/WHITE/USA	1360(mg)/2014-08-06 (133)	13	14	2014-08-13 (140)/8	PATHOLOGICAL FRACTURE OF FEMUR/病的骨折	4	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
		100091	48/F/WHITE/USA	976(mg)/2014-03-28 (2)	1	2	2014-03-30 (4)/3	ABDOMINAL PAIN/腹痛	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				976(mg)/2014-07-25 (121)	12	16		SPINAL CANAL STENOSIS/脊柱管狭窄症	4	DRUG WITHDRAWN	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				976(mg)/2014-07-25 (121)	12	16		SPINAL CORD COMPRESSION/脊髄圧迫	4	DRUG WITHDRAWN	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Onset Date (Study Day)	Number of DARA Infusions Before AE Onset	Days Since Last DARA Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious	Infusion Related Reaction
	US10767	100085	62/M/WHITE/USA	1504(mg)/2014-04-15 (16)	3	2	2014-04-18 (19)/4	BILATERAL PNEUMONIA/肺炎	3	DRUG INTERRUPTED	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
		100158	65/M/WHITE/USA	1232(mg)/2014-10-26 (160)	16	7	2014-10-27 (161)/2	DEEP VEIN THROMBOSIS/深部静脈血栓症	3	DOSE NOT CHANGED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
	US10769	100083	59/F/BLACK OR AFRICAN AMERICAN/USA	960(mg)/2014-05-27 (51)	7	9	2014-05-28 (52)/2	HYPERKALEMIA/高カリウム血症	3	NOT APPLICABLE	NOT RELATED	RECOVERED/ RESOLVED WITH SEQUELAE	Y	N
				960(mg)/2014-05-27 (51)	7	9	2014-05-29 (53)/3	CREATININE INCREASED/腎機能障害	3	NOT APPLICABLE	NOT RELATED	RECOVERED/ RESOLVED WITH SEQUELAE	Y	N
				960(mg)/2014-05-27 (51)	7	9	2014-05-29 (53)/3	HYPERCALCEMIA/高カルシウム血症	4	NOT APPLICABLE	NOT RELATED	RECOVERED/ RESOLVED WITH SEQUELAE	Y	N
		100089	77/F/WHITE/USA	944(mg)/2014-11-27 (220)	18	24		SPINAL COMPRESSION FRACTURE/脊椎圧迫骨折	3	NOT APPLICABLE	NOT RELATED	RECOVERING /RESOLVING	Y	NA
	US10782	100065	74/M/NOT REPORTED/USA	928(mg)/2014-08-19 (169)	17	1	2014-08-19 (169)/1	CHEST WALL PAIN/ 筋骨格系胸痛	2	NOT APPLICABLE	DOUBTFUL	RECOVERED/ RESOLVED	Y	N
				944(mg)/2014-06-30 (119)	13	7		PAIN (RIGHT MID-RIB AREA)/筋骨格系胸痛	3	DOSE NOT CHANGED	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				944(mg)/2014-06-30 (119)	13	7	2014-07-01 (120)/2	FEVER/発熱	1	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N
				944(mg)/2014-06-30 (119)	13	7	2014-07-02 (121)/3	HYPOTENSION/低血圧	3	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N

LSFAE-JST02_2002: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study 54767414MMY2002)

Actual Treatment Group	Site ID	Subject ID	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Onset Date (Study Day)	Number of DARA Infusions Before AE Onset	Days Since Last DARA Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Action Taken	Relation	Outcome	Serious	Infusion Related Reaction
		100070	66/M/BLACK OR AFRICAN AMERICAN/USA	1632(mg)/2014-05-12 (49)	7	6		COLONIC OBSTRUCTION/大腸閉塞	4	DOSE NOT CHANGED	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
				1632(mg)/2014-05-12 (49)	7	6		URINARY TRACT OBSTRUCTION/尿路閉塞	3	DOSE NOT CHANGED	NOT RELATED	NOT RECOVERED/ NOT RESOLVED	Y	N
	US10796	100017	64/F/WHITE/USA	982.4(mg)/2013-11-17 (13)	2	5	2013-11-27 (23)/11	HERPES ZOSTER REACTIVATION/帯状疱疹	3	DRUG INTERRUPTED	POSSIBLE	RECOVERED/ RESOLVED	Y	N
		100027	66/M/BLACK OR AFRICAN AMERICAN/USA	1568(mg)/2013-11-30 (13)	2	5	2013-12-01 (14)/2	UPPER RESPIRATORY TRACT INFECTION/上気道感染	3	DOSE NOT CHANGED	POSSIBLE	RECOVERED/ RESOLVED	Y	NA
		100050	65/F/WHITE/USA	1088(mg)/2014-02-26 (3)	1	3	2014-02-28 (5)/3	DIASTOLIC CONGESTIVE HEART FAILURE/うっ血性心不全	1	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	Y	N

Note: Adverse events are reported using MedDRA version 17.0
Adverse events with onset date the same as infusion date and missing onset time were considered as having onset time after infusion start.

LSFAE-JST02_501P1: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN501 Part1)

Dose Level	Site ID	Enrollment No	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Start Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Serious ?	Infusion Related Reaction ?	Relationship to Study Drug	Action Taken	Outcome
0.005 mg/kg	DK01	501001	67/M/WHITE/DNK	0.000283(mg/kg)/2008-04-02 (8)	2	7	2008-06-11 (78)/71	ABDOMINAL PAIN/腹痛	5	Y	N	NOT RELATED	DOSE NOT CHANGED	FATAL
0.1 mg/kg	DK02	501008	65/M/WHITE/DNK	0.1(mg/kg)/2010-03-10 (31)	5	1	2010-03-11 (32)/2	CYTOKINE RELEASE SYNDROME/サイトカイン放出症候群	2	Y	Y	POSSIBLE /PROBABLE	DRUG WITHDRAWN	RECOVERED /RESOLVED
	SE01	501005	62/F/WHITE/SWE	0.1(mg/kg)/2009-02-02 (22)	2	21	2009-02-05 (25)/4	ANEMIA/貧血	3	Y	N	POSSIBLE /PROBABLE	DOSE NOT CHANGED	RECOVERED /RESOLVED
				0.1(mg/kg)/2009-02-04 (24)	4	2	2009-04-03 (82)/59	THROMBOCYTOPENIA /血小板減少症	4	Y	N	POSSIBLE /PROBABLE	DOSE NOT CHANGED	RECOVERED /RESOLVED
0.5 mg/kg	DK02	501010	60/F/WHITE/DNK	0.5(mg/kg)/2010-10-04 (50)	7	7	2010-10-04 (50)/1	ATRIAL FIBRILLATION/心房細動	2	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				0.5(mg/kg)/2010-10-12 (58)	9	1	2010-10-13 (59)/2	INCREASED FREE HAEMAGLOBIN/遊離ヘモグロビン陽性	1	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
1 mg/kg	DK02	501012	61/F/WHITE/DNK	1(mg/kg)/2010-12-29 (31)	5	1	2010-12-30 (32)/2	INCREASED ASAT (FUNCTION LIVER ABNORMAL)/肝機能異常	2	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				1(mg/kg)/2011-01-05 (38)	6	1	2011-01-13 (46)/9	INCREASED ASAT (FUNCTION LIVER ABNORMAL)/肝機能異常	3	Y	N	POSSIBLE /PROBABLE	DRUG WITHDRAWN	RECOVERED /RESOLVED
	NL01	501016	65/F/WHITE/NLD	1.074(mg/kg)/2011-03-08 (28)	4	7	2011-03-28 (48)/21	COLLAPSE TH6/脊椎圧迫骨折	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED WITH SEQUELAE
2 mg/kg	DK01	501018	60/M/WHITE/DNK	2.144(mg/kg)/2011-05-06 (25)	4	3	2011-05-07 (26)/2	BRONCHOSPASM/気管支痙攣	3	Y	Y	POSSIBLE /PROBABLE	DRUG WITHDRAWN	RECOVERED /RESOLVED
				2.144(mg/kg)/2011-05-27 (46)	4	24	2011-06-01 (51)/6	FEVER WITH UNKNOWN ORIGIN/発熱	2	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED

LSFAE-JST02_501P1: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN501 Part1)

Dose Level	Site ID	Enrollment No	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Start Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Serious ?	Infusion Related Reaction ?	Relationship to Study Drug	Action Taken	Outcome
8 mg/kg	DK02	501026	68/M/WHITE/DNK	8(mg/kg)/2011-11-27 (7)	2	6	2011-12-01 (11)/5	INFECTION METAPNEUMOVIRUS/メタニューモウイルス感染	1	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				8(mg/kg)/2011-12-27 (37)	5	7	2011-12-31 (41)/5	FEVER U.K FOCUS/発熱	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
16 mg/kg	DK02	501029	51/M/WHITE/DNK	16(mg/kg)/2012-02-19 (7)	2	6	2012-02-22 (10)/4	FEVER WITH UNKNOWN ORIGIN/発熱	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				16(mg/kg)/2012-02-28 (16)	2	15		CONFUSION/錯乱状態	3	Y	N	NOT RELATED	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED
		501031	54/M/WHITE/DNK	16(mg/kg)/2012-05-18 (68)	9	10	2012-05-23 (73)/6	PNEUMONIA/肺炎	2	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
24 mg/kg	NL01	501033	50/M/WHITE/NLD	25.08(mg/kg)/2012-07-25 (24)	4	2	2012-07-26 (25)/2	BRONCHOSPASMS/気管支痙攣	2	Y	Y	POSSIBLE /PROBABLE	DOSE NOT CHANGED	RECOVERED /RESOLVED
	SE01	501034	69/M/WHITE/SWE	24(mg/kg)/2012-09-03 (8)	2	7	2012-09-20 (25)/18	URINARY TRACT INFECTION/尿路感染	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				24(mg/kg)/2012-09-24 (29)	4	7	2012-10-05 (40)/12	URINARY TRACT INFECTION/尿路感染	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED

Note: Adverse events are reported using MedDRA version 17.0
Adverse events with onset date the same as infusion date and missing onset time were considered as having onset time after infusion start.

LSFAE-JST02_501P2: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN501 Part2)

Dose Level	Site ID	Enrollment No	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Start Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Serious ?	Infusion Related Reaction ?	Relationship to Study Drug	Action Taken	Outcome
SCHEDULE A - 8 mg/kg	50122	501209	49/F/WHITE/DNK	776(mg)/2013-02-04 (15)	2	14		INCREASED CREATININE/腎機能障害	3	Y	N	NOT RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED
		501210	76/F/WHITE/DNK	487.2(mg)/2013-04-03 (66)	9	16		ANEMIA/貧血	3	Y	N	NOT RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED
	50123	501208	58/M//NLD	752(mg)/2013-05-24 (124)	14	4		L1 FRACTURE, OSTEOPOROSIC (PREV OSTEOPOROSIC FRACTURE VERTEBRA T12)/骨粗鬆症性骨折	3	Y	N	NOT RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED
		501213	73/M//NLD	712(mg)/2013-03-05 (22)	4	7	2013-03-12 (29)/8	PNEUMONIA/肺炎	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED
	50124	501206	60/M/WHITE/SWE	448(mg)/2013-01-12 (5)	2	4	2013-01-22 (15)/11	INFLUENZA A, INFECTION/インフルエンザ	2	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED
				432(mg)/2013-02-23 (47)	7	5	2013-03-01 (53)/7	RS VIRUS INFECTION/ＲＳウイルス感染	2	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED
				424(mg)/2013-03-09 (61)	8	6	2013-03-13 (65)/5	FEVER/発熱	2	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED
		501207	54/M/WHITE/SWE	792(mg)/2013-03-05 (55)	9	7	2013-03-13 (63)/9	PNEUMONIA/肺炎	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED
				768(mg)/2013-05-17 (128)	13	24	2013-06-01 (143)/16	FINGER TRAUMA AMPUTATION/四肢外傷性切断	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE
	50125	501214	60/M/WHITE/USA	760(mg)/2013-03-08 (16)	2	15	2013-03-18 (26)/11	BACTEREMIA/菌血症	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED
SCHEDULE B - 8 mg/kg	50122	501223	67/M/WHITE/DNK	488(mg)/2013-07-05 (19)	4	5	2013-07-10 (24)/6	PNEUMONIA/肺炎	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED

LSFAE-JST02_501P2: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN501 Part2)

Dose Level	Site ID	Enrollment No	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Start Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Serious ?	Infusion Related Reaction ?	Relationship to Study Drug	Action Taken	Outcome
				464(mg)/2013-08-02 (47)	7	5	2014-08-11 (421)/375	PNEUMONIA/肺炎	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
	50123	501217	53/F//NLD	680(mg)/2013-08-26 (106)	12	18	2013-09-09 (120)/15	ABDUCENS PALSY/第６脳神経麻痺	3	Y	N	NOT RELATED	DRUG WITHDRAWN	RECOVERED /RESOLVED
SCHEDULE C - 8 mg/kg	50122	501226	72/F/WHITE/DNK	560(mg)/2013-08-29 (50)	8	2	2013-08-30 (51)/2	INR-INCREASED/国際標準比増加	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
	50125	501229	67/M/WHITE/USA	628(mg)/2014-02-02 (187)	16	13	2014-02-04 (189)/3	CHEST PAIN/胸痛	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
		501230	44/F/WHITE/USA	517.6(mg)/2013-10-16 (66)	7	9	2013-10-25 (75)/10	THROMBOCYTOPENIA/血小板減少症	4	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
				524.8(mg)/2013-11-22 (103)	11	8	2013-11-26 (107)/5	THROMBOCYTOPENIA/血小板減少症	4	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
SCHEDULE D - 16 mg/kg	50123	501238	66/F//NLD	920(mg)/2013-11-11 (14)	1	14	2013-11-12 (15)/2	HYPOMAGNESEMIA/低マグネシウム血症	2	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
	50125	501239	66/F/WHITE/USA	1027.2(mg)/2013-11-20 (21)	1	21	2013-11-20 (21)/1	HYPOKALEMIA/低カリウム血症	4	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
		501242	59/F/WHITE/USA	1152(mg)/2014-08-26 (288)	19	1		PERIPHERAL EDEMA/末梢性浮腫	3	Y	N	NOT RELATED	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED
	50127	501248	61/M/WHITE/SWE	1488(mg)/2014-02-08 (13)	1	13	2014-02-10 (15)/3	FEVER/発熱	1	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				1488(mg)/2014-03-26 (59)	6	9	2014-03-27 (60)/2	FEVER/発熱	2	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
				1488(mg)/2014-04-03 (67)	7	3		IMPOSSIBLE TO TO BASAL BLOODSCREENING OR CROSSMATCH TO FIND MATCHING BLOOD TRANSFUSION FOR PATIENT/交差適合試験不適合		Y	N	POSSIBLE/ PROBABLE	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED
SCHEDULE E - 16 mg/kg	50121	501252	76/F/WHITE/DNK	1024(mg)/2014-04-01 (9)	1	9	2014-04-14 (22)/14	NEUTROPHENIA/好中球減少症	4	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED

LSFAE-JST02_501P2: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN501 Part2)

Dose Level	Site ID	Enrollment No	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Start Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Serious ?	Infusion Related Reaction ?	Relationship to Study Drug	Action Taken	Outcome
		501264	67/M/WHITE/DNK	1264(mg)/2014-07-04 (39)	4	3		FRACTURA COMPRESSIO L3/脊椎圧迫骨折	3	Y	N	NOT RELATED	DOSE NOT CHANGED	UNKNOWN
		501265	53/M/WHITE/DNK	1488(mg)/2014-11-22 (186)	15	26	2014-12-02 (196)/11	VARICELLA/水痘	2	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
	50122	501268	61/F/WHITE/DNK	1300(mg)/2014-07-05 (40)	4	5	2014-07-06 (41)/2	FEVER OF UNKNOWN ORIGIN/発熱	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
	50125	501259	44/M/BLACK OR AFRICAN AMERICAN/USA	1422(mg)/2014-11-12 (202)	16	13	2014-12-01 (221)/20	PNEUMONIA/肺炎	3	Y	N	POSSIBLE/ PROBABLE	DOSE NOT CHANGED	RECOVERED /RESOLVED
		501262	61/M/WHITE/USA	693(mg)/2014-05-23 (15)	1	15	2014-05-28 (20)/6	BONE PAIN/骨痛	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				693(mg)/2014-05-23 (15)	1	15	2014-05-28 (20)/6	NAUSEA/悪心	2	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				693(mg)/2014-05-31 (23)	1	23	2014-06-01 (24)/2	BONE PAIN/骨痛	3	Y	N	NOT RELATED	DOSE NOT CHANGED	RECOVERED /RESOLVED
				658.1(mg)/2014-06-08 (31)	2	7	2014-06-14 (37)/7	PNEUMONIA/肺炎	5	Y	N	NOT RELATED	DRUG WITHDRAWN	FATAL
		501263	73/F/WHITE/USA	931(mg)/2014-07-08 (57)	6	1	2014-09-26 (137)/81	SHINGLES/帯状疱疹	3	Y	N	POSSIBLE/ PROBABLE	DRUG INTERRUPTED	RECOVERED /RESOLVED
				931(mg)/2014-08-21 (101)	6	45	2014-09-26 (137)/37	PNEUMONIA/肺炎	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
		501272	72/M/WHITE/USA	1275(mg)/2014-08-07 (57)	6	8	2014-08-11 (61)/5	ATRIAL FLUTTER/心房粗動	3	Y	N	NOT RELATED	DRUG INTERRUPTED	RECOVERED /RESOLVED
				1232(mg)/2014-09-01 (82)	8	7	2014-09-01 (82)/1	ATRIAL FLUTTER/心房粗動	3	Y	N	NOT RELATED	NOT APPLICABLE	RECOVERED /RESOLVED
	50127	501251	72/F/WHITE/SWE	928(mg)/2014-05-14 (71)	8	7		IMPOSSIBLE TO TO BASAL BLOODSCREENING OR CROSSMATCH TO FIND MATCHING BLOOD TRANSFUSION FOR PATIENT/交差適合試験不適合		Y	N	POSSIBLE/ PROBABLE	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED

LSFAE-JST02_501P2: List of Treatment-emergent Serious Adverse Events; All Treated Analysis Set (Study GEN501 Part2)

Dose Level	Site ID	Enrollment No	Age (years)/ Sex/ Race/ Country	Onset Dose (unit)AE Start Date (Study Day)	Number of Dara Doses Before AE Onset	Days Since Last Dara Infusion	AE End Date (Study Day)/ AE Duration (days)	Reported Term/ MedDRA Preferred Term	NCI CTCAE Grade	Serious ?	Infusion Related Reaction ?	Relationship to Study Drug	Action Taken	Outcome
		501254	49/F/WHITE/SWE	688(mg)/2014-04-09 (1)	1	1		IMPOSSIBLE TO TO BASAL BLOODSCREENING OR CROSSMATCH TO FIND MATCHING BLOOD TRANSFUSION FOR PATIENT/交差適合試験不適合		Y	N	POSSIBLE/ PROBABLE	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED

Note: Adverse events are reported using MedDRA version 17.0
Adverse events with onset date the same as infusion date and missing onset time were considered as having onset time after infusion start.

表 2.7.4-付録-60 Number of Subjects with Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE04: Number of Subjects with Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Number of subjects with any serious TEAEs	1 (25.0%)	2 (40.0%)	3 (33.3%)
MedDRA system organ class/preferred term			
感染症および寄生虫症	0	1 (20.0%)	1 (11.1%)
肺炎	0	1 (20.0%)	1 (11.1%)
血液およびリンパ系障害	1 (25.0%)	0	1 (11.1%)
血小板減少症	1 (25.0%)	0	1 (11.1%)
神経系障害	0	1 (20.0%)	1 (11.1%)
頭痛	0	1 (20.0%)	1 (11.1%)
一般・全身障害および投与部位の状態	0	1 (20.0%)	1 (11.1%)
発熱	0	1 (20.0%)	1 (11.1%)

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.

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表 2.7.4-付録-61 Listing of Serious Adverse Events other than Death; All Treated Analysis Population (Study 54767414MMY1002)

LSFAE03: Listing of Serious Adverse Events other than Death; All Treated Analysis Population (Study 54767414MMY1002)

Treatment Group	Subject ID	Sex/ Age	Race	Reported Term	Preferred Term[a]	TEAE	Onset Date/ (Study Day)	Outcome Date/ (Study Day)	Duration[b]	Outcome	Toxicity Grade	Action Taken	Causality	Serious Event	DLT Evaluated?
Daratumumab 8 mg/kg	810101	F/ 64	ASIAN	PLATELET COUNT DECREASED	血小板減少症	Y	2014-06-03/ (15)			NOT RECOVERED/NOT RESOLVED	4	DOSE NOT CHANGED	NOT RELATED	Y	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	HEADACHE	頭痛	Y	2014-08-28/ (24)	2014-09-01/ (28)	5	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	POSSIBLE	Y	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	FEVER	発熱	Y	2014-08-30/ (26)	2014-09-25/ (52)	27	RECOVERED/RESOLVED	1	DOSE NOT CHANGED	POSSIBLE	Y	
Daratumumab 16 mg/kg	810104	M/ 65	ASIAN	PNEUMONIA	肺炎		2014-08-28/ (-13)	2014-09-24/ (15)	28	RECOVERED/RESOLVED	2	NOT APPLICABLE	NOT RELATED	Y	
Daratumumab 16 mg/kg	810104	M/ 65	ASIAN	PNEUMONIA	肺炎	Y	2014-09-24/ (15)	2014-11-05/ (57)	43	RECOVERED/RESOLVED	3	NOT APPLICABLE	POSSIBLE	Y	

[a] Adverse Events are coded using MedDRA 18.0.
[b] Calculated as the number of days between Onset Date and Outcome Date when outcome is Recovered or Recovering.

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表 2.7.4-付録-62 Treatment-Emergent Adverse Events Leading to Infusion Modification Prior to Infusion Start by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE08: Treatment-Emergent Adverse Events Leading to Infusion Modification Prior to Infusion Start by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
Analysis set: safety[a]	243	283	103	629
Total number of subjects with TEAE leading to infusion modification prior to infusion start[b]	87 (35.8%)	105 (37.1%)	50 (48.5%)	242 (38.5%)
MedDRA system organ class / Preferred term				
感染症および寄生虫症	34 (14.0%)	61 (21.6%)	18 (17.5%)	113 (18.0%)
肺炎	11 (4.5%)	10 (3.5%)	3 (2.9%)	24 (3.8%)
上気道感染	4 (1.6%)	6 (2.1%)	3 (2.9%)	13 (2.1%)
気管支炎	5 (2.1%)	5 (1.8%)	0	10 (1.6%)
インフルエンザ	2 (0.8%)	5 (1.8%)	1 (1.0%)	8 (1.3%)
下気道感染	1 (0.4%)	5 (1.8%)	0	6 (1.0%)
鼻咽頭炎	0	5 (1.8%)	0	5 (0.8%)
ＲＳウイルス感染	1 (0.4%)	1 (0.4%)	3 (2.9%)	5 (0.8%)
尿路感染	0	4 (1.4%)	1 (1.0%)	5 (0.8%)
帯状疱疹	3 (1.2%)	0	1 (1.0%)	4 (0.6%)
肺感染	1 (0.4%)	2 (0.7%)	1 (1.0%)	4 (0.6%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	2 (1.9%)	4 (0.6%)
インフルエンザ性肺炎	0	3 (1.1%)	0	3 (0.5%)
敗血症	0	1 (0.4%)	2 (1.9%)	3 (0.5%)
胃腸炎	1 (0.4%)	1 (0.4%)	0	2 (0.3%)
気道感染	0	2 (0.7%)	0	2 (0.3%)
鼻炎	1 (0.4%)	1 (0.4%)	0	2 (0.3%)
副鼻腔炎	1 (0.4%)	1 (0.4%)	0	2 (0.3%)
細菌感染	0	1 (0.4%)	0	1 (0.2%)
細気管支炎	0	1 (0.4%)	0	1 (0.2%)
細菌性気管支炎	0	1 (0.4%)	0	1 (0.2%)
気管支肺炎	0	1 (0.4%)	0	1 (0.2%)
コロナウイルス感染	0	0	1 (1.0%)	1 (0.2%)
憩室炎	0	0	1 (1.0%)	1 (0.2%)
喉頭蓋炎	0	1 (0.4%)	0	1 (0.2%)
伝染性紅斑	1 (0.4%)	0	0	1 (0.2%)

TSFAE08: Treatment-Emergent Adverse Events Leading to Infusion Modification Prior to Infusion Start by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
消化管感染	1 (0.4%)	0	0	1 (0.2%)
陰部ヘルペス	1 (0.4%)	0	0	1 (0.2%)
歯肉炎	0	1 (0.4%)	0	1 (0.2%)
鼻膿瘍	0	1 (0.4%)	0	1 (0.2%)
好中球減少性敗血症	0	1 (0.4%)	0	1 (0.2%)
急性中耳炎	0	1 (0.4%)	0	1 (0.2%)
細菌性肺炎	0	1 (0.4%)	0	1 (0.2%)
サイトメガロウイルス性肺炎	1 (0.4%)	0	0	1 (0.2%)
ヘモフィルス性肺炎	0	1 (0.4%)	0	1 (0.2%)
クレブシエラ菌性肺炎	0	1 (0.4%)	0	1 (0.2%)
レジオネラ菌性肺炎	0	1 (0.4%)	0	1 (0.2%)
進行性多巣性白質脳症	0	0	1 (1.0%)	1 (0.2%)
肺敗血症	1 (0.4%)	0	0	1 (0.2%)
ウイルス性気道感染	1 (0.4%)	0	0	1 (0.2%)
サルモネラ性菌血症	0	1 (0.4%)	0	1 (0.2%)
唾液腺炎	1 (0.4%)	0	0	1 (0.2%)
脊髄感染	0	0	1 (1.0%)	1 (0.2%)
細菌性上気道感染	0	1 (0.4%)	0	1 (0.2%)
血液およびリンパ系障害	32 (13.2%)	33 (11.7%)	27 (26.2%)	92 (14.6%)
好中球減少症	5 (2.1%)	29 (10.2%)	24 (23.3%)	58 (9.2%)
血小板減少症	28 (11.5%)	5 (1.8%)	9 (8.7%)	42 (6.7%)
発熱性好中球減少症	3 (1.2%)	4 (1.4%)	3 (2.9%)	10 (1.6%)
貧血	2 (0.8%)	2 (0.7%)	4 (3.9%)	8 (1.3%)
白血球減少症	0	1 (0.4%)	3 (2.9%)	4 (0.6%)
溶血	0	0	1 (1.0%)	1 (0.2%)
リンパ節症	0	1 (0.4%)	0	1 (0.2%)
リンパ球減少症	0	1 (0.4%)	0	1 (0.2%)
胃腸障害	9 (3.7%)	12 (4.2%)	1 (1.0%)	22 (3.5%)
下痢	5 (2.1%)	7 (2.5%)	1 (1.0%)	13 (2.1%)
悪心	0	2 (0.7%)	0	2 (0.3%)
嘔吐	0	2 (0.7%)	0	2 (0.3%)
便秘	0	1 (0.4%)	0	1 (0.2%)
十二指腸潰瘍	1 (0.4%)	0	0	1 (0.2%)
白色便	1 (0.4%)	0	0	1 (0.2%)

TSFAE08: Treatment-Emergent Adverse Events Leading to Infusion Modification Prior to Infusion Start by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
出血性胃腸管血管異形成	0	1 (0.4%)	0	1 (0.2%)
鼠径ヘルニア	0	1 (0.4%)	0	1 (0.2%)
腸閉塞	1 (0.4%)	0	0	1 (0.2%)
口腔内潰瘍形成	0	1 (0.4%)	0	1 (0.2%)
舌浮腫	1 (0.4%)	0	0	1 (0.2%)
一般・全身障害および投与部位の状態	7 (2.9%)	13 (4.6%)	2 (1.9%)	22 (3.5%)
発熱	5 (2.1%)	7 (2.5%)	2 (1.9%)	14 (2.2%)
無力症	0	3 (1.1%)	0	3 (0.5%)
疲労	1 (0.4%)	2 (0.7%)	0	3 (0.5%)
インフルエンザ様疾患	1 (0.4%)	1 (0.4%)	0	2 (0.3%)
全身健康状態低下	0	1 (0.4%)	0	1 (0.2%)
疼痛	1 (0.4%)	0	0	1 (0.2%)
呼吸器、胸郭および縦隔障害	5 (2.1%)	2 (0.7%)	5 (4.9%)	12 (1.9%)
呼吸困難	1 (0.4%)	1 (0.4%)	2 (1.9%)	4 (0.6%)
咳嗽	1 (0.4%)	1 (0.4%)	1 (1.0%)	3 (0.5%)
気管支肺症	0	0	1 (1.0%)	1 (0.2%)
慢性閉塞性肺疾患	1 (0.4%)	0	0	1 (0.2%)
発声障害	0	0	1 (1.0%)	1 (0.2%)
労作性呼吸困難	1 (0.4%)	0	0	1 (0.2%)
間質性肺疾患	0	0	1 (1.0%)	1 (0.2%)
胸水	1 (0.4%)	0	0	1 (0.2%)
湿性咳嗽	1 (0.4%)	0	0	1 (0.2%)
臨床検査	2 (0.8%)	4 (1.4%)	4 (3.9%)	10 (1.6%)
アラニンアミノトランスフェラーゼ増加	1 (0.4%)	3 (1.1%)	1 (1.0%)	5 (0.8%)
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (0.7%)	2 (1.9%)	4 (0.6%)
血中アルカリホスファターゼ増加	0	2 (0.7%)	1 (1.0%)	3 (0.5%)
血中クレアチニン増加	1 (0.4%)	0	1 (1.0%)	2 (0.3%)
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	0	2 (0.3%)
血中乳酸脱水素酵素増加	0	1 (0.4%)	0	1 (0.2%)
血圧低下	0	1 (0.4%)	0	1 (0.2%)
神経系障害	3 (1.2%)	3 (1.1%)	4 (3.9%)	10 (1.6%)
末梢性感覚ニューロパチー	1 (0.4%)	0	1 (1.0%)	2 (0.3%)
失神	0	1 (0.4%)	1 (1.0%)	2 (0.3%)
平衡障害	1 (0.4%)	0	0	1 (0.2%)

TSFAE08: Treatment-Emergent Adverse Events Leading to Infusion Modification Prior to Infusion Start by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
浮動性めまい	0	0	1 (1.0%)	1 (0.2%)
嗜眠	0	1 (0.4%)	0	1 (0.2%)
意識消失	0	0	1 (1.0%)	1 (0.2%)
一過性脳虚血発作	0	1 (0.4%)	0	1 (0.2%)
第６脳神経麻痺	1 (0.4%)	0	0	1 (0.2%)
代謝および栄養障害	2 (0.8%)	2 (0.7%)	3 (2.9%)	7 (1.1%)
高血糖	1 (0.4%)	1 (0.4%)	0	2 (0.3%)
脱水	1 (0.4%)	0	0	1 (0.2%)
電解質失調	0	1 (0.4%)	0	1 (0.2%)
高カルシウム血症	0	0	1 (1.0%)	1 (0.2%)
低カリウム血症	0	0	1 (1.0%)	1 (0.2%)
低ナトリウム血症	0	0	1 (1.0%)	1 (0.2%)
皮膚および皮下組織障害	0	4 (1.4%)	2 (1.9%)	6 (1.0%)
全身性皮疹	0	1 (0.4%)	1 (1.0%)	2 (0.3%)
ざ瘡様皮膚炎	0	0	1 (1.0%)	1 (0.2%)
薬疹	0	1 (0.4%)	0	1 (0.2%)
そう痒症	0	0	1 (1.0%)	1 (0.2%)
発疹	0	1 (0.4%)	0	1 (0.2%)
斑状丘疹状皮疹	0	1 (0.4%)	0	1 (0.2%)
蕁麻疹	0	1 (0.4%)	0	1 (0.2%)
肝胆道系障害	0	2 (0.7%)	2 (1.9%)	4 (0.6%)
高ビリルビン血症	0	1 (0.4%)	2 (1.9%)	3 (0.5%)
肝機能異常	0	1 (0.4%)	0	1 (0.2%)
筋骨格系および結合組織障害	2 (0.8%)	2 (0.7%)	0	4 (0.6%)
関節痛	0	1 (0.4%)	0	1 (0.2%)
筋痙縮	0	1 (0.4%)	0	1 (0.2%)
筋肉痛	1 (0.4%)	0	0	1 (0.2%)
病的骨折	1 (0.4%)	0	0	1 (0.2%)
腎および尿路障害	2 (0.8%)	2 (0.7%)	0	4 (0.6%)
急性腎不全	2 (0.8%)	1 (0.4%)	0	3 (0.5%)
腎不全	0	1 (0.4%)	0	1 (0.2%)
血管障害	2 (0.8%)	2 (0.7%)	0	4 (0.6%)
塞栓症	0	1 (0.4%)	0	1 (0.2%)
高血圧クリーゼ	1 (0.4%)	0	0	1 (0.2%)

TSFAE08: Treatment-Emergent Adverse Events Leading to Infusion Modification Prior to Infusion Start by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
低血圧	0	1 (0.4%)	0	1 (0.2%)
起立性低血圧	1 (0.4%)	0	0	1 (0.2%)
血栓性静脈炎	0	1 (0.4%)	0	1 (0.2%)
心臓障害	2 (0.8%)	1 (0.4%)	0	3 (0.5%)
狭心症	0	1 (0.4%)	0	1 (0.2%)
上室性不整脈	1 (0.4%)	0	0	1 (0.2%)
心房細動	1 (0.4%)	0	0	1 (0.2%)
傷害、中毒および処置合併症	1 (0.4%)	0	2 (1.9%)	3 (0.5%)
骨盤骨折	0	0	1 (1.0%)	1 (0.2%)
肋骨骨折	1 (0.4%)	0	0	1 (0.2%)
脊椎圧迫骨折	0	0	1 (1.0%)	1 (0.2%)
耳および迷路障害	1 (0.4%)	0	0	1 (0.2%)
乳突洞滲出液	1 (0.4%)	0	0	1 (0.2%)
眼障害	1 (0.4%)	0	0	1 (0.2%)
複視	1 (0.4%)	0	0	1 (0.2%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.4%)	0	1 (0.2%)
基底細胞癌	0	1 (0.4%)	0	1 (0.2%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a]GEN503 is excluded from this summary as it did not collect dose delay and dose skip information.
[b]Infusion modification prior to infusion start includes infusion skipping or delay.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE08.SAS] 09JUN2016, 13:46

表 2.7.4-付録-63 Summary of Reasons for Daratumumab Dose Modification; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSIEXP04: Summary of Reasons for Daratumumab Dose Modification; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd	MMY3003+GEN 503 DRd	MMY1001 DPd	Total Dara Combined
Analysis set: safety (excluding GEN503)[a]	243	283	103	629
Subjects with Daratumumab dose delays	15 (6.2%)	36 (12.7%)	12 (11.7%)	63 (10.0%)
Reason for dose delays				
Adverse event	11 (4.5%)	26 (9.2%)	12 (11.7%)	49 (7.8%)
Other	4 (1.6%)	12 (4.2%)	0	16 (2.5%)
Subjects with Daratumumab dose skipped	82 (33.7%)	94 (33.2%)	50 (48.5%)	226 (35.9%)
Reason for skipping				
Adverse event	80 (32.9%)	87 (30.7%)	46 (44.7%)	213 (33.9%)
Other	9 (3.7%)	16 (5.7%)	6 (5.8%)	31 (4.9%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
[a] GEN503 did not collect reason for dose delay and dose skipping on the eCRF.
Note: For Daratumumab dose delay and dose skipping, percentages are calculated with safety subjects from the studies collecting this data (GEN503 is not included).

[TSIEXP04.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSIEXP04.SAS] 14JUL2016, 10:28

表 2.7.4-付録-64 Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Daratumumab Prior to Infusion Start by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE18C: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Daratumumab Prior to Infusion Start by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to dose modifications of daratumumab	4 (50.0%)	4 (50.0%)	0
MedDRA system organ class/Preferred term			
血液およびリンパ系障害	2 (25.0%)	2 (25.0%)	0
血小板減少症	2 (25.0%)	2 (25.0%)	0
肝胆道系障害	1 (12.5%)	1 (12.5%)	0
薬物性肝障害	1 (12.5%)	1 (12.5%)	0
感染症および寄生虫症	1 (12.5%)	1 (12.5%)	0
鼻咽頭炎	1 (12.5%)	1 (12.5%)	0
臨床検査	1 (12.5%)	1 (12.5%)	0
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0
代謝および栄養障害	1 (12.5%)	0	0
脱水	1 (12.5%)	0	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE18C.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE18C.SAS] 28SEP2016, 04:20

表 2.7.4-付録-65 Summary of Treatment Cycle Delays and Reasons for Study Treatment Dose Modifications; All-treated Analysis Set (Study 54767414MMY1005)

TSIEXP05: Summary of Treatment Cycle Delays and Reasons for Study Treatment Dose Modifications; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Subjects with cycle delays	6 (75.0%)
Reason for cycle delays	
Adverse event	4 (50.0%)
Other	2 (25.0%)
Subjects with dose delays	
Bortezomib	0
Reason for delays	
Adverse event	0
Other	0
Dexamethasone	1 (12.5%)
Reason for delays	
Adverse event	1 (12.5%)
Other	0
Daratumumab	1 (12.5%)
Reason for delays	
Adverse event	1 (12.5%)
Other	0
Subjects with dose skipped	
Bortezomib	2 (25.0%)
Reason for skipping	
Adverse event	2 (25.0%)
Other	0
Dexamethasone	7 (87.5%)
Reason for skipping	
Adverse event	7 (87.5%)
Other	0
Daratumumab	4 (50.0%)
Reason for skipping	
Adverse event	4 (50.0%)
Other	0
Subjects with doses reduced	
Bortezomib	5 (62.5%)
Reason for reduction	
Adverse event	4 (50.0%)
Other	1 (12.5%)
Dexamethasone	6 (75.0%)
Reason for reduction	
Adverse event	6 (75.0%)
Other	0
Subjects with schedule change	
Bortezomib	4 (50.0%)
Reason for schedule change	
Adverse event	4 (50.0%)
Other	0
Subjects with study treatment permanently discontinued	
Bortezomib	0
Reason for discontinuing	
Adverse event	0
Other	0
Dexamethasone	0
Reason for discontinuing	
Adverse event	0
Other	0
Daratumumab	0

TSIEXP05: Summary of Treatment Cycle Delays and Reasons for Study Treatment Dose Modifications; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Reason for discontinuing	
Adverse event	0
Other	0

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSIEXP05.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSIEXP05.SAS] 28SEP2016, 04:38

表 2.7.4-付録-66 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE08C_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd	
	All Grades n (%)	Grade 3 or 4 n (%)
Total[a]		
Analysis set: safety	283	
Total number of subjects with TEAE leading to Daratumumab dose modifications[c]	105 (37.1%)	73 (25.8%)
MedDRA system organ class/Preferred term		
感染症および寄生虫症	61 (21.6%)	33 (11.7%)
肺炎	10 (3.5%)	8 (2.8%)
上気道感染	6 (2.1%)	1 (0.4%)
気管支炎	5 (1.8%)	1 (0.4%)
インフルエンザ	5 (1.8%)	4 (1.4%)
下気道感染	5 (1.8%)	2 (0.7%)
鼻咽頭炎	5 (1.8%)	0
尿路感染	4 (1.4%)	2 (0.7%)
インフルエンザ性肺炎	3 (1.1%)	2 (0.7%)
肺感染	2 (0.7%)	1 (0.4%)
気道感染	2 (0.7%)	0
細菌感染	1 (0.4%)	1 (0.4%)
細気管支炎	1 (0.4%)	1 (0.4%)
細菌性気管支炎	1 (0.4%)	0
気管支肺炎	1 (0.4%)	1 (0.4%)
喉頭蓋炎	1 (0.4%)	1 (0.4%)
胃腸炎	1 (0.4%)	1 (0.4%)
歯肉炎	1 (0.4%)	0
鼻膿瘍	1 (0.4%)	1 (0.4%)
好中球減少性敗血症	1 (0.4%)	1 (0.4%)
急性中耳炎	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)
細菌性肺炎	1 (0.4%)	0
ヘモフィルス性肺炎	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	1 (0.4%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)
ＲＳウイルス感染	1 (0.4%)	1 (0.4%)
鼻炎	1 (0.4%)	0
サルモネラ性菌血症	1 (0.4%)	1 (0.4%)
敗血症	1 (0.4%)	1 (0.4%)
副鼻腔炎	1 (0.4%)	0
細菌性上気道感染	1 (0.4%)	1 (0.4%)
血液およびリンパ系障害	33 (11.7%)	31 (11.0%)
好中球減少症	29 (10.2%)	27 (9.5%)
血小板減少症	5 (1.8%)	4 (1.4%)
発熱性好中球減少症	4 (1.4%)	4 (1.4%)
貧血	2 (0.7%)	1 (0.4%)
白血球減少症	1 (0.4%)	1 (0.4%)
リンパ節症	1 (0.4%)	0
リンパ球減少症	1 (0.4%)	1 (0.4%)
一般・全身障害および投与部位の状態	13 (4.6%)	6 (2.1%)
発熱	7 (2.5%)	1 (0.4%)
無力症	3 (1.1%)	3 (1.1%)

TSFAE08C_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd	
	All Grades n (%)	Grade 3 or 4 n (%)
疲労	2 (0.7%)	2 (0.7%)
全身健康状態低下	1 (0.4%)	0
インフルエンザ様疾患	1 (0.4%)	0
胃腸障害	12 (4.2%)	5 (1.8%)
下痢	7 (2.5%)	3 (1.1%)
悪心	2 (0.7%)	0
嘔吐	2 (0.7%)	0
便秘	1 (0.4%)	1 (0.4%)
出血性胃腸管血管異形成	1 (0.4%)	1 (0.4%)
鼠径ヘルニア	1 (0.4%)	0
口腔内潰瘍形成	1 (0.4%)	0
臨床検査	4 (1.4%)	3 (1.1%)
アラニンアミノトランスフェラーゼ増加	3 (1.1%)	1 (0.4%)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.7%)	1 (0.4%)
血中アルカリホスファターゼ増加	2 (0.7%)	1 (0.4%)
血中乳酸脱水素酵素増加	1 (0.4%)	0
血圧低下	1 (0.4%)	0
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)
皮膚および皮下組織障害	4 (1.4%)	3 (1.1%)
薬疹	1 (0.4%)	1 (0.4%)
発疹	1 (0.4%)	0
全身性皮疹	1 (0.4%)	1 (0.4%)
斑状丘疹状皮疹	1 (0.4%)	1 (0.4%)
蕁麻疹	1 (0.4%)	1 (0.4%)
神経系障害	3 (1.1%)	2 (0.7%)
嗜眠	1 (0.4%)	1 (0.4%)
失神	1 (0.4%)	1 (0.4%)
一過性脳虚血発作	1 (0.4%)	0
肝胆道系障害	2 (0.7%)	1 (0.4%)
肝機能異常	1 (0.4%)	0
高ビリルビン血症	1 (0.4%)	1 (0.4%)
代謝および栄養障害	2 (0.7%)	2 (0.7%)
電解質失調	1 (0.4%)	1 (0.4%)
高血糖	1 (0.4%)	1 (0.4%)
筋骨格系および結合組織障害	2 (0.7%)	2 (0.7%)
関節痛	1 (0.4%)	1 (0.4%)
筋痙縮	1 (0.4%)	1 (0.4%)
腎および尿路障害	2 (0.7%)	1 (0.4%)
急性腎不全	1 (0.4%)	0
腎不全	1 (0.4%)	1 (0.4%)
呼吸器、胸郭および縦隔障害	2 (0.7%)	1 (0.4%)
咳嗽	1 (0.4%)	0
呼吸困難	1 (0.4%)	1 (0.4%)
血管障害	2 (0.7%)	0
塞栓症	1 (0.4%)	0
低血圧	1 (0.4%)	0
血栓性静脈炎	1 (0.4%)	0
心臓障害	1 (0.4%)	1 (0.4%)
狭心症	1 (0.4%)	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	0
基底細胞癌	1 (0.4%)	0

Japanese

TSFAE08C_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd	
	All Grades n (%)	Grade 3 or 4 n (%)
Analysis set: safety	20	
Total number of subjects with TEAE leading to Daratumumab dose modifications[c]	9 (45.0%)	5 (25.0%)
MedDRA system organ class/Preferred term		
感染症および寄生虫症	3 (15.0%)	1 (5.0%)
肺炎	0	0
上気道感染	1 (5.0%)	0
気管支炎	0	0
インフルエンザ	0	0
下気道感染	0	0
鼻咽頭炎	1 (5.0%)	0
尿路感染	0	0
インフルエンザ性肺炎	0	0
肺感染	0	0
気道感染	0	0
細菌感染	1 (5.0%)	1 (5.0%)
細気管支炎	0	0
細菌性気管支炎	0	0
気管支肺炎	0	0
喉頭蓋炎	0	0
胃腸炎	0	0
歯肉炎	0	0
鼻膿瘍	0	0
好中球減少性敗血症	0	0
急性中耳炎	0	0
パラインフルエンザウイルス感染	0	0
細菌性肺炎	0	0
ヘモフィルス性肺炎	0	0
クレブシエラ菌性肺炎	0	0
レジオネラ菌性肺炎	0	0
ＲＳウイルス感染	0	0
鼻炎	0	0
サルモネラ性菌血症	0	0
敗血症	0	0
副鼻腔炎	0	0
細菌性上気道感染	0	0
血液およびリンパ系障害	2 (10.0%)	2 (10.0%)
好中球減少症	2 (10.0%)	2 (10.0%)
血小板減少症	1 (5.0%)	1 (5.0%)
発熱性好中球減少症	0	0
貧血	0	0
白血球減少症	0	0
リンパ節症	0	0
リンパ球減少症	1 (5.0%)	1 (5.0%)
一般・全身障害および投与部位の状態	0	0
発熱	0	0
無力症	0	0
疲労	0	0
全身健康状態低下	0	0
インフルエンザ様疾患	0	0
胃腸障害	0	0
下痢	0	0
悪心	0	0
嘔吐	0	0

TSFAE08C_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd	
	All Grades n (%)	Grade 3 or 4 n (%)
便秘	0	0
出血性胃腸管血管異形成	0	0
鼠径ヘルニア	0	0
口腔内潰瘍形成	0	0
臨床検査	2 (10.0%)	1 (5.0%)
アラニンアミノトランスフェラーゼ増加	1 (5.0%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (5.0%)	0
血中アルカリホスファターゼ増加	1 (5.0%)	0
血中乳酸脱水素酵素増加	0	0
血圧低下	1 (5.0%)	0
γ－グルタミルトランスフェラーゼ増加	1 (5.0%)	1 (5.0%)
皮膚および皮下組織障害	2 (10.0%)	1 (5.0%)
薬疹	1 (5.0%)	1 (5.0%)
発疹	1 (5.0%)	0
全身性皮疹	0	0
斑状丘疹状皮疹	0	0
蕁麻疹	0	0
神経系障害	0	0
嗜眠	0	0
失神	0	0
一過性脳虚血発作	0	0
肝胆道系障害	1 (5.0%)	0
肝機能異常	1 (5.0%)	0
高ビリルビン血症	0	0
代謝および栄養障害	0	0
電解質失調	0	0
高血糖	0	0
筋骨格系および結合組織障害	0	0
関節痛	0	0
筋痙縮	0	0
腎および尿路障害	0	0
急性腎不全	0	0
腎不全	0	0
呼吸器、胸郭および縦隔障害	0	0
咳嗽	0	0
呼吸困難	0	0
血管障害	1 (5.0%)	0
塞栓症	1 (5.0%)	0
低血圧	0	0
血栓性静脈炎	1 (5.0%)	0
心臓障害	0	0
狭心症	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0
基底細胞癌	0	0
East Asian[b]		
Analysis set: safety	51	
Total number of subjects with TEAE leading to Daratumumab dose modifications[c]	17 (33.3%)	12 (23.5%)
MedDRA system organ class/Preferred term		
感染症および寄生虫症	7 (13.7%)	4 (7.8%)
肺炎	0	0

TSFAE08C_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd	
	All Grades n (%)	Grade 3 or 4 n (%)
上気道感染	1 (2.0%)	0
気管支炎	0	0
インフルエンザ	0	0
下気道感染	0	0
鼻咽頭炎	1 (2.0%)	0
尿路感染	0	0
インフルエンザ性肺炎	0	0
肺感染	0	0
気道感染	0	0
細菌感染	1 (2.0%)	1 (2.0%)
細気管支炎	1 (2.0%)	1 (2.0%)
細菌性気管支炎	0	0
気管支肺炎	0	0
喉頭蓋炎	0	0
胃腸炎	0	0
歯肉炎	0	0
鼻膿瘍	0	0
好中球減少性敗血症	0	0
急性中耳炎	1 (2.0%)	1 (2.0%)
パラインフルエンザウイルス感染	0	0
細菌性肺炎	0	0
ヘモフィルス性肺炎	0	0
クレブシエラ菌性肺炎	0	0
レジオネラ菌性肺炎	0	0
ＲＳウイルス感染	0	0
鼻炎	0	0
サルモネラ性菌血症	1 (2.0%)	1 (2.0%)
敗血症	0	0
副鼻腔炎	1 (2.0%)	0
細菌性上気道感染	0	0
血液およびリンパ系障害	7 (13.7%)	7 (13.7%)
好中球減少症	7 (13.7%)	7 (13.7%)
血小板減少症	2 (3.9%)	2 (3.9%)
発熱性好中球減少症	0	0
貧血	0	0
白血球減少症	1 (2.0%)	1 (2.0%)
リンパ節症	0	0
リンパ球減少症	1 (2.0%)	1 (2.0%)
一般・全身障害および投与部位の状態	1 (2.0%)	0
発熱	1 (2.0%)	0
無力症	0	0
疲労	0	0
全身健康状態低下	0	0
インフルエンザ様疾患	0	0
胃腸障害	0	0
下痢	0	0
悪心	0	0
嘔吐	0	0
便秘	0	0
出血性胃腸管血管異形成	0	0
鼠径ヘルニア	0	0
口腔内潰瘍形成	0	0
臨床検査	2 (3.9%)	1 (2.0%)
アラニンアミノトランスフェラーゼ増加	1 (2.0%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (2.0%)	0

TSFAE08C_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Daratumumab Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd	
	All Grades n (%)	Grade 3 or 4 n (%)
血中アルカリホスファターゼ増加	1 (2.0%)	0
血中乳酸脱水素酵素増加	0	0
血圧低下	1 (2.0%)	0
γ－グルタミルトランスフェラーゼ増加	1 (2.0%)	1 (2.0%)
皮膚および皮下組織障害	3 (5.9%)	2 (3.9%)
薬疹	1 (2.0%)	1 (2.0%)
発疹	1 (2.0%)	0
全身性皮疹	0	0
斑状丘疹状皮疹	1 (2.0%)	1 (2.0%)
蕁麻疹	1 (2.0%)	1 (2.0%)
神経系障害	0	0
嗜眠	0	0
失神	0	0
一過性脳虚血発作	0	0
肝胆道系障害	1 (2.0%)	0
肝機能異常	1 (2.0%)	0
高ビリルビン血症	0	0
代謝および栄養障害	0	0
電解質失調	0	0
高血糖	0	0
筋骨格系および結合組織障害	0	0
関節痛	0	0
筋痙縮	0	0
腎および尿路障害	0	0
急性腎不全	0	0
腎不全	0	0
呼吸器、胸郭および縦隔障害	0	0
咳嗽	0	0
呼吸困難	0	0
血管障害	1 (2.0%)	0
塞栓症	1 (2.0%)	0
低血圧	0	0
血栓性静脈炎	1 (2.0%)	0
心臓障害	0	0
狭心症	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0
基底細胞癌	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes adverse events leading to daratumumab dose modifications (i.e., dose delays, or dose skipping).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08C_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE08C_3003.SAS] 30JUN2016, 22:03

表 2.7.4-付録-67 Summary of Treatment Cycle Delays and Reasons for Study Treatment Dose Modifications; Safety Analysis Set (Study 54767414MMY3003)

TSIEXP04_3003: Summary of Treatment Cycle Delays and Reasons for Study Treatment Dose Modifications; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Analysis set: safety	15	44	281	20	51	283
Subjects with cycle delays	3 (20.0%)	13 (29.5%)	133 (47.3%)	5 (25.0%)	13 (25.5%)	136 (48.1%)
Reason for cycle delays						
Adverse event	2 (13.3%)	9 (20.5%)	105 (37.4%)	5 (25.0%)	9 (17.6%)	104 (36.7%)
Other	1 (6.7%)	5 (11.4%)	51 (18.1%)	1 (5.0%)	5 (9.8%)	59 (20.8%)
Subjects with dose delays						
Lenalidomide	0	3 (6.8%)	18 (6.4%)	0	2 (3.9%)	21 (7.4%)
Reason for delays						
Adverse event	0	2 (4.5%)	15 (5.3%)	0	2 (3.9%)	20 (7.1%)
Other	0	1 (2.3%)	3 (1.1%)	0	0	3 (1.1%)
Dexamethasone	0	1 (2.3%)	21 (7.5%)	0	2 (3.9%)	23 (8.1%)
Reason for delays						
Adverse event	0	0	12 (4.3%)	0	2 (3.9%)	19 (6.7%)
Other	0	1 (2.3%)	10 (3.6%)	0	0	4 (1.4%)
Daratumumab	0	0	0	1 (5.0%)	3 (5.9%)	36 (12.7%)
Reason for delays						
Adverse event	0	0	0	1 (5.0%)	3 (5.9%)	26 (9.2%)
Other	0	0	0	0	0	12 (4.2%)
Subjects with dose skipped						
Lenalidomide	13 (86.7%)	28 (63.6%)	135 (48.0%)	17 (85.0%)	35 (68.6%)	181 (64.0%)
Reason for skipping						
Adverse event	9 (60.0%)	23 (52.3%)	112 (39.9%)	17 (85.0%)	35 (68.6%)	168 (59.4%)
Other	6 (40.0%)	9 (20.5%)	54 (19.2%)	8 (40.0%)	12 (23.5%)	59 (20.8%)
Dexamethasone	5 (33.3%)	13 (29.5%)	86 (30.6%)	8 (40.0%)	21 (41.2%)	159 (56.2%)
Reason for skipping						
Adverse event	5 (33.3%)	9 (20.5%)	73 (26.0%)	7 (35.0%)	12 (23.5%)	128 (45.2%)
Other	1 (6.7%)	6 (13.6%)	21 (7.5%)	1 (5.0%)	10 (19.6%)	71 (25.1%)
Daratumumab	0	0	0	9 (45.0%)	16 (31.4%)	94 (33.2%)
Reason for skipping						
Adverse event	0	0	0	8 (40.0%)	15 (29.4%)	87 (30.7%)
Other	0	0	0	2 (10.0%)	2 (3.9%)	16 (5.7%)

TSIEXP04_3003: Summary of Treatment Cycle Delays and Reasons for Study Treatment Dose Modifications; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)			DRd n (%)		
	Japanese	East Asian[a]	Total[b]	Japanese	East Asian[a]	Total[b]
Subjects with doses reduced						
Lenalidomide	8 (53.3%)	23 (52.3%)	132 (47.0%)	17 (85.0%)	39 (76.5%)	171 (60.4%)
Reason for reduction						
Adverse event	5 (33.3%)	14 (31.8%)	89 (31.7%)	14 (70.0%)	27 (52.9%)	128 (45.2%)
Other	3 (20.0%)	11 (25.0%)	58 (20.6%)	10 (50.0%)	21 (41.2%)	72 (25.4%)
Dexamethasone	2 (13.3%)	3 (6.8%)	83 (29.5%)	3 (15.0%)	5 (9.8%)	100 (35.3%)
Reason for reduction						
Adverse event	2 (13.3%)	3 (6.8%)	71 (25.3%)	3 (15.0%)	4 (7.8%)	76 (26.9%)
Other	0	0	13 (4.6%)	0	1 (2.0%)	30 (10.6%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Percentages calculated with the number of subjects in each treatment group as denominator.

[TSIEXP04_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSIEXP04_3003.SAS] 30JUN2016, 23:07

表 2.7.4-付録-68 Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

TSFAE08A: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Analysis set: safety	237		243	
Total number of subjects with TEAE leading to dose modifications of bortezomib[a]	129 (54.4%)	72 (30.4%)	155 (63.8%)	82 (33.7%)
MedDRA system organ class/Preferred term				
神経系障害	72 (30.4%)	18 (7.6%)	85 (35.0%)	14 (5.8%)
末梢性感覚ニューロパチー	55 (23.2%)	14 (5.9%)	77 (31.7%)	11 (4.5%)
神経痛	23 (9.7%)	1 (0.4%)	26 (10.7%)	2 (0.8%)
末梢性運動ニューロパチー	5 (2.1%)	2 (0.8%)	6 (2.5%)	0
浮動性めまい	5 (2.1%)	0	2 (0.8%)	0
平衡障害	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
異常感覚	1 (0.4%)	0	1 (0.4%)	0
錯感覚	0	0	2 (0.8%)	0
末梢性感覚運動ニューロパチー	1 (0.4%)	0	1 (0.4%)	0
運動失調	1 (0.4%)	0	0	0
自律神経ニューロパチー	1 (0.4%)	1 (0.4%)	0	0
脳虚血	1 (0.4%)	0	0	0
脳症	1 (0.4%)	1 (0.4%)	0	0
記憶障害	0	0	1 (0.4%)	0
末梢性ニューロパチー	0	0	1 (0.4%)	0
失神寸前の状態	0	0	1 (0.4%)	1 (0.4%)
下肢静止不能症候群	1 (0.4%)	1 (0.4%)	0	0
一過性脳虚血発作	0	0	1 (0.4%)	0
感染症および寄生虫症	33 (13.9%)	22 (9.3%)	41 (16.9%)	23 (9.5%)
肺炎	11 (4.6%)	11 (4.6%)	12 (4.9%)	11 (4.5%)
上気道感染	8 (3.4%)	1 (0.4%)	4 (1.6%)	1 (0.4%)
気管支炎	3 (1.3%)	1 (0.4%)	5 (2.1%)	2 (0.8%)
帯状疱疹	2 (0.8%)	0	4 (1.6%)	3 (1.2%)
インフルエンザ	3 (1.3%)	2 (0.8%)	3 (1.2%)	1 (0.4%)
胃腸炎	2 (0.8%)	2 (0.8%)	1 (0.4%)	0

TSFAE08A: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
細菌感染	1 (0.4%)	0	0	0
気管支肺炎	0	0	1 (0.4%)	0
結膜炎	1 (0.4%)	1 (0.4%)	0	0
精巣上体炎	1 (0.4%)	1 (0.4%)	0	0
丹毒	0	0	1 (0.4%)	0
伝染性紅斑	0	0	1 (0.4%)	0
壊疽	1 (0.4%)	1 (0.4%)	0	0
消化管感染	1 (0.4%)	0	0	0
麦粒腫	0	0	1 (0.4%)	0
下気道感染	0	0	1 (0.4%)	0
メタニューモウイルス感染	0	0	1 (0.4%)	1 (0.4%)
口腔ヘルペス	0	0	1 (0.4%)	0
中耳炎	0	0	1 (0.4%)	1 (0.4%)
腹膜炎	0	0	1 (0.4%)	1 (0.4%)
ニューモシスチス・イロベチイ肺炎	0	0	1 (0.4%)	1 (0.4%)
サイトメガロウイルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
慢性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)
ライノウイルス感染	1 (0.4%)	0	0	0
敗血症	1 (0.4%)	1 (0.4%)	0	0
唾液腺炎	0	0	1 (0.4%)	0
ブドウ球菌性咽頭炎	0	0	1 (0.4%)	0
血液およびリンパ系障害	27 (11.4%)	27 (11.4%)	35 (14.4%)	35 (14.4%)
血小板減少症	26 (11.0%)	26 (11.0%)	32 (13.2%)	32 (13.2%)
好中球減少症	1 (0.4%)	1 (0.4%)	6 (2.5%)	6 (2.5%)
発熱性好中球減少症	0	0	2 (0.8%)	2 (0.8%)
貧血	0	0	1 (0.4%)	1 (0.4%)
白血球減少症	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	9 (3.8%)	4 (1.7%)	19 (7.8%)	6 (2.5%)
下痢	4 (1.7%)	1 (0.4%)	14 (5.8%)	5 (2.1%)
腹痛	2 (0.8%)	1 (0.4%)	2 (0.8%)	0
便秘	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
嘔吐	1 (0.4%)	0	1 (0.4%)	0
腹部不快感	0	0	1 (0.4%)	0

TSFAE08A: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
憩室穿孔	0	0	1 (0.4%)	1 (0.4%)
糞塊	1 (0.4%)	0	0	0
胃炎	1 (0.4%)	1 (0.4%)	0	0
小腸閉塞	0	0	1 (0.4%)	1 (0.4%)
一般・全身障害および投与部位の状態	14 (5.9%)	4 (1.7%)	11 (4.5%)	6 (2.5%)
疲労	7 (3.0%)	2 (0.8%)	5 (2.1%)	5 (2.1%)
発熱	2 (0.8%)	0	4 (1.6%)	1 (0.4%)
インフルエンザ様疾患	2 (0.8%)	0	2 (0.8%)	0
無力症	2 (0.8%)	1 (0.4%)	0	0
全身健康状態低下	1 (0.4%)	1 (0.4%)	0	0
限局性浮腫	1 (0.4%)	0	0	0
疼痛	0	0	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	8 (3.4%)	1 (0.4%)	8 (3.3%)	5 (2.1%)
呼吸困難	3 (1.3%)	0	3 (1.2%)	2 (0.8%)
鼻出血	2 (0.8%)	0	1 (0.4%)	0
喘息	0	0	1 (0.4%)	1 (0.4%)
慢性閉塞性肺疾患	0	0	1 (0.4%)	1 (0.4%)
喀血	0	0	1 (0.4%)	0
胸水	1 (0.4%)	0	0	0
胸膜炎	1 (0.4%)	0	0	0
肺動脈血栓症	0	0	1 (0.4%)	1 (0.4%)
呼吸不全	1 (0.4%)	1 (0.4%)	0	0
代謝および栄養障害	5 (2.1%)	2 (0.8%)	6 (2.5%)	4 (1.6%)
食欲減退	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
低ナトリウム血症	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)
脱水	0	0	1 (0.4%)	1 (0.4%)
高カルシウム血症	1 (0.4%)	0	0	0
高血糖	0	0	1 (0.4%)	0
低カリウム血症	0	0	1 (0.4%)	1 (0.4%)
代謝性アシドーシス	1 (0.4%)	0	0	0
筋骨格系および結合組織障害	4 (1.7%)	2 (0.8%)	7 (2.9%)	3 (1.2%)
四肢痛	3 (1.3%)	1 (0.4%)	4 (1.6%)	1 (0.4%)
骨痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
四肢不快感	0	0	1 (0.4%)	0

TSFAE08A: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
筋肉痛	0	0	1 (0.4%)	1 (0.4%)
血管障害	5 (2.1%)	3 (1.3%)	4 (1.6%)	0
起立性低血圧	2 (0.8%)	1 (0.4%)	2 (0.8%)	0
低血圧	2 (0.8%)	1 (0.4%)	0	0
血腫	0	0	1 (0.4%)	0
高血圧	1 (0.4%)	1 (0.4%)	0	0
血栓性静脈炎	0	0	1 (0.4%)	0
心臓障害	2 (0.8%)	2 (0.8%)	5 (2.1%)	4 (1.6%)
心房細動	1 (0.4%)	1 (0.4%)	3 (1.2%)	2 (0.8%)
急性心筋梗塞	0	0	1 (0.4%)	1 (0.4%)
上室性不整脈	0	0	1 (0.4%)	0
心不全	0	0	1 (0.4%)	1 (0.4%)
心室性期外収縮	1 (0.4%)	1 (0.4%)	0	0
耳および迷路障害	2 (0.8%)	0	3 (1.2%)	0
耳鳴	2 (0.8%)	0	0	0
回転性めまい	0	0	2 (0.8%)	0
乳突洞滲出液	0	0	1 (0.4%)	0
傷害、中毒および処置合併症	2 (0.8%)	0	3 (1.2%)	3 (1.2%)
挫傷	1 (0.4%)	0	0	0
転倒	1 (0.4%)	0	0	0
大腿骨骨折	0	0	1 (0.4%)	1 (0.4%)
上腕骨骨折	0	0	1 (0.4%)	1 (0.4%)
肋骨骨折	0	0	1 (0.4%)	1 (0.4%)
上肢骨折	0	0	1 (0.4%)	1 (0.4%)
腎および尿路障害	2 (0.8%)	0	1 (0.4%)	1 (0.4%)
急性腎不全	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
頻尿	1 (0.4%)	0	0	0
眼障害	0	0	2 (0.8%)	1 (0.4%)
結膜出血	0	0	1 (0.4%)	0
複視	0	0	1 (0.4%)	1 (0.4%)
臨床検査	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
アラニンアミノトランスフェラーゼ増加	0	0	1 (0.4%)	1 (0.4%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.4%)	0

TSFAE08A: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (0.4%)	1 (0.4%)
移行上皮癌	0	0	1 (0.4%)	1 (0.4%)
精神障害	1 (0.4%)	0	0	0
錯乱状態	1 (0.4%)	0	0	0
皮膚および皮下組織障害	1 (0.4%)	0	0	0
皮膚障害	1 (0.4%)	0	0	0

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Includes adverse events leading to bortezomib dose modifications (i.e., dose delays, dose skipping, schedule change or dose reduction).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08A.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\TSFAE08A.SAS] 05APR2016, 16:06

表 2.7.4-付録-69 Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

TSFAE08B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Analysis set: safety	237		243	
Total number of subjects with TEAE leading to dose modifications of dexamethasone[a]	93 (39.2%)	45 (19.0%)	111 (45.7%)	54 (22.2%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	34 (14.3%)	15 (6.3%)	39 (16.0%)	19 (7.8%)
上気道感染	11 (4.6%)	0	8 (3.3%)	1 (0.4%)
肺炎	9 (3.8%)	9 (3.8%)	9 (3.7%)	8 (3.3%)
気管支炎	2 (0.8%)	1 (0.4%)	6 (2.5%)	2 (0.8%)
帯状疱疹	3 (1.3%)	0	4 (1.6%)	3 (1.2%)
インフルエンザ	1 (0.4%)	0	3 (1.2%)	1 (0.4%)
胃腸炎	2 (0.8%)	2 (0.8%)	1 (0.4%)	0
サイトメガロウイルス性肺炎	0	0	2 (0.8%)	2 (0.8%)
鼻炎	1 (0.4%)	0	1 (0.4%)	0
副鼻腔炎	0	0	2 (0.8%)	0
急性副鼻腔炎	1 (0.4%)	0	0	0
細菌感染	1 (0.4%)	0	0	0
気管支肺炎	1 (0.4%)	0	0	0
カンジダ感染	1 (0.4%)	0	0	0
憩室炎	0	0	1 (0.4%)	0
精巣上体炎	1 (0.4%)	1 (0.4%)	0	0
伝染性紅斑	0	0	1 (0.4%)	0
せつ	1 (0.4%)	0	0	0
壊疽	1 (0.4%)	1 (0.4%)	0	0
消化管感染	1 (0.4%)	0	0	0
下気道感染	0	0	1 (0.4%)	0
メタニューモウイルス感染	0	0	1 (0.4%)	1 (0.4%)
鼻咽頭炎	0	0	1 (0.4%)	0
口腔カンジダ症	0	0	1 (0.4%)	0
腹膜炎	0	0	1 (0.4%)	1 (0.4%)

TSFAE08B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)
ライノウイルス感染	1 (0.4%)	0	0	0
敗血症	1 (0.4%)	1 (0.4%)	0	0
唾液腺炎	0	0	1 (0.4%)	0
ブドウ球菌性咽頭炎	0	0	1 (0.4%)	0
神経系障害	24 (10.1%)	4 (1.7%)	17 (7.0%)	5 (2.1%)
末梢性感覚ニューロパチー	9 (3.8%)	2 (0.8%)	7 (2.9%)	1 (0.4%)
浮動性めまい	5 (2.1%)	0	2 (0.8%)	1 (0.4%)
振戦	5 (2.1%)	1 (0.4%)	2 (0.8%)	2 (0.8%)
神経痛	5 (2.1%)	0	1 (0.4%)	0
頭痛	0	0	4 (1.6%)	0
末梢性運動ニューロパチー	2 (0.8%)	0	1 (0.4%)	0
運動失調	1 (0.4%)	0	0	0
自律神経ニューロパチー	1 (0.4%)	1 (0.4%)	0	0
平衡障害	0	0	1 (0.4%)	1 (0.4%)
脳虚血	1 (0.4%)	0	0	0
認知障害	1 (0.4%)	0	0	0
注意力障害	0	0	1 (0.4%)	0
虚血性脳卒中	0	0	1 (0.4%)	1 (0.4%)
腓骨神経麻痺	0	0	1 (0.4%)	0
下肢静止不能症候群	1 (0.4%)	1 (0.4%)	0	0
一過性脳虚血発作	0	0	1 (0.4%)	0
一般・全身障害および投与部位の状態	18 (7.6%)	4 (1.7%)	19 (7.8%)	4 (1.6%)
疲労	8 (3.4%)	2 (0.8%)	4 (1.6%)	2 (0.8%)
発熱	2 (0.8%)	0	7 (2.9%)	1 (0.4%)
浮腫	1 (0.4%)	0	4 (1.6%)	1 (0.4%)
末梢性浮腫	1 (0.4%)	0	4 (1.6%)	0
インフルエンザ様疾患	2 (0.8%)	0	1 (0.4%)	0
無力症	2 (0.8%)	1 (0.4%)	0	0
悪寒	1 (0.4%)	0	0	0
全身健康状態低下	1 (0.4%)	1 (0.4%)	0	0
全身性浮腫	1 (0.4%)	0	0	0
限局性浮腫	1 (0.4%)	0	0	0
倦怠感	0	0	1 (0.4%)	0

TSFAE08B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
疼痛	0	0	1 (0.4%)	0
胃腸障害	14 (5.9%)	3 (1.3%)	15 (6.2%)	5 (2.1%)
下痢	3 (1.3%)	0	8 (3.3%)	1 (0.4%)
腹痛	2 (0.8%)	1 (0.4%)	2 (0.8%)	0
便秘	3 (1.3%)	1 (0.4%)	0	0
消化不良	3 (1.3%)	0	0	0
腹部膨満	0	0	2 (0.8%)	0
胃炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
胃食道逆流性疾患	1 (0.4%)	0	1 (0.4%)	0
嘔吐	1 (0.4%)	0	1 (0.4%)	0
上腹部痛	1 (0.4%)	0	0	0
憩室穿孔	0	0	1 (0.4%)	1 (0.4%)
十二指腸潰瘍	0	0	1 (0.4%)	1 (0.4%)
胃潰瘍	1 (0.4%)	0	0	0
悪心	1 (0.4%)	0	0	0
慢性膵炎	0	0	1 (0.4%)	1 (0.4%)
小腸閉塞	0	0	1 (0.4%)	1 (0.4%)
代謝および栄養障害	12 (5.1%)	6 (2.5%)	13 (5.3%)	8 (3.3%)
高血糖	7 (3.0%)	5 (2.1%)	6 (2.5%)	5 (2.1%)
食欲減退	1 (0.4%)	0	1 (0.4%)	0
糖尿病	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
体液貯留	1 (0.4%)	0	1 (0.4%)	0
脱水	0	0	1 (0.4%)	1 (0.4%)
コントロール不良の糖尿病	0	0	1 (0.4%)	0
糖尿病性ケトアシドーシス	1 (0.4%)	1 (0.4%)	0	0
高カルシウム血症	1 (0.4%)	0	0	0
低アルブミン血症	0	0	1 (0.4%)	0
低カリウム血症	0	0	1 (0.4%)	1 (0.4%)
代謝性アシドーシス	1 (0.4%)	0	0	0
精神障害	12 (5.1%)	2 (0.8%)	12 (4.9%)	2 (0.8%)
不眠症	5 (2.1%)	2 (0.8%)	4 (1.6%)	0
落ち着きのなさ	3 (1.3%)	0	4 (1.6%)	0
激越	2 (0.8%)	0	2 (0.8%)	1 (0.4%)
錯乱状態	1 (0.4%)	0	1 (0.4%)	0

TSFAE08B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
うつ病	2 (0.8%)	0	0	0
転導性	1 (0.4%)	0	1 (0.4%)	0
不安	1 (0.4%)	0	0	0
易刺激性	1 (0.4%)	0	0	0
気分変化	0	0	1 (0.4%)	1 (0.4%)
精神的機能代償不全	0	0	1 (0.4%)	0
物質誘発性精神病性障害	1 (0.4%)	0	0	0
血液およびリンパ系障害	8 (3.4%)	8 (3.4%)	10 (4.1%)	10 (4.1%)
血小板減少症	6 (2.5%)	6 (2.5%)	8 (3.3%)	8 (3.3%)
好中球減少症	0	0	2 (0.8%)	2 (0.8%)
貧血	1 (0.4%)	1 (0.4%)	0	0
発熱性好中球減少症	0	0	1 (0.4%)	1 (0.4%)
白血球減少症	1 (0.4%)	1 (0.4%)	0	0
呼吸器、胸郭および縦隔障害	6 (2.5%)	1 (0.4%)	9 (3.7%)	4 (1.6%)
咳嗽	1 (0.4%)	0	3 (1.2%)	0
呼吸困難	1 (0.4%)	0	3 (1.2%)	1 (0.4%)
喘息	0	0	1 (0.4%)	1 (0.4%)
慢性閉塞性肺疾患	0	0	1 (0.4%)	1 (0.4%)
鼻出血	1 (0.4%)	0	0	0
口腔咽頭痛	0	0	1 (0.4%)	0
胸水	1 (0.4%)	0	0	0
胸膜炎	1 (0.4%)	0	0	0
肺動脈血栓症	0	0	1 (0.4%)	1 (0.4%)
呼吸不全	1 (0.4%)	1 (0.4%)	0	0
筋骨格系および結合組織障害	6 (2.5%)	1 (0.4%)	5 (2.1%)	0
ミオパチー	2 (0.8%)	0	3 (1.2%)	0
筋力低下	3 (1.3%)	1 (0.4%)	1 (0.4%)	0
筋肉痛	1 (0.4%)	0	0	0
骨粗鬆症	0	0	1 (0.4%)	0
心臓障害	2 (0.8%)	2 (0.8%)	8 (3.3%)	4 (1.6%)
心房細動	0	0	2 (0.8%)	1 (0.4%)
心不全	0	0	2 (0.8%)	1 (0.4%)
うっ血性心不全	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
急性冠動脈症候群	0	0	1 (0.4%)	1 (0.4%)

TSFAE08B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
急性心筋梗塞	0	0	1 (0.4%)	1 (0.4%)
上室性不整脈	0	0	1 (0.4%)	0
左脚ブロック	0	0	1 (0.4%)	0
動悸	0	0	1 (0.4%)	0
心室性期外収縮	1 (0.4%)	1 (0.4%)	0	0
内分泌障害	3 (1.3%)	1 (0.4%)	7 (2.9%)	0
クッシング様症状	3 (1.3%)	1 (0.4%)	5 (2.1%)	0
クッシング症候群	0	0	2 (0.8%)	0
傷害、中毒および処置合併症	2 (0.8%)	0	4 (1.6%)	3 (1.2%)
挫傷	1 (0.4%)	0	0	0
転倒	1 (0.4%)	0	0	0
大腿骨骨折	0	0	1 (0.4%)	1 (0.4%)
上腕骨骨折	0	0	1 (0.4%)	1 (0.4%)
肋骨骨折	0	0	1 (0.4%)	1 (0.4%)
上肢骨折	0	0	1 (0.4%)	1 (0.4%)
創傷	0	0	1 (0.4%)	0
眼障害	1 (0.4%)	0	4 (1.6%)	1 (0.4%)
結膜出血	0	0	1 (0.4%)	0
複視	0	0	1 (0.4%)	1 (0.4%)
流涙増加	0	0	1 (0.4%)	0
霧視	1 (0.4%)	0	0	0
視力障害	0	0	1 (0.4%)	0
血管障害	3 (1.3%)	3 (1.3%)	2 (0.8%)	1 (0.4%)
起立性低血圧	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
循環虚脱	1 (0.4%)	1 (0.4%)	0	0
高血圧	1 (0.4%)	1 (0.4%)	0	0
高血圧クリーゼ	0	0	1 (0.4%)	1 (0.4%)
耳および迷路障害	1 (0.4%)	0	3 (1.2%)	0
回転性めまい	0	0	2 (0.8%)	0
乳突洞滲出液	0	0	1 (0.4%)	0
耳鳴	1 (0.4%)	0	0	0
臨床検査	1 (0.4%)	0	3 (1.2%)	0
体重増加	1 (0.4%)	0	3 (1.2%)	0
皮膚および皮下組織障害	0	0	1 (0.4%)	0

TSFAE08B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd		DVd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
紅斑	0	0	1 (0.4%)	0

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Includes adverse events leading to dexamethasone dose modifications (i.e., dose delays, dose skipping or dose reduction).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08B.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\TSFAE08B.SAS] 05APR2016, 16:06

表 2.7.4-付録-70 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Analysis set: safety	281		283	
Total number of subjects with TEAE leading to lenalidomide dose modifications[a]	153 (54.4%)	112 (39.9%)	200 (70.7%)	150 (53.0%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	80 (28.5%)	68 (24.2%)	111 (39.2%)	104 (36.7%)
好中球減少症	63 (22.4%)	57 (20.3%)	97 (34.3%)	93 (32.9%)
血小板減少症	17 (6.0%)	11 (3.9%)	21 (7.4%)	15 (5.3%)
貧血	14 (5.0%)	9 (3.2%)	10 (3.5%)	2 (0.7%)
発熱性好中球減少症	5 (1.8%)	5 (1.8%)	10 (3.5%)	10 (3.5%)
白血球減少症	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
リンパ球減少症	0	0	2 (0.7%)	2 (0.7%)
出血性障害	1 (0.4%)	0	0	0
リンパ節症	0	0	1 (0.4%)	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	1 (0.4%)	1 (0.4%)	0	0
感染症および寄生虫症	45 (16.0%)	26 (9.3%)	64 (22.6%)	36 (12.7%)
肺炎	12 (4.3%)	8 (2.8%)	13 (4.6%)	11 (3.9%)
上気道感染	7 (2.5%)	1 (0.4%)	8 (2.8%)	2 (0.7%)
気道感染	4 (1.4%)	0	6 (2.1%)	2 (0.7%)
気管支炎	5 (1.8%)	2 (0.7%)	4 (1.4%)	0
インフルエンザ	3 (1.1%)	1 (0.4%)	5 (1.8%)	3 (1.1%)
下気道感染	2 (0.7%)	2 (0.7%)	4 (1.4%)	1 (0.4%)
鼻咽頭炎	0	0	4 (1.4%)	0
肺感染	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
尿路感染	1 (0.4%)	0	2 (0.7%)	2 (0.7%)
虫垂炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細気管支炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0
胃腸炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
帯状疱疹	2 (0.7%)	1 (0.4%)	0	0
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
耳下腺炎	0	0	2 (0.7%)	0
インフルエンザ性肺炎	0	0	2 (0.7%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
敗血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
急性副鼻腔炎	0	0	1 (0.4%)	0
細菌感染	0	0	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	1 (0.4%)	0
ウイルス性気管支炎	1 (0.4%)	1 (0.4%)	0	0
気管支肺炎	0	0	1 (0.4%)	1 (0.4%)
ウイルス性腸炎	0	0	1 (0.4%)	0
喉頭蓋炎	0	0	1 (0.4%)	1 (0.4%)
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	0	0
消化管感染	1 (0.4%)	1 (0.4%)	0	0
歯肉炎	0	0	1 (0.4%)	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0
感染	1 (0.4%)	1 (0.4%)	0	0
リステリア性敗血症	0	0	1 (0.4%)	1 (0.4%)
鼻膿瘍	0	0	1 (0.4%)	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	1 (0.4%)
咽頭炎	1 (0.4%)	1 (0.4%)	0	0
細菌性肺炎	1 (0.4%)	0	0	0
ヘモフィルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
レンサ球菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
急性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)
鼻炎	0	0	1 (0.4%)	0
サルモネラ性菌血症	0	0	1 (0.4%)	1 (0.4%)
副鼻腔炎	0	0	1 (0.4%)	0
細菌性上気道感染	0	0	1 (0.4%)	1 (0.4%)
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0
一般・全身障害および投与部位の状態	13 (4.6%)	9 (3.2%)	41 (14.5%)	20 (7.1%)

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
疲労	4 (1.4%)	3 (1.1%)	24 (8.5%)	12 (4.2%)
発熱	2 (0.7%)	1 (0.4%)	10 (3.5%)	2 (0.7%)
無力症	4 (1.4%)	4 (1.4%)	7 (2.5%)	5 (1.8%)
倦怠感	1 (0.4%)	0	3 (1.1%)	1 (0.4%)
悪寒	0	0	2 (0.7%)	0
末梢性浮腫	2 (0.7%)	1 (0.4%)	0	0
胸部不快感	0	0	1 (0.4%)	0
胸痛	1 (0.4%)	0	0	0
全身性浮腫	1 (0.4%)	0	0	0
全身性炎症反応症候群	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	14 (5.0%)	6 (2.1%)	31 (11.0%)	12 (4.2%)
下痢	9 (3.2%)	5 (1.8%)	21 (7.4%)	6 (2.1%)
悪心	0	0	6 (2.1%)	2 (0.7%)
嘔吐	3 (1.1%)	1 (0.4%)	3 (1.1%)	0
便秘	0	0	3 (1.1%)	2 (0.7%)
上腹部痛	1 (0.4%)	0	0	0
肛門出血	0	0	1 (0.4%)	1 (0.4%)
大腸炎	1 (0.4%)	1 (0.4%)	0	0
憩室穿孔	0	0	1 (0.4%)	1 (0.4%)
嚥下障害	0	0	1 (0.4%)	0
出血性胃腸管血管異形成	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	0	0	1 (0.4%)	0
鼠径ヘルニア	0	0	1 (0.4%)	0
下部消化管出血	1 (0.4%)	0	0	0
腎および尿路障害	11 (3.9%)	3 (1.1%)	18 (6.4%)	1 (0.4%)
腎機能障害	7 (2.5%)	0	16 (5.7%)	0
急性腎不全	2 (0.7%)	1 (0.4%)	0	0
慢性腎臓病	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
腎不全	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
神経系障害	12 (4.3%)	4 (1.4%)	14 (4.9%)	6 (2.1%)
末梢性ニューロパチー	2 (0.7%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
末梢性感覚ニューロパチー	3 (1.1%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
失神	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
振戦	1 (0.4%)	0	1 (0.4%)	0

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
脳梗塞	1 (0.4%)	1 (0.4%)	0	0
脳血管発作	0	0	1 (0.4%)	1 (0.4%)
認知障害	0	0	1 (0.4%)	1 (0.4%)
注意力障害	1 (0.4%)	0	0	0
浮動性めまい	1 (0.4%)	0	0	0
体位性めまい	0	0	1 (0.4%)	0
知覚過敏	0	0	1 (0.4%)	0
感覚鈍麻	0	0	1 (0.4%)	0
意識消失	1 (0.4%)	0	0	0
不随意性筋収縮	1 (0.4%)	0	0	0
失神寸前の状態	0	0	1 (0.4%)	0
痙攣発作	0	0	1 (0.4%)	0
傾眠	1 (0.4%)	0	0	0
一過性脳虚血発作	0	0	1 (0.4%)	0
三叉神経障害	0	0	1 (0.4%)	0
臨床検査	10 (3.6%)	1 (0.4%)	15 (5.3%)	6 (2.1%)
血中クレアチニン増加	6 (2.1%)	0	6 (2.1%)	0
アラニンアミノトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	8 (2.8%)	4 (1.4%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	4 (1.4%)	2 (0.7%)
腎クレアチニン・クリアランス減少	2 (0.7%)	0	1 (0.4%)	0
血中アルカリホスファターゼ増加	0	0	2 (0.7%)	1 (0.4%)
γ－グルタミルトランスフェラーゼ増加	0	0	2 (0.7%)	2 (0.7%)
糸球体濾過率減少	2 (0.7%)	0	0	0
血中乳酸脱水素酵素増加	0	0	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	9 (3.2%)	5 (1.8%)	15 (5.3%)	6 (2.1%)
肺塞栓症	3 (1.1%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
咳嗽	2 (0.7%)	0	2 (0.7%)	0
呼吸困難	2 (0.7%)	0	2 (0.7%)	2 (0.7%)
慢性閉塞性肺疾患	0	0	2 (0.7%)	1 (0.4%)
湿性咳嗽	1 (0.4%)	0	1 (0.4%)	0
急性肺水腫	0	0	1 (0.4%)	1 (0.4%)
急性呼吸不全	1 (0.4%)	1 (0.4%)	0	0
労作性呼吸困難	0	0	1 (0.4%)	0
低酸素症	0	0	1 (0.4%)	0

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
喉頭浮腫	0	0	1 (0.4%)	0
肺障害	1 (0.4%)	1 (0.4%)	0	0
肺腫瘤	0	0	1 (0.4%)	0
肺水腫	0	0	1 (0.4%)	1 (0.4%)
代謝および栄養障害	4 (1.4%)	2 (0.7%)	11 (3.9%)	4 (1.4%)
高血糖	1 (0.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
脱水	0	0	3 (1.1%)	0
食欲減退	1 (0.4%)	0	1 (0.4%)	0
低カリウム血症	2 (0.7%)	1 (0.4%)	0	0
食物不耐性	0	0	1 (0.4%)	0
低カルシウム血症	0	0	1 (0.4%)	1 (0.4%)
低ナトリウム血症	0	0	1 (0.4%)	1 (0.4%)
低リン酸血症	0	0	1 (0.4%)	0
筋骨格系および結合組織障害	7 (2.5%)	3 (1.1%)	8 (2.8%)	3 (1.1%)
筋痙縮	5 (1.8%)	2 (0.7%)	6 (2.1%)	2 (0.7%)
関節痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
背部痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
側腹部痛	0	0	1 (0.4%)	0
筋力低下	1 (0.4%)	0	0	0
四肢痛	1 (0.4%)	1 (0.4%)	0	0
脊椎痛	1 (0.4%)	1 (0.4%)	0	0
皮膚および皮下組織障害	6 (2.1%)	0	9 (3.2%)	5 (1.8%)
発疹	1 (0.4%)	0	4 (1.4%)	0
全身性皮疹	0	0	2 (0.7%)	1 (0.4%)
斑状皮疹	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
斑状丘疹状皮疹	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
薬疹	0	0	1 (0.4%)	1 (0.4%)
多汗症	1 (0.4%)	0	0	0
寝汗	1 (0.4%)	0	0	0
そう痒症	0	0	1 (0.4%)	1 (0.4%)
壊疽性膿皮症	1 (0.4%)	0	0	0
蕁麻疹	0	0	1 (0.4%)	1 (0.4%)
血管障害	6 (2.1%)	4 (1.4%)	9 (3.2%)	2 (0.7%)
深部静脈血栓症	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
低血圧	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
静脈炎	0	0	2 (0.7%)	0
血栓症	0	0	2 (0.7%)	1 (0.4%)
塞栓症	0	0	1 (0.4%)	0
起立性低血圧	1 (0.4%)	1 (0.4%)	0	0
血栓性静脈炎	0	0	1 (0.4%)	0
表在性血栓性静脈炎	0	0	1 (0.4%)	0
静脈血栓症	0	0	1 (0.4%)	0
心臓障害	3 (1.1%)	3 (1.1%)	7 (2.5%)	4 (1.4%)
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
狭心症	0	0	1 (0.4%)	1 (0.4%)
心房細動	0	0	1 (0.4%)	0
心房粗動	0	0	1 (0.4%)	0
心アミロイドーシス	0	0	1 (0.4%)	0
うっ血性心不全	0	0	1 (0.4%)	1 (0.4%)
心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
洞性不整脈	0	0	1 (0.4%)	1 (0.4%)
洞性頻脈	0	0	1 (0.4%)	1 (0.4%)
上室性頻脈	1 (0.4%)	1 (0.4%)	0	0
肝胆道系障害	0	0	3 (1.1%)	2 (0.7%)
高ビリルビン血症	0	0	2 (0.7%)	2 (0.7%)
肝機能異常	0	0	1 (0.4%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.7%)	0	1 (0.4%)	0
基底細胞癌	0	0	1 (0.4%)	0
形質細胞性白血病	1 (0.4%)	0	0	0
扁平上皮癌	1 (0.4%)	0	0	0
精神障害	2 (0.7%)	2 (0.7%)	1 (0.4%)	0
錯乱状態	1 (0.4%)	1 (0.4%)	0	0
譫妄	1 (0.4%)	1 (0.4%)	0	0
うつ病	0	0	1 (0.4%)	0
耳および迷路障害	0	0	2 (0.7%)	0
耳鳴	0	0	1 (0.4%)	0
回転性めまい	0	0	1 (0.4%)	0

TSFAE08A: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
関節脱臼	1 (0.4%)	1 (0.4%)	0	0
脊椎圧迫骨折	0	0	1 (0.4%)	0
生殖系および乳房障害	1 (0.4%)	0	0	0
前立腺炎	1 (0.4%)	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Includes adverse events leading to lenalidomide dose modifications (i.e., dose delays, dose skipping, or dose reduction).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08A.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_CSR\PROD\TSFAE08A.SAS] 13MAY2016, 14:52

表 2.7.4-付録-71 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Analysis set: safety	281		283	
Total number of subjects with TEAE leading to dexamethasone dose modifications[a]	125 (44.5%)	64 (22.8%)	165 (58.3%)	87 (30.7%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	41 (14.6%)	21 (7.5%)	67 (23.7%)	38 (13.4%)
肺炎	9 (3.2%)	7 (2.5%)	11 (3.9%)	9 (3.2%)
気管支炎	6 (2.1%)	1 (0.4%)	8 (2.8%)	1 (0.4%)
上気道感染	5 (1.8%)	0	6 (2.1%)	2 (0.7%)
インフルエンザ	3 (1.1%)	1 (0.4%)	7 (2.5%)	4 (1.4%)
気道感染	4 (1.4%)	0	5 (1.8%)	1 (0.4%)
下気道感染	1 (0.4%)	0	5 (1.8%)	2 (0.7%)
鼻咽頭炎	2 (0.7%)	0	2 (0.7%)	0
尿路感染	1 (0.4%)	0	3 (1.1%)	2 (0.7%)
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
肺感染	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
虫垂炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
気管支肺炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0
胃腸炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
耳下腺炎	0	0	2 (0.7%)	0
細菌性肺炎	1 (0.4%)	0	1 (0.4%)	0
インフルエンザ性肺炎	0	0	2 (0.7%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
鼻炎	0	0	2 (0.7%)	0
敗血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細菌感染	0	0	1 (0.4%)	1 (0.4%)
細気管支炎	0	0	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	1 (0.4%)	0
ウイルス性気管支炎	1 (0.4%)	1 (0.4%)	0	0

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
蜂巣炎	1 (0.4%)	1 (0.4%)	0	0
ウイルス性腸炎	0	0	1 (0.4%)	0
喉頭蓋炎	0	0	1 (0.4%)	1 (0.4%)
歯肉炎	0	0	1 (0.4%)	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0
帯状疱疹	1 (0.4%)	0	0	0
感染	0	0	1 (0.4%)	0
リステリア性敗血症	0	0	1 (0.4%)	1 (0.4%)
鼻膿瘍	0	0	1 (0.4%)	1 (0.4%)
好中球減少性敗血症	0	0	1 (0.4%)	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	0	0	1 (0.4%)	1 (0.4%)
咽頭炎	1 (0.4%)	1 (0.4%)	0	0
ヘモフィルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)
サルモネラ性菌血症	0	0	1 (0.4%)	1 (0.4%)
敗血症性ショック	0	0	1 (0.4%)	1 (0.4%)
細菌性上気道感染	0	0	1 (0.4%)	1 (0.4%)
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0
水痘	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	1 (0.4%)	0	0
精神障害	35 (12.5%)	6 (2.1%)	31 (11.0%)	3 (1.1%)
不眠症	13 (4.6%)	1 (0.4%)	11 (3.9%)	1 (0.4%)
不安	5 (1.8%)	2 (0.7%)	4 (1.4%)	1 (0.4%)
激越	4 (1.4%)	1 (0.4%)	4 (1.4%)	0
気分変化	4 (1.4%)	0	2 (0.7%)	1 (0.4%)
神経過敏	5 (1.8%)	1 (0.4%)	0	0
うつ病	0	0	4 (1.4%)	0
易刺激性	2 (0.7%)	0	2 (0.7%)	0
精神障害	1 (0.4%)	0	2 (0.7%)	0
落ち着きのなさ	1 (0.4%)	0	2 (0.7%)	0
抑うつ気分	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
気分動揺	0	0	2 (0.7%)	0

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
睡眠障害	0	0	2 (0.7%)	0
譫妄	1 (0.4%)	1 (0.4%)	0	0
気分変調性障害	1 (0.4%)	0	0	0
精神病性障害	1 (0.4%)	0	0	0
血液およびリンパ系障害	23 (8.2%)	19 (6.8%)	27 (9.5%)	26 (9.2%)
好中球減少症	12 (4.3%)	12 (4.3%)	20 (7.1%)	19 (6.7%)
発熱性好中球減少症	4 (1.4%)	4 (1.4%)	8 (2.8%)	8 (2.8%)
貧血	6 (2.1%)	4 (1.4%)	3 (1.1%)	1 (0.4%)
血小板減少症	6 (2.1%)	3 (1.1%)	3 (1.1%)	2 (0.7%)
白血球減少症	1 (0.4%)	0	0	0
リンパ節症	0	0	1 (0.4%)	0
リンパ球減少症	1 (0.4%)	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	1 (0.4%)	1 (0.4%)	0	0
一般・全身障害および投与部位の状態	20 (7.1%)	7 (2.5%)	28 (9.9%)	7 (2.5%)
疲労	9 (3.2%)	2 (0.7%)	14 (4.9%)	3 (1.1%)
発熱	3 (1.1%)	1 (0.4%)	6 (2.1%)	1 (0.4%)
無力症	4 (1.4%)	3 (1.1%)	4 (1.4%)	2 (0.7%)
末梢性浮腫	3 (1.1%)	1 (0.4%)	0	0
薬物不耐性	0	0	2 (0.7%)	0
顔面浮腫	2 (0.7%)	0	0	0
倦怠感	0	0	2 (0.7%)	1 (0.4%)
胸痛	1 (0.4%)	0	0	0
脂肪組織増加	0	0	1 (0.4%)	0
歩行障害	0	0	1 (0.4%)	0
全身健康状態低下	0	0	1 (0.4%)	0
全身性浮腫	1 (0.4%)	0	0	0
インフルエンザ様疾患	0	0	1 (0.4%)	0
末梢腫脹	1 (0.4%)	0	0	0
筋骨格系および結合組織障害	16 (5.7%)	2 (0.7%)	22 (7.8%)	3 (1.1%)
筋力低下	9 (3.2%)	0	14 (4.9%)	0
筋痙縮	5 (1.8%)	1 (0.4%)	3 (1.1%)	1 (0.4%)
ミオパチー	2 (0.7%)	0	2 (0.7%)	0
筋萎縮症	0	0	1 (0.4%)	1 (0.4%)
背部痛	0	0	1 (0.4%)	1 (0.4%)

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
関節腫脹	0	0	1 (0.4%)	0
四肢痛	0	0	1 (0.4%)	0
脊椎痛	1 (0.4%)	1 (0.4%)	0	0
神経系障害	17 (6.0%)	2 (0.7%)	12 (4.2%)	3 (1.1%)
振戦	6 (2.1%)	0	6 (2.1%)	1 (0.4%)
浮動性めまい	2 (0.7%)	0	1 (0.4%)	0
感覚鈍麻	1 (0.4%)	0	1 (0.4%)	0
錯感覚	0	0	2 (0.7%)	0
労作性めまい	1 (0.4%)	0	0	0
頭痛	1 (0.4%)	0	0	0
意識消失	1 (0.4%)	0	0	0
記憶障害	1 (0.4%)	1 (0.4%)	0	0
神経系障害	0	0	1 (0.4%)	1 (0.4%)
末梢性ニューロパチー	1 (0.4%)	1 (0.4%)	0	0
末梢性感覚ニューロパチー	1 (0.4%)	0	0	0
精神運動亢進	1 (0.4%)	0	0	0
失神	0	0	1 (0.4%)	1 (0.4%)
一過性脳虚血発作	0	0	1 (0.4%)	0
第７脳神経麻痺	1 (0.4%)	0	0	0
代謝および栄養障害	11 (3.9%)	6 (2.1%)	15 (5.3%)	10 (3.5%)
高血糖	7 (2.5%)	4 (1.4%)	13 (4.6%)	8 (2.8%)
低カリウム血症	3 (1.1%)	2 (0.7%)	0	0
食欲減退	1 (0.4%)	0	1 (0.4%)	0
低カルシウム血症	0	0	2 (0.7%)	1 (0.4%)
糖尿病	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	10 (3.6%)	4 (1.4%)	15 (5.3%)	4 (1.4%)
下痢	4 (1.4%)	3 (1.1%)	5 (1.8%)	2 (0.7%)
嘔吐	3 (1.1%)	1 (0.4%)	1 (0.4%)	0
上腹部痛	0	0	2 (0.7%)	0
大腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
悪心	0	0	2 (0.7%)	0
腹部不快感	0	0	1 (0.4%)	0
腹痛	1 (0.4%)	0	0	0
憩室穿孔	0	0	1 (0.4%)	1 (0.4%)

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
口内乾燥	1 (0.4%)	0	0	0
心窩部不快感	0	0	1 (0.4%)	0
胃炎	0	0	1 (0.4%)	0
鼠径ヘルニア	0	0	1 (0.4%)	0
下部消化管出血	1 (0.4%)	0	0	0
口腔内潰瘍形成	0	0	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	8 (2.8%)	3 (1.1%)	8 (2.8%)	4 (1.4%)
呼吸困難	4 (1.4%)	0	1 (0.4%)	0
咳嗽	2 (0.7%)	0	2 (0.7%)	0
肺塞栓症	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
肺障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
肺水腫	0	0	2 (0.7%)	2 (0.7%)
無気肺	1 (0.4%)	1 (0.4%)	0	0
低酸素症	0	0	1 (0.4%)	0
湿性咳嗽	1 (0.4%)	0	0	0
血管障害	5 (1.8%)	2 (0.7%)	8 (2.8%)	0
潮紅	2 (0.7%)	0	2 (0.7%)	0
深部静脈血栓症	3 (1.1%)	2 (0.7%)	0	0
低血圧	0	0	2 (0.7%)	0
塞栓症	0	0	1 (0.4%)	0
高血圧	1 (0.4%)	0	0	0
静脈炎	0	0	1 (0.4%)	0
血栓性静脈炎	0	0	1 (0.4%)	0
表在性血栓性静脈炎	0	0	1 (0.4%)	0
静脈血栓症	0	0	1 (0.4%)	0
皮膚および皮下組織障害	6 (2.1%)	0	5 (1.8%)	1 (0.4%)
多汗症	3 (1.1%)	0	1 (0.4%)	0
発疹	2 (0.7%)	0	0	0
紅斑	1 (0.4%)	0	0	0
毛髪成長異常	0	0	1 (0.4%)	0
男性型多毛症	0	0	1 (0.4%)	0
寝汗	1 (0.4%)	0	0	0
点状出血	0	0	1 (0.4%)	0
そう痒症	1 (0.4%)	0	0	0

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
全身性皮疹	0	0	1 (0.4%)	1 (0.4%)
顔面腫脹	0	0	1 (0.4%)	0
心臓障害	4 (1.4%)	2 (0.7%)	6 (2.1%)	3 (1.1%)
心房細動	1 (0.4%)	0	1 (0.4%)	0
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
狭心症	0	0	1 (0.4%)	1 (0.4%)
心房粗動	0	0	1 (0.4%)	0
徐脈	0	0	1 (0.4%)	0
心アミロイドーシス	0	0	1 (0.4%)	0
心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
心嚢液貯留	1 (0.4%)	0	0	0
洞性不整脈	0	0	1 (0.4%)	1 (0.4%)
洞性頻脈	0	0	1 (0.4%)	1 (0.4%)
眼障害	2 (0.7%)	0	5 (1.8%)	1 (0.4%)
白内障	1 (0.4%)	0	4 (1.4%)	1 (0.4%)
霧視	1 (0.4%)	0	1 (0.4%)	0
水晶体混濁	1 (0.4%)	0	0	0
内分泌障害	3 (1.1%)	1 (0.4%)	2 (0.7%)	0
クッシング様症状	2 (0.7%)	0	1 (0.4%)	0
高コルチコイド症	0	0	1 (0.4%)	0
ステロイド離脱症候群	1 (0.4%)	1 (0.4%)	0	0
臨床検査	1 (0.4%)	0	4 (1.4%)	3 (1.1%)
アラニンアミノトランスフェラーゼ増加	0	0	4 (1.4%)	2 (0.7%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	3 (1.1%)	1 (0.4%)
γ－グルタミルトランスフェラーゼ増加	0	0	2 (0.7%)	2 (0.7%)
血中アルカリホスファターゼ増加	0	0	1 (0.4%)	0
血中クレアチニン増加	1 (0.4%)	0	0	0
傷害、中毒および処置合併症	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
各種物質毒性	1 (0.4%)	0	1 (0.4%)	0
関節脱臼	1 (0.4%)	1 (0.4%)	0	0
腎および尿路障害	1 (0.4%)	0	2 (0.7%)	1 (0.4%)
急性腎不全	1 (0.4%)	0	1 (0.4%)	0
腎不全	0	0	1 (0.4%)	1 (0.4%)
肝胆道系障害	0	0	2 (0.7%)	1 (0.4%)

TSFAE08B: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
肝機能異常	0	0	1 (0.4%)	0
高ビリルビン血症	0	0	1 (0.4%)	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	0	1 (0.4%)	0
基底細胞癌	0	0	1 (0.4%)	0
扁平上皮癌	1 (0.4%)	0	0	0
生殖系および乳房障害	1 (0.4%)	0	1 (0.4%)	0
前立腺炎	1 (0.4%)	0	1 (0.4%)	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Includes adverse events leading to dexamethasone dose modifications (i.e., dose delays, dose skipping, or dose reduction).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08B.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_CSR\PROD\TSFAE08B.SAS] 13MAY2016, 14:52

表 2.7.4-付録-72 Treatment-emergent Adverse Events Leading to Pomalidomide Dose Modifications by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1001)

TSFAE09DP2: Treatment-emergent Adverse Events Leading to Pomalidomide Dose Modifications by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1001)

	D-Pom-dex	
	All Grades	Grade 3 or 4
Analysis set: safety	103	
Total number of subjects with TEAE leading to Pomalidomide dose modifications[a]	75 (72.8%)	69 (67.0%)
MedDRA system organ class/Preferred term		
血液およびリンパ系障害	55 (53.4%)	52 (50.5%)
好中球減少症	49 (47.6%)	48 (46.6%)
白血球減少症	8 (7.8%)	7 (6.8%)
血小板減少症	7 (6.8%)	6 (5.8%)
貧血	5 (4.9%)	3 (2.9%)
発熱性好中球減少症	5 (4.9%)	5 (4.9%)
感染症および寄生虫症	15 (14.6%)	12 (11.7%)
上気道感染	3 (2.9%)	1 (1.0%)
肺炎	2 (1.9%)	2 (1.9%)
敗血症	2 (1.9%)	2 (1.9%)
クロストリジウム・ディフィシレ大腸炎	1 (1.0%)	1 (1.0%)
コロナウイルス感染	1 (1.0%)	0
胃腸炎	1 (1.0%)	0
帯状疱疹	1 (1.0%)	1 (1.0%)
インフルエンザ	1 (1.0%)	1 (1.0%)
肺感染	1 (1.0%)	1 (1.0%)
シュードモナス性敗血症	1 (1.0%)	1 (1.0%)
ＲＳウイルス感染	1 (1.0%)	0
脊髄感染	1 (1.0%)	1 (1.0%)
歯感染	1 (1.0%)	1 (1.0%)
一般・全身障害および投与部位の状態	11 (10.7%)	6 (5.8%)
疲労	7 (6.8%)	6 (5.8%)
発熱	3 (2.9%)	0
末梢性浮腫	2 (1.9%)	1 (1.0%)
無力症	1 (1.0%)	0
呼吸器、胸郭および縦隔障害	9 (8.7%)	4 (3.9%)
呼吸困難	3 (2.9%)	1 (1.0%)
気管支肺症	1 (1.0%)	1 (1.0%)
慢性閉塞性肺疾患	1 (1.0%)	0
発声障害	1 (1.0%)	1 (1.0%)
しゃっくり	1 (1.0%)	1 (1.0%)
間質性肺疾患	1 (1.0%)	1 (1.0%)
咽喉刺激感	1 (1.0%)	0
喘鳴	1 (1.0%)	0
神経系障害	8 (7.8%)	5 (4.9%)
錯感覚	2 (1.9%)	0
末梢性感覚ニューロパチー	2 (1.9%)	2 (1.9%)
異痛症	1 (1.0%)	0
運動失調	1 (1.0%)	1 (1.0%)
浮動性めまい	1 (1.0%)	1 (1.0%)
感覚鈍麻	1 (1.0%)	0
末梢性ニューロパチー	1 (1.0%)	1 (1.0%)
失神寸前の状態	1 (1.0%)	0
皮膚および皮下組織障害	7 (6.8%)	4 (3.9%)
発疹	2 (1.9%)	0
全身性皮疹	2 (1.9%)	2 (1.9%)
ざ瘡様皮膚炎	1 (1.0%)	0
薬疹	1 (1.0%)	0
多形紅斑	1 (1.0%)	1 (1.0%)
そう痒症	1 (1.0%)	1 (1.0%)

TSFAE09DP2: Treatment-emergent Adverse Events Leading to Pomalidomide Dose Modifications by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1001)

	D-Pom-dex	
	All Grades	Grade 3 or 4
胃腸障害	4 (3.9%)	2 (1.9%)
腹痛	1 (1.0%)	0
下痢	1 (1.0%)	1 (1.0%)
小腸閉塞	1 (1.0%)	1 (1.0%)
嘔吐	1 (1.0%)	0
代謝および栄養障害	4 (3.9%)	3 (2.9%)
食欲減退	1 (1.0%)	0
高カルシウム血症	1 (1.0%)	1 (1.0%)
高血糖	1 (1.0%)	1 (1.0%)
低ナトリウム血症	1 (1.0%)	1 (1.0%)
臨床検査	3 (2.9%)	3 (2.9%)
アスパラギン酸アミノトランスフェラーゼ増加	3 (2.9%)	2 (1.9%)
アラニンアミノトランスフェラーゼ増加	2 (1.9%)	2 (1.9%)
血中アルカリホスファターゼ増加	2 (1.9%)	0
肝胆道系障害	2 (1.9%)	1 (1.0%)
高ビリルビン血症	2 (1.9%)	1 (1.0%)
傷害、中毒および処置合併症	2 (1.9%)	2 (1.9%)
転倒	1 (1.0%)	1 (1.0%)
大腿骨骨折	1 (1.0%)	1 (1.0%)
上肢骨折	1 (1.0%)	1 (1.0%)
精神障害	2 (1.9%)	2 (1.9%)
錯乱状態	2 (1.9%)	2 (1.9%)
血管障害	2 (1.9%)	2 (1.9%)
大動脈解離	1 (1.0%)	1 (1.0%)
血腫	1 (1.0%)	1 (1.0%)
心臓障害	1 (1.0%)	0
動悸	1 (1.0%)	0
免疫系障害	1 (1.0%)	0
サイトカイン放出症候群	1 (1.0%)	0
筋骨格系および結合組織障害	1 (1.0%)	0
関節痛	1 (1.0%)	0

Keys: TEAE = Treatment-emergent adverse event; D-Pom-dex = daratumumab-pomalidomide-dexamethasone
[a]Includes adverse events leading to pomalidomide dose modifications (i.e., dose delays, dose skip, dose re-escalation, or dose reduction).
Note: Adverse events are reported using MedDRA version 18.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE09DP2.RTF] [JNJ-54767414\MMY1001\DBR_SBLA_2016\RE_SBLA_2016\PROD\TSFAE09DP2.SAS] 05MAY2016, 19:11

表 2.7.4-付録-73 Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE18A: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Bortezomib by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to dose modifications of bortezomib	8 (100.0%)	6 (75.0%)	0
MedDRA system organ class/Preferred term			
血液およびリンパ系障害	4 (50.0%)	4 (50.0%)	0
血小板減少症	4 (50.0%)	4 (50.0%)	0
一般・全身障害および投与部位の状態	2 (25.0%)	1 (12.5%)	0
疲労	2 (25.0%)	1 (12.5%)	0
感染症および寄生虫症	2 (25.0%)	2 (25.0%)	0
帯状疱疹	1 (12.5%)	1 (12.5%)	0
鼻咽頭炎	1 (12.5%)	1 (12.5%)	0
神経系障害	2 (25.0%)	0	0
神経痛	1 (12.5%)	0	0
末梢性感覚ニューロパチー	1 (12.5%)	0	0
代謝および栄養障害	1 (12.5%)	0	0
脱水	1 (12.5%)	0	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE18A.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE18A.SAS] 28SEP2016, 04:19

表 2.7.4-付録-74 Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE18B: Number of Subjects with 1 or More Treatment-emergent Adverse Events Leading to Dose Modifications of Dexamethasone by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to dose modifications of dexamethasone	7 (87.5%)	4 (50.0%)	0
MedDRA system organ class/Preferred term			
代謝および栄養障害	3 (37.5%)	2 (25.0%)	0
高血糖	2 (25.0%)	2 (25.0%)	0
脱水	1 (12.5%)	0	0
胃腸障害	2 (25.0%)	0	0
腹部膨満	1 (12.5%)	0	0
消化不良	1 (12.5%)	0	0
胃炎	1 (12.5%)	0	0
筋骨格系および結合組織障害	2 (25.0%)	0	0
筋力低下	1 (12.5%)	0	0
ミオパチー	1 (12.5%)	0	0
感染症および寄生虫症	1 (12.5%)	1 (12.5%)	0
鼻咽頭炎	1 (12.5%)	1 (12.5%)	0
臨床検査	1 (12.5%)	1 (12.5%)	0
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0
神経系障害	1 (12.5%)	0	0
ヘルペス後神経痛	1 (12.5%)	0	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE18B.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE18B.SAS] 28SEP2016, 04:20

表 2.7.4-付録-75 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Total[a]				
Analysis set: safety	281		283	
Total number of subjects with TEAE leading to Lenalidomide dose modifications[c]	153 (54.4%)	112 (39.9%)	200 (70.7%)	150 (53.0%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	80 (28.5%)	68 (24.2%)	111 (39.2%)	104 (36.7%)
好中球減少症	63 (22.4%)	57 (20.3%)	97 (34.3%)	93 (32.9%)
血小板減少症	17 (6.0%)	11 (3.9%)	21 (7.4%)	15 (5.3%)
貧血	14 (5.0%)	9 (3.2%)	10 (3.5%)	2 (0.7%)
発熱性好中球減少症	5 (1.8%)	5 (1.8%)	10 (3.5%)	10 (3.5%)
リンパ球減少症	0	0	2 (0.7%)	2 (0.7%)
白血球減少症	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
リンパ節症	0	0	1 (0.4%)	0
出血性障害	1 (0.4%)	0	0	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	1 (0.4%)	1 (0.4%)	0	0
感染症および寄生虫症	45 (16.0%)	26 (9.3%)	64 (22.6%)	36 (12.7%)
肺炎	12 (4.3%)	8 (2.8%)	13 (4.6%)	11 (3.9%)
上気道感染	7 (2.5%)	1 (0.4%)	8 (2.8%)	2 (0.7%)
気道感染	4 (1.4%)	0	6 (2.1%)	2 (0.7%)
インフルエンザ	3 (1.1%)	1 (0.4%)	5 (1.8%)	3 (1.1%)
気管支炎	5 (1.8%)	2 (0.7%)	4 (1.4%)	0
下気道感染	2 (0.7%)	2 (0.7%)	4 (1.4%)	1 (0.4%)
鼻咽頭炎	0	0	4 (1.4%)	0
耳下腺炎	0	0	2 (0.7%)	0
インフルエンザ性肺炎	0	0	2 (0.7%)	1 (0.4%)
尿路感染	1 (0.4%)	0	2 (0.7%)	2 (0.7%)
急性副鼻腔炎	0	0	1 (0.4%)	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
虫垂炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細菌感染	0	0	1 (0.4%)	1 (0.4%)
細気管支炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	1 (0.4%)	0
気管支肺炎	0	0	1 (0.4%)	1 (0.4%)
ウイルス性腸炎	0	0	1 (0.4%)	0
喉頭蓋炎	0	0	1 (0.4%)	1 (0.4%)
胃腸炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
歯肉炎	0	0	1 (0.4%)	0
リステリア性敗血症	0	0	1 (0.4%)	1 (0.4%)
肺感染	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
鼻膿瘍	0	0	1 (0.4%)	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ヘモフィルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
レンサ球菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)
鼻炎	0	0	1 (0.4%)	0
サルモネラ性菌血症	0	0	1 (0.4%)	1 (0.4%)
敗血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
副鼻腔炎	0	0	1 (0.4%)	0
細菌性上気道感染	0	0	1 (0.4%)	1 (0.4%)
ウイルス性気管支炎	1 (0.4%)	1 (0.4%)	0	0
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	0	0
消化管感染	1 (0.4%)	1 (0.4%)	0	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0
帯状疱疹	2 (0.7%)	1 (0.4%)	0	0
感染	1 (0.4%)	1 (0.4%)	0	0
咽頭炎	1 (0.4%)	1 (0.4%)	0	0
細菌性肺炎	1 (0.4%)	0	0	0
急性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0
一般・全身障害および投与部位の状態	13 (4.6%)	9 (3.2%)	41 (14.5%)	20 (7.1%)
疲労	4 (1.4%)	3 (1.1%)	24 (8.5%)	12 (4.2%)
発熱	2 (0.7%)	1 (0.4%)	10 (3.5%)	2 (0.7%)
無力症	4 (1.4%)	4 (1.4%)	7 (2.5%)	5 (1.8%)
倦怠感	1 (0.4%)	0	3 (1.1%)	1 (0.4%)
悪寒	0	0	2 (0.7%)	0
胸部不快感	0	0	1 (0.4%)	0
全身性炎症反応症候群	0	0	1 (0.4%)	1 (0.4%)
胸痛	1 (0.4%)	0	0	0
全身性浮腫	1 (0.4%)	0	0	0
末梢性浮腫	2 (0.7%)	1 (0.4%)	0	0
胃腸障害	14 (5.0%)	6 (2.1%)	31 (11.0%)	12 (4.2%)
下痢	9 (3.2%)	5 (1.8%)	21 (7.4%)	6 (2.1%)
悪心	0	0	6 (2.1%)	2 (0.7%)
便秘	0	0	3 (1.1%)	2 (0.7%)
嘔吐	3 (1.1%)	1 (0.4%)	3 (1.1%)	0
肛門出血	0	0	1 (0.4%)	1 (0.4%)
憩室穿孔	0	0	1 (0.4%)	1 (0.4%)
嚥下障害	0	0	1 (0.4%)	0
出血性胃腸管血管異形成	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	0	0	1 (0.4%)	0
鼠径ヘルニア	0	0	1 (0.4%)	0
上腹部痛	1 (0.4%)	0	0	0
大腸炎	1 (0.4%)	1 (0.4%)	0	0
下部消化管出血	1 (0.4%)	0	0	0
腎および尿路障害	11 (3.9%)	3 (1.1%)	18 (6.4%)	1 (0.4%)
腎機能障害	7 (2.5%)	0	16 (5.7%)	0
慢性腎臓病	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
腎不全	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
急性腎不全	2 (0.7%)	1 (0.4%)	0	0
臨床検査	10 (3.6%)	1 (0.4%)	15 (5.3%)	6 (2.1%)
アラニンアミノトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	8 (2.8%)	4 (1.4%)
血中クレアチニン増加	6 (2.1%)	0	6 (2.1%)	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	4 (1.4%)	2 (0.7%)
血中アルカリホスファターゼ増加	0	0	2 (0.7%)	1 (0.4%)
γ－グルタミルトランスフェラーゼ増加	0	0	2 (0.7%)	2 (0.7%)
血中乳酸脱水素酵素増加	0	0	1 (0.4%)	0
腎クレアチニン・クリアランス減少	2 (0.7%)	0	1 (0.4%)	0
糸球体濾過率減少	2 (0.7%)	0	0	0
呼吸器、胸郭および縦隔障害	9 (3.2%)	5 (1.8%)	15 (5.3%)	6 (2.1%)
肺塞栓症	3 (1.1%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
慢性閉塞性肺疾患	0	0	2 (0.7%)	1 (0.4%)
咳嗽	2 (0.7%)	0	2 (0.7%)	0
呼吸困難	2 (0.7%)	0	2 (0.7%)	2 (0.7%)
急性肺水腫	0	0	1 (0.4%)	1 (0.4%)
労作性呼吸困難	0	0	1 (0.4%)	0
低酸素症	0	0	1 (0.4%)	0
喉頭浮腫	0	0	1 (0.4%)	0
湿性咳嗽	1 (0.4%)	0	1 (0.4%)	0
肺腫瘤	0	0	1 (0.4%)	0
肺水腫	0	0	1 (0.4%)	1 (0.4%)
急性呼吸不全	1 (0.4%)	1 (0.4%)	0	0
肺障害	1 (0.4%)	1 (0.4%)	0	0
神経系障害	12 (4.3%)	4 (1.4%)	14 (4.9%)	6 (2.1%)
末梢性ニューロパチー	2 (0.7%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
失神	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
脳血管発作	0	0	1 (0.4%)	1 (0.4%)
認知障害	0	0	1 (0.4%)	1 (0.4%)
体位性めまい	0	0	1 (0.4%)	0
知覚過敏	0	0	1 (0.4%)	0
感覚鈍麻	0	0	1 (0.4%)	0
末梢性感覚ニューロパチー	3 (1.1%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
失神寸前の状態	0	0	1 (0.4%)	0
痙攣発作	0	0	1 (0.4%)	0
一過性脳虚血発作	0	0	1 (0.4%)	0
振戦	1 (0.4%)	0	1 (0.4%)	0
三叉神経障害	0	0	1 (0.4%)	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
脳梗塞	1 (0.4%)	1 (0.4%)	0	0
注意力障害	1 (0.4%)	0	0	0
浮動性めまい	1 (0.4%)	0	0	0
意識消失	1 (0.4%)	0	0	0
不随意性筋収縮	1 (0.4%)	0	0	0
傾眠	1 (0.4%)	0	0	0
代謝および栄養障害	4 (1.4%)	2 (0.7%)	11 (3.9%)	4 (1.4%)
脱水	0	0	3 (1.1%)	0
高血糖	1 (0.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
食欲減退	1 (0.4%)	0	1 (0.4%)	0
食物不耐性	0	0	1 (0.4%)	0
低カルシウム血症	0	0	1 (0.4%)	1 (0.4%)
低ナトリウム血症	0	0	1 (0.4%)	1 (0.4%)
低リン酸血症	0	0	1 (0.4%)	0
低カリウム血症	2 (0.7%)	1 (0.4%)	0	0
皮膚および皮下組織障害	6 (2.1%)	0	9 (3.2%)	5 (1.8%)
発疹	1 (0.4%)	0	4 (1.4%)	0
全身性皮疹	0	0	2 (0.7%)	1 (0.4%)
薬疹	0	0	1 (0.4%)	1 (0.4%)
そう痒症	0	0	1 (0.4%)	1 (0.4%)
斑状皮疹	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
斑状丘疹状皮疹	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
蕁麻疹	0	0	1 (0.4%)	1 (0.4%)
多汗症	1 (0.4%)	0	0	0
寝汗	1 (0.4%)	0	0	0
壊疽性膿皮症	1 (0.4%)	0	0	0
血管障害	6 (2.1%)	4 (1.4%)	9 (3.2%)	2 (0.7%)
静脈炎	0	0	2 (0.7%)	0
血栓症	0	0	2 (0.7%)	1 (0.4%)
深部静脈血栓症	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
塞栓症	0	0	1 (0.4%)	0
低血圧	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
血栓性静脈炎	0	0	1 (0.4%)	0
表在性血栓性静脈炎	0	0	1 (0.4%)	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
静脈血栓症	0	0	1 (0.4%)	0
起立性低血圧	1 (0.4%)	1 (0.4%)	0	0
筋骨格系および結合組織障害	7 (2.5%)	3 (1.1%)	8 (2.8%)	3 (1.1%)
筋痙縮	5 (1.8%)	2 (0.7%)	6 (2.1%)	2 (0.7%)
関節痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
背部痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
側腹部痛	0	0	1 (0.4%)	0
筋力低下	1 (0.4%)	0	0	0
四肢痛	1 (0.4%)	1 (0.4%)	0	0
脊椎痛	1 (0.4%)	1 (0.4%)	0	0
心臓障害	3 (1.1%)	3 (1.1%)	7 (2.5%)	4 (1.4%)
狭心症	0	0	1 (0.4%)	1 (0.4%)
心房細動	0	0	1 (0.4%)	0
心房粗動	0	0	1 (0.4%)	0
心アミロイドーシス	0	0	1 (0.4%)	0
うっ血性心不全	0	0	1 (0.4%)	1 (0.4%)
洞性不整脈	0	0	1 (0.4%)	1 (0.4%)
洞性頻脈	0	0	1 (0.4%)	1 (0.4%)
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
上室性頻脈	1 (0.4%)	1 (0.4%)	0	0
肝胆道系障害	0	0	3 (1.1%)	2 (0.7%)
高ビリルビン血症	0	0	2 (0.7%)	2 (0.7%)
肝機能異常	0	0	1 (0.4%)	0
耳および迷路障害	0	0	2 (0.7%)	0
耳鳴	0	0	1 (0.4%)	0
回転性めまい	0	0	1 (0.4%)	0
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
脊椎圧迫骨折	0	0	1 (0.4%)	0
関節脱臼	1 (0.4%)	1 (0.4%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.7%)	0	1 (0.4%)	0
基底細胞癌	0	0	1 (0.4%)	0
形質細胞性白血病	1 (0.4%)	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
扁平上皮癌	1 (0.4%)	0	0	0
精神障害	2 (0.7%)	2 (0.7%)	1 (0.4%)	0
うつ病	0	0	1 (0.4%)	0
錯乱状態	1 (0.4%)	1 (0.4%)	0	0
譫妄	1 (0.4%)	1 (0.4%)	0	0
生殖系および乳房障害	1 (0.4%)	0	0	0
前立腺炎	1 (0.4%)	0	0	0
Japanese				
Analysis set: safety	15		20	
Total number of subjects with TEAE leading to Lenalidomide dose modifications[c]	9 (60.0%)	6 (40.0%)	18 (90.0%)	15 (75.0%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	7 (46.7%)	5 (33.3%)	8 (40.0%)	8 (40.0%)
好中球減少症	4 (26.7%)	3 (20.0%)	7 (35.0%)	7 (35.0%)
血小板減少症	1 (6.7%)	0	1 (5.0%)	1 (5.0%)
貧血	2 (13.3%)	2 (13.3%)	0	0
発熱性好中球減少症	0	0	0	0
リンパ球減少症	0	0	2 (10.0%)	2 (10.0%)
白血球減少症	1 (6.7%)	0	0	0
リンパ節症	0	0	0	0
出血性障害	0	0	0	0
鉄芽球性貧血	0	0	0	0
血栓性血小板減少性紫斑病	0	0	0	0
感染症および寄生虫症	2 (13.3%)	1 (6.7%)	4 (20.0%)	2 (10.0%)
肺炎	1 (6.7%)	1 (6.7%)	1 (5.0%)	1 (5.0%)
上気道感染	0	0	1 (5.0%)	0
気道感染	0	0	0	0
インフルエンザ	0	0	0	0
気管支炎	0	0	0	0
下気道感染	0	0	0	0
鼻咽頭炎	0	0	1 (5.0%)	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
耳下腺炎	0	0	0	0
インフルエンザ性肺炎	0	0	0	0
尿路感染	0	0	0	0
急性副鼻腔炎	0	0	0	0
虫垂炎	0	0	0	0
細菌感染	0	0	1 (5.0%)	1 (5.0%)
細気管支炎	0	0	0	0
細菌性気管支炎	0	0	0	0
気管支肺炎	0	0	0	0
ウイルス性腸炎	0	0	1 (5.0%)	0
喉頭蓋炎	0	0	0	0
胃腸炎	0	0	0	0
歯肉炎	0	0	0	0
リステリア性敗血症	0	0	0	0
肺感染	0	0	0	0
鼻膿瘍	0	0	0	0
急性中耳炎	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
レンサ球菌性肺炎	0	0	0	0
ＲＳウイルス感染	0	0	0	0
鼻炎	0	0	0	0
サルモネラ性菌血症	0	0	0	0
敗血症	0	0	0	0
副鼻腔炎	0	0	0	0
細菌性上気道感染	0	0	0	0
ウイルス性気管支炎	0	0	0	0
感染性小腸結腸炎	0	0	0	0
ウイルス性胃腸炎	0	0	0	0
消化管感染	0	0	0	0
ヘモフィルス感染	0	0	0	0
帯状疱疹	1 (6.7%)	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
感染	0	0	0	0
咽頭炎	0	0	0	0
細菌性肺炎	0	0	0	0
急性腎盂腎炎	0	0	0	0
尿路性敗血症	0	0	0	0
一般・全身障害および投与部位の状態	0	0	2 (10.0%)	0
疲労	0	0	0	0
発熱	0	0	1 (5.0%)	0
無力症	0	0	0	0
倦怠感	0	0	1 (5.0%)	0
悪寒	0	0	0	0
胸部不快感	0	0	0	0
全身性炎症反応症候群	0	0	0	0
胸痛	0	0	0	0
全身性浮腫	0	0	0	0
末梢性浮腫	0	0	0	0
胃腸障害	1 (6.7%)	0	1 (5.0%)	0
下痢	0	0	0	0
悪心	0	0	1 (5.0%)	0
便秘	0	0	0	0
嘔吐	1 (6.7%)	0	0	0
肛門出血	0	0	0	0
憩室穿孔	0	0	0	0
嚥下障害	0	0	0	0
出血性胃腸管血管異形成	0	0	0	0
胃腸障害	0	0	0	0
鼠径ヘルニア	0	0	0	0
上腹部痛	0	0	0	0
大腸炎	0	0	0	0
下部消化管出血	0	0	0	0
腎および尿路障害	1 (6.7%)	1 (6.7%)	2 (10.0%)	0
腎機能障害	0	0	2 (10.0%)	0
慢性腎臓病	0	0	0	0
腎不全	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
急性腎不全	1 (6.7%)	1 (6.7%)	0	0
臨床検査	1 (6.7%)	0	3 (15.0%)	3 (15.0%)
アラニンアミノトランスフェラーゼ増加	0	0	3 (15.0%)	2 (10.0%)
血中クレアチニン増加	1 (6.7%)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (5.0%)	0
血中アルカリホスファターゼ増加	0	0	1 (5.0%)	0
γ－グルタミルトランスフェラーゼ増加	0	0	1 (5.0%)	1 (5.0%)
血中乳酸脱水素酵素増加	0	0	0	0
腎クレアチニン・クリアランス減少	0	0	0	0
糸球体濾過率減少	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	1 (5.0%)	0
肺塞栓症	0	0	0	0
慢性閉塞性肺疾患	0	0	0	0
咳嗽	0	0	0	0
呼吸困難	0	0	0	0
急性肺水腫	0	0	0	0
労作性呼吸困難	0	0	0	0
低酸素症	0	0	1 (5.0%)	0
喉頭浮腫	0	0	0	0
湿性咳嗽	0	0	0	0
肺腫瘤	0	0	0	0
肺水腫	0	0	0	0
急性呼吸不全	0	0	0	0
肺障害	0	0	0	0
神経系障害	0	0	1 (5.0%)	1 (5.0%)
末梢性ニューロパチー	0	0	1 (5.0%)	1 (5.0%)
失神	0	0	0	0
脳血管発作	0	0	0	0
認知障害	0	0	0	0
体位性めまい	0	0	0	0
知覚過敏	0	0	0	0
感覚鈍麻	0	0	0	0
末梢性感覚ニューロパチー	0	0	0	0
失神寸前の状態	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
痙攣発作	0	0	0	0
一過性脳虚血発作	0	0	0	0
振戦	0	0	0	0
三叉神経障害	0	0	0	0
脳梗塞	0	0	0	0
注意力障害	0	0	0	0
浮動性めまい	0	0	0	0
意識消失	0	0	0	0
不随意性筋収縮	0	0	0	0
傾眠	0	0	0	0
代謝および栄養障害	0	0	1 (5.0%)	0
脱水	0	0	0	0
高血糖	0	0	0	0
食欲減退	0	0	1 (5.0%)	0
食物不耐性	0	0	0	0
低カルシウム血症	0	0	0	0
低ナトリウム血症	0	0	0	0
低リン酸血症	0	0	0	0
低カリウム血症	0	0	0	0
皮膚および皮下組織障害	1 (6.7%)	0	2 (10.0%)	1 (5.0%)
発疹	1 (6.7%)	0	1 (5.0%)	0
全身性皮疹	0	0	0	0
薬疹	0	0	1 (5.0%)	1 (5.0%)
そう痒症	0	0	0	0
斑状皮疹	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
蕁麻疹	0	0	0	0
多汗症	0	0	0	0
寝汗	0	0	0	0
壊疽性膿皮症	0	0	0	0
血管障害	0	0	2 (10.0%)	0
静脈炎	0	0	0	0
血栓症	0	0	1 (5.0%)	0
深部静脈血栓症	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
塞栓症	0	0	1 (5.0%)	0
低血圧	0	0	0	0
血栓性静脈炎	0	0	1 (5.0%)	0
表在性血栓性静脈炎	0	0	0	0
静脈血栓症	0	0	0	0
起立性低血圧	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0
筋痙縮	0	0	0	0
関節痛	0	0	0	0
背部痛	0	0	0	0
側腹部痛	0	0	0	0
筋力低下	0	0	0	0
四肢痛	0	0	0	0
脊椎痛	0	0	0	0
心臓障害	0	0	0	0
狭心症	0	0	0	0
心房細動	0	0	0	0
心房粗動	0	0	0	0
心アミロイドーシス	0	0	0	0
うっ血性心不全	0	0	0	0
洞性不整脈	0	0	0	0
洞性頻脈	0	0	0	0
急性心筋梗塞	0	0	0	0
心筋梗塞	0	0	0	0
上室性頻脈	0	0	0	0
肝胆道系障害	0	0	1 (5.0%)	0
高ビリルビン血症	0	0	0	0
肝機能異常	0	0	1 (5.0%)	0
耳および迷路障害	0	0	0	0
耳鳴	0	0	0	0
回転性めまい	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
脊椎圧迫骨折	0	0	0	0
関節脱臼	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0
基底細胞癌	0	0	0	0
形質細胞性白血病	0	0	0	0
扁平上皮癌	0	0	0	0
精神障害	0	0	0	0
うつ病	0	0	0	0
錯乱状態	0	0	0	0
譫妄	0	0	0	0
生殖系および乳房障害	0	0	0	0
前立腺炎	0	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Total number of subjects with TEAE leading to Lenalidomide dose modifications[c]	24 (54.5%)	20 (45.5%)	37 (72.5%)	33 (64.7%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	19 (43.2%)	17 (38.6%)	24 (47.1%)	24 (47.1%)
好中球減少症	16 (36.4%)	15 (34.1%)	23 (45.1%)	23 (45.1%)
血小板減少症	1 (2.3%)	0	2 (3.9%)	2 (3.9%)
貧血	3 (6.8%)	3 (6.8%)	1 (2.0%)	1 (2.0%)
発熱性好中球減少症	1 (2.3%)	1 (2.3%)	1 (2.0%)	1 (2.0%)
リンパ球減少症	0	0	2 (3.9%)	2 (3.9%)
白血球減少症	1 (2.3%)	0	1 (2.0%)	1 (2.0%)
リンパ節症	0	0	0	0
出血性障害	0	0	0	0
鉄芽球性貧血	0	0	0	0
血栓性血小板減少性紫斑病	0	0	0	0
感染症および寄生虫症	7 (15.9%)	4 (9.1%)	8 (15.7%)	5 (9.8%)
肺炎	3 (6.8%)	2 (4.5%)	1 (2.0%)	1 (2.0%)
上気道感染	0	0	1 (2.0%)	0
気道感染	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
インフルエンザ	1 (2.3%)	0	0	0
気管支炎	1 (2.3%)	0	0	0
下気道感染	0	0	0	0
鼻咽頭炎	0	0	1 (2.0%)	0
耳下腺炎	0	0	0	0
インフルエンザ性肺炎	0	0	0	0
尿路感染	0	0	0	0
急性副鼻腔炎	0	0	0	0
虫垂炎	0	0	0	0
細菌感染	0	0	1 (2.0%)	1 (2.0%)
細気管支炎	0	0	1 (2.0%)	1 (2.0%)
細菌性気管支炎	0	0	0	0
気管支肺炎	0	0	0	0
ウイルス性腸炎	0	0	1 (2.0%)	0
喉頭蓋炎	0	0	0	0
胃腸炎	0	0	0	0
歯肉炎	0	0	0	0
リステリア性敗血症	0	0	0	0
肺感染	0	0	0	0
鼻膿瘍	0	0	0	0
急性中耳炎	0	0	1 (2.0%)	1 (2.0%)
パラインフルエンザウイルス感染	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
レンサ球菌性肺炎	0	0	0	0
ＲＳウイルス感染	0	0	0	0
鼻炎	0	0	0	0
サルモネラ性菌血症	0	0	1 (2.0%)	1 (2.0%)
敗血症	0	0	0	0
副鼻腔炎	0	0	1 (2.0%)	0
細菌性上気道感染	0	0	0	0
ウイルス性気管支炎	0	0	0	0
感染性小腸結腸炎	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
ウイルス性胃腸炎	0	0	0	0
消化管感染	0	0	0	0
ヘモフィルス感染	0	0	0	0
帯状疱疹	2 (4.5%)	1 (2.3%)	0	0
感染	0	0	0	0
咽頭炎	0	0	0	0
細菌性肺炎	0	0	0	0
急性腎盂腎炎	1 (2.3%)	1 (2.3%)	0	0
尿路性敗血症	0	0	0	0
一般・全身障害および投与部位の状態	1 (2.3%)	1 (2.3%)	5 (9.8%)	2 (3.9%)
疲労	0	0	2 (3.9%)	1 (2.0%)
発熱	0	0	2 (3.9%)	1 (2.0%)
無力症	1 (2.3%)	1 (2.3%)	1 (2.0%)	1 (2.0%)
倦怠感	0	0	1 (2.0%)	0
悪寒	0	0	0	0
胸部不快感	0	0	0	0
全身性炎症反応症候群	0	0	0	0
胸痛	0	0	0	0
全身性浮腫	0	0	0	0
末梢性浮腫	0	0	0	0
胃腸障害	2 (4.5%)	1 (2.3%)	3 (5.9%)	2 (3.9%)
下痢	1 (2.3%)	1 (2.3%)	2 (3.9%)	2 (3.9%)
悪心	0	0	1 (2.0%)	0
便秘	0	0	0	0
嘔吐	1 (2.3%)	0	0	0
肛門出血	0	0	0	0
憩室穿孔	0	0	0	0
嚥下障害	0	0	0	0
出血性胃腸管血管異形成	0	0	0	0
胃腸障害	0	0	0	0
鼠径ヘルニア	0	0	0	0
上腹部痛	0	0	0	0
大腸炎	0	0	0	0
下部消化管出血	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
腎および尿路障害	2 (4.5%)	2 (4.5%)	3 (5.9%)	0
腎機能障害	0	0	2 (3.9%)	0
慢性腎臓病	1 (2.3%)	1 (2.3%)	1 (2.0%)	0
腎不全	0	0	0	0
急性腎不全	1 (2.3%)	1 (2.3%)	0	0
臨床検査	1 (2.3%)	0	3 (5.9%)	3 (5.9%)
アラニンアミノトランスフェラーゼ増加	0	0	3 (5.9%)	2 (3.9%)
血中クレアチニン増加	1 (2.3%)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (2.0%)	0
血中アルカリホスファターゼ増加	0	0	1 (2.0%)	0
γ－グルタミルトランスフェラーゼ増加	0	0	1 (2.0%)	1 (2.0%)
血中乳酸脱水素酵素増加	0	0	0	0
腎クレアチニン・クリアランス減少	0	0	0	0
糸球体濾過率減少	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	2 (3.9%)	0
肺塞栓症	0	0	0	0
慢性閉塞性肺疾患	0	0	0	0
咳嗽	0	0	1 (2.0%)	0
呼吸困難	0	0	0	0
急性肺水腫	0	0	0	0
労作性呼吸困難	0	0	0	0
低酸素症	0	0	1 (2.0%)	0
喉頭浮腫	0	0	0	0
湿性咳嗽	0	0	0	0
肺腫瘤	0	0	0	0
肺水腫	0	0	0	0
急性呼吸不全	0	0	0	0
肺障害	0	0	0	0
神経系障害	0	0	1 (2.0%)	1 (2.0%)
末梢性ニューロパチー	0	0	1 (2.0%)	1 (2.0%)
失神	0	0	0	0
脳血管発作	0	0	0	0
認知障害	0	0	0	0
体位性めまい	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
知覚過敏	0	0	0	0
感覚鈍麻	0	0	0	0
末梢性感覚ニューロパチー	0	0	0	0
失神寸前の状態	0	0	0	0
痙攣発作	0	0	0	0
一過性脳虚血発作	0	0	0	0
振戦	0	0	0	0
三叉神経障害	0	0	0	0
脳梗塞	0	0	0	0
注意力障害	0	0	0	0
浮動性めまい	0	0	0	0
意識消失	0	0	0	0
不随意性筋収縮	0	0	0	0
傾眠	0	0	0	0
代謝および栄養障害	0	0	2 (3.9%)	1 (2.0%)
脱水	0	0	0	0
高血糖	0	0	1 (2.0%)	1 (2.0%)
食欲減退	0	0	1 (2.0%)	0
食物不耐性	0	0	0	0
低カルシウム血症	0	0	0	0
低ナトリウム血症	0	0	0	0
低リン酸血症	0	0	0	0
低カリウム血症	0	0	0	0
皮膚および皮下組織障害	2 (4.5%)	0	3 (5.9%)	2 (3.9%)
発疹	1 (2.3%)	0	1 (2.0%)	0
全身性皮疹	0	0	0	0
薬疹	0	0	1 (2.0%)	1 (2.0%)
そう痒症	0	0	0	0
斑状皮疹	0	0	0	0
斑状丘疹状皮疹	0	0	1 (2.0%)	1 (2.0%)
蕁麻疹	0	0	1 (2.0%)	1 (2.0%)
多汗症	0	0	0	0
寝汗	0	0	0	0
壊疽性膿皮症	1 (2.3%)	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
血管障害	0	0	2 (3.9%)	0
静脈炎	0	0	0	0
血栓症	0	0	1 (2.0%)	0
深部静脈血栓症	0	0	0	0
塞栓症	0	0	1 (2.0%)	0
低血圧	0	0	0	0
血栓性静脈炎	0	0	1 (2.0%)	0
表在性血栓性静脈炎	0	0	0	0
静脈血栓症	0	0	0	0
起立性低血圧	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0
筋痙縮	0	0	0	0
関節痛	0	0	0	0
背部痛	0	0	0	0
側腹部痛	0	0	0	0
筋力低下	0	0	0	0
四肢痛	0	0	0	0
脊椎痛	0	0	0	0
心臓障害	0	0	0	0
狭心症	0	0	0	0
心房細動	0	0	0	0
心房粗動	0	0	0	0
心アミロイドーシス	0	0	0	0
うっ血性心不全	0	0	0	0
洞性不整脈	0	0	0	0
洞性頻脈	0	0	0	0
急性心筋梗塞	0	0	0	0
心筋梗塞	0	0	0	0
上室性頻脈	0	0	0	0
肝胆道系障害	0	0	1 (2.0%)	0
高ビリルビン血症	0	0	0	0
肝機能異常	0	0	1 (2.0%)	0
耳および迷路障害	0	0	0	0
耳鳴	0	0	0	0

TSFAE08A_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Lenalidomide Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
回転性めまい	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
脊椎圧迫骨折	0	0	0	0
関節脱臼	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0
基底細胞癌	0	0	0	0
形質細胞性白血病	0	0	0	0
扁平上皮癌	0	0	0	0
精神障害	0	0	0	0
うつ病	0	0	0	0
錯乱状態	0	0	0	0
譫妄	0	0	0	0
生殖系および乳房障害	0	0	0	0
前立腺炎	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes adverse events leading to lenalidomide dose modifications (i.e., dose delays, dose skipping, or dose reduction).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE08A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE08A_3003.SAS] 30JUN2016, 21:56

表 2.7.4-付録-76 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Total[a]				
Analysis set: safety	281		283	
Total number of subjects with TEAE leading to Dexamethasone dose modifications[c]	125 (44.5%)	64 (22.8%)	165 (58.3%)	87 (30.7%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	41 (14.6%)	21 (7.5%)	67 (23.7%)	38 (13.4%)
肺炎	9 (3.2%)	7 (2.5%)	11 (3.9%)	9 (3.2%)
気管支炎	6 (2.1%)	1 (0.4%)	8 (2.8%)	1 (0.4%)
インフルエンザ	3 (1.1%)	1 (0.4%)	7 (2.5%)	4 (1.4%)
上気道感染	5 (1.8%)	0	6 (2.1%)	2 (0.7%)
下気道感染	1 (0.4%)	0	5 (1.8%)	2 (0.7%)
気道感染	4 (1.4%)	0	5 (1.8%)	1 (0.4%)
尿路感染	1 (0.4%)	0	3 (1.1%)	2 (0.7%)
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
鼻咽頭炎	2 (0.7%)	0	2 (0.7%)	0
耳下腺炎	0	0	2 (0.7%)	0
インフルエンザ性肺炎	0	0	2 (0.7%)	1 (0.4%)
鼻炎	0	0	2 (0.7%)	0
虫垂炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細菌感染	0	0	1 (0.4%)	1 (0.4%)
細気管支炎	0	0	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	1 (0.4%)	0
気管支肺炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
ウイルス性腸炎	0	0	1 (0.4%)	0
喉頭蓋炎	0	0	1 (0.4%)	1 (0.4%)
胃腸炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
歯肉炎	0	0	1 (0.4%)	0
感染	0	0	1 (0.4%)	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
リステリア性敗血症	0	0	1 (0.4%)	1 (0.4%)
肺感染	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
鼻膿瘍	0	0	1 (0.4%)	1 (0.4%)
好中球減少性敗血症	0	0	1 (0.4%)	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	0	0	1 (0.4%)	1 (0.4%)
細菌性肺炎	1 (0.4%)	0	1 (0.4%)	0
ヘモフィルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)
サルモネラ性菌血症	0	0	1 (0.4%)	1 (0.4%)
敗血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
敗血症性ショック	0	0	1 (0.4%)	1 (0.4%)
細菌性上気道感染	0	0	1 (0.4%)	1 (0.4%)
ウイルス性気管支炎	1 (0.4%)	1 (0.4%)	0	0
蜂巣炎	1 (0.4%)	1 (0.4%)	0	0
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0
帯状疱疹	1 (0.4%)	0	0	0
咽頭炎	1 (0.4%)	1 (0.4%)	0	0
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0
水痘	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	1 (0.4%)	0	0
精神障害	35 (12.5%)	6 (2.1%)	31 (11.0%)	3 (1.1%)
不眠症	13 (4.6%)	1 (0.4%)	11 (3.9%)	1 (0.4%)
激越	4 (1.4%)	1 (0.4%)	4 (1.4%)	0
不安	5 (1.8%)	2 (0.7%)	4 (1.4%)	1 (0.4%)
うつ病	0	0	4 (1.4%)	0
易刺激性	2 (0.7%)	0	2 (0.7%)	0
精神障害	1 (0.4%)	0	2 (0.7%)	0
気分変化	4 (1.4%)	0	2 (0.7%)	1 (0.4%)
気分動揺	0	0	2 (0.7%)	0
落ち着きのなさ	1 (0.4%)	0	2 (0.7%)	0

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	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
睡眠障害	0	0	2 (0.7%)	0
抑うつ気分	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
譫妄	1 (0.4%)	1 (0.4%)	0	0
気分変調性障害	1 (0.4%)	0	0	0
神経過敏	5 (1.8%)	1 (0.4%)	0	0
精神病性障害	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	20 (7.1%)	7 (2.5%)	28 (9.9%)	7 (2.5%)
疲労	9 (3.2%)	2 (0.7%)	14 (4.9%)	3 (1.1%)
発熱	3 (1.1%)	1 (0.4%)	6 (2.1%)	1 (0.4%)
無力症	4 (1.4%)	3 (1.1%)	4 (1.4%)	2 (0.7%)
薬物不耐性	0	0	2 (0.7%)	0
倦怠感	0	0	2 (0.7%)	1 (0.4%)
脂肪組織増加	0	0	1 (0.4%)	0
歩行障害	0	0	1 (0.4%)	0
全身健康状態低下	0	0	1 (0.4%)	0
インフルエンザ様疾患	0	0	1 (0.4%)	0
胸痛	1 (0.4%)	0	0	0
顔面浮腫	2 (0.7%)	0	0	0
全身性浮腫	1 (0.4%)	0	0	0
末梢性浮腫	3 (1.1%)	1 (0.4%)	0	0
末梢腫脹	1 (0.4%)	0	0	0
血液およびリンパ系障害	23 (8.2%)	19 (6.8%)	27 (9.5%)	26 (9.2%)
好中球減少症	12 (4.3%)	12 (4.3%)	20 (7.1%)	19 (6.7%)
発熱性好中球減少症	4 (1.4%)	4 (1.4%)	8 (2.8%)	8 (2.8%)
貧血	6 (2.1%)	4 (1.4%)	3 (1.1%)	1 (0.4%)
血小板減少症	6 (2.1%)	3 (1.1%)	3 (1.1%)	2 (0.7%)
リンパ節症	0	0	1 (0.4%)	0
白血球減少症	1 (0.4%)	0	0	0
リンパ球減少症	1 (0.4%)	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	1 (0.4%)	1 (0.4%)	0	0
筋骨格系および結合組織障害	16 (5.7%)	2 (0.7%)	22 (7.8%)	3 (1.1%)
筋力低下	9 (3.2%)	0	14 (4.9%)	0
筋痙縮	5 (1.8%)	1 (0.4%)	3 (1.1%)	1 (0.4%)
ミオパチー	2 (0.7%)	0	2 (0.7%)	0

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	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
筋萎縮症	0	0	1 (0.4%)	1 (0.4%)
背部痛	0	0	1 (0.4%)	1 (0.4%)
関節腫脹	0	0	1 (0.4%)	0
四肢痛	0	0	1 (0.4%)	0
脊椎痛	1 (0.4%)	1 (0.4%)	0	0
胃腸障害	10 (3.6%)	4 (1.4%)	15 (5.3%)	4 (1.4%)
下痢	4 (1.4%)	3 (1.1%)	5 (1.8%)	2 (0.7%)
上腹部痛	0	0	2 (0.7%)	0
悪心	0	0	2 (0.7%)	0
腹部不快感	0	0	1 (0.4%)	0
大腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
憩室穿孔	0	0	1 (0.4%)	1 (0.4%)
心窩部不快感	0	0	1 (0.4%)	0
胃炎	0	0	1 (0.4%)	0
鼠径ヘルニア	0	0	1 (0.4%)	0
口腔内潰瘍形成	0	0	1 (0.4%)	0
嘔吐	3 (1.1%)	1 (0.4%)	1 (0.4%)	0
腹痛	1 (0.4%)	0	0	0
口内乾燥	1 (0.4%)	0	0	0
下部消化管出血	1 (0.4%)	0	0	0
代謝および栄養障害	11 (3.9%)	6 (2.1%)	15 (5.3%)	10 (3.5%)
高血糖	7 (2.5%)	4 (1.4%)	13 (4.6%)	8 (2.8%)
低カルシウム血症	0	0	2 (0.7%)	1 (0.4%)
食欲減退	1 (0.4%)	0	1 (0.4%)	0
糖尿病	0	0	1 (0.4%)	1 (0.4%)
低カリウム血症	3 (1.1%)	2 (0.7%)	0	0
神経系障害	17 (6.0%)	2 (0.7%)	12 (4.2%)	3 (1.1%)
振戦	6 (2.1%)	0	6 (2.1%)	1 (0.4%)
錯感覚	0	0	2 (0.7%)	0
浮動性めまい	2 (0.7%)	0	1 (0.4%)	0
感覚鈍麻	1 (0.4%)	0	1 (0.4%)	0
神経系障害	0	0	1 (0.4%)	1 (0.4%)
失神	0	0	1 (0.4%)	1 (0.4%)
一過性脳虚血発作	0	0	1 (0.4%)	0

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	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
労作性めまい	1 (0.4%)	0	0	0
頭痛	1 (0.4%)	0	0	0
意識消失	1 (0.4%)	0	0	0
記憶障害	1 (0.4%)	1 (0.4%)	0	0
末梢性ニューロパチー	1 (0.4%)	1 (0.4%)	0	0
末梢性感覚ニューロパチー	1 (0.4%)	0	0	0
精神運動亢進	1 (0.4%)	0	0	0
第７脳神経麻痺	1 (0.4%)	0	0	0
呼吸器、胸郭および縦隔障害	8 (2.8%)	3 (1.1%)	8 (2.8%)	4 (1.4%)
咳嗽	2 (0.7%)	0	2 (0.7%)	0
肺塞栓症	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
肺水腫	0	0	2 (0.7%)	2 (0.7%)
呼吸困難	4 (1.4%)	0	1 (0.4%)	0
低酸素症	0	0	1 (0.4%)	0
肺障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
無気肺	1 (0.4%)	1 (0.4%)	0	0
湿性咳嗽	1 (0.4%)	0	0	0
血管障害	5 (1.8%)	2 (0.7%)	8 (2.8%)	0
潮紅	2 (0.7%)	0	2 (0.7%)	0
低血圧	0	0	2 (0.7%)	0
塞栓症	0	0	1 (0.4%)	0
静脈炎	0	0	1 (0.4%)	0
血栓性静脈炎	0	0	1 (0.4%)	0
表在性血栓性静脈炎	0	0	1 (0.4%)	0
静脈血栓症	0	0	1 (0.4%)	0
深部静脈血栓症	3 (1.1%)	2 (0.7%)	0	0
高血圧	1 (0.4%)	0	0	0
心臓障害	4 (1.4%)	2 (0.7%)	6 (2.1%)	3 (1.1%)
狭心症	0	0	1 (0.4%)	1 (0.4%)
心房細動	1 (0.4%)	0	1 (0.4%)	0
心房粗動	0	0	1 (0.4%)	0
徐脈	0	0	1 (0.4%)	0
心アミロイドーシス	0	0	1 (0.4%)	0
洞性不整脈	0	0	1 (0.4%)	1 (0.4%)

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	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
洞性頻脈	0	0	1 (0.4%)	1 (0.4%)
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
心嚢液貯留	1 (0.4%)	0	0	0
眼障害	2 (0.7%)	0	5 (1.8%)	1 (0.4%)
白内障	1 (0.4%)	0	4 (1.4%)	1 (0.4%)
霧視	1 (0.4%)	0	1 (0.4%)	0
水晶体混濁	1 (0.4%)	0	0	0
皮膚および皮下組織障害	6 (2.1%)	0	5 (1.8%)	1 (0.4%)
毛髪成長異常	0	0	1 (0.4%)	0
男性型多毛症	0	0	1 (0.4%)	0
多汗症	3 (1.1%)	0	1 (0.4%)	0
点状出血	0	0	1 (0.4%)	0
全身性皮疹	0	0	1 (0.4%)	1 (0.4%)
顔面腫脹	0	0	1 (0.4%)	0
紅斑	1 (0.4%)	0	0	0
寝汗	1 (0.4%)	0	0	0
そう痒症	1 (0.4%)	0	0	0
発疹	2 (0.7%)	0	0	0
臨床検査	1 (0.4%)	0	4 (1.4%)	3 (1.1%)
アラニンアミノトランスフェラーゼ増加	0	0	4 (1.4%)	2 (0.7%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	3 (1.1%)	1 (0.4%)
γ－グルタミルトランスフェラーゼ増加	0	0	2 (0.7%)	2 (0.7%)
血中アルカリホスファターゼ増加	0	0	1 (0.4%)	0
血中クレアチニン増加	1 (0.4%)	0	0	0
内分泌障害	3 (1.1%)	1 (0.4%)	2 (0.7%)	0
クッシング様症状	2 (0.7%)	0	1 (0.4%)	0
高コルチコイド症	0	0	1 (0.4%)	0
ステロイド離脱症候群	1 (0.4%)	1 (0.4%)	0	0
肝胆道系障害	0	0	2 (0.7%)	1 (0.4%)
肝機能異常	0	0	1 (0.4%)	0
高ビリルビン血症	0	0	1 (0.4%)	1 (0.4%)
腎および尿路障害	1 (0.4%)	0	2 (0.7%)	1 (0.4%)
急性腎不全	1 (0.4%)	0	1 (0.4%)	0

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	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
腎不全	0	0	1 (0.4%)	1 (0.4%)
傷害、中毒および処置合併症	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
各種物質毒性	1 (0.4%)	0	1 (0.4%)	0
関節脱臼	1 (0.4%)	1 (0.4%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	0	1 (0.4%)	0
基底細胞癌	0	0	1 (0.4%)	0
扁平上皮癌	1 (0.4%)	0	0	0
生殖系および乳房障害	1 (0.4%)	0	1 (0.4%)	0
前立腺炎	1 (0.4%)	0	1 (0.4%)	0
Japanese				
Analysis set: safety	15		20	
Total number of subjects with TEAE leading to Dexamethasone dose modifications[c]	7 (46.7%)	1 (6.7%)	8 (40.0%)	5 (25.0%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	2 (13.3%)	0	2 (10.0%)	2 (10.0%)
肺炎	0	0	1 (5.0%)	1 (5.0%)
気管支炎	0	0	0	0
インフルエンザ	0	0	0	0
上気道感染	0	0	0	0
下気道感染	0	0	0	0
気道感染	0	0	0	0
尿路感染	0	0	0	0
ウイルス性胃腸炎	0	0	0	0
鼻咽頭炎	0	0	0	0
耳下腺炎	0	0	0	0
インフルエンザ性肺炎	0	0	0	0
鼻炎	0	0	0	0
虫垂炎	0	0	0	0
細菌感染	0	0	1 (5.0%)	1 (5.0%)
細気管支炎	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
細菌性気管支炎	0	0	0	0
気管支肺炎	1 (6.7%)	0	0	0
ウイルス性腸炎	0	0	1 (5.0%)	0
喉頭蓋炎	0	0	0	0
胃腸炎	0	0	0	0
歯肉炎	0	0	0	0
感染	0	0	0	0
リステリア性敗血症	0	0	0	0
肺感染	0	0	0	0
鼻膿瘍	0	0	0	0
好中球減少性敗血症	0	0	0	0
急性中耳炎	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0
細菌性肺炎	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
ＲＳウイルス感染	0	0	0	0
サルモネラ性菌血症	0	0	0	0
敗血症	0	0	0	0
敗血症性ショック	0	0	0	0
細菌性上気道感染	0	0	0	0
ウイルス性気管支炎	0	0	0	0
蜂巣炎	0	0	0	0
感染性小腸結腸炎	0	0	0	0
ヘモフィルス感染	0	0	0	0
帯状疱疹	1 (6.7%)	0	0	0
咽頭炎	0	0	0	0
尿路性敗血症	0	0	0	0
水痘	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0
精神障害	0	0	0	0
不眠症	0	0	0	0
激越	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
不安	0	0	0	0
うつ病	0	0	0	0
易刺激性	0	0	0	0
精神障害	0	0	0	0
気分変化	0	0	0	0
気分動揺	0	0	0	0
落ち着きのなさ	0	0	0	0
睡眠障害	0	0	0	0
抑うつ気分	0	0	0	0
譫妄	0	0	0	0
気分変調性障害	0	0	0	0
神経過敏	0	0	0	0
精神病性障害	0	0	0	0
一般・全身障害および投与部位の状態	0	0	1 (5.0%)	0
疲労	0	0	1 (5.0%)	0
発熱	0	0	0	0
無力症	0	0	0	0
薬物不耐性	0	0	0	0
倦怠感	0	0	0	0
脂肪組織増加	0	0	0	0
歩行障害	0	0	0	0
全身健康状態低下	0	0	0	0
インフルエンザ様疾患	0	0	0	0
胸痛	0	0	0	0
顔面浮腫	0	0	0	0
全身性浮腫	0	0	0	0
末梢性浮腫	0	0	0	0
末梢腫脹	0	0	0	0
血液およびリンパ系障害	1 (6.7%)	1 (6.7%)	0	0
好中球減少症	0	0	0	0
発熱性好中球減少症	0	0	0	0
貧血	0	0	0	0
血小板減少症	0	0	0	0
リンパ節症	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
白血球減少症	0	0	0	0
リンパ球減少症	1 (6.7%)	1 (6.7%)	0	0
血栓性血小板減少性紫斑病	0	0	0	0
筋骨格系および結合組織障害	2 (13.3%)	0	0	0
筋力低下	1 (6.7%)	0	0	0
筋痙縮	0	0	0	0
ミオパチー	1 (6.7%)	0	0	0
筋萎縮症	0	0	0	0
背部痛	0	0	0	0
関節腫脹	0	0	0	0
四肢痛	0	0	0	0
脊椎痛	0	0	0	0
胃腸障害	1 (6.7%)	0	1 (5.0%)	0
下痢	0	0	0	0
上腹部痛	0	0	0	0
悪心	0	0	1 (5.0%)	0
腹部不快感	0	0	0	0
大腸炎	0	0	0	0
憩室穿孔	0	0	0	0
心窩部不快感	0	0	0	0
胃炎	0	0	0	0
鼠径ヘルニア	0	0	0	0
口腔内潰瘍形成	0	0	0	0
嘔吐	1 (6.7%)	0	0	0
腹痛	0	0	0	0
口内乾燥	0	0	0	0
下部消化管出血	0	0	0	0
代謝および栄養障害	0	0	3 (15.0%)	2 (10.0%)
高血糖	0	0	2 (10.0%)	2 (10.0%)
低カルシウム血症	0	0	0	0
食欲減退	0	0	1 (5.0%)	0
糖尿病	0	0	0	0
低カリウム血症	0	0	0	0
神経系障害	1 (6.7%)	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
振戦	0	0	0	0
錯感覚	0	0	0	0
浮動性めまい	0	0	0	0
感覚鈍麻	0	0	0	0
神経系障害	0	0	0	0
失神	0	0	0	0
一過性脳虚血発作	0	0	0	0
労作性めまい	0	0	0	0
頭痛	0	0	0	0
意識消失	0	0	0	0
記憶障害	0	0	0	0
末梢性ニューロパチー	0	0	0	0
末梢性感覚ニューロパチー	0	0	0	0
精神運動亢進	0	0	0	0
第７脳神経麻痺	1 (6.7%)	0	0	0
呼吸器、胸郭および縦隔障害	0	0	1 (5.0%)	0
咳嗽	0	0	0	0
肺塞栓症	0	0	0	0
肺水腫	0	0	0	0
呼吸困難	0	0	0	0
低酸素症	0	0	1 (5.0%)	0
肺障害	0	0	0	0
無気肺	0	0	0	0
湿性咳嗽	0	0	0	0
血管障害	0	0	1 (5.0%)	0
潮紅	0	0	0	0
低血圧	0	0	0	0
塞栓症	0	0	1 (5.0%)	0
静脈炎	0	0	0	0
血栓性静脈炎	0	0	1 (5.0%)	0
表在性血栓性静脈炎	0	0	0	0
静脈血栓症	0	0	0	0
深部静脈血栓症	0	0	0	0
高血圧	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
心臓障害	0	0	0	0
狭心症	0	0	0	0
心房細動	0	0	0	0
心房粗動	0	0	0	0
徐脈	0	0	0	0
心アミロイドーシス	0	0	0	0
洞性不整脈	0	0	0	0
洞性頻脈	0	0	0	0
急性心筋梗塞	0	0	0	0
心筋梗塞	0	0	0	0
心嚢液貯留	0	0	0	0
眼障害	0	0	0	0
白内障	0	0	0	0
霧視	0	0	0	0
水晶体混濁	0	0	0	0
皮膚および皮下組織障害	0	0	0	0
毛髪成長異常	0	0	0	0
男性型多毛症	0	0	0	0
多汗症	0	0	0	0
点状出血	0	0	0	0
全身性皮疹	0	0	0	0
顔面腫脹	0	0	0	0
紅斑	0	0	0	0
寝汗	0	0	0	0
そう痒症	0	0	0	0
発疹	0	0	0	0
臨床検査	0	0	1 (5.0%)	1 (5.0%)
アラニンアミノトランスフェラーゼ増加	0	0	1 (5.0%)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (5.0%)	0
γ－グルタミルトランスフェラーゼ増加	0	0	1 (5.0%)	1 (5.0%)
血中アルカリホスファターゼ増加	0	0	1 (5.0%)	0
血中クレアチニン増加	0	0	0	0
内分泌障害	0	0	0	0
クッシング様症状	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
高コルチコイド症	0	0	0	0
ステロイド離脱症候群	0	0	0	0
肝胆道系障害	0	0	1 (5.0%)	0
肝機能異常	0	0	1 (5.0%)	0
高ビリルビン血症	0	0	0	0
腎および尿路障害	0	0	0	0
急性腎不全	0	0	0	0
腎不全	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
各種物質毒性	0	0	0	0
関節脱臼	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0
基底細胞癌	0	0	0	0
扁平上皮癌	0	0	0	0
生殖系および乳房障害	0	0	0	0
前立腺炎	0	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Total number of subjects with TEAE leading to Dexamethasone dose modifications[c]	11 (25.0%)	3 (6.8%)	14 (27.5%)	10 (19.6%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	5 (11.4%)	2 (4.5%)	5 (9.8%)	5 (9.8%)
肺炎	1 (2.3%)	1 (2.3%)	1 (2.0%)	1 (2.0%)
気管支炎	1 (2.3%)	0	0	0
インフルエンザ	0	0	0	0
上気道感染	0	0	0	0
下気道感染	0	0	0	0
気道感染	0	0	0	0
尿路感染	0	0	0	0
ウイルス性胃腸炎	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
鼻咽頭炎	0	0	0	0
耳下腺炎	0	0	0	0
インフルエンザ性肺炎	0	0	0	0
鼻炎	0	0	0	0
虫垂炎	0	0	0	0
細菌感染	0	0	1 (2.0%)	1 (2.0%)
細気管支炎	0	0	1 (2.0%)	1 (2.0%)
細菌性気管支炎	0	0	0	0
気管支肺炎	1 (2.3%)	0	0	0
ウイルス性腸炎	0	0	1 (2.0%)	0
喉頭蓋炎	0	0	0	0
胃腸炎	0	0	0	0
歯肉炎	0	0	0	0
感染	0	0	0	0
リステリア性敗血症	0	0	0	0
肺感染	0	0	0	0
鼻膿瘍	0	0	0	0
好中球減少性敗血症	0	0	0	0
急性中耳炎	0	0	1 (2.0%)	1 (2.0%)
パラインフルエンザウイルス感染	0	0	0	0
細菌性肺炎	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
ＲＳウイルス感染	0	0	0	0
サルモネラ性菌血症	0	0	1 (2.0%)	1 (2.0%)
敗血症	1 (2.3%)	1 (2.3%)	0	0
敗血症性ショック	0	0	0	0
細菌性上気道感染	0	0	0	0
ウイルス性気管支炎	0	0	0	0
蜂巣炎	0	0	0	0
感染性小腸結腸炎	0	0	0	0
ヘモフィルス感染	0	0	0	0
帯状疱疹	1 (2.3%)	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
咽頭炎	0	0	0	0
尿路性敗血症	0	0	0	0
水痘	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0
精神障害	0	0	0	0
不眠症	0	0	0	0
激越	0	0	0	0
不安	0	0	0	0
うつ病	0	0	0	0
易刺激性	0	0	0	0
精神障害	0	0	0	0
気分変化	0	0	0	0
気分動揺	0	0	0	0
落ち着きのなさ	0	0	0	0
睡眠障害	0	0	0	0
抑うつ気分	0	0	0	0
譫妄	0	0	0	0
気分変調性障害	0	0	0	0
神経過敏	0	0	0	0
精神病性障害	0	0	0	0
一般・全身障害および投与部位の状態	2 (4.5%)	1 (2.3%)	3 (5.9%)	0
疲労	1 (2.3%)	0	2 (3.9%)	0
発熱	0	0	1 (2.0%)	0
無力症	1 (2.3%)	1 (2.3%)	0	0
薬物不耐性	0	0	0	0
倦怠感	0	0	0	0
脂肪組織増加	0	0	0	0
歩行障害	0	0	0	0
全身健康状態低下	0	0	0	0
インフルエンザ様疾患	0	0	0	0
胸痛	0	0	0	0
顔面浮腫	0	0	0	0
全身性浮腫	0	0	0	0
末梢性浮腫	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
末梢腫脹	0	0	0	0
血液およびリンパ系障害	1 (2.3%)	1 (2.3%)	3 (5.9%)	3 (5.9%)
好中球減少症	0	0	2 (3.9%)	2 (3.9%)
発熱性好中球減少症	0	0	1 (2.0%)	1 (2.0%)
貧血	0	0	0	0
血小板減少症	0	0	0	0
リンパ節症	0	0	0	0
白血球減少症	0	0	0	0
リンパ球減少症	1 (2.3%)	1 (2.3%)	0	0
血栓性血小板減少性紫斑病	0	0	0	0
筋骨格系および結合組織障害	3 (6.8%)	0	0	0
筋力低下	2 (4.5%)	0	0	0
筋痙縮	0	0	0	0
ミオパチー	1 (2.3%)	0	0	0
筋萎縮症	0	0	0	0
背部痛	0	0	0	0
関節腫脹	0	0	0	0
四肢痛	0	0	0	0
脊椎痛	0	0	0	0
胃腸障害	1 (2.3%)	0	1 (2.0%)	0
下痢	0	0	0	0
上腹部痛	0	0	0	0
悪心	0	0	1 (2.0%)	0
腹部不快感	0	0	0	0
大腸炎	0	0	0	0
憩室穿孔	0	0	0	0
心窩部不快感	0	0	0	0
胃炎	0	0	0	0
鼠径ヘルニア	0	0	0	0
口腔内潰瘍形成	0	0	0	0
嘔吐	1 (2.3%)	0	0	0
腹痛	0	0	0	0
口内乾燥	0	0	0	0
下部消化管出血	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
代謝および栄養障害	0	0	4 (7.8%)	3 (5.9%)
高血糖	0	0	3 (5.9%)	3 (5.9%)
低カルシウム血症	0	0	0	0
食欲減退	0	0	1 (2.0%)	0
糖尿病	0	0	0	0
低カリウム血症	0	0	0	0
神経系障害	2 (4.5%)	0	0	0
振戦	0	0	0	0
錯感覚	0	0	0	0
浮動性めまい	0	0	0	0
感覚鈍麻	1 (2.3%)	0	0	0
神経系障害	0	0	0	0
失神	0	0	0	0
一過性脳虚血発作	0	0	0	0
労作性めまい	0	0	0	0
頭痛	0	0	0	0
意識消失	0	0	0	0
記憶障害	0	0	0	0
末梢性ニューロパチー	0	0	0	0
末梢性感覚ニューロパチー	0	0	0	0
精神運動亢進	0	0	0	0
第７脳神経麻痺	1 (2.3%)	0	0	0
呼吸器、胸郭および縦隔障害	0	0	1 (2.0%)	0
咳嗽	0	0	0	0
肺塞栓症	0	0	0	0
肺水腫	0	0	0	0
呼吸困難	0	0	0	0
低酸素症	0	0	1 (2.0%)	0
肺障害	0	0	0	0
無気肺	0	0	0	0
湿性咳嗽	0	0	0	0
血管障害	0	0	1 (2.0%)	0
潮紅	0	0	0	0
低血圧	0	0	0	0

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
塞栓症	0	0	1 (2.0%)	0
静脈炎	0	0	0	0
血栓性静脈炎	0	0	1 (2.0%)	0
表在性血栓性静脈炎	0	0	0	0
静脈血栓症	0	0	0	0
深部静脈血栓症	0	0	0	0
高血圧	0	0	0	0
心臓障害	0	0	0	0
狭心症	0	0	0	0
心房細動	0	0	0	0
心房粗動	0	0	0	0
徐脈	0	0	0	0
心アミロイドーシス	0	0	0	0
洞性不整脈	0	0	0	0
洞性頻脈	0	0	0	0
急性心筋梗塞	0	0	0	0
心筋梗塞	0	0	0	0
心嚢液貯留	0	0	0	0
眼障害	0	0	0	0
白内障	0	0	0	0
霧視	0	0	0	0
水晶体混濁	0	0	0	0
皮膚および皮下組織障害	0	0	0	0
毛髪成長異常	0	0	0	0
男性型多毛症	0	0	0	0
多汗症	0	0	0	0
点状出血	0	0	0	0
全身性皮疹	0	0	0	0
顔面腫脹	0	0	0	0
紅斑	0	0	0	0
寝汗	0	0	0	0
そう痒症	0	0	0	0
発疹	0	0	0	0
臨床検査	0	0	1 (2.0%)	1 (2.0%)

TSFAE08B_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Dexamethasone Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
アラニンアミノトランスフェラーゼ増加	0	0	1 (2.0%)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (2.0%)	0
γ－グルタミルトランスフェラーゼ増加	0	0	1 (2.0%)	1 (2.0%)
血中アルカリホスファターゼ増加	0	0	1 (2.0%)	0
血中クレアチニン増加	0	0	0	0
内分泌障害	1 (2.3%)	0	0	0
クッシング様症状	1 (2.3%)	0	0	0
高コルチコイド症	0	0	0	0
ステロイド離脱症候群	0	0	0	0
肝胆道系障害	0	0	1 (2.0%)	0
肝機能異常	0	0	1 (2.0%)	0
高ビリルビン血症	0	0	0	0
腎および尿路障害	0	0	0	0
急性腎不全	0	0	0	0
腎不全	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
各種物質毒性	0	0	0	0
関節脱臼	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0
基底細胞癌	0	0	0	0
扁平上皮癌	0	0	0	0
生殖系および乳房障害	0	0	0	0
前立腺炎	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes adverse events leading to dexamethasone dose modifications (i.e., dose delays, dose skipping, or dose reduction).
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-77 Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term by Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE13A: Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term by Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd			MMY3003+GEN503 DRd			MMY1001 DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: safety	243			318			103		
Total number of subjects with TEAE leading to discontinuation daratumumab[a]	23 (9.5%)	15 (6.2%)	5 (2.1%)	29 (9.1%)	20 (6.3%)	6 (1.9%)	16 (15.5%)	12 (11.7%)	3 (2.9%)
MedDRA system organ class/Preferred term									
感染症および寄生虫症	8 (3.3%)	6 (2.5%)	0	10 (3.1%)	6 (1.9%)	4 (1.3%)	5 (4.9%)	4 (3.9%)	1 (1.0%)
肺炎	4 (1.6%)	3 (1.2%)	0	4 (1.3%)	4 (1.3%)	0	1 (1.0%)	1 (1.0%)	0
敗血症性ショック	0	0	0	3 (0.9%)	1 (0.3%)	2 (0.6%)	0	0	0
細菌性気管支炎	0	0	0	1 (0.3%)	0	0	0	0	0
細菌性肺炎	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
ウイルス性肺炎	0	0	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	0	0	0
気管支炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
真菌性食道炎	1 (0.4%)	0	0	0	0	0	0	0	0
胃腸炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
乳腺炎	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
進行性多巣性白質脳症	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
敗血症	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (1.0%)	0	1 (1.0%)
尿路感染	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
一般・全身障害および投与部位の状態	0	0	0	5 (1.6%)	3 (0.9%)	1 (0.3%)	0	0	0
全身健康状態低下	0	0	0	3 (0.9%)	2 (0.6%)	0	0	0	0
多臓器不全	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
疼痛	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	1 (0.4%)	0	3 (0.9%)	3 (0.9%)	0	0	0	0
急性単球性白血病	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
胃腺癌	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0

TSFAE13A: Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term by Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd			MMY3003+GEN503 DRd			MMY1001 DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
移行上皮癌	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
神経系障害	4 (1.6%)	1 (0.4%)	2 (0.8%)	3 (0.9%)	2 (0.6%)	0	1 (1.0%)	0	1 (1.0%)
脳梗塞	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0	0	0
脳血管発作	0	0	0	1 (0.3%)	0	0	1 (1.0%)	0	1 (1.0%)
認知障害	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
味覚異常	1 (0.4%)	0	0	0	0	0	0	0	0
虚血性脳卒中	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
末梢性感覚ニューロパチー	1 (0.4%)	0	0	0	0	0	0	0	0
失神寸前の状態	1 (0.4%)	0	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	6 (2.5%)	4 (1.6%)	1 (0.4%)	3 (0.9%)	3 (0.9%)	0	5 (4.9%)	4 (3.9%)	1 (1.0%)
喉頭浮腫	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	2 (0.6%)	0	0	0	0
発声障害	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
呼吸困難	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	0
呼吸不全	1 (0.4%)	0	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	0	1 (1.0%)
喘鳴	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
気管支痙攣	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0	0
労作性呼吸困難	1 (0.4%)	0	0	0	0	0	0	0	0
胸水症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
低酸素症	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
間質性肺疾患	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
胸水	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
胃腸障害	2 (0.8%)	1 (0.4%)	0	2 (0.6%)	1 (0.3%)	0	0	0	0
憩室穿孔	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
消化不良	0	0	0	1 (0.3%)	0	0	0	0	0
十二指腸潰瘍	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
十二指腸炎	1 (0.4%)	0	0	0	0	0	0	0	0
代謝および栄養障害	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	1 (0.3%)	0	0	0	0
高カルシウム血症	0	0	0	2 (0.6%)	1 (0.3%)	0	0	0	0
代謝性アシドーシス	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
心臓障害	4 (1.6%)	1 (0.4%)	2 (0.8%)	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	1 (1.0%)	0
心肺不全	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
急性冠動脈症候群	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0

TSFAE13A: Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term by Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd			MMY3003+GEN503 DRd			MMY1001 DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
狭心症	0	0	0	0	0	0	1 (1.0%)	0	0
心房細動	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
心停止	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
うっ血性心不全	1 (0.4%)	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
精神障害	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
うつ病	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
腎および尿路障害	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
腎不全	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
皮膚および皮下組織障害	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
全身性皮疹	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
発疹	1 (0.4%)	0	0	0	0	0	0	0	0
血液およびリンパ系障害	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
血小板減少症	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
脊椎骨折	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
筋骨格系および結合組織障害	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (1.0%)	0
筋力低下	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
脊椎痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
血管障害	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
大動脈解離	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] TEAEs with an action taken of drug withdrawal for any study treatment on the AE CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-78 Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events but stayed on Backbone therapy by MedDRA System-Organ Class and Preferred Term by Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE13A1: Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events but stayed on Backbone therapy by MedDRA System-Organ Class and Preferred Term by Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004			MMY3003+GEN503			MMY1001		
	DVd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: safety	243			318			103		
Total number of subjects with TEAE leading to discontinuation daratumumab but stayed on backbone therapya[a]	4 (1.6%)	3 (1.2%)	0	2 (0.6%)	2 (0.6%)	0	0	0	0
MedDRA system organ class/Preferred term									
呼吸器、胸郭および縦隔障害	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	2 (0.6%)	0	0	0	0
発声障害	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
呼吸困難	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
喉頭浮腫	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
呼吸不全	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
喘鳴	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
気管支痙攣	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
胃腸障害	0	0	0	1 (0.3%)	0	0	0	0	0
消化不良	0	0	0	1 (0.3%)	0	0	0	0	0
感染症および寄生虫症	3 (1.2%)	2 (0.8%)	0	0	0	0	0	0	0
気管支炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
胃腸炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
肺炎	1 (0.4%)	0	0	0	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Subjects who discontinued daratumumab based on AE action taken without discontinuing one of the other two drugs (per action of other drugs) and last cycle of Dara is prior to last cycle of Len, Vel, or Pom.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE13A1.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE13A1.SAS] 14JUL2016, 10:58

表 2.7.4-付録-79 Number of Subjects with Treatment-emergent Adverse Events Leading to Study Treatment Discontinuation by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE05B: Number of Subjects with Treatment-emergent Adverse Events Leading to Study Treatment Discontinuation by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to study treatment discontinuation[a]	1 (12.5%)	1 (12.5%)	0
MedDRA system organ class/Preferred term			
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)	1 (12.5%)	0
前立腺癌	1 (12.5%)	1 (12.5%)	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
[a] Includes those subjects indicated as having discontinued treatment due to an adverse event on the end of treatment CRF page.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE05B.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE05B.SAS] 28SEP2016, 04:15

表 2.7.4-付録-80 Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE05A3: Number of Subjects Who Discontinued Daratumumab Because of 1 or More Treatment-emergent Adverse Events by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to discontinuation of daratumumab	1 (12.5%)	1 (12.5%)	0
MedDRA system organ class/Preferred term			
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)	1 (12.5%)	0
前立腺癌	1 (12.5%)	1 (12.5%)	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE05A3.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE05A3.SAS] 28SEP2016, 04:14

表 2.7.4-付録-81 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE14_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Total[a]						
Analysis set: safety	281			283		
Total number of subjects with TEAE leading to discontinuation of study treatment[c]	22 (7.8%)	16 (5.7%)	6 (2.1%)	19 (6.7%)	14 (4.9%)	2 (0.7%)
MedDRA system organ class/Preferred term						
感染症および寄生虫症	5 (1.8%)	4 (1.4%)	1 (0.4%)	7 (2.5%)	5 (1.8%)	1 (0.4%)
肺炎	2 (0.7%)	2 (0.7%)	0	3 (1.1%)	3 (1.1%)	0
敗血症性ショック	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	0	1 (0.4%)	0	0
細菌性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0
感染	1 (0.4%)	1 (0.4%)	0	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
敗血症	1 (0.4%)	0	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	0	0	0	3 (1.1%)	2 (0.7%)	0
全身健康状態低下	0	0	0	3 (1.1%)	2 (0.7%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (1.1%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	0
急性単球性白血病	0	0	0	1 (0.4%)	1 (0.4%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.4%)	1 (0.4%)	0
肺腺癌	1 (0.4%)	0	1 (0.4%)	0	0	0
前立腺癌	1 (0.4%)	1 (0.4%)	0	0	0	0
直腸腺癌	1 (0.4%)	1 (0.4%)	0	0	0	0
神経系障害	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	0
脳梗塞	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
認知障害	0	0	0	1 (0.4%)	1 (0.4%)	0
脳出血	1 (0.4%)	0	1 (0.4%)	0	0	0
心臓障害	2 (0.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)

TSFAE14_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
心肺不全	0	0	0	1 (0.4%)	0	1 (0.4%)
心停止	1 (0.4%)	0	1 (0.4%)	0	0	0
心膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
胃腸障害	0	0	0	1 (0.4%)	1 (0.4%)	0
憩室穿孔	0	0	0	1 (0.4%)	1 (0.4%)	0
代謝および栄養障害	0	0	0	1 (0.4%)	0	0
高カルシウム血症	0	0	0	1 (0.4%)	0	0
精神障害	0	0	0	1 (0.4%)	1 (0.4%)	0
うつ病	0	0	0	1 (0.4%)	1 (0.4%)	0
腎および尿路障害	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	1 (0.4%)	0
腎不全	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	1 (0.4%)	0
皮膚および皮下組織障害	0	0	0	1 (0.4%)	1 (0.4%)	0
全身性皮疹	0	0	0	1 (0.4%)	1 (0.4%)	0
血液およびリンパ系障害	3 (1.1%)	3 (1.1%)	0	0	0	0
貧血	1 (0.4%)	1 (0.4%)	0	0	0	0
好中球減少症	1 (0.4%)	1 (0.4%)	0	0	0	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0	0	0
血小板減少症	1 (0.4%)	1 (0.4%)	0	0	0	0
筋骨格系および結合組織障害	1 (0.4%)	1 (0.4%)	0	0	0	0
脊柱管狭窄症	1 (0.4%)	1 (0.4%)	0	0	0	0
呼吸器、胸郭および縦隔障害	5 (1.8%)	3 (1.1%)	2 (0.7%)	0	0	0
急性呼吸不全	1 (0.4%)	0	1 (0.4%)	0	0	0
肺塞栓症	3 (1.1%)	3 (1.1%)	0	0	0	0
肺水腫	1 (0.4%)	0	1 (0.4%)	0	0	0
血管障害	1 (0.4%)	0	0	0	0	0
深部静脈血栓症	1 (0.4%)	0	0	0	0	0
Japanese						
Analysis set: safety	15			20		
Total number of subjects with TEAE leading to discontinuation of study treatment[c]	0	0	0	2 (10.0%)	2 (10.0%)	0
MedDRA system organ class/Preferred term						

TSFAE14_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
感染症および寄生虫症	0	0	0	0	0	0
肺炎	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0
細菌性気管支炎	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0
感染	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0
敗血症	0	0	0	0	0	0
一般・全身障害および投与部位の状態	0	0	0	0	0	0
全身健康状態低下	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (5.0%)	1 (5.0%)	0
急性単球性白血病	0	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (5.0%)	1 (5.0%)	0
肺腺癌	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0
直腸腺癌	0	0	0	0	0	0
神経系障害	0	0	0	1 (5.0%)	1 (5.0%)	0
脳梗塞	0	0	0	1 (5.0%)	1 (5.0%)	0
認知障害	0	0	0	0	0	0
脳出血	0	0	0	0	0	0
心臓障害	0	0	0	0	0	0
心肺不全	0	0	0	0	0	0
心停止	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0
胃腸障害	0	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0
代謝および栄養障害	0	0	0	0	0	0
高カルシウム血症	0	0	0	0	0	0
精神障害	0	0	0	0	0	0
うつ病	0	0	0	0	0	0
腎および尿路障害	0	0	0	0	0	0
腎不全	0	0	0	0	0	0

TSFAE14_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
皮膚および皮下組織障害	0	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0
血液およびリンパ系障害	0	0	0	0	0	0
貧血	0	0	0	0	0	0
好中球減少症	0	0	0	0	0	0
鉄芽球性貧血	0	0	0	0	0	0
血小板減少症	0	0	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	0	0
急性呼吸不全	0	0	0	0	0	0
肺塞栓症	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0
血管障害	0	0	0	0	0	0
深部静脈血栓症	0	0	0	0	0	0
East Asian[b]						
Analysis set: safety	44			51		
Total number of subjects with TEAE leading to discontinuation of study treatment[c]	1 (2.3%)	0	1 (2.3%)	3 (5.9%)	3 (5.9%)	0
MedDRA system organ class/Preferred term						
感染症および寄生虫症	1 (2.3%)	0	1 (2.3%)	1 (2.0%)	1 (2.0%)	0
肺炎	0	0	0	1 (2.0%)	1 (2.0%)	0
敗血症性ショック	0	0	0	0	0	0
細菌性気管支炎	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0
感染	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0
敗血症	1 (2.3%)	0	1 (2.3%)	0	0	0
一般・全身障害および投与部位の状態	0	0	0	0	0	0
全身健康状態低下	0	0	0	0	0	0

TSFAE14_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (2.0%)	1 (2.0%)	0
急性単球性白血病	0	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (2.0%)	1 (2.0%)	0
肺腺癌	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0
直腸腺癌	0	0	0	0	0	0
神経系障害	0	0	0	1 (2.0%)	1 (2.0%)	0
脳梗塞	0	0	0	1 (2.0%)	1 (2.0%)	0
認知障害	0	0	0	0	0	0
脳出血	0	0	0	0	0	0
心臓障害	0	0	0	0	0	0
心肺不全	0	0	0	0	0	0
心停止	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0
胃腸障害	0	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0
代謝および栄養障害	0	0	0	0	0	0
高カルシウム血症	0	0	0	0	0	0
精神障害	0	0	0	0	0	0
うつ病	0	0	0	0	0	0
腎および尿路障害	0	0	0	0	0	0
腎不全	0	0	0	0	0	0
皮膚および皮下組織障害	0	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0
血液およびリンパ系障害	0	0	0	0	0	0
貧血	0	0	0	0	0	0
好中球減少症	0	0	0	0	0	0
鉄芽球性貧血	0	0	0	0	0	0
血小板減少症	0	0	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	0	0

TSFAE14_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Discontinuation of Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
急性呼吸不全	0	0	0	0	0	0
肺塞栓症	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0
血管障害	0	0	0	0	0	0
深部静脈血栓症	0	0	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes those subjects indicated as having discontinued treatment due to an adverse event on the end of treatment CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-82 Number of Subjects Who Discontinued Daratumumab Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE13A_3003: Number of Subjects Who Discontinued Daratumumab Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Total[a]			
Analysis set: safety	283		
Total number of subjects with TEAE leading to discontinuation of Daratumumab[c]	25 (8.8%)	17 (6.0%)	5 (1.8%)
MedDRA system organ class/Preferred term			
感染症および寄生虫症	9 (3.2%)	5 (1.8%)	3 (1.1%)
肺炎	4 (1.4%)	4 (1.4%)	0
敗血症性ショック	3 (1.1%)	1 (0.4%)	2 (0.7%)
細菌性気管支炎	1 (0.4%)	0	0
細菌性肺炎	1 (0.4%)	0	1 (0.4%)
一般・全身障害および投与部位の状態	5 (1.8%)	3 (1.1%)	1 (0.4%)
全身健康状態低下	3 (1.1%)	2 (0.7%)	0
多臓器不全	1 (0.4%)	0	1 (0.4%)
疼痛	1 (0.4%)	1 (0.4%)	0
胃腸障害	2 (0.7%)	1 (0.4%)	0
憩室穿孔	1 (0.4%)	1 (0.4%)	0
消化不良	1 (0.4%)	0	0
代謝および栄養障害	2 (0.7%)	1 (0.4%)	0
高カルシウム血症	2 (0.7%)	1 (0.4%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.7%)	2 (0.7%)	0
急性単球性白血病	1 (0.4%)	1 (0.4%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	1 (0.4%)	1 (0.4%)	0
神経系障害	2 (0.7%)	2 (0.7%)	0
脳梗塞	1 (0.4%)	1 (0.4%)	0
認知障害	1 (0.4%)	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	2 (0.7%)	2 (0.7%)	0
発声障害	1 (0.4%)	1 (0.4%)	0
呼吸困難	1 (0.4%)	1 (0.4%)	0
喉頭浮腫	1 (0.4%)	1 (0.4%)	0
呼吸不全	1 (0.4%)	1 (0.4%)	0
喘鳴	1 (0.4%)	1 (0.4%)	0
心臓障害	1 (0.4%)	0	1 (0.4%)
心肺不全	1 (0.4%)	0	1 (0.4%)
精神障害	1 (0.4%)	1 (0.4%)	0
うつ病	1 (0.4%)	1 (0.4%)	0
腎および尿路障害	1 (0.4%)	1 (0.4%)	0
腎不全	1 (0.4%)	1 (0.4%)	0
皮膚および皮下組織障害	1 (0.4%)	1 (0.4%)	0
全身性皮疹	1 (0.4%)	1 (0.4%)	0
Japanese			
Analysis set: safety	20		
Total number of subjects with TEAE leading to discontinuation of Daratumumab[c]	3 (15.0%)	3 (15.0%)	0

TSFAE13A_3003: Number of Subjects Who Discontinued Daratumumab Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
MedDRA system organ class/Preferred term			
感染症および寄生虫症	1 (5.0%)	1 (5.0%)	0
肺炎	1 (5.0%)	1 (5.0%)	0
敗血症性ショック	0	0	0
細菌性気管支炎	0	0	0
細菌性肺炎	0	0	0
一般・全身障害および投与部位の状態	0	0	0
全身健康状態低下	0	0	0
多臓器不全	0	0	0
疼痛	0	0	0
胃腸障害	0	0	0
憩室穿孔	0	0	0
消化不良	0	0	0
代謝および栄養障害	0	0	0
高カルシウム血症	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (5.0%)	1 (5.0%)	0
急性単球性白血病	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	1 (5.0%)	1 (5.0%)	0
神経系障害	1 (5.0%)	1 (5.0%)	0
脳梗塞	1 (5.0%)	1 (5.0%)	0
認知障害	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0
発声障害	0	0	0
呼吸困難	0	0	0
喉頭浮腫	0	0	0
呼吸不全	0	0	0
喘鳴	0	0	0
心臓障害	0	0	0
心肺不全	0	0	0
精神障害	0	0	0
うつ病	0	0	0
腎および尿路障害	0	0	0
腎不全	0	0	0
皮膚および皮下組織障害	0	0	0
全身性皮疹	0	0	0
East Asian[b]			
Analysis set: safety	51		
Total number of subjects with TEAE leading to discontinuation of Daratumumab[c]	5 (9.8%)	4 (7.8%)	1 (2.0%)
MedDRA system organ class/Preferred term			
感染症および寄生虫症	2 (3.9%)	2 (3.9%)	0
肺炎	2 (3.9%)	2 (3.9%)	0
敗血症性ショック	0	0	0
細菌性気管支炎	0	0	0
細菌性肺炎	0	0	0
一般・全身障害および投与部位の状態	1 (2.0%)	0	1 (2.0%)
全身健康状態低下	0	0	0
多臓器不全	1 (2.0%)	0	1 (2.0%)
疼痛	0	0	0
胃腸障害	0	0	0

TSFAE13A_3003: Number of Subjects Who Discontinued Daratumumab Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
憩室穿孔	0	0	0
消化不良	0	0	0
代謝および栄養障害	0	0	0
高カルシウム血症	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (2.0%)	1 (2.0%)	0
急性単球性白血病	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	1 (2.0%)	1 (2.0%)	0
神経系障害	1 (2.0%)	1 (2.0%)	0
脳梗塞	1 (2.0%)	1 (2.0%)	0
認知障害	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0
発声障害	0	0	0
呼吸困難	0	0	0
喉頭浮腫	0	0	0
呼吸不全	0	0	0
喘鳴	0	0	0
心臓障害	0	0	0
心肺不全	0	0	0
精神障害	0	0	0
うつ病	0	0	0
腎および尿路障害	0	0	0
腎不全	0	0	0
皮膚および皮下組織障害	0	0	0
全身性皮疹	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] TEAEs with an action taken of drug withdrawal for Daratumumab on the AE CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE13A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE13A_3003.SAS] 30JUN2016, 22:09

表 2.7.4-付録-83 Treatment-Emergent Adverse Events Leading to Infusion Delay by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE09: Treatment-Emergent Adverse Events Leading to Infusion Delay by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with TEAEs leading to infusion delay	2 (8.7%)	0	13 (23.6%)	2 (3.6%)	24 (15.4%)	4 (2.6%)	1 (33.3%)	0	40 (16.9%)	6 (2.5%)
MedDRA system organ class/Preferred term										
感染症および寄生虫症	0	0	7 (12.7%)	1 (1.8%)	12 (7.7%)	3 (1.9%)	1 (33.3%)	0	20 (8.4%)	4 (1.7%)
肺炎	0	0	2 (3.6%)	0	3 (1.9%)	1 (0.6%)	0	0	5 (2.1%)	1 (0.4%)
上気道感染	0	0	2 (3.6%)	1 (1.8%)	3 (1.9%)	1 (0.6%)	0	0	5 (2.1%)	2 (0.8%)
気管支炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
帯状疱疹	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
インフルエンザ	0	0	2 (3.6%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
鼻咽頭炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
レンサ球菌性肺炎	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
気道感染	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
敗血症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
水痘	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
菌血症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
ＲＳウイルス感染	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
尿路感染	0	0	0	0	0	0	1 (33.3%)	0	1 (0.4%)	0
一般・全身障害および投与部位の状態	0	0	4 (7.3%)	1 (1.8%)	3 (1.9%)	0	0	0	7 (3.0%)	1 (0.4%)
発熱	0	0	4 (7.3%)	1 (1.8%)	2 (1.3%)	0	0	0	6 (2.5%)	1 (0.4%)
インフルエンザ様疾患	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
悪寒	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
胃腸障害	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
下痢	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
便失禁	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
傷害、中毒および処置合併症	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0
上腕骨骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
手首関節骨折	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脊椎圧迫骨折	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
臨床検査	1 (4.3%)	0	0	0	2 (1.3%)	0	0	0	3 (1.3%)	0

TSFAE09: Treatment-Emergent Adverse Events Leading to Infusion Delay by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
血中クレアチンホスホキナーゼ増加	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図異常Q波	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図異常T波	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心電図QT延長	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
代謝および栄養障害	0	0	2 (3.6%)	0	2 (1.3%)	0	0	0	4 (1.7%)	0
高カルシウム血症	0	0	2 (3.6%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
高尿酸血症	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋骨格系および結合組織障害	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
筋骨格系胸痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
四肢痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
脊椎痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
神経系障害	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
傾眠	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
振戦	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心臓障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
心房粗動	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
呼吸器、胸郭および縦隔障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
急性肺水腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
皮膚および皮下組織障害	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
接触性皮膚炎	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
血液およびリンパ系障害	0	0	2 (3.6%)	0	0	0	0	0	2 (0.8%)	0
血小板減少症	0	0	2 (3.6%)	0	0	0	0	0	2 (0.8%)	0

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
501P1/P2: ORAEACN="POSTPONED".
2002/1002: Adverse events reported as the reason for action 'infusion delayed within the cycle' on the Daratumumab infusion CRF page, or for cycle delay on the cycle delay CRF page are summarized.

[TSFAE09.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae09.sas] 16MAR2015, 12:04

表 2.7.4-付録-84 Number of Subjects with Treatment-emergent Adverse Events Leading to Dose Delay by System Organ Class, Preferred Term and Relationship; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE16: Number of Subjects with Treatment-emergent Adverse Events Leading to Dose Delay by System Organ Class, Preferred Term and Relationship; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab					
	8 mg/kg		16 mg/kg		All groups	
	Total	Related	Total	Related	Total	Related
Analysis set: All Treated Analysis Population	4		5		9	
Total number of subjects with any TEAEs leading to dose delay	1 (25.0%)	1 (25.0%)	0	0	1 (11.1%)	1 (11.1%)
MedDRA system organ class/preferred term						
感染症および寄生虫症	1 (25.0%)	1 (25.0%)	-	-	1 (11.1%)	1 (11.1%)
上気道感染	1 (25.0%)	1 (25.0%)	-	-	1 (11.1%)	1 (11.1%)

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.

[TSFAE16.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae16.sas] 22FEB2016, 11:18

表 2.7.4-付録-85 Treatment-Emergent Adverse Events Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE10: Treatment-Emergent Adverse Events Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with TEAEs leading to interruption during infusion	3 (13.0%)	3 (13.0%)	28 (50.9%)	27 (49.1%)	62 (39.7%)	56 (35.9%)	2 (66.7%)	2 (66.7%)	95 (40.1%)	88 (37.1%)
MedDRA system organ class/Preferred term										
呼吸器、胸郭および縦隔障害	2 (8.7%)	2 (8.7%)	21 (38.2%)	21 (38.2%)	44 (28.2%)	44 (28.2%)	2 (66.7%)	2 (66.7%)	69 (29.1%)	69 (29.1%)
鼻閉	0	0	3 (5.5%)	3 (5.5%)	12 (7.7%)	12 (7.7%)	1 (33.3%)	1 (33.3%)	16 (6.8%)	16 (6.8%)
アレルギー性鼻炎	0	0	12 (21.8%)	12 (21.8%)	10 (6.4%)	10 (6.4%)	0	0	22 (9.3%)	22 (9.3%)
咳嗽	0	0	2 (3.6%)	2 (3.6%)	9 (5.8%)	9 (5.8%)	1 (33.3%)	1 (33.3%)	12 (5.1%)	12 (5.1%)
呼吸困難	1 (4.3%)	1 (4.3%)	3 (5.5%)	3 (5.5%)	8 (5.1%)	8 (5.1%)	0	0	12 (5.1%)	12 (5.1%)
咽喉刺激感	0	0	0	0	5 (3.2%)	5 (3.2%)	0	0	5 (2.1%)	5 (2.1%)
くしゃみ	0	0	0	0	3 (1.9%)	3 (1.9%)	0	0	3 (1.3%)	3 (1.3%)
咽喉絞扼感	0	0	0	0	3 (1.9%)	3 (1.9%)	0	0	3 (1.3%)	3 (1.3%)
気管支痙攣	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	4 (1.7%)	4 (1.7%)
低酸素症	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
喘鳴	0	0	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	3 (1.3%)	3 (1.3%)
アレルギー性咳嗽	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
喉頭浮腫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
アレルギー性喉頭炎	0	0	3 (5.5%)	3 (5.5%)	1 (0.6%)	1 (0.6%)	0	0	4 (1.7%)	4 (1.7%)
鼻部障害	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
口腔咽頭痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
発声障害	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
一般・全身障害および投与部位の状態	0	0	6 (10.9%)	6 (10.9%)	14 (9.0%)	13 (8.3%)	0	0	20 (8.4%)	19 (8.0%)
悪寒	0	0	3 (5.5%)	3 (5.5%)	11 (7.1%)	11 (7.1%)	0	0	14 (5.9%)	14 (5.9%)
胸部不快感	0	0	2 (3.6%)	2 (3.6%)	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	3 (1.3%)
胸痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
注射部位浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
発熱	0	0	2 (3.6%)	2 (3.6%)	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	3 (1.3%)
非心臓性胸痛	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	1 (4.3%)	1 (4.3%)	6 (10.9%)	6 (10.9%)	9 (5.8%)	8 (5.1%)	1 (33.3%)	1 (33.3%)	17 (7.2%)	16 (6.8%)

TSFAE10: Treatment-Emergent Adverse Events Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
嘔吐	0	0	4 (7.3%)	4 (7.3%)	6 (3.8%)	5 (3.2%)	1 (33.3%)	1 (33.3%)	11 (4.6%)	10 (4.2%)
悪心	1 (4.3%)	1 (4.3%)	3 (5.5%)	3 (5.5%)	5 (3.2%)	5 (3.2%)	0	0	9 (3.8%)	9 (3.8%)
上腹部痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
消化不良	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
口唇浮腫	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
筋骨格系および結合組織障害	0	0	1 (1.8%)	1 (1.8%)	4 (2.6%)	3 (1.9%)	0	0	5 (2.1%)	4 (1.7%)
背部痛	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
筋骨格痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋肉痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
側腹部痛	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
心臓障害	1 (4.3%)	1 (4.3%)	0	0	3 (1.9%)	3 (1.9%)	0	0	4 (1.7%)	4 (1.7%)
動悸	1 (4.3%)	1 (4.3%)	0	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
洞性頻脈	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
頻脈	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
精神障害	0	0	1 (1.8%)	0	3 (1.9%)	2 (1.3%)	0	0	4 (1.7%)	2 (0.8%)
不安	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
譫妄	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
神経過敏	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
血管障害	0	0	3 (5.5%)	3 (5.5%)	3 (1.9%)	2 (1.3%)	0	0	6 (2.5%)	5 (2.1%)
高血圧	0	0	2 (3.6%)	2 (3.6%)	2 (1.3%)	1 (0.6%)	0	0	4 (1.7%)	3 (1.3%)
潮紅	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
眼障害	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
霧視	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
免疫系障害	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	4 (1.7%)	4 (1.7%)
サイトカイン放出症候群	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
季節性アレルギー	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
過敏症	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
神経系障害	0	0	2 (3.6%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	4 (1.7%)	3 (1.3%)
頭痛	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
浮動性めまい	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
振戦	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
皮膚および皮下組織障害	1 (4.3%)	1 (4.3%)	2 (3.6%)	2 (3.6%)	2 (1.3%)	1 (0.6%)	0	0	5 (2.1%)	4 (1.7%)
そう痒症	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	3 (1.3%)	2 (0.8%)
斑状皮疹	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)

TSFAE10: Treatment-Emergent Adverse Events Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
発疹	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
蕁麻疹	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
形質細胞性白血病	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
501P1: ORAEACN="INTERRUPTED".
501P2: ORAEACN="INFUSION TEMPORARILY INTERRUPTED".
2002/1002: Adverse events reported as the reason for action 'infusion interrupted' on the Daratumumab infusion CRF page are summarized.

[TSFAE10.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae10.sas] 16MAR2015, 12:04

表 2.7.4-付録-86 Infusion Interruption due to Treatment-emergent Adverse Events During Infusion by Preferred Term and Relationship; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE17: Infusion Interruption due to Treatment-emergent Adverse Events During Infusion by Preferred Term and Relationship; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab					
	8 mg/kg		16 mg/kg		All groups	
	Total	Related	Total	Related	Total	Related
Analysis set: All Treated Analysis Population	4		5		9	
Total number of subjects with infusion interruption due to TEAEs	1 (25.0%)	1 (25.0%)	1 (20.0%)	1 (20.0%)	2 (22.2%)	2 (22.2%)
Preferred term						
悪寒	0	0	1 (20.0%)	1 (20.0%)	1 (11.1%)	1 (11.1%)
頭痛	0	0	1 (20.0%)	1 (20.0%)	1 (11.1%)	1 (11.1%)
低酸素症	0	0	1 (20.0%)	1 (20.0%)	1 (11.1%)	1 (11.1%)
口腔咽頭痛	0	0	1 (20.0%)	1 (20.0%)	1 (11.1%)	1 (11.1%)
発熱	1 (25.0%)	1 (25.0%)	1 (20.0%)	1 (20.0%)	2 (22.2%)	2 (22.2%)

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.

[TSFAE17.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae17.sas] 22FEB2016, 11:19

表 2.7.4-付録-87 Number of Subjects with Treatment-emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE05: Number of Subjects with Treatment-emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Number of subjects with any TEAEs leading to study drug discontinuation	0	0	0

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.

[TSFAE05.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsfae05.sas] 22FEB2016, 11:14

表 2.7.4-付録-88 Number of Subjects with Treatment-emergent Infusion Related Reactions by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE14: Number of Subjects with Treatment-emergent Infusion Related Reactions by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8			
Total number of subjects with treatment-emergent infusion related reactions	5 (62.5%)	0	0	0
Total number of subjects with treatment-emergent infusion related reactions in more than 1 infusion	0	0	0	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	4 (50.0%)	0	0	0
低酸素症	2 (25.0%)	0	0	0
喘鳴	2 (25.0%)	0	0	0
口腔咽頭不快感	1 (12.5%)	0	0	0
口腔咽頭痛	1 (12.5%)	0	0	0
一般・全身障害および投与部位の状態	2 (25.0%)	0	0	0
悪寒	2 (25.0%)	0	0	0
発熱	1 (12.5%)	0	0	0
臨床検査	1 (12.5%)	0	0	0
血圧上昇	1 (12.5%)	0	0	0
血管障害	1 (12.5%)	0	0	0
高血圧	1 (12.5%)	0	0	0

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in safety population in ‘All Grades’ column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE14.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE14.SAS] 28SEP2016, 04:17

表 2.7.4-付録-89 Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Total[a]				
Analysis set: safety	283			
Total number of subjects with infusion related reactions	135 (47.7%)	15 (5.3%)	0	0
Total number of subjects with infusion related reactions in more than 1 infusion	13 (4.6%)	3 (1.1%)	0	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	87 (30.7%)	6 (2.1%)	0	0
咳嗽	24 (8.5%)	0	0	0
呼吸困難	24 (8.5%)	2 (0.7%)	0	0
気管支痙攣	13 (4.6%)	1 (0.4%)	0	0
咽喉刺激感	8 (2.8%)	0	0	0
鼻閉	7 (2.5%)	0	0	0
喉頭浮腫	6 (2.1%)	1 (0.4%)	0	0
鼻漏	6 (2.1%)	0	0	0
喘鳴	6 (2.1%)	2 (0.7%)	0	0
アレルギー性鼻炎	5 (1.8%)	0	0	0
低酸素症	4 (1.4%)	1 (0.4%)	0	0
発声障害	3 (1.1%)	1 (0.4%)	0	0
アレルギー性呼吸器症状	2 (0.7%)	0	0	0
鼻閉塞	2 (0.7%)	0	0	0
湿性咳嗽	2 (0.7%)	0	0	0
くしゃみ	2 (0.7%)	0	0	0
窒息	1 (0.4%)	0	0	0
喉頭不快感	1 (0.4%)	0	0	0
喉頭狭窄	1 (0.4%)	0	0	0
喉頭刺激感	1 (0.4%)	0	0	0
鼻部不快感	1 (0.4%)	0	0	0
口腔咽頭痛	1 (0.4%)	0	0	0
呼気延長	1 (0.4%)	0	0	0
肺水腫	1 (0.4%)	1 (0.4%)	0	0
副鼻腔障害	1 (0.4%)	0	0	0
上気道性喘鳴	1 (0.4%)	0	0	0
窒息感	1 (0.4%)	0	0	0
咽喉絞扼感	1 (0.4%)	0	0	0
一般・全身障害および投与部位の状態	34 (12.0%)	1 (0.4%)	0	0
悪寒	13 (4.6%)	1 (0.4%)	0	0
発熱	6 (2.1%)	0	0	0
胸部不快感	5 (1.8%)	0	0	0
冷感	5 (1.8%)	1 (0.4%)	0	0
疲労	2 (0.7%)	0	0	0
溢出	1 (0.4%)	0	0	0
高熱	1 (0.4%)	0	0	0
インフルエンザ様疾患	1 (0.4%)	0	0	0
注入部位発疹	1 (0.4%)	0	0	0
非心臓性胸痛	1 (0.4%)	0	0	0
分泌物分泌	1 (0.4%)	0	0	0
苦悶感	1 (0.4%)	0	0	0

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
胃腸障害	31 (11.0%)	1 (0.4%)	0	0
嘔吐	16 (5.7%)	1 (0.4%)	0	0
悪心	14 (4.9%)	0	0	0
腹痛	3 (1.1%)	0	0	0
嚥下障害	2 (0.7%)	0	0	0
口の錯感覚	2 (0.7%)	0	0	0
消化不良	1 (0.4%)	0	0	0
口唇そう痒症	1 (0.4%)	0	0	0
口唇腫脹	1 (0.4%)	0	0	0
嚥下痛	1 (0.4%)	0	0	0
皮膚および皮下組織障害	26 (9.2%)	1 (0.4%)	0	0
そう痒症	8 (2.8%)	1 (0.4%)	0	0
多汗症	5 (1.8%)	0	0	0
蕁麻疹	4 (1.4%)	0	0	0
紅斑	3 (1.1%)	0	0	0
発疹	3 (1.1%)	0	0	0
冷汗	1 (0.4%)	0	0	0
アレルギー性そう痒症	1 (0.4%)	0	0	0
斑状丘疹状皮疹	1 (0.4%)	0	0	0
そう痒性皮疹	1 (0.4%)	0	0	0
血管障害	16 (5.7%)	3 (1.1%)	0	0
高血圧	5 (1.8%)	2 (0.7%)	0	0
低血圧	5 (1.8%)	1 (0.4%)	0	0
潮紅	4 (1.4%)	0	0	0
ほてり	2 (0.7%)	0	0	0
神経系障害	12 (4.2%)	1 (0.4%)	0	0
頭痛	7 (2.5%)	0	0	0
錯感覚	2 (0.7%)	0	0	0
浮動性めまい	1 (0.4%)	0	0	0
味覚異常	1 (0.4%)	0	0	0
失神	1 (0.4%)	1 (0.4%)	0	0
眼障害	10 (3.5%)	0	0	0
流涙増加	5 (1.8%)	0	0	0
眼刺激	2 (0.7%)	0	0	0
眼部腫脹	2 (0.7%)	0	0	0
眼のアレルギー	1 (0.4%)	0	0	0
眼充血	1 (0.4%)	0	0	0
心臓障害	9 (3.2%)	1 (0.4%)	0	0
頻脈	5 (1.8%)	0	0	0
洞性頻脈	2 (0.7%)	1 (0.4%)	0	0
狭心症	1 (0.4%)	0	0	0
動悸	1 (0.4%)	0	0	0
上室性頻脈	1 (0.4%)	0	0	0
筋骨格系および結合組織障害	5 (1.8%)	2 (0.7%)	0	0
筋骨格系胸痛	3 (1.1%)	1 (0.4%)	0	0
背部痛	1 (0.4%)	0	0	0
筋骨格痛	1 (0.4%)	1 (0.4%)	0	0
感染症および寄生虫症	3 (1.1%)	0	0	0
結膜炎	1 (0.4%)	0	0	0
鼻咽頭炎	1 (0.4%)	0	0	0
上気道感染	1 (0.4%)	0	0	0
臨床検査	2 (0.7%)	0	0	0
心電図ＱＴ延長	1 (0.4%)	0	0	0
酸素飽和度低下	1 (0.4%)	0	0	0
血液およびリンパ系障害	1 (0.4%)	0	0	0

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
貧血	1 (0.4%)	0	0	0
血小板減少症	1 (0.4%)	0	0	0
免疫系障害	1 (0.4%)	0	0	0
薬物過敏症	1 (0.4%)	0	0	0
精神障害	1 (0.4%)	0	0	0
うつ病	1 (0.4%)	0	0	0
Japanese				
Analysis set: safety	20			
Total number of subjects with infusion related reactions	8 (40.0%)	1 (5.0%)	0	0
Total number of subjects with infusion related reactions in more than 1 infusion	1 (5.0%)	0	0	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	6 (30.0%)	1 (5.0%)	0	0
咳嗽	0	0	0	0
呼吸困難	2 (10.0%)	1 (5.0%)	0	0
気管支痙攣	0	0	0	0
咽喉刺激感	0	0	0	0
鼻閉	0	0	0	0
喉頭浮腫	0	0	0	0
鼻漏	1 (5.0%)	0	0	0
喘鳴	0	0	0	0
アレルギー性鼻炎	0	0	0	0
低酸素症	1 (5.0%)	0	0	0
発声障害	0	0	0	0
アレルギー性呼吸器症状	0	0	0	0
鼻閉塞	0	0	0	0
湿性咳嗽	0	0	0	0
くしゃみ	0	0	0	0
窒息	0	0	0	0
喉頭不快感	0	0	0	0
喉頭狭窄	1 (5.0%)	0	0	0
喉頭刺激感	0	0	0	0
鼻部不快感	0	0	0	0
口腔咽頭痛	0	0	0	0
呼気延長	0	0	0	0
肺水腫	0	0	0	0
副鼻腔障害	0	0	0	0
上気道性喘鳴	1 (5.0%)	0	0	0
窒息感	0	0	0	0
咽喉絞扼感	0	0	0	0
一般・全身障害および投与部位の状態	2 (10.0%)	0	0	0
悪寒	1 (5.0%)	0	0	0
発熱	1 (5.0%)	0	0	0
胸部不快感	0	0	0	0
冷感	0	0	0	0
疲労	0	0	0	0
溢出	0	0	0	0
高熱	0	0	0	0
インフルエンザ様疾患	0	0	0	0
注入部位発疹	0	0	0	0
非心臓性胸痛	0	0	0	0

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
分泌物分泌	0	0	0	0
苦悶感	0	0	0	0
胃腸障害	0	0	0	0
嘔吐	0	0	0	0
悪心	0	0	0	0
腹痛	0	0	0	0
嚥下障害	0	0	0	0
口の錯感覚	0	0	0	0
消化不良	0	0	0	0
口唇そう痒症	0	0	0	0
口唇腫脹	0	0	0	0
嚥下痛	0	0	0	0
皮膚および皮下組織障害	0	0	0	0
そう痒症	0	0	0	0
多汗症	0	0	0	0
蕁麻疹	0	0	0	0
紅斑	0	0	0	0
発疹	0	0	0	0
冷汗	0	0	0	0
アレルギー性そう痒症	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
そう痒性皮疹	0	0	0	0
血管障害	2 (10.0%)	0	0	0
高血圧	0	0	0	0
低血圧	1 (5.0%)	0	0	0
潮紅	1 (5.0%)	0	0	0
ほてり	0	0	0	0
神経系障害	1 (5.0%)	0	0	0
頭痛	1 (5.0%)	0	0	0
錯感覚	0	0	0	0
浮動性めまい	0	0	0	0
味覚異常	0	0	0	0
失神	0	0	0	0
眼障害	0	0	0	0
流涙増加	0	0	0	0
眼刺激	0	0	0	0
眼部腫脹	0	0	0	0
眼のアレルギー	0	0	0	0
眼充血	0	0	0	0
心臓障害	0	0	0	0
頻脈	0	0	0	0
洞性頻脈	0	0	0	0
狭心症	0	0	0	0
動悸	0	0	0	0
上室性頻脈	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0
筋骨格系胸痛	0	0	0	0
背部痛	0	0	0	0
筋骨格痛	0	0	0	0
感染症および寄生虫症	1 (5.0%)	0	0	0
結膜炎	0	0	0	0
鼻咽頭炎	1 (5.0%)	0	0	0
上気道感染	0	0	0	0
臨床検査	0	0	0	0
心電図ＱＴ延長	0	0	0	0

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
酸素飽和度低下	0	0	0	0
血液およびリンパ系障害	0	0	0	0
貧血	0	0	0	0
血小板減少症	0	0	0	0
免疫系障害	0	0	0	0
薬物過敏症	0	0	0	0
精神障害	0	0	0	0
うつ病	0	0	0	0
East Asian[b]				
Analysis set: safety	51			
Total number of subjects with infusion related reactions	26 (51.0%)	6 (11.8%)	0	0
Total number of subjects with infusion related reactions in more than 1 infusion	4 (7.8%)	1 (2.0%)	0	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	17 (33.3%)	4 (7.8%)	0	0
咳嗽	2 (3.9%)	0	0	0
呼吸困難	5 (9.8%)	1 (2.0%)	0	0
気管支痙攣	0	0	0	0
咽喉刺激感	0	0	0	0
鼻閉	0	0	0	0
喉頭浮腫	0	0	0	0
鼻漏	2 (3.9%)	0	0	0
喘鳴	1 (2.0%)	1 (2.0%)	0	0
アレルギー性鼻炎	1 (2.0%)	0	0	0
低酸素症	3 (5.9%)	1 (2.0%)	0	0
発声障害	1 (2.0%)	0	0	0
アレルギー性呼吸器症状	2 (3.9%)	0	0	0
鼻閉塞	1 (2.0%)	0	0	0
湿性咳嗽	1 (2.0%)	0	0	0
くしゃみ	0	0	0	0
窒息	0	0	0	0
喉頭不快感	0	0	0	0
喉頭狭窄	1 (2.0%)	0	0	0
喉頭刺激感	0	0	0	0
鼻部不快感	0	0	0	0
口腔咽頭痛	0	0	0	0
呼気延長	0	0	0	0
肺水腫	1 (2.0%)	1 (2.0%)	0	0
副鼻腔障害	0	0	0	0
上気道性喘鳴	1 (2.0%)	0	0	0
窒息感	0	0	0	0
咽喉絞扼感	0	0	0	0
一般・全身障害および投与部位の状態	9 (17.6%)	1 (2.0%)	0	0
悪寒	3 (5.9%)	1 (2.0%)	0	0
発熱	2 (3.9%)	0	0	0
胸部不快感	2 (3.9%)	0	0	0
冷感	3 (5.9%)	1 (2.0%)	0	0
疲労	0	0	0	0
溢出	0	0	0	0
高熱	0	0	0	0
インフルエンザ様疾患	0	0	0	0

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
注入部位発疹	0	0	0	0
非心臓性胸痛	0	0	0	0
分泌物分泌	0	0	0	0
苦悶感	0	0	0	0
胃腸障害	3 (5.9%)	0	0	0
嘔吐	2 (3.9%)	0	0	0
悪心	1 (2.0%)	0	0	0
腹痛	0	0	0	0
嚥下障害	0	0	0	0
口の錯感覚	0	0	0	0
消化不良	0	0	0	0
口唇そう痒症	0	0	0	0
口唇腫脹	1 (2.0%)	0	0	0
嚥下痛	0	0	0	0
皮膚および皮下組織障害	2 (3.9%)	0	0	0
そう痒症	0	0	0	0
多汗症	0	0	0	0
蕁麻疹	1 (2.0%)	0	0	0
紅斑	0	0	0	0
発疹	0	0	0	0
冷汗	1 (2.0%)	0	0	0
アレルギー性そう痒症	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
そう痒性皮疹	0	0	0	0
血管障害	6 (11.8%)	1 (2.0%)	0	0
高血圧	1 (2.0%)	0	0	0
低血圧	4 (7.8%)	1 (2.0%)	0	0
潮紅	1 (2.0%)	0	0	0
ほてり	0	0	0	0
神経系障害	1 (2.0%)	0	0	0
頭痛	1 (2.0%)	0	0	0
錯感覚	0	0	0	0
浮動性めまい	0	0	0	0
味覚異常	0	0	0	0
失神	0	0	0	0
眼障害	0	0	0	0
流涙増加	0	0	0	0
眼刺激	0	0	0	0
眼部腫脹	0	0	0	0
眼のアレルギー	0	0	0	0
眼充血	0	0	0	0
心臓障害	3 (5.9%)	0	0	0
頻脈	2 (3.9%)	0	0	0
洞性頻脈	0	0	0	0
狭心症	1 (2.0%)	0	0	0
動悸	1 (2.0%)	0	0	0
上室性頻脈	0	0	0	0
筋骨格系および結合組織障害	1 (2.0%)	1 (2.0%)	0	0
筋骨格系胸痛	1 (2.0%)	1 (2.0%)	0	0
背部痛	0	0	0	0
筋骨格痛	0	0	0	0
感染症および寄生虫症	1 (2.0%)	0	0	0
結膜炎	0	0	0	0
鼻咽頭炎	1 (2.0%)	0	0	0
上気道感染	0	0	0	0

TSFAE06A_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
臨床検査	0	0	0	0
心電図ＱＴ延長	0	0	0	0
酸素飽和度低下	0	0	0	0
血液およびリンパ系障害	0	0	0	0
貧血	0	0	0	0
血小板減少症	0	0	0	0
免疫系障害	0	0	0	0
薬物過敏症	0	0	0	0
精神障害	0	0	0	0
うつ病	0	0	0	0

Key: DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE06A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE06A_3003.SAS] 14JUL2016, 09:35

表 2.7.4-付録-90 Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE06BPART1OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503			
	DVd				DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
Analysis set: safety	243				318			
Total number of subjects treated within window	243	243	238	232	318	318	315	311
Total number of subjects with infusion related reactions	110 (45.3%)	108 (44.4%)	2 (0.8%)	4 (1.7%)	154 (48.4%)	148 (46.5%)	6 (1.9%)	17 (5.5%)
MedDRA system organ class/Preferred term								
呼吸器、胸郭および縦隔障害	83 (34.2%)	83 (34.2%)	0	2 (0.9%)	101 (31.8%)	100 (31.4%)	1 (0.3%)	3 (1.0%)
呼吸困難	26 (10.7%)	26 (10.7%)	0	1 (0.4%)	26 (8.2%)	26 (8.2%)	0	0
咳嗽	17 (7.0%)	16 (6.6%)	0	1 (0.4%)	32 (10.1%)	31 (9.7%)	0	2 (0.6%)
気管支痙攣	22 (9.1%)	22 (9.1%)	0	0	14 (4.4%)	14 (4.4%)	0	0
咽喉刺激感	12 (4.9%)	12 (4.9%)	0	0	9 (2.8%)	8 (2.5%)	1 (0.3%)	0
鼻閉	10 (4.1%)	10 (4.1%)	0	0	9 (2.8%)	9 (2.8%)	0	0
アレルギー性鼻炎	3 (1.2%)	3 (1.2%)	0	0	9 (2.8%)	9 (2.8%)	0	0
喘鳴	4 (1.6%)	3 (1.2%)	0	1 (0.4%)	6 (1.9%)	6 (1.9%)	0	0
喉頭浮腫	2 (0.8%)	2 (0.8%)	0	0	7 (2.2%)	7 (2.2%)	0	0
鼻漏	4 (1.6%)	4 (1.6%)	0	0	6 (1.9%)	6 (1.9%)	0	0
くしゃみ	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0
低酸素症	0	0	0	0	4 (1.3%)	4 (1.3%)	0	0
咽喉絞扼感	4 (1.6%)	4 (1.6%)	0	0	1 (0.3%)	0	0	1 (0.3%)
発声障害	0	0	0	0	4 (1.3%)	4 (1.3%)	0	0
湿性咳嗽	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	2 (0.6%)	0	0
アレルギー性咳嗽	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0
鼻閉塞	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	2 (0.6%)	0	0
口腔咽頭痛	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0
アレルギー性呼吸器症状	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0
喉頭刺激感	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0

TSFAE06BPART1OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd				MMY3003+GEN503 DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
窒息	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
喘息	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
喀血	0	0	0	0	0	0	0	0
喉頭不快感	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
喉頭狭窄	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
鼻部不快感	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
口腔咽頭不快感	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
口腔咽頭腫脹	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
副鼻腔不快感	0	0	0	0	0	0	0	0
咽頭浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
呼気延長	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
肺水腫	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
気道うっ血	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
低音性連続性ラ音	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
副鼻腔うっ血	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
副鼻腔障害	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
上気道性喘鳴	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
窒息感	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
上気道咳症候群	0	0	0	0	0	0	0	0
一般・全身障害および投与部位の状態	21 (8.6%)	21 (8.6%)	0	0	34 (10.7%)	31 (9.7%)	2 (0.6%)	3 (1.0%)
悪寒	10 (4.1%)	10 (4.1%)	0	0	13 (4.1%)	12 (3.8%)	1 (0.3%)	1 (0.3%)
発熱	4 (1.6%)	4 (1.6%)	0	0	6 (1.9%)	6 (1.9%)	0	0
胸部不快感	2 (0.8%)	2 (0.8%)	0	0	5 (1.6%)	5 (1.6%)	0	0
冷感	0	0	0	0	5 (1.6%)	5 (1.6%)	0	0
非心臓性胸痛	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
疲労	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	0	1 (0.3%)	1 (0.3%)
高熱	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
インフルエンザ様疾患	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0
溢出	0	0	0	0	1 (0.3%)	0	0	1 (0.3%)
注入部位そう痒感	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
注入部位発疹	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0

TSFAE06BPART1OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd				MMY3003+GEN503 DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
倦怠感	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
粘膜浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
疼痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
分泌物分泌	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
苦悶感	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
胃腸障害	21 (8.6%)	20 (8.2%)	0	1 (0.4%)	37 (11.6%)	35 (11.0%)	0	2 (0.6%)
悪心	6 (2.5%)	6 (2.5%)	0	0	17 (5.3%)	16 (5.0%)	0	1 (0.3%)
嘔吐	9 (3.7%)	8 (3.3%)	0	1 (0.4%)	19 (6.0%)	19 (6.0%)	0	0
下痢	4 (1.6%)	4 (1.6%)	0	0	0	0	0	0
腹痛	0	0	0	0	3 (0.9%)	3 (0.9%)	0	0
嚥下障害	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	2 (0.6%)	0	0
口唇腫脹	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0
口の錯感覚	0	0	0	0	2 (0.6%)	1 (0.3%)	0	1 (0.3%)
上腹部痛	1 (0.4%)	0	0	1 (0.4%)	0	0	0	0
消化不良	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
口唇そう痒症	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
嚥下痛	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
口蓋浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
舌そう痒症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
血管障害	14 (5.8%)	11 (4.5%)	2 (0.8%)	1 (0.4%)	19 (6.0%)	17 (5.3%)	0	2 (0.6%)
高血圧	8 (3.3%)	8 (3.3%)	0	0	6 (1.9%)	6 (1.9%)	0	0
潮紅	2 (0.8%)	1 (0.4%)	0	1 (0.4%)	5 (1.6%)	5 (1.6%)	0	0
低血圧	3 (1.2%)	1 (0.4%)	2 (0.8%)	0	6 (1.9%)	4 (1.3%)	0	2 (0.6%)
ほてり	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	2 (0.6%)	0	0
血管拡張	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
皮膚および皮下組織障害	9 (3.7%)	9 (3.7%)	0	0	26 (8.2%)	24 (7.5%)	0	2 (0.6%)
そう痒症	3 (1.2%)	3 (1.2%)	0	0	8 (2.5%)	8 (2.5%)	0	0
多汗症	1 (0.4%)	1 (0.4%)	0	0	5 (1.6%)	3 (0.9%)	0	2 (0.6%)
蕁麻疹	1 (0.4%)	1 (0.4%)	0	0	4 (1.3%)	4 (1.3%)	0	0
発疹	1 (0.4%)	1 (0.4%)	0	0	3 (0.9%)	3 (0.9%)	0	0
紅斑	0	0	0	0	3 (0.9%)	3 (0.9%)	0	0
アレルギー性皮膚炎	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0

TSFAE06BPART1OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd				MMY3003+GEN503 DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
冷汗	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
多形紅斑	0	0	0	0	0	0	0	0
アレルギー性そう痒症	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
紅斑性皮疹	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
斑状丘疹状皮疹	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
そう痒性皮疹	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
顔面腫脹	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
眼障害	11 (4.5%)	11 (4.5%)	0	0	11 (3.5%)	11 (3.5%)	0	0
流涙増加	5 (2.1%)	5 (2.1%)	0	0	6 (1.9%)	6 (1.9%)	0	0
結膜浮腫	3 (1.2%)	3 (1.2%)	0	0	0	0	0	0
眼刺激	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0
眼部腫脹	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0
眼のアレルギー	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
眼脂	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
眼の障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
眼そう痒症	0	0	0	0	0	0	0	0
眼瞼浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
眼充血	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
神経系障害	5 (2.1%)	5 (2.1%)	0	0	12 (3.8%)	12 (3.8%)	1 (0.3%)	1 (0.3%)
頭痛	2 (0.8%)	2 (0.8%)	0	0	7 (2.2%)	7 (2.2%)	1 (0.3%)	1 (0.3%)
浮動性めまい	2 (0.8%)	2 (0.8%)	0	0	1 (0.3%)	1 (0.3%)	0	0
錯感覚	1 (0.4%)	1 (0.4%)	0	0	2 (0.6%)	2 (0.6%)	0	0
味覚異常	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
会話障害	0	0	0	0	0	0	0	0
失神	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
心臓障害	5 (2.1%)	5 (2.1%)	0	0	9 (2.8%)	7 (2.2%)	2 (0.6%)	2 (0.6%)
洞性頻脈	3 (1.2%)	3 (1.2%)	0	0	2 (0.6%)	1 (0.3%)	0	1 (0.3%)
頻脈	0	0	0	0	5 (1.6%)	4 (1.3%)	2 (0.6%)	0
狭心症	0	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (0.3%)
上室性頻脈	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	1 (0.3%)	0	0
徐脈	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
動悸	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0

TSFAE06BPART1OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd				MMY3003+GEN503 DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
筋骨格系および結合組織障害	5 (2.1%)	5 (2.1%)	0	0	5 (1.6%)	5 (1.6%)	0	0
背部痛	4 (1.6%)	4 (1.6%)	0	0	1 (0.3%)	1 (0.3%)	0	0
筋骨格系胸痛	0	0	0	0	3 (0.9%)	3 (0.9%)	0	0
骨痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
筋骨格痛	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
筋肉痛	0	0	0	0	0	0	0	0
臨床検査	0	0	0	0	3 (0.9%)	3 (0.9%)	0	1 (0.3%)
血圧上昇	0	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (0.3%)
心電図ＱＴ延長	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
心拍数増加	0	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (0.3%)
酸素飽和度低下	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
耳および迷路障害	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0
耳そう痒症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
回転性めまい	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
感染症および寄生虫症	0	0	0	0	3 (0.9%)	1 (0.3%)	0	2 (0.6%)
結膜炎	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
鼻咽頭炎	0	0	0	0	1 (0.3%)	0	0	1 (0.3%)
上気道感染	0	0	0	0	1 (0.3%)	0	0	1 (0.3%)
免疫系障害	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
サイトカイン放出症候群	0	0	0	0	0	0	0	0
薬物過敏症	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
血液およびリンパ系障害	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
貧血	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
血小板減少症	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
傷害、中毒および処置合併症	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
注入に伴う反応	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
精神障害	0	0	0	0	1 (0.3%)	0	0	1 (0.3%)
うつ病	0	0	0	0	1 (0.3%)	0	0	1 (0.3%)

TSFAE06BPART1OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503			
	DVd				DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects treated within each window as denominator.

[TSFAE06BPART1OF2.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE06B.SAS] 01JUN2016, 10:39

TSFAE06BPART2OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd				Total Dara Combined			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
Analysis set: safety	103				664			
Total number of subjects treated within window	103	103	95	92	664	664	648	635
Total number of subjects with infusion related reactions	51 (49.5%)	51 (49.5%)	1 (1.1%)	0	315 (47.4%)	307 (46.2%)	9 (1.4%)	21 (3.3%)
MedDRA system organ class/Preferred term								
呼吸器、胸郭および縦隔障害	37 (35.9%)	37 (35.9%)	1 (1.1%)	0	221 (33.3%)	220 (33.1%)	2 (0.3%)	5 (0.8%)
呼吸困難	11 (10.7%)	11 (10.7%)	0	0	63 (9.5%)	63 (9.5%)	0	1 (0.2%)
咳嗽	11 (10.7%)	11 (10.7%)	0	0	60 (9.0%)	58 (8.7%)	0	3 (0.5%)
気管支痙攣	0	0	0	0	36 (5.4%)	36 (5.4%)	0	0
咽喉刺激感	7 (6.8%)	7 (6.8%)	0	0	28 (4.2%)	27 (4.1%)	1 (0.2%)	0
鼻閉	7 (6.8%)	7 (6.8%)	0	0	26 (3.9%)	26 (3.9%)	0	0
アレルギー性鼻炎	1 (1.0%)	1 (1.0%)	0	0	13 (2.0%)	13 (2.0%)	0	0
喘鳴	3 (2.9%)	3 (2.9%)	0	0	13 (2.0%)	12 (1.8%)	0	1 (0.2%)
喉頭浮腫	2 (1.9%)	2 (1.9%)	1 (1.1%)	0	11 (1.7%)	11 (1.7%)	1 (0.2%)	0
鼻漏	0	0	0	0	10 (1.5%)	10 (1.5%)	0	0
くしゃみ	5 (4.9%)	5 (4.9%)	0	0	7 (1.1%)	7 (1.1%)	0	0
低酸素症	2 (1.9%)	2 (1.9%)	0	0	6 (0.9%)	6 (0.9%)	0	0
咽喉絞扼感	1 (1.0%)	1 (1.0%)	0	0	6 (0.9%)	5 (0.8%)	0	1 (0.2%)
発声障害	0	0	0	0	4 (0.6%)	4 (0.6%)	0	0
湿性咳嗽	1 (1.0%)	1 (1.0%)	0	0	4 (0.6%)	4 (0.6%)	0	0
アレルギー性咳嗽	1 (1.0%)	1 (1.0%)	0	0	3 (0.5%)	3 (0.5%)	0	0
鼻閉塞	0	0	0	0	3 (0.5%)	3 (0.5%)	0	0
口腔咽頭痛	1 (1.0%)	1 (1.0%)	0	0	3 (0.5%)	3 (0.5%)	0	0
アレルギー性呼吸器症状	0	0	0	0	2 (0.3%)	2 (0.3%)	0	0
喉頭刺激感	1 (1.0%)	1 (1.0%)	0	0	2 (0.3%)	2 (0.3%)	0	0
窒息	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
喘息	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
喀血	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0

TSFAE06BPART2OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd				Total Dara Combined			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
喉頭不快感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
喉頭狭窄	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
鼻部不快感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
口腔咽頭不快感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
口腔咽頭腫脹	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
副鼻腔不快感	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
咽頭浮腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
呼気延長	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
肺水腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
気道うっ血	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
低音性連続性ラ音	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
副鼻腔うっ血	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
副鼻腔障害	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
上気道性喘鳴	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
窒息感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
上気道咳症候群	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
一般・全身障害および投与部位の状態	22 (21.4%)	22 (21.4%)	0	0	77 (11.6%)	74 (11.1%)	2 (0.3%)	3 (0.5%)
悪寒	15 (14.6%)	15 (14.6%)	0	0	38 (5.7%)	37 (5.6%)	1 (0.2%)	1 (0.2%)
発熱	5 (4.9%)	5 (4.9%)	0	0	15 (2.3%)	15 (2.3%)	0	0
胸部不快感	2 (1.9%)	2 (1.9%)	0	0	9 (1.4%)	9 (1.4%)	0	0
冷感	1 (1.0%)	1 (1.0%)	0	0	6 (0.9%)	6 (0.9%)	0	0
非心臓性胸痛	3 (2.9%)	3 (2.9%)	0	0	4 (0.6%)	4 (0.6%)	0	0
疲労	0	0	0	0	3 (0.5%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
高熱	1 (1.0%)	1 (1.0%)	0	0	2 (0.3%)	2 (0.3%)	0	0
インフルエンザ様疾患	0	0	0	0	2 (0.3%)	2 (0.3%)	0	0
溢出	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
注入部位そう痒感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
注入部位発疹	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
倦怠感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
粘膜浮腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
疼痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

TSFAE06BPART2OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd				Total Dara Combined			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
分泌物分泌	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
苦悶感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
胃腸障害	10 (9.7%)	10 (9.7%)	0	0	68 (10.2%)	65 (9.8%)	0	3 (0.5%)
悪心	9 (8.7%)	9 (8.7%)	0	0	32 (4.8%)	31 (4.7%)	0	1 (0.2%)
嘔吐	4 (3.9%)	4 (3.9%)	0	0	32 (4.8%)	31 (4.7%)	0	1 (0.2%)
下痢	1 (1.0%)	1 (1.0%)	0	0	5 (0.8%)	5 (0.8%)	0	0
腹痛	1 (1.0%)	1 (1.0%)	0	0	4 (0.6%)	4 (0.6%)	0	0
嚥下障害	0	0	0	0	3 (0.5%)	3 (0.5%)	0	0
口唇腫脹	0	0	0	0	2 (0.3%)	2 (0.3%)	0	0
口の錯感覚	0	0	0	0	2 (0.3%)	1 (0.2%)	0	1 (0.2%)
上腹部痛	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
消化不良	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
口唇そう痒症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
嚥下痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
口蓋浮腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
舌そう痒症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
血管障害	6 (5.8%)	6 (5.8%)	0	0	39 (5.9%)	34 (5.1%)	2 (0.3%)	3 (0.5%)
高血圧	2 (1.9%)	2 (1.9%)	0	0	16 (2.4%)	16 (2.4%)	0	0
潮紅	3 (2.9%)	3 (2.9%)	0	0	10 (1.5%)	9 (1.4%)	0	1 (0.2%)
低血圧	0	0	0	0	9 (1.4%)	5 (0.8%)	2 (0.3%)	2 (0.3%)
ほてり	1 (1.0%)	1 (1.0%)	0	0	4 (0.6%)	4 (0.6%)	0	0
血管拡張	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
皮膚および皮下組織障害	2 (1.9%)	2 (1.9%)	0	0	37 (5.6%)	35 (5.3%)	0	2 (0.3%)
そう痒症	0	0	0	0	11 (1.7%)	11 (1.7%)	0	0
多汗症	1 (1.0%)	1 (1.0%)	0	0	7 (1.1%)	5 (0.8%)	0	2 (0.3%)
蕁麻疹	0	0	0	0	5 (0.8%)	5 (0.8%)	0	0
発疹	0	0	0	0	4 (0.6%)	4 (0.6%)	0	0
紅斑	0	0	0	0	3 (0.5%)	3 (0.5%)	0	0
アレルギー性皮膚炎	0	0	0	0	2 (0.3%)	2 (0.3%)	0	0
冷汗	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
多形紅斑	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
アレルギー性そう痒症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

TSFAE06BPART2OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd				Total Dara Combined			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
紅斑性皮疹	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
斑状丘疹状皮疹	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
そう痒性皮疹	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
顔面腫脹	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
眼障害	4 (3.9%)	4 (3.9%)	0	0	26 (3.9%)	26 (3.9%)	0	0
流涙増加	2 (1.9%)	2 (1.9%)	0	0	13 (2.0%)	13 (2.0%)	0	0
結膜浮腫	0	0	0	0	3 (0.5%)	3 (0.5%)	0	0
眼刺激	1 (1.0%)	1 (1.0%)	0	0	3 (0.5%)	3 (0.5%)	0	0
眼部腫脹	0	0	0	0	2 (0.3%)	2 (0.3%)	0	0
眼のアレルギー	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
眼脂	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
眼の障害	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
眼そう痒症	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
眼瞼浮腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
眼充血	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
神経系障害	4 (3.9%)	4 (3.9%)	0	0	21 (3.2%)	21 (3.2%)	1 (0.2%)	1 (0.2%)
頭痛	1 (1.0%)	1 (1.0%)	0	0	10 (1.5%)	10 (1.5%)	1 (0.2%)	1 (0.2%)
浮動性めまい	1 (1.0%)	1 (1.0%)	0	0	4 (0.6%)	4 (0.6%)	0	0
錯感覚	1 (1.0%)	1 (1.0%)	0	0	4 (0.6%)	4 (0.6%)	0	0
味覚異常	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
会話障害	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
失神	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
心臓障害	3 (2.9%)	3 (2.9%)	0	0	17 (2.6%)	15 (2.3%)	2 (0.3%)	2 (0.3%)
洞性頻脈	1 (1.0%)	1 (1.0%)	0	0	6 (0.9%)	5 (0.8%)	0	1 (0.2%)
頻脈	1 (1.0%)	1 (1.0%)	0	0	6 (0.9%)	5 (0.8%)	2 (0.3%)	0
狭心症	1 (1.0%)	1 (1.0%)	0	0	2 (0.3%)	2 (0.3%)	0	1 (0.2%)
上室性頻脈	0	0	0	0	2 (0.3%)	2 (0.3%)	0	0
徐脈	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
動悸	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
筋骨格系および結合組織障害	2 (1.9%)	2 (1.9%)	0	0	12 (1.8%)	12 (1.8%)	0	0
背部痛	1 (1.0%)	1 (1.0%)	0	0	6 (0.9%)	6 (0.9%)	0	0
筋骨格系胸痛	0	0	0	0	3 (0.5%)	3 (0.5%)	0	0

TSFAE06BPART2OF2: Number of Subjects with 1 or more Treatment-emergent Infusion Related Reactions by MedDRA System-organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd				Total Dara Combined			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
骨痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
筋骨格痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
筋肉痛	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
臨床検査	1 (1.0%)	1 (1.0%)	0	0	4 (0.6%)	4 (0.6%)	0	1 (0.2%)
血圧上昇	1 (1.0%)	1 (1.0%)	0	0	2 (0.3%)	2 (0.3%)	0	1 (0.2%)
心電図ＱＴ延長	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
心拍数増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	1 (0.2%)
酸素飽和度低下	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
耳および迷路障害	1 (1.0%)	1 (1.0%)	0	0	3 (0.5%)	3 (0.5%)	0	0
耳そう痒症	1 (1.0%)	1 (1.0%)	0	0	2 (0.3%)	2 (0.3%)	0	0
回転性めまい	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
感染症および寄生虫症	0	0	0	0	3 (0.5%)	1 (0.2%)	0	2 (0.3%)
結膜炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
鼻咽頭炎	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
上気道感染	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
免疫系障害	1 (1.0%)	1 (1.0%)	0	0	2 (0.3%)	2 (0.3%)	0	0
サイトカイン放出症候群	1 (1.0%)	1 (1.0%)	0	0	1 (0.2%)	1 (0.2%)	0	0
薬物過敏症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
血液およびリンパ系障害	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
貧血	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
血小板減少症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
傷害、中毒および処置合併症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
注入に伴う反応	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
精神障害	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
うつ病	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects treated within each window as denominator.

表 2.7.4-付録-91 Time to Onset of Infusion Related Reaction; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE06CPART1OF2: GEN503)	**Time to Onset of Infusion Related Reaction; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and**							
	MMY3004				MMY3003+GEN503			
	DVd				DRd			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
Analysis set: safety	243				318			
Total number of subjects with event of infusion related reactions	110	108 (98.2%)	2 (1.8%)	4 (3.6%)	154	148 (96.1%)	6 (3.9%)	17 (11.0%)
Total number of infusion related reactions	215	207 (96.3%)	2 (0.9%)	6 (2.8%)	344	315 (91.6%)	6 (1.7%)	23 (6.7%)
Time to onset of infusion related reactions (minutes)								
N[a]	211	205	2	4	306	291	4	11
Mean (SD)	98.3 (121.35)	99.3 (122.98)	70.0 (14.14)	65.0 (11.55)	116.9 (253.18)	116.8 (258.96)	118.5 (45.01)	117.8 (98.51)
Median	80.0	84.0	70.0	65.0	90.0	90.0	124.5	65.0
Range	(15; 1695)	(15; 1695)	(60; 80)	(55; 75)	(5; 4370)	(5; 4370)	(60; 165)	(20; 320)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
[a]Infusion related reactions with no onset time are excluded.
Note: Percentage of the number of infusion related reactions in each event onset sub-group are calculated with the number of 'Total' column in each group as denominator.
Note: Time to onset of infusion related reactions in minutes are calculated as the start of the infusion related reaction minus the start of the latest infusion which is prior to this event.

[TSFAE06CPART1OF2.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE06C.SAS] 01JUN2016, 10:39

TSFAE06CPART2OF2: Time to Onset of Infusion Related Reaction; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd				Total Dara Combined			
		Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
Analysis set: safety	103				664			
Total number of subjects with event of infusion related reactions	51	51 (100.0%)	1 (2.0%)	0	315	307 (97.5%)	9 (2.9%)	21 (6.7%)
Total number of infusion related reactions	126	125 (99.2%)	1 (0.8%)	0	685	647 (94.5%)	9 (1.3%)	29 (4.2%)
Time to onset of infusion related reactions (minutes)								
N[a]	125	124	1	0	642	620	7	15
Mean (SD)	93.4 (111.09)	91.7 (109.81)	310.0 (-)	-	106.2 (194.47)	106.0 (197.25)	132.0 (87.92)	103.7 (86.86)
Median	76.0	76.0	310.0	-	85.0	85.0	110.0	65.0
Range	(7; 1200)	(7; 1200)	(310; 310)	-	(5; 4370)	(5; 4370)	(60; 310)	(20; 320)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
[a]Infusion related reactions with no onset time are excluded.
Note: Percentage of the number of infusion related reactions in each event onset sub-group are calculated with the number of 'Total' column in each group as denominator.
Note: Time to onset of infusion related reactions in minutes are calculated as the start of the infusion related reaction minus the start of the latest infusion which is prior to this event.

[TSFAE06CPART2OF2.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE06C.SAS] 01JUN2016, 10:39

表 2.7.4-付録-92 Number of Subjects with Treatment-emergent Infusion Related Reactions by System Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY1005)

TSFAE15: Number of Subjects with Treatment-emergent Infusion Related Reactions by System Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)			
		Event Onset Time		
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
Analysis set: Safety	8			
Total number of subjects treated within window	8	8	8	8
Total number of subjects with infusion related reactions	5 (62.5%)	5 (62.5%)	0	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	4 (50.0%)	4 (50.0%)	0	0
低酸素症	2 (25.0%)	2 (25.0%)	0	0
喘鳴	2 (25.0%)	2 (25.0%)	0	0
口腔咽頭不快感	1 (12.5%)	1 (12.5%)	0	0
口腔咽頭痛	1 (12.5%)	1 (12.5%)	0	0
一般・全身障害および投与部位の状態	2 (25.0%)	2 (25.0%)	0	0
悪寒	2 (25.0%)	2 (25.0%)	0	0
発熱	1 (12.5%)	1 (12.5%)	0	0
臨床検査	1 (12.5%)	1 (12.5%)	0	0
血圧上昇	1 (12.5%)	1 (12.5%)	0	0
血管障害	1 (12.5%)	1 (12.5%)	0	0
高血圧	1 (12.5%)	1 (12.5%)	0	0

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in safety population within each window as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE15.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE15.SAS] 28SEP2016, 04:17

表 2.7.4-付録-93 Time to Onset of Infusion Related Reaction; Safety Analysis Set (Study 54767414MMY1005)

TSFAE15A: Time to Onset of Infusion Related Reaction; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)			
		Event Onset Time		
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
Analysis set: Safety	8			
Total number of subjects with infusion related reactions	5	5 (100.0%)	0	0
Total number of infusion related reactions	11	11 (100.0%)	0	0
Time to onset of infusion related reactions (minutes)				
N[a]	11	11	0	0
Mean (SD)	78.5 (43.06)	78.5 (43.06)	-	-
Median	85.0	85.0	-	-
Range	(20; 184)	(20; 184)	-	-

Key: Vd = bortezomib-dexamethasone.
[a] Infusion related reactions with missing onset time are excluded.
Note: Percentages of the number of infusion related reactions in each event onset subgroup are calculated with the number of total column in each group as denominator.
Note: Time to onset of infusion related reactions in minutes are calculated as the start of the infusion related reaction minus the start of the last infusion which is prior to this event.

[TSFAE15A.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE15A.SAS] 28SEP2016, 04:17

表 2.7.4-付録-94 Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
Total[a]				
Analysis set: safety	283			
Total number of subjects treated within window	283	283	281	277
Total number of subjects with infusion related reactions	135 (47.7%)	129 (45.6%)	6 (2.1%)	14 (5.1%)
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	87 (30.7%)	87 (30.7%)	1 (0.4%)	2 (0.7%)
咳嗽	24 (8.5%)	24 (8.5%)	0	1 (0.4%)
呼吸困難	24 (8.5%)	24 (8.5%)	0	0
気管支痙攣	13 (4.6%)	13 (4.6%)	0	0
咽喉刺激感	8 (2.8%)	7 (2.5%)	1 (0.4%)	0
鼻閉	7 (2.5%)	7 (2.5%)	0	0
喉頭浮腫	6 (2.1%)	6 (2.1%)	0	0
鼻漏	6 (2.1%)	6 (2.1%)	0	0
喘鳴	6 (2.1%)	6 (2.1%)	0	0
アレルギー性鼻炎	5 (1.8%)	5 (1.8%)	0	0
低酸素症	4 (1.4%)	4 (1.4%)	0	0
発声障害	3 (1.1%)	3 (1.1%)	0	0
アレルギー性呼吸器症状	2 (0.7%)	2 (0.7%)	0	0
鼻閉塞	2 (0.7%)	2 (0.7%)	0	0
湿性咳嗽	2 (0.7%)	2 (0.7%)	0	0
くしゃみ	2 (0.7%)	2 (0.7%)	0	0
窒息	1 (0.4%)	1 (0.4%)	0	0
喉頭不快感	1 (0.4%)	1 (0.4%)	0	0
喉頭狭窄	1 (0.4%)	1 (0.4%)	0	0
喉頭刺激感	1 (0.4%)	1 (0.4%)	0	0
鼻部不快感	1 (0.4%)	1 (0.4%)	0	0
口腔咽頭痛	1 (0.4%)	1 (0.4%)	0	0
呼気延長	1 (0.4%)	1 (0.4%)	0	0
肺水腫	1 (0.4%)	1 (0.4%)	0	0
副鼻腔障害	1 (0.4%)	1 (0.4%)	0	0
上気道性喘鳴	1 (0.4%)	1 (0.4%)	0	0
窒息感	1 (0.4%)	1 (0.4%)	0	0
咽喉絞扼感	1 (0.4%)	0	0	1 (0.4%)
一般・全身障害および投与部位の状態	34 (12.0%)	31 (11.0%)	2 (0.7%)	3 (1.1%)
悪寒	13 (4.6%)	12 (4.2%)	1 (0.4%)	1 (0.4%)
発熱	6 (2.1%)	6 (2.1%)	0	0
胸部不快感	5 (1.8%)	5 (1.8%)	0	0
冷感	5 (1.8%)	5 (1.8%)	0	0
疲労	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
溢出	1 (0.4%)	0	0	1 (0.4%)
高熱	1 (0.4%)	1 (0.4%)	0	0
インフルエンザ様疾患	1 (0.4%)	1 (0.4%)	0	0
注入部位発疹	1 (0.4%)	1 (0.4%)	0	0
非心臓性胸痛	1 (0.4%)	1 (0.4%)	0	0
分泌物分泌	1 (0.4%)	1 (0.4%)	0	0
苦悶感	1 (0.4%)	1 (0.4%)	0	0

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
胃腸障害	31 (11.0%)	30 (10.6%)	0	1 (0.4%)
嘔吐	16 (5.7%)	16 (5.7%)	0	0
悪心	14 (4.9%)	14 (4.9%)	0	0
腹痛	3 (1.1%)	3 (1.1%)	0	0
嚥下障害	2 (0.7%)	2 (0.7%)	0	0
口の錯感覚	2 (0.7%)	1 (0.4%)	0	1 (0.4%)
消化不良	1 (0.4%)	1 (0.4%)	0	0
口唇そう痒症	1 (0.4%)	1 (0.4%)	0	0
口唇腫脹	1 (0.4%)	1 (0.4%)	0	0
嚥下痛	1 (0.4%)	1 (0.4%)	0	0
皮膚および皮下組織障害	26 (9.2%)	24 (8.5%)	0	2 (0.7%)
そう痒症	8 (2.8%)	8 (2.8%)	0	0
多汗症	5 (1.8%)	3 (1.1%)	0	2 (0.7%)
蕁麻疹	4 (1.4%)	4 (1.4%)	0	0
紅斑	3 (1.1%)	3 (1.1%)	0	0
発疹	3 (1.1%)	3 (1.1%)	0	0
冷汗	1 (0.4%)	1 (0.4%)	0	0
アレルギー性そう痒症	1 (0.4%)	1 (0.4%)	0	0
斑状丘疹状皮疹	1 (0.4%)	1 (0.4%)	0	0
そう痒性皮疹	1 (0.4%)	1 (0.4%)	0	0
血管障害	16 (5.7%)	14 (4.9%)	0	2 (0.7%)
高血圧	5 (1.8%)	5 (1.8%)	0	0
低血圧	5 (1.8%)	3 (1.1%)	0	2 (0.7%)
潮紅	4 (1.4%)	4 (1.4%)	0	0
ほてり	2 (0.7%)	2 (0.7%)	0	0
神経系障害	12 (4.2%)	12 (4.2%)	1 (0.4%)	1 (0.4%)
頭痛	7 (2.5%)	7 (2.5%)	1 (0.4%)	1 (0.4%)
錯感覚	2 (0.7%)	2 (0.7%)	0	0
浮動性めまい	1 (0.4%)	1 (0.4%)	0	0
味覚異常	1 (0.4%)	1 (0.4%)	0	0
失神	1 (0.4%)	1 (0.4%)	0	0
眼障害	10 (3.5%)	10 (3.5%)	0	0
流涙増加	5 (1.8%)	5 (1.8%)	0	0
眼刺激	2 (0.7%)	2 (0.7%)	0	0
眼部腫脹	2 (0.7%)	2 (0.7%)	0	0
眼のアレルギー	1 (0.4%)	1 (0.4%)	0	0
眼充血	1 (0.4%)	1 (0.4%)	0	0
心臓障害	9 (3.2%)	7 (2.5%)	2 (0.7%)	2 (0.7%)
頻脈	5 (1.8%)	4 (1.4%)	2 (0.7%)	0
洞性頻脈	2 (0.7%)	1 (0.4%)	0	1 (0.4%)
狭心症	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
動悸	1 (0.4%)	1 (0.4%)	0	0
上室性頻脈	1 (0.4%)	1 (0.4%)	0	0
筋骨格系および結合組織障害	5 (1.8%)	5 (1.8%)	0	0
筋骨格系胸痛	3 (1.1%)	3 (1.1%)	0	0
背部痛	1 (0.4%)	1 (0.4%)	0	0
筋骨格痛	1 (0.4%)	1 (0.4%)	0	0
感染症および寄生虫症	3 (1.1%)	1 (0.4%)	0	2 (0.7%)
結膜炎	1 (0.4%)	1 (0.4%)	0	0
鼻咽頭炎	1 (0.4%)	0	0	1 (0.4%)
上気道感染	1 (0.4%)	0	0	1 (0.4%)
臨床検査	2 (0.7%)	2 (0.7%)	0	0
心電図ＱＴ延長	1 (0.4%)	1 (0.4%)	0	0
酸素飽和度低下	1 (0.4%)	1 (0.4%)	0	0

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
血液およびリンパ系障害	1 (0.4%)	1 (0.4%)	0	0
貧血	1 (0.4%)	1 (0.4%)	0	0
血小板減少症	1 (0.4%)	1 (0.4%)	0	0
免疫系障害	1 (0.4%)	1 (0.4%)	0	0
薬物過敏症	1 (0.4%)	1 (0.4%)	0	0
精神障害	1 (0.4%)	0	0	1 (0.4%)
うつ病	1 (0.4%)	0	0	1 (0.4%)
Japanese				
Analysis set: safety	20			
Total number of subjects treated within window	20	20	20	20
Total number of subjects with infusion related reactions	8 (40.0%)	6 (30.0%)	1 (5.0%)	3 (15.0%)
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	6 (30.0%)	6 (30.0%)	0	0
咳嗽	0	0	0	0
呼吸困難	2 (10.0%)	2 (10.0%)	0	0
気管支痙攣	0	0	0	0
咽喉刺激感	0	0	0	0
鼻閉	0	0	0	0
喉頭浮腫	0	0	0	0
鼻漏	1 (5.0%)	1 (5.0%)	0	0
喘鳴	0	0	0	0
アレルギー性鼻炎	0	0	0	0
低酸素症	1 (5.0%)	1 (5.0%)	0	0
発声障害	0	0	0	0
アレルギー性呼吸器症状	0	0	0	0
鼻閉塞	0	0	0	0
湿性咳嗽	0	0	0	0
くしゃみ	0	0	0	0
窒息	0	0	0	0
喉頭不快感	0	0	0	0
喉頭狭窄	1 (5.0%)	1 (5.0%)	0	0
喉頭刺激感	0	0	0	0
鼻部不快感	0	0	0	0
口腔咽頭痛	0	0	0	0
呼気延長	0	0	0	0
肺水腫	0	0	0	0
副鼻腔障害	0	0	0	0
上気道性喘鳴	1 (5.0%)	1 (5.0%)	0	0
窒息感	0	0	0	0
咽喉絞扼感	0	0	0	0
一般・全身障害および投与部位の状態	2 (10.0%)	2 (10.0%)	0	0
悪寒	1 (5.0%)	1 (5.0%)	0	0
発熱	1 (5.0%)	1 (5.0%)	0	0
胸部不快感	0	0	0	0
冷感	0	0	0	0
疲労	0	0	0	0
溢出	0	0	0	0
高熱	0	0	0	0
インフルエンザ様疾患	0	0	0	0
注入部位発疹	0	0	0	0

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
非心臓性胸痛	0	0	0	0
分泌物分泌	0	0	0	0
苦悶感	0	0	0	0
胃腸障害	0	0	0	0
嘔吐	0	0	0	0
悪心	0	0	0	0
腹痛	0	0	0	0
嚥下障害	0	0	0	0
口の錯感覚	0	0	0	0
消化不良	0	0	0	0
口唇そう痒症	0	0	0	0
口唇腫脹	0	0	0	0
嚥下痛	0	0	0	0
皮膚および皮下組織障害	0	0	0	0
そう痒症	0	0	0	0
多汗症	0	0	0	0
蕁麻疹	0	0	0	0
紅斑	0	0	0	0
発疹	0	0	0	0
冷汗	0	0	0	0
アレルギー性そう痒症	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
そう痒性皮疹	0	0	0	0
血管障害	2 (10.0%)	1 (5.0%)	0	1 (5.0%)
高血圧	0	0	0	0
低血圧	1 (5.0%)	0	0	1 (5.0%)
潮紅	1 (5.0%)	1 (5.0%)	0	0
ほてり	0	0	0	0
神経系障害	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
頭痛	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)
錯感覚	0	0	0	0
浮動性めまい	0	0	0	0
味覚異常	0	0	0	0
失神	0	0	0	0
眼障害	0	0	0	0
流涙増加	0	0	0	0
眼刺激	0	0	0	0
眼部腫脹	0	0	0	0
眼のアレルギー	0	0	0	0
眼充血	0	0	0	0
心臓障害	0	0	0	0
頻脈	0	0	0	0
洞性頻脈	0	0	0	0
狭心症	0	0	0	0
動悸	0	0	0	0
上室性頻脈	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0
筋骨格系胸痛	0	0	0	0
背部痛	0	0	0	0
筋骨格痛	0	0	0	0
感染症および寄生虫症	1 (5.0%)	0	0	1 (5.0%)
結膜炎	0	0	0	0
鼻咽頭炎	1 (5.0%)	0	0	1 (5.0%)
上気道感染	0	0	0	0

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
臨床検査	0	0	0	0
心電図ＱＴ延長	0	0	0	0
酸素飽和度低下	0	0	0	0
血液およびリンパ系障害	0	0	0	0
貧血	0	0	0	0
血小板減少症	0	0	0	0
免疫系障害	0	0	0	0
薬物過敏症	0	0	0	0
精神障害	0	0	0	0
うつ病	0	0	0	0
East Asian[b]				
Analysis set: safety	51			
Total number of subjects treated within window	51	51	51	51
Total number of subjects with infusion related reactions	26 (51.0%)	24 (47.1%)	2 (3.9%)	5 (9.8%)
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	17 (33.3%)	17 (33.3%)	0	0
咳嗽	2 (3.9%)	2 (3.9%)	0	0
呼吸困難	5 (9.8%)	5 (9.8%)	0	0
気管支痙攣	0	0	0	0
咽喉刺激感	0	0	0	0
鼻閉	0	0	0	0
喉頭浮腫	0	0	0	0
鼻漏	2 (3.9%)	2 (3.9%)	0	0
喘鳴	1 (2.0%)	1 (2.0%)	0	0
アレルギー性鼻炎	1 (2.0%)	1 (2.0%)	0	0
低酸素症	3 (5.9%)	3 (5.9%)	0	0
発声障害	1 (2.0%)	1 (2.0%)	0	0
アレルギー性呼吸器症状	2 (3.9%)	2 (3.9%)	0	0
鼻閉塞	1 (2.0%)	1 (2.0%)	0	0
湿性咳嗽	1 (2.0%)	1 (2.0%)	0	0
くしゃみ	0	0	0	0
窒息	0	0	0	0
喉頭不快感	0	0	0	0
喉頭狭窄	1 (2.0%)	1 (2.0%)	0	0
喉頭刺激感	0	0	0	0
鼻部不快感	0	0	0	0
口腔咽頭痛	0	0	0	0
呼気延長	0	0	0	0
肺水腫	1 (2.0%)	1 (2.0%)	0	0
副鼻腔障害	0	0	0	0
上気道性喘鳴	1 (2.0%)	1 (2.0%)	0	0
窒息感	0	0	0	0
咽喉絞扼感	0	0	0	0
一般・全身障害および投与部位の状態	9 (17.6%)	9 (17.6%)	0	0
悪寒	3 (5.9%)	3 (5.9%)	0	0
発熱	2 (3.9%)	2 (3.9%)	0	0
胸部不快感	2 (3.9%)	2 (3.9%)	0	0
冷感	3 (5.9%)	3 (5.9%)	0	0
疲労	0	0	0	0
溢出	0	0	0	0

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
高熱	0	0	0	0
インフルエンザ様疾患	0	0	0	0
注入部位発疹	0	0	0	0
非心臓性胸痛	0	0	0	0
分泌物分泌	0	0	0	0
苦悶感	0	0	0	0
胃腸障害	3 (5.9%)	3 (5.9%)	0	0
嘔吐	2 (3.9%)	2 (3.9%)	0	0
悪心	1 (2.0%)	1 (2.0%)	0	0
腹痛	0	0	0	0
嚥下障害	0	0	0	0
口の錯感覚	0	0	0	0
消化不良	0	0	0	0
口唇そう痒症	0	0	0	0
口唇腫脹	1 (2.0%)	1 (2.0%)	0	0
嚥下痛	0	0	0	0
皮膚および皮下組織障害	2 (3.9%)	2 (3.9%)	0	0
そう痒症	0	0	0	0
多汗症	0	0	0	0
蕁麻疹	1 (2.0%)	1 (2.0%)	0	0
紅斑	0	0	0	0
発疹	0	0	0	0
冷汗	1 (2.0%)	1 (2.0%)	0	0
アレルギー性そう痒症	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
そう痒性皮疹	0	0	0	0
血管障害	6 (11.8%)	4 (7.8%)	0	2 (3.9%)
高血圧	1 (2.0%)	1 (2.0%)	0	0
低血圧	4 (7.8%)	2 (3.9%)	0	2 (3.9%)
潮紅	1 (2.0%)	1 (2.0%)	0	0
ほてり	0	0	0	0
神経系障害	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
頭痛	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)
錯感覚	0	0	0	0
浮動性めまい	0	0	0	0
味覚異常	0	0	0	0
失神	0	0	0	0
眼障害	0	0	0	0
流涙増加	0	0	0	0
眼刺激	0	0	0	0
眼部腫脹	0	0	0	0
眼のアレルギー	0	0	0	0
眼充血	0	0	0	0
心臓障害	3 (5.9%)	3 (5.9%)	1 (2.0%)	1 (2.0%)
頻脈	2 (3.9%)	2 (3.9%)	1 (2.0%)	0
洞性頻脈	0	0	0	0
狭心症	1 (2.0%)	1 (2.0%)	0	1 (2.0%)
動悸	1 (2.0%)	1 (2.0%)	0	0
上室性頻脈	0	0	0	0
筋骨格系および結合組織障害	1 (2.0%)	1 (2.0%)	0	0
筋骨格系胸痛	1 (2.0%)	1 (2.0%)	0	0
背部痛	0	0	0	0
筋骨格痛	0	0	0	0
感染症および寄生虫症	1 (2.0%)	0	0	1 (2.0%)

TSFAE06B_3003: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Event Onset Time; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
	Event Onset Time			
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
結膜炎	0	0	0	0
鼻咽頭炎	1 (2.0%)	0	0	1 (2.0%)
上気道感染	0	0	0	0
臨床検査	0	0	0	0
心電図ＱＴ延長	0	0	0	0
酸素飽和度低下	0	0	0	0
血液およびリンパ系障害	0	0	0	0
貧血	0	0	0	0
血小板減少症	0	0	0	0
免疫系障害	0	0	0	0
薬物過敏症	0	0	0	0
精神障害	0	0	0	0
うつ病	0	0	0	0

Key: DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE06B_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE06B_3003.SAS] 14JUL2016, 09:36

表 2.7.4-付録-95 Summary of Time to Onset of Infusion Related Reaction; Safety Analysis Set (Study 54767414MMY3003)

TSFAE06C_3003: Summary of Time to Onset of Infusion Related Reaction; Safety Analysis Set (Study 54767414MMY3003)

	DRd			
		Event Onset Time		
	Total	1st Infusion	2nd Infusion	Subsequent Infusion
Total[a]				
Analysis set: safety	283			
Total number of subjects with infusion related reactions	135	129 (95.6%)	6 (4.4%)	14 (10.4%)
Total number of infusion related reactions	307	283 (92.2%)	6 (2.0%)	18 (5.9%)
Time to onset of infusion related reactions (minutes)				
N[c]	280	267	4	9
Mean (SD)	121.6 (263.80)	121.3 (269.53)	118.5 (45.01)	134.0 (102.52)
Median	90.0	90.0	124.5	120.0
Range	(7; 4370)	(7; 4370)	(60; 165)	(20; 320)
Japanese				
Analysis set: safety	20			
Total number of subjects with infusion related reactions	8	6 (75.0%)	1 (12.5%)	3 (37.5%)
Total number of infusion related reactions	15	10 (66.7%)	1 (6.7%)	4 (26.7%)
Time to onset of infusion related reactions (minutes)				
N[c]	8	7	0	1
Mean (SD)	82.5 (39.80)	77.1 (39.75)	-	120.0 (-)
Median	86.5	80.0	-	120.0
Range	(23; 138)	(23; 138)	-	(120; 120)
East Asian[b]				
Analysis set: safety	51			
Total number of subjects with infusion related reactions	26	24 (92.3%)	2 (7.7%)	5 (19.2%)
Total number of infusion related reactions	56	48 (85.7%)	2 (3.6%)	6 (10.7%)
Time to onset of infusion related reactions (minutes)				
N[c]	49	45	1	3
Mean (SD)	129.6 (97.87)	125.1 (100.07)	165.0 (-)	186.0 (60.89)
Median	120.0	96.0	165.0	198.0
Range	(23; 540)	(23; 540)	(165; 165)	(120; 240)

Keys: DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Infusion related reactions with missing onset time are excluded.
Note: Percentage of the number of infection related reactions in each event onset sub-group are calculated with the number of 'Total' column in each group as denominator.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Time to onset of infusion related reactions in minutes are calculated as the start of the infusion related reaction minus the start of the latest infusion which is prior to this event.

[TSFAE06C_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE06C_3003.SAS] 01JUL2016, 15:34

表 2.7.4-付録-96 Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE06D: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
Analysis set: safety	243	318	103	664
Total number of subjects with IRRs leading to infusion modification during infusion	104 (42.8%)	129 (40.6%)	47 (45.6%)	280 (42.2%)
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	80 (32.9%)	89 (28.0%)	35 (34.0%)	204 (30.7%)
咳嗽	16 (6.6%)	27 (8.5%)	11 (10.7%)	54 (8.1%)
呼吸困難	25 (10.3%)	26 (8.2%)	11 (10.7%)	62 (9.3%)
気管支痙攣	22 (9.1%)	13 (4.1%)	0	35 (5.3%)
鼻閉	10 (4.1%)	9 (2.8%)	7 (6.8%)	26 (3.9%)
喉頭浮腫	2 (0.8%)	7 (2.2%)	2 (1.9%)	11 (1.7%)
咽喉刺激感	11 (4.5%)	7 (2.2%)	6 (5.8%)	24 (3.6%)
アレルギー性鼻炎	3 (1.2%)	6 (1.9%)	1 (1.0%)	10 (1.5%)
鼻漏	3 (1.2%)	6 (1.9%)	0	9 (1.4%)
喘鳴	3 (1.2%)	5 (1.6%)	3 (2.9%)	11 (1.7%)
発声障害	0	3 (0.9%)	0	3 (0.5%)
低酸素症	0	3 (0.9%)	2 (1.9%)	5 (0.8%)
アレルギー性呼吸器症状	0	2 (0.6%)	0	2 (0.3%)
湿性咳嗽	1 (0.4%)	2 (0.6%)	1 (1.0%)	4 (0.6%)
くしゃみ	0	2 (0.6%)	3 (2.9%)	5 (0.8%)
窒息	0	1 (0.3%)	0	1 (0.2%)
喉頭狭窄	0	1 (0.3%)	0	1 (0.2%)
喉頭刺激感	0	1 (0.3%)	1 (1.0%)	2 (0.3%)
鼻部不快感	0	1 (0.3%)	0	1 (0.2%)
鼻閉塞	0	1 (0.3%)	0	1 (0.2%)
口腔咽頭痛	1 (0.4%)	1 (0.3%)	1 (1.0%)	3 (0.5%)
呼気延長	0	1 (0.3%)	0	1 (0.2%)
肺水腫	0	1 (0.3%)	0	1 (0.2%)
副鼻腔うっ血	0	1 (0.3%)	0	1 (0.2%)

TSFAE06D: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
副鼻腔障害	0	1 (0.3%)	0	1 (0.2%)
上気道性喘鳴	0	1 (0.3%)	0	1 (0.2%)
アレルギー性咳嗽	2 (0.8%)	0	1 (1.0%)	3 (0.5%)
喀血	0	0	1 (1.0%)	1 (0.2%)
口腔咽頭不快感	1 (0.4%)	0	0	1 (0.2%)
口腔咽頭腫脹	1 (0.4%)	0	0	1 (0.2%)
副鼻腔不快感	0	0	1 (1.0%)	1 (0.2%)
咽頭浮腫	1 (0.4%)	0	0	1 (0.2%)
気道うっ血	1 (0.4%)	0	0	1 (0.2%)
低音性連続性ラ音	1 (0.4%)	0	0	1 (0.2%)
咽喉絞扼感	3 (1.2%)	0	1 (1.0%)	4 (0.6%)
上気道咳症候群	0	0	1 (1.0%)	1 (0.2%)
胃腸障害	18 (7.4%)	31 (9.7%)	7 (6.8%)	56 (8.4%)
嘔吐	9 (3.7%)	18 (5.7%)	2 (1.9%)	29 (4.4%)
悪心	4 (1.6%)	13 (4.1%)	6 (5.8%)	23 (3.5%)
腹痛	0	3 (0.9%)	1 (1.0%)	4 (0.6%)
嚥下障害	1 (0.4%)	2 (0.6%)	0	3 (0.5%)
消化不良	0	1 (0.3%)	0	1 (0.2%)
口唇そう痒症	0	1 (0.3%)	0	1 (0.2%)
口唇腫脹	1 (0.4%)	1 (0.3%)	0	2 (0.3%)
嚥下痛	0	1 (0.3%)	0	1 (0.2%)
口の錯感覚	0	1 (0.3%)	0	1 (0.2%)
上腹部痛	1 (0.4%)	0	0	1 (0.2%)
下痢	2 (0.8%)	0	0	2 (0.3%)
口蓋浮腫	1 (0.4%)	0	0	1 (0.2%)
一般・全身障害および投与部位の状態	18 (7.4%)	27 (8.5%)	21 (20.4%)	66 (9.9%)
悪寒	10 (4.1%)	11 (3.5%)	15 (14.6%)	36 (5.4%)
胸部不快感	2 (0.8%)	5 (1.6%)	2 (1.9%)	9 (1.4%)
冷感	0	5 (1.6%)	1 (1.0%)	6 (0.9%)
発熱	2 (0.8%)	5 (1.6%)	4 (3.9%)	11 (1.7%)
高熱	0	1 (0.3%)	1 (1.0%)	2 (0.3%)
インフルエンザ様疾患	1 (0.4%)	1 (0.3%)	0	2 (0.3%)
注入部位発疹	0	1 (0.3%)	0	1 (0.2%)

TSFAE06D: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
非心臓性胸痛	0	1 (0.3%)	3 (2.9%)	4 (0.6%)
苦悶感	0	1 (0.3%)	0	1 (0.2%)
疲労	1 (0.4%)	0	0	1 (0.2%)
注入部位そう痒感	1 (0.4%)	0	0	1 (0.2%)
粘膜浮腫	1 (0.4%)	0	0	1 (0.2%)
疼痛	1 (0.4%)	0	0	1 (0.2%)
皮膚および皮下組織障害	6 (2.5%)	20 (6.3%)	2 (1.9%)	28 (4.2%)
そう痒症	1 (0.4%)	6 (1.9%)	0	7 (1.1%)
多汗症	1 (0.4%)	5 (1.6%)	1 (1.0%)	7 (1.1%)
紅斑	0	3 (0.9%)	0	3 (0.5%)
蕁麻疹	0	3 (0.9%)	0	3 (0.5%)
冷汗	0	1 (0.3%)	0	1 (0.2%)
アレルギー性そう痒症	0	1 (0.3%)	0	1 (0.2%)
発疹	1 (0.4%)	1 (0.3%)	0	2 (0.3%)
そう痒性皮疹	0	1 (0.3%)	0	1 (0.2%)
アレルギー性皮膚炎	2 (0.8%)	0	0	2 (0.3%)
多形紅斑	0	0	1 (1.0%)	1 (0.2%)
顔面腫脹	1 (0.4%)	0	0	1 (0.2%)
血管障害	11 (4.5%)	13 (4.1%)	6 (5.8%)	30 (4.5%)
潮紅	1 (0.4%)	4 (1.3%)	3 (2.9%)	8 (1.2%)
高血圧	7 (2.9%)	4 (1.3%)	2 (1.9%)	13 (2.0%)
低血圧	3 (1.2%)	4 (1.3%)	0	7 (1.1%)
ほてり	0	1 (0.3%)	1 (1.0%)	2 (0.3%)
眼障害	9 (3.7%)	8 (2.5%)	4 (3.9%)	21 (3.2%)
流涙増加	4 (1.6%)	4 (1.3%)	2 (1.9%)	10 (1.5%)
眼刺激	0	2 (0.6%)	1 (1.0%)	3 (0.5%)
眼部腫脹	0	2 (0.6%)	0	2 (0.3%)
眼充血	0	1 (0.3%)	0	1 (0.2%)
結膜浮腫	3 (1.2%)	0	0	3 (0.5%)
眼脂	1 (0.4%)	0	0	1 (0.2%)
眼の障害	1 (0.4%)	0	0	1 (0.2%)
眼そう痒症	0	0	1 (1.0%)	1 (0.2%)
神経系障害	3 (1.2%)	8 (2.5%)	3 (2.9%)	14 (2.1%)
頭痛	1 (0.4%)	5 (1.6%)	1 (1.0%)	7 (1.1%)

TSFAE06D: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined
錯感覚	1 (0.4%)	2 (0.6%)	0	3 (0.5%)
味覚異常	0	1 (0.3%)	0	1 (0.2%)
浮動性めまい	1 (0.4%)	0	1 (1.0%)	2 (0.3%)
会話障害	0	0	1 (1.0%)	1 (0.2%)
心臓障害	5 (2.1%)	5 (1.6%)	2 (1.9%)	12 (1.8%)
頻脈	0	3 (0.9%)	0	3 (0.5%)
狭心症	0	1 (0.3%)	1 (1.0%)	2 (0.3%)
動悸	0	1 (0.3%)	0	1 (0.2%)
洞性頻脈	3 (1.2%)	1 (0.3%)	1 (1.0%)	5 (0.8%)
徐脈	1 (0.4%)	0	0	1 (0.2%)
上室性頻脈	1 (0.4%)	0	0	1 (0.2%)
筋骨格系および結合組織障害	4 (1.6%)	4 (1.3%)	2 (1.9%)	10 (1.5%)
筋骨格系胸痛	0	3 (0.9%)	0	3 (0.5%)
背部痛	3 (1.2%)	1 (0.3%)	1 (1.0%)	5 (0.8%)
骨痛	1 (0.4%)	0	0	1 (0.2%)
筋肉痛	0	0	1 (1.0%)	1 (0.2%)
臨床検査	0	2 (0.6%)	1 (1.0%)	3 (0.5%)
血圧上昇	0	1 (0.3%)	1 (1.0%)	2 (0.3%)
心拍数増加	0	1 (0.3%)	0	1 (0.2%)
酸素飽和度低下	0	1 (0.3%)	0	1 (0.2%)
免疫系障害	0	1 (0.3%)	1 (1.0%)	2 (0.3%)
薬物過敏症	0	1 (0.3%)	0	1 (0.2%)
サイトカイン放出症候群	0	0	1 (1.0%)	1 (0.2%)
感染症および寄生虫症	0	1 (0.3%)	0	1 (0.2%)
結膜炎	0	1 (0.3%)	0	1 (0.2%)
傷害、中毒および処置合併症	0	1 (0.3%)	0	1 (0.2%)
注入に伴う反応	0	1 (0.3%)	0	1 (0.2%)
耳および迷路障害	2 (0.8%)	0	1 (1.0%)	3 (0.5%)
耳そう痒症	1 (0.4%)	0	1 (1.0%)	2 (0.3%)
回転性めまい	1 (0.4%)	0	0	1 (0.2%)

TSFAE06D: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001	Total
	DVd	DRd	DPd	Dara Combined

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Note: Infusion modification during infusion includes Infusion interruption, abortion (or drug withdrawn in GEN503) and infusion rate decrease.

[TSFAE06D.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE06D.SAS] 01JUN2016, 10:39

表 2.7.4-付録-97 Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE34: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with IRRs leading to infusion modification during infusion	5 (62.5%)	0	0
MedDRA system organ class/Preferred term			
呼吸器、胸郭および縦隔障害	4 (50.0%)	0	0
低酸素症	2 (25.0%)	0	0
喘鳴	2 (25.0%)	0	0
口腔咽頭不快感	1 (12.5%)	0	0
口腔咽頭痛	1 (12.5%)	0	0
一般・全身障害および投与部位の状態	2 (25.0%)	0	0
悪寒	2 (25.0%)	0	0
発熱	1 (12.5%)	0	0
臨床検査	1 (12.5%)	0	0
血圧上昇	1 (12.5%)	0	0
血管障害	1 (12.5%)	0	0
高血圧	1 (12.5%)	0	0

Keys: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE34.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE34.SAS] 28SEP2016, 04:24

表 2.7.4-付録-98 Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE_J01_3003: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd n (%)		
	Japanese	East Asian[a]	Total[b]
Analysis set: safety	20	51	283
Total number of subjects with infusion related reaction leading to infusion modification	7 (35.0%)	22 (43.1%)	113 (39.9%)
MedDRA system organ class/Preferred term			
呼吸器、胸郭および縦隔障害	6 (30.0%)	16 (31.4%)	76 (26.9%)
呼吸困難	2 (10.0%)	5 (9.8%)	24 (8.5%)
咳嗽	0	2 (3.9%)	20 (7.1%)
気管支痙攣	0	0	12 (4.2%)
鼻閉	0	0	7 (2.5%)
喉頭浮腫	0	0	6 (2.1%)
鼻漏	1 (5.0%)	2 (3.9%)	6 (2.1%)
咽喉刺激感	0	0	6 (2.1%)
喘鳴	0	1 (2.0%)	5 (1.8%)
低酸素症	1 (5.0%)	2 (3.9%)	3 (1.1%)
アレルギー性鼻炎	0	0	3 (1.1%)
アレルギー性呼吸器症状	0	2 (3.9%)	2 (0.7%)
発声障害	0	1 (2.0%)	2 (0.7%)
湿性咳嗽	0	1 (2.0%)	2 (0.7%)
くしゃみ	0	0	2 (0.7%)
窒息	0	0	1 (0.4%)
喉頭狭窄	1 (5.0%)	1 (2.0%)	1 (0.4%)
喉頭刺激感	0	0	1 (0.4%)
鼻部不快感	0	0	1 (0.4%)
鼻閉塞	0	1 (2.0%)	1 (0.4%)
口腔咽頭痛	0	0	1 (0.4%)
呼気延長	0	0	1 (0.4%)
肺水腫	0	1 (2.0%)	1 (0.4%)
副鼻腔障害	0	0	1 (0.4%)
上気道性喘鳴	1 (5.0%)	1 (2.0%)	1 (0.4%)
胃腸障害	0	3 (5.9%)	27 (9.5%)
嘔吐	0	2 (3.9%)	15 (5.3%)
悪心	0	1 (2.0%)	12 (4.2%)
腹痛	0	0	3 (1.1%)
嚥下障害	0	0	2 (0.7%)
消化不良	0	0	1 (0.4%)
口唇そう痒症	0	0	1 (0.4%)
口唇腫脹	0	1 (2.0%)	1 (0.4%)
嚥下痛	0	0	1 (0.4%)
口の錯感覚	0	0	1 (0.4%)
一般・全身障害および投与部位の状態	1 (5.0%)	7 (13.7%)	27 (9.5%)
悪寒	1 (5.0%)	2 (3.9%)	11 (3.9%)
胸部不快感	0	2 (3.9%)	5 (1.8%)
冷感	0	3 (5.9%)	5 (1.8%)
発熱	0	1 (2.0%)	5 (1.8%)
高熱	0	0	1 (0.4%)
インフルエンザ様疾患	0	0	1 (0.4%)
注入部位発疹	0	0	1 (0.4%)
非心臓性胸痛	0	0	1 (0.4%)
苦悶感	0	0	1 (0.4%)
皮膚および皮下組織障害	0	1 (2.0%)	20 (7.1%)

TSFAE_J01_3003: Infusion Related Reactions Leading to Infusion Modification During Infusion by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	DRd n (%)		
	Japanese	East Asian[a]	Total[b]
そう痒症	0	0	6 (2.1%)
多汗症	0	0	5 (1.8%)
紅斑	0	0	3 (1.1%)
蕁麻疹	0	0	3 (1.1%)
冷汗	0	1 (2.0%)	1 (0.4%)
アレルギー性そう痒症	0	0	1 (0.4%)
発疹	0	0	1 (0.4%)
そう痒性皮疹	0	0	1 (0.4%)
血管障害	1 (5.0%)	3 (5.9%)	11 (3.9%)
高血圧	0	1 (2.0%)	4 (1.4%)
潮紅	0	0	3 (1.1%)
低血圧	1 (5.0%)	2 (3.9%)	3 (1.1%)
ほてり	0	0	1 (0.4%)
神経系障害	0	0	8 (2.8%)
頭痛	0	0	5 (1.8%)
錯感覚	0	0	2 (0.7%)
味覚異常	0	0	1 (0.4%)
眼障害	0	0	7 (2.5%)
流涙増加	0	0	3 (1.1%)
眼刺激	0	0	2 (0.7%)
眼部腫脹	0	0	2 (0.7%)
眼充血	0	0	1 (0.4%)
心臓障害	0	3 (5.9%)	5 (1.8%)
頻脈	0	2 (3.9%)	3 (1.1%)
狭心症	0	1 (2.0%)	1 (0.4%)
動悸	0	1 (2.0%)	1 (0.4%)
洞性頻脈	0	0	1 (0.4%)
筋骨格系および結合組織障害	0	1 (2.0%)	4 (1.4%)
筋骨格系胸痛	0	1 (2.0%)	3 (1.1%)
背部痛	0	0	1 (0.4%)
免疫系障害	0	0	1 (0.4%)
薬物過敏症	0	0	1 (0.4%)
感染症および寄生虫症	0	0	1 (0.4%)
結膜炎	0	0	1 (0.4%)
臨床検査	0	0	1 (0.4%)
酸素飽和度低下	0	0	1 (0.4%)

Key: DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Infusion modification during infusion includes Infusion interruption, abortion and infusion rate decrease.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events are reported using MedDRA version 18.0.

[TSFAE_J01_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE_J01_3003.SAS] 01JUL2016, 14:49

表 2.7.4-付録-99 Discontinuation of Daratumumab Due to Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE11: Discontinuation of Daratumumab Due to Infusion Related Reactions by MedDRA System-Organ Class, Preferred Term and Relationship; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004 DVd		MMY3003+GEN503 DRd		MMY1001 DPd		Total Dara Combined	
	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: safety	243		318		103		664	
Total number of subjects with IRRs leading to discontinuation of daratumumab	2 (0.8%)	2 (0.8%)	2 (0.6%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	5 (0.8%)	5 (0.8%)
MedDRA system organ class/Preferred term								
呼吸器、胸郭および縦隔障害	2 (0.8%)	2 (0.8%)	2 (0.6%)	2 (0.6%)	1 (1.0%)	1 (1.0%)	5 (0.8%)	5 (0.8%)
低酸素症	0	0	0	0	1 (1.0%)	1 (1.0%)	1 (0.2%)	1 (0.2%)
気管支痙攣	2 (0.8%)	2 (0.8%)	0	0	0	0	2 (0.3%)	2 (0.3%)
発声障害	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
呼吸困難	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
喉頭浮腫	1 (0.4%)	1 (0.4%)	2 (0.6%)	2 (0.6%)	0	0	3 (0.5%)	3 (0.5%)
喘鳴	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
胃腸障害	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
消化不良	0	0	1 (0.3%)	1 (0.3%)	0	0	1 (0.2%)	1 (0.2%)
皮膚および皮下組織障害	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.2%)	1 (0.2%)
発疹	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.2%)	1 (0.2%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-100 Discontinuation of Daratumumab Due to Infusion Related Reactions by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY1005)

TSFAE36: Discontinuation of Daratumumab Due to Infusion Related Reactions by System Organ Class, Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)	
	Total	Related
Analysis set: Safety	8	
Total number of subjects with IRRs leading to discontinuation of daratumumab	0	0
MedDRA system organ class/Preferred term		
No data to report		

Keys: Vd = bortezomib-dexamethasone.
Note: Percentages are calculated with the number of subjects in safety population as denominator.
Note: Adverse events related to study treatments are adverse events with a relationship to study treatments of very likely, probably or possible.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE36.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE36.SAS] 28SEP2016, 04:25

表 2.7.4-付録-101 Discontinuation of Daratumumab Due to Infusion Related Reactions by Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

TSFAE_J04_3003: Discontinuation of Daratumumab Due to Infusion Related Reactions by Preferred Term and Relationship; Safety Analysis Set (Study 54767414MMY3003)

	DRd n (%)					
	Japanese		East Asian[a]		Total[b]	
	Total	Related	Total	Related	Total	Related
Analysis set: safety	20		51		283	
Total number of subjects with IRRs leading to Daratumumab discontinuation	0	0	0	0	1 (0.4%)	1 (0.4%)
Preferred term						
消化不良	0	0	0	0	1 (0.4%)	1 (0.4%)
発声障害	0	0	0	0	1 (0.4%)	1 (0.4%)
呼吸困難	0	0	0	0	1 (0.4%)	1 (0.4%)
喉頭浮腫	0	0	0	0	1 (0.4%)	1 (0.4%)
喘鳴	0	0	0	0	1 (0.4%)	1 (0.4%)

Key: DRd = daratumumab-lenalidomide-dexamethasone.
Key: IRRs = infusion related reactions.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events are reported using MedDRA version 18.0.

[TSFAE_J04_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE_J04_3003.SAS] 05JUL2016, 10:40

表 2.7.4-付録-102 Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSICM02: Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001
	DVd	DRd	DPd
Analysis set: safety	243	318	103
Total number of subjects received pre-infusion medications	243 (100.0%)	318 (100.0%)	103 (100.0%)
Therapeutic class/pharmacologic class/preferred term			
Antihistamines for systemic use	243 (100.0%)	318 (100.0%)	103 (100.0%)
Antihistamines for systemic use	243 (100.0%)	318 (100.0%)	103 (100.0%)
Diphenhydramine	66 (27.2%)	94 (29.6%)	81 (78.6%)
Chlorphenamine	27 (11.1%)	61 (19.2%)	0
Dexchlorpheniramine	10 (4.1%)	54 (17.0%)	22 (21.4%)
Clemastine	44 (18.1%)	51 (16.0%)	0
Cetirizine	32 (13.2%)	27 (8.5%)	3 (2.9%)
Promethazine	6 (2.5%)	22 (6.9%)	0
Levocetirizine	0	19 (6.0%)	3 (2.9%)
Loratadine	13 (5.3%)	11 (3.5%)	0
Dimetindene	17 (7.0%)	6 (1.9%)	0
Pheniramine	6 (2.5%)	4 (1.3%)	0
Chloropyramine	22 (9.1%)	3 (0.9%)	0
Piprinhydrinate	4 (1.6%)	3 (0.9%)	0
Desloratadine	0	1 (0.3%)	2 (1.9%)
Fexofenadine	0	1 (0.3%)	0
Antihistamines	1 (0.4%)	0	0
Astemizole	1 (0.4%)	0	0
Bisulepin	11 (4.5%)	0	0
Chlorphenoxamine	1 (0.4%)	0	0
Uncoded	1 (0.4%)	2 (0.6%)	0
Antihistamines for systemic use	1 (0.4%)	2 (0.6%)	0
Analgesics	241 (99.2%)	317 (99.7%)	103 (100.0%)
Other analgesics and antipyretics	241 (99.2%)	317 (99.7%)	103 (100.0%)
Paracetamol	241 (99.2%)	317 (99.7%)	103 (100.0%)
Acetylsalicylic acid	0	3 (0.9%)	0
Metamizole	0	1 (0.3%)	0
Opioids	0	1 (0.3%)	1 (1.0%)
Procet /01554201/	0	1 (0.3%)	0

TSICM02: Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001
	DVd	DRd	DPd
Hydromorphone	0	0	1 (1.0%)
Drugs for acid related disorders	19 (7.8%)	12 (3.8%)	2 (1.9%)
Drugs for peptic ulcer and gastro-oesophageal reflux disease (gord)	19 (7.8%)	12 (3.8%)	2 (1.9%)
Ranitidine	16 (6.6%)	11 (3.5%)	2 (1.9%)
Famotidine	2 (0.8%)	1 (0.3%)	0
Omeprazole	2 (0.8%)	0	0
Drugs for obstructive airway diseases	1 (0.4%)	8 (2.5%)	12 (11.7%)
Other systemic drugs for obstructive airway diseases	0	6 (1.9%)	12 (11.7%)
Montelukast	0	6 (1.9%)	12 (11.7%)
Adrenergics, inhalants	0	2 (0.6%)	0
Duovent	0	2 (0.6%)	0
Other drugs for obstructive airway diseases, inhalants	1 (0.4%)	0	0
Ipratropium	1 (0.4%)	0	0
Antiemetics and antinauseants	14 (5.8%)	6 (1.9%)	2 (1.9%)
Antiemetics and antinauseants	14 (5.8%)	6 (1.9%)	2 (1.9%)
Ondansetron	9 (3.7%)	6 (1.9%)	0
Antiemetics and antinauseants	1 (0.4%)	0	0
Granisetron	5 (2.1%)	0	2 (1.9%)
Blood substitutes and perfusion solutions	7 (2.9%)	2 (0.6%)	0
Irrigating solutions	7 (2.9%)	2 (0.6%)	0
Sodium chloride	6 (2.5%)	2 (0.6%)	0
Sodium bicarbonate	0	1 (0.3%)	0
Salt solutions	1 (0.4%)	0	0
Drugs for functional gastrointestinal disorders	4 (1.6%)	2 (0.6%)	0
Propulsives	4 (1.6%)	2 (0.6%)	0
Alizapride	1 (0.4%)	1 (0.3%)	0
Metoclopramide	3 (1.2%)	1 (0.3%)	0
Psycholeptics	0	2 (0.6%)	0
Antipsychotics	0	1 (0.3%)	0
Prochlorperazine	0	1 (0.3%)	0
Anxiolytics	0	1 (0.3%)	0
Lorazepam	0	1 (0.3%)	0
General nutrients	0	1 (0.3%)	0
Other nutrients	0	1 (0.3%)	0
Glucose	0	1 (0.3%)	0
Other nervous system drugs	0	1 (0.3%)	0
Antivertigo preparations	0	1 (0.3%)	0

TSICM02: Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001
	DVd	DRd	DPd
Cinnarizine	0	1 (0.3%)	0
Anesthetics	1 (0.4%)	0	0
Anesthetics, local	1 (0.4%)	0	0
Lidocaine	1 (0.4%)	0	0
Antibacterials for systemic use	3 (1.2%)	0	0
Sulfonamides and trimethoprim	3 (1.2%)	0	0
Trimethoprim	3 (1.2%)	0	0
Antigout preparations	1 (0.4%)	0	0
Antigout preparations	1 (0.4%)	0	0
Allopurinol	1 (0.4%)	0	0
Antiinflammatory and antirheumatic products	1 (0.4%)	0	0
Antiinflammatory and antirheumatic products, non-steroids	1 (0.4%)	0	0
Ketoprofen	1 (0.4%)	0	0
Diuretics	1 (0.4%)	0	0
High-ceiling diuretics	1 (0.4%)	0	0
Furosemide	1 (0.4%)	0	0
Drugs for treatment of bone diseases	1 (0.4%)	0	0
Drugs affecting bone structure and mineralization	1 (0.4%)	0	0
Zoledronic acid	1 (0.4%)	0	0
Mineral supplements	1 (0.4%)	0	0
Potassium	1 (0.4%)	0	0
Potassium	1 (0.4%)	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: Corticosteroids for systemic use are excluded.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSICM02.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSICM02.SAS] 01JUN2016, 10:46

表 2.7.4-付録-103 Summary of Pre-infusion Medication; All-treated Analysis Set (Study 54767414MMY1005)

TSICM04: Summary of Pre-infusion Medication; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Total number of subjects with 1 or more pre-infusion medications	8 (100.0%)
Therapeutic class/pharmacologic class/preferred term	
Analgesics	8 (100.0%)
Other analgesics and antipyretics	8 (100.0%)
Paracetamol	8 (100.0%)
Antihistamines for systemic use	8 (100.0%)
Antihistamines for systemic use	8 (100.0%)
Diphenhydramine	7 (87.5%)
Chlorphenamine maleate	1 (12.5%)
Corticosteroids for systemic use	8 (100.0%)
Corticosteroids for systemic use, plain	8 (100.0%)
Dexamethasone	8 (100.0%)

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSICM04.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSICM04.SAS] 28SEP2016, 04:30

表 2.7.4-付録-104 Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Study 54767414MMY3003)

TSICM02_3003: Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Study 54767414MMY3003)

	DRd		
	Japanese	East Asian[a]	Total[b]
Analysis set: safety	20	51	283
Total number of subjects with 1 or more pre-infusion medications	20 (100.0%)	51 (100.0%)	283 (100.0%)
Therapeutic class/pharmacologic class/drug			
Analgesics	20 (100.0%)	51 (100.0%)	283 (100.0%)
Other analgesics and antipyretics	20 (100.0%)	51 (100.0%)	283 (100.0%)
Paracetamol	20 (100.0%)	51 (100.0%)	283 (100.0%)
Acetylsalicylic acid	0	0	2 (0.7%)
Metamizole	0	0	1 (0.4%)
Opioids	0	0	1 (0.4%)
Procet /01554201/	0	0	1 (0.4%)
Antihistamines for systemic use	20 (100.0%)	51 (100.0%)	283 (100.0%)
Antihistamines for systemic use	20 (100.0%)	51 (100.0%)	283 (100.0%)
Diphenhydramine	15 (75.0%)	26 (51.0%)	91 (32.2%)
Dexchlorpheniramine	3 (15.0%)	3 (5.9%)	50 (17.7%)
Chlorphenamine	2 (10.0%)	19 (37.3%)	48 (17.0%)
Clemastine	0	0	45 (15.9%)
Promethazine	0	0	22 (7.8%)
Cetirizine	0	0	15 (5.3%)
Levocetirizine	0	0	12 (4.2%)
Loratadine	1 (5.0%)	1 (2.0%)	10 (3.5%)
Dimetindene	0	0	6 (2.1%)
Pheniramine	0	4 (7.8%)	4 (1.4%)
Chloropyramine	0	0	3 (1.1%)
Piprinhydrinate	0	3 (5.9%)	3 (1.1%)
Fexofenadine	0	0	1 (0.4%)
Uncoded	0	0	2 (0.7%)
Antihistamines for systemic use	0	0	2 (0.7%)
Drugs for acid related disorders	0	0	12 (4.2%)
Drugs for peptic ulcer and gastro-oesophageal reflux disease (gord)	0	0	12 (4.2%)
Ranitidine	0	0	11 (3.9%)
Famotidine	0	0	1 (0.4%)
Corticosteroids for systemic use	1 (5.0%)	1 (2.0%)	9 (3.2%)
Corticosteroids for systemic use, plain	1 (5.0%)	1 (2.0%)	9 (3.2%)
Dexamethasone	1 (5.0%)	1 (2.0%)	3 (1.1%)
Prednisone	0	0	3 (1.1%)
Hydrocortisone	0	0	2 (0.7%)
Prednisolone	0	0	1 (0.4%)
Drugs for obstructive airway diseases	0	0	8 (2.8%)
Other systemic drugs for obstructive airway diseases	0	0	6 (2.1%)
Montelukast	0	0	6 (2.1%)
Adrenergics, inhalants	0	0	2 (0.7%)
Duovent	0	0	2 (0.7%)
Antiemetics and antinauseants	0	0	6 (2.1%)
Antiemetics and antinauseants	0	0	6 (2.1%)
Ondansetron	0	0	6 (2.1%)
Blood substitutes and perfusion solutions	0	0	2 (0.7%)
Irrigating solutions	0	0	2 (0.7%)
Sodium chloride	0	0	2 (0.7%)
Sodium bicarbonate	0	0	1 (0.4%)
Drugs for functional gastrointestinal disorders	0	0	2 (0.7%)
Propulsives	0	0	2 (0.7%)
Alizapride	0	0	1 (0.4%)
Metoclopramide	0	0	1 (0.4%)
Psycholeptics	0	0	2 (0.7%)
Antipsychotics	0	0	1 (0.4%)
Prochlorperazine	0	0	1 (0.4%)
Anxiolytics	0	0	1 (0.4%)
Lorazepam	0	0	1 (0.4%)

TSICM02_3003: Summary of Pre-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Study 54767414MMY3003)

	DRd		
	Japanese	East Asian[a]	Total[b]
General nutrients	0	1 (2.0%)	1 (0.4%)
Other nutrients	0	1 (2.0%)	1 (0.4%)
Glucose	0	1 (2.0%)	1 (0.4%)
Other nervous system drugs	1 (5.0%)	1 (2.0%)	1 (0.4%)
Antivertigo preparations	1 (5.0%)	1 (2.0%)	1 (0.4%)
Cinnarizine	1 (5.0%)	1 (2.0%)	1 (0.4%)

Keys: DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Percentages calculated with the number of subjects in each treatment group as denominator.

[TSICM02_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSICM02_3003.SAS] 30JUN2016, 22:31

表 2.7.4-付録-105 Summary of Post-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug;Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSICM04: Summary of Post-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug;Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001
	DVd	DRd	DPd
Analysis set: safety	243	318	103
Total number of subjects received post-infusion medications	21 (8.6%)	30 (9.4%)	0
Therapeutic class/pharmacologic class/preferred term			
Antihistamines For Systemic Use	14 (5.8%)	22 (6.9%)	0
Antihistamines For Systemic Use	14 (5.8%)	22 (6.9%)	0
Cetirizine	0	6 (1.9%)	0
Clemastine	1 (0.4%)	6 (1.9%)	0
Diphenhydramine	1 (0.4%)	4 (1.3%)	0
Dexchlorpheniramine	0	3 (0.9%)	0
Chlorphenamine	10 (4.1%)	1 (0.3%)	0
Loratadine	0	1 (0.3%)	0
Promethazine	0	1 (0.3%)	0
Desloratadine	1 (0.4%)	0	0
Pheniramine	1 (0.4%)	0	0
Piprinhydrinate	1 (0.4%)	0	0
Analgesics	1 (0.4%)	9 (2.8%)	0
Other Analgesics And Antipyretics	1 (0.4%)	7 (2.2%)	0
Paracetamol	1 (0.4%)	7 (2.2%)	0
Opioids	0	2 (0.6%)	0
Lamaline /01708901/	0	1 (0.3%)	0
Oxycodone	0	1 (0.3%)	0
Tramadol	0	1 (0.3%)	0
Drugs For Obstructive Airway Diseases	6 (2.5%)	6 (1.9%)	0
Adrenergics, Inhalants	6 (2.5%)	6 (1.9%)	0
Salbutamol	5 (2.1%)	6 (1.9%)	0
Budesonide W/Formoterol	1 (0.4%)	0	0
Duovent	1 (0.4%)	0	0
Epinephrine	1 (0.4%)	0	0
Other Drugs For Obstructive Airway Diseases, Inhalants	1 (0.4%)	0	0
Fluticasone	1 (0.4%)	0	0
Other Systemic Drugs For Obstructive Airway Diseases	1 (0.4%)	0	0
Aminophylline	1 (0.4%)	0	0

TSICM04: Summary of Post-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug;Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004	MMY3003+GEN503	MMY1001
	DVd	DRd	DPd
All Other Therapeutic Products	0	1 (0.3%)	0
All Other Therapeutic Products	0	1 (0.3%)	0
Oxygen	0	1 (0.3%)	0
Antiemetics And Antinauseants	0	1 (0.3%)	0
Antiemetics And Antinauseants	0	1 (0.3%)	0
Ondansetron	0	1 (0.3%)	0
Drugs For Acid Related Disorders	1 (0.4%)	1 (0.3%)	0
Drugs For Peptic Ulcer And Gastro-Oesophageal Reflux Disease (Gord)	1 (0.4%)	1 (0.3%)	0
Famotidine	0	1 (0.3%)	0
Omeprazole	1 (0.4%)	0	0
Drugs For Functional Gastrointestinal Disorders	0	1 (0.3%)	0
Propulsives	0	1 (0.3%)	0
Metoclopramide	0	1 (0.3%)	0
Antithrombotic Agents	2 (0.8%)	0	0
Antithrombotic Agents	2 (0.8%)	0	0
Heparin	1 (0.4%)	0	0
Nadroparin	1 (0.4%)	0	0
Blood Substitutes And Perfusion Solutions	1 (0.4%)	0	0
Irrigating Solutions	1 (0.4%)	0	0
Salt Solutions	1 (0.4%)	0	0
Diuretics	1 (0.4%)	0	0
High-Ceiling Diuretics	1 (0.4%)	0	0
Furosemide	1 (0.4%)	0	0
Drugs For Treatment Of Bone Diseases	3 (1.2%)	0	0
Drugs Affecting Bone Structure And Mineralization	3 (1.2%)	0	0
Pamidronic Acid	3 (1.2%)	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: Corticosteroids for systemic use are excluded and corticosteroids were the only post-infusion medications utilized for the DPd arm.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-106 Summary of Post-infusion Medication; All-treated Analysis Set (Study 54767414MMY1005)

TSICM05: Summary of Post-infusion Medication; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Total number of subjects with 1 or more post-infusion medications	1 (12.5%)
Therapeutic class/pharmacologic class/preferred term	
Antihistamines for systemic use	1 (12.5%)
Antihistamines for systemic use	1 (12.5%)
Diphenhydramine hydrochloride	1 (12.5%)
Drugs for obstructive airway diseases	1 (12.5%)
Adrenergics, inhalants	1 (12.5%)
Salbutamol sulfate	1 (12.5%)

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSICM05.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSICM05.SAS] 28SEP2016, 04:30

表 2.7.4-付録-107 Summary of Post-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Study 54767414MMY3003)

TSICM04_3003: Summary of Post-infusion Medications by Therapeutic Class, Pharmacologic Class, and Drug; Safety Analysis Set (Study 54767414MMY3003)

	DRd		
	Japanese	East Asian[a]	Total[b]
Analysis set: safety	20	51	283
Total number of subjects with 1 or more post-infusion medications	0	0	21 (7.4%)
Therapeutic class/pharmacologic class/drug			
Antihistamines for systemic use	0	0	16 (5.7%)
Antihistamines for systemic use	0	0	16 (5.7%)
Cetirizine	0	0	6 (2.1%)
Diphenhydramine	0	0	4 (1.4%)
Dexchlorpheniramine	0	0	3 (1.1%)
Chlorphenamine	0	0	1 (0.4%)
Loratadine	0	0	1 (0.4%)
Promethazine	0	0	1 (0.4%)
Drugs for obstructive airway diseases	0	0	6 (2.1%)
Adrenergics, inhalants	0	0	6 (2.1%)
Salbutamol	0	0	6 (2.1%)
Analgesics	0	0	4 (1.4%)
Other analgesics and antipyretics	0	0	4 (1.4%)
Paracetamol	0	0	4 (1.4%)
All other therapeutic products	0	0	1 (0.4%)
All other therapeutic products	0	0	1 (0.4%)
Oxygen	0	0	1 (0.4%)
Antiemetics and antinauseants	0	0	1 (0.4%)
Antiemetics and antinauseants	0	0	1 (0.4%)
Ondansetron	0	0	1 (0.4%)
Corticosteroids for systemic use	0	0	1 (0.4%)
Corticosteroids for systemic use, plain	0	0	1 (0.4%)
Dexamethasone	0	0	1 (0.4%)
Drugs for acid related disorders	0	0	1 (0.4%)
Drugs for peptic ulcer and gastro-oesophageal reflux disease (gord)	0	0	1 (0.4%)
Famotidine	0	0	1 (0.4%)
Drugs for functional gastrointestinal disorders	0	0	1 (0.4%)
Propulsives	0	0	1 (0.4%)
Metoclopramide	0	0	1 (0.4%)

Keys: DRd = daratumumab-lenalidomide-dexamethasone.
[a] East Asian: Japan, Korea and Taiwan.
[b] Total column include all subjects of the group.
Note: Percentages calculated with the number of subjects in each treatment group as denominator.

[TSICM04_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSICM04_3003.SAS] 30JUN2016, 22:32

表 2.7.4-付録-108 Infusion Related Reactions by System Organ Class, Preferred Term and Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE20: Infusion Related Reactions by System Organ Class, Preferred Term and Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with infusion related reactions	15 (65.2%)	2 (8.7%)	30 (54.5%)	2 (3.6%)	80 (51.3%)	6 (3.8%)	3 (100.0%)	0	128 (54.0%)	10 (4.2%)
MedDRA system organ class/Preferred term										
呼吸器、胸郭および縦隔障害	3 (13.0%)	1 (4.3%)	24 (43.6%)	0	55 (35.3%)	4 (2.6%)	2 (66.7%)	0	84 (35.4%)	5 (2.1%)
鼻閉	0	0	3 (5.5%)	0	17 (10.9%)	0	1 (33.3%)	0	21 (8.9%)	0
咳嗽	0	0	6 (10.9%)	0	12 (7.7%)	0	1 (33.3%)	0	19 (8.0%)	0
アレルギー性鼻炎	1 (4.3%)	0	12 (21.8%)	0	10 (6.4%)	0	0	0	23 (9.7%)	0
咽喉刺激感	0	0	0	0	9 (5.8%)	0	0	0	9 (3.8%)	0
呼吸困難	1 (4.3%)	0	3 (5.5%)	0	8 (5.1%)	1 (0.6%)	0	0	12 (5.1%)	1 (0.4%)
気管支痙攣	1 (4.3%)	1 (4.3%)	1 (1.8%)	0	4 (2.6%)	2 (1.3%)	1 (33.3%)	0	7 (3.0%)	3 (1.3%)
くしゃみ	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
咽喉絞扼感	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
低酸素症	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
口腔咽頭痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
喘鳴	0	0	1 (1.8%)	0	2 (1.3%)	0	0	0	3 (1.3%)	0
アレルギー性咳嗽	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
喉頭浮腫	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
アレルギー性喉頭炎	0	0	3 (5.5%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
鼻部障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
発声障害	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
一般・全身障害および投与部位の状態	9 (39.1%)	0	9 (16.4%)	1 (1.8%)	20 (12.8%)	0	0	0	38 (16.0%)	1 (0.4%)
悪寒	0	0	5 (9.1%)	1 (1.8%)	11 (7.1%)	0	0	0	16 (6.8%)	1 (0.4%)
発熱	6 (26.1%)	0	4 (7.3%)	0	5 (3.2%)	0	0	0	15 (6.3%)	0
胸部不快感	0	0	2 (3.6%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
胸痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
疲労	2 (8.7%)	0	0	0	1 (0.6%)	0	0	0	3 (1.3%)	0
インフルエンザ様疾患	3 (13.0%)	0	0	0	1 (0.6%)	0	0	0	4 (1.7%)	0
注入部位内出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE20: Infusion Related Reactions by System Organ Class, Preferred Term and Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
疼痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
非心臓性胸痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
胃腸障害	3 (13.0%)	0	7 (12.7%)	0	11 (7.1%)	0	1 (33.3%)	0	22 (9.3%)	0
悪心	2 (8.7%)	0	3 (5.5%)	0	8 (5.1%)	0	0	0	13 (5.5%)	0
嘔吐	0	0	5 (9.1%)	0	7 (4.5%)	0	1 (33.3%)	0	13 (5.5%)	0
上腹部痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
下痢	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口の錯感覚	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口内乾燥	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
消化不良	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
口唇浮腫	1 (4.3%)	0	0	0	0	0	0	0	1 (0.4%)	0
皮膚および皮下組織障害	1 (4.3%)	0	3 (5.5%)	0	6 (3.8%)	0	0	0	10 (4.2%)	0
そう痒症	1 (4.3%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	5 (2.1%)	0
発疹	1 (4.3%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	3 (1.3%)	0
斑状皮疹	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
蕁麻疹	0	0	1 (1.8%)	0	1 (0.6%)	0	0	0	2 (0.8%)	0
多汗症	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
眼障害	0	0	0	0	5 (3.2%)	0	0	0	5 (2.1%)	0
眼そう痒症	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
霧視	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
白内障	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋骨格系および結合組織障害	0	0	2 (3.6%)	0	4 (2.6%)	0	0	0	6 (2.5%)	0
背部痛	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
鼡径部痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
筋肉痛	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
側腹部痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
筋骨格痛	0	0	1 (1.8%)	0	0	0	0	0	1 (0.4%)	0
血管障害	4 (17.4%)	0	4 (7.3%)	1 (1.8%)	4 (2.6%)	2 (1.3%)	0	0	12 (5.1%)	3 (1.3%)
高血圧	1 (4.3%)	0	2 (3.6%)	1 (1.8%)	3 (1.9%)	2 (1.3%)	0	0	6 (2.5%)	3 (1.3%)
潮紅	2 (8.7%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
低血圧	2 (8.7%)	0	1 (1.8%)	0	0	0	0	0	3 (1.3%)	0
血液およびリンパ系障害	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
貧血	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
赤血球凝集	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE20: Infusion Related Reactions by System Organ Class, Preferred Term and Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
心臓障害	3 (13.0%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	7 (3.0%)	0
動悸	1 (4.3%)	0	0	0	1 (0.6%)	0	0	0	2 (0.8%)	0
洞性頻脈	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
頻脈	2 (8.7%)	0	1 (1.8%)	0	1 (0.6%)	0	0	0	4 (1.7%)	0
神経系障害	3 (13.0%)	0	1 (1.8%)	0	3 (1.9%)	0	0	0	7 (3.0%)	0
頭痛	1 (4.3%)	0	0	0	3 (1.9%)	0	0	0	4 (1.7%)	0
浮動性めまい	2 (8.7%)	0	1 (1.8%)	0	0	0	0	0	3 (1.3%)	0
精神障害	0	0	0	0	3 (1.9%)	0	0	0	3 (1.3%)	0
不安	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
譫妄	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
免疫系障害	3 (13.0%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	0	0	0	6 (2.5%)	2 (0.8%)
サイトカイン放出症候群	1 (4.3%)	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	3 (1.3%)	1 (0.4%)
季節性アレルギー	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
過敏症	2 (8.7%)	1 (4.3%)	0	0	0	0	0	0	2 (0.8%)	1 (0.4%)
感染症および寄生虫症	0	0	0	0	0	0	1 (33.3%)	0	1 (0.4%)	0
鼻咽頭炎	0	0	0	0	0	0	1 (33.3%)	0	1 (0.4%)	0

Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE20.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae20.sas] 16MAR2015, 12:05

表 2.7.4-付録-109 Summary of Subjects who Experienced Bronchospasm IRRs (Studies: MMY2002 and GEN501)

Table 14: Summary of Subjects who Experienced Bronchospasm IRRs (Studies: MMY2002 and GEN501)

Subject ID	Age	Sex	Past Medical History	Treatment Group	Study Day of TEAE	Serious/ Toxicity Grade	Drug Relationship	Action Taken With Study Drug	Pre-Infusion Steroids Y/N	Post-Infusion Steroids Y/N	Start of IRR	Dose Resumed after IRR and Completed?	Subject Received Future Doses?
MMY2002-100079	55	F	No h/o airway disease	16mg/kg	1	N/2	Very likely	Interrupted	Y	Y	60 minutes after start of first dose	Y	Y
MMY2002-100095	61	F	h/o Grade 1 dyspnoea at study entry	16 mg/kg	1	N/3	Very likely	Interrupted	Y	Y	90 minutes after start of first dose	Y	Y
MMY2002-100149	70	F	h/o Grade 1 COPD and Grade 1 asthma at study entry	16 mg/kg	1	N/3	Very likely	Interrupted	Y	Y	90 minutes after start of first dose	N	Y
MMY2002-100153	74	M	No h/o airway disease	16 mg/kg	1	N/2	Very likely	Interrupted	Y	Y	90 minutes after start of first dose	N	Y
GEN501-501018 (Part 1)	60	M	h/o COPD at study entry	2 mg/kg	2	N/2	Possibly/probably	Interrupted	Y	Y[a]	Approximately 180 minutes after start of first dose	Y	Y
					23	N/2	Possibly/probably	Withdrawn	Y	Y[a]	Approximately 210 minutes after start of first dose	Y	N
					25	Y/3	Possibly/probably	Withdrawn	Y	Y[a]	2 days after d/c from study drug	N/A	N/A
GEN501-501209[b] (Part 2)	49	F	h/o pneumonia	8 mg/kg	2	N/1	Possibly/probably	Interrupted	Y	Y	45 minutes after the start of 1st full dose	Y	N
GEN501-501033 (Part 1)	50	M	h/o asthma at study entry	24 mg/kg	24	Y/2	Possibly/probably	Dose not changed	Y	Y	Approximately 24 hours after the 2nd full dose	N/A	Y
					31	N/2	Possibly/probably	Withdrawn	Y	Y	Approximately 24 hours after the 3rd full dose was administered	N/A	N

COPD=chronic obstructive pulmonary disease; F=female; h/o=history of; IRR=infusion-related reaction; M=male; N=no; N/A=not applicable; TEAE=treatment-emergent adverse event; Y=yes

[a] post-infusion steroids were not mandated as prophylaxis per protocol, but given as treatment for the TEAE.

[b] Subject was assigned to Schedule A, 500 mL for first infusion.

参照元: MMY2002 CSR_Attachment Subject Narratives, GEN501 CSR_Attachment Subject Narratives

表 2.7.4-付録-110 Infusion Related Reactions; All Treated Analysis Population (Study 54767414MMY1002)

LSFAE05: Infusion Related Reactions; All Treated Analysis Population (Study 54767414MMY1002)

Treatment Group	Subject ID	Sex/ Age	Race	Reported Term	Preferred Term[a]	TEAE	Onset Date/ (Study Day)	Outcome Date/ (Study Day)	Duration[b]	Outcome	Toxicity Grade	Action Taken	Causality	Serious Event	DLT Evaluated?
Daratumumab 8 mg/kg	810201	M/ 66	ASIAN	FEVER	発熱	Y	2014-05-15T14:10/ (1)	2014-05-15T14:58/ (1)	1	RECOVERED/RESOLVED	1	DRUG INTERRUPTED	VERY LIKELY	N	
Daratumumab 8 mg/kg	810201	M/ 66	ASIAN	FEVER	発熱	Y	2014-05-15T14:59/ (1)	2014-05-15T16:08/ (1)	1	RECOVERED/RESOLVED	2	DRUG INTERRUPTED	VERY LIKELY	N	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	CHILLS	悪寒	Y	2014-08-05T11:50/ (1)	2014-08-05T13:35/ (1)	1	RECOVERED/RESOLVED	2	DRUG INTERRUPTED	PROBABLE	N	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	HEADACHE	頭痛	Y	2014-08-05T11:50/ (1)	2014-08-05T13:35/ (1)	1	RECOVERED/RESOLVED	2	DRUG INTERRUPTED	PROBABLE	N	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	PAIN IN THE THROAT	口腔咽頭痛	Y	2014-08-05T11:50/ (1)	2014-08-05T13:35/ (1)	1	RECOVERED/RESOLVED	2	DRUG INTERRUPTED	PROBABLE	N	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	HYPOXIA	低酸素症	Y	2014-08-05T11:50/ (1)	2014-08-05T17:30/ (1)	1	RECOVERED/RESOLVED	2	DRUG INTERRUPTED	PROBABLE	N	
Daratumumab 16 mg/kg	810103	F/ 72	ASIAN	FEVER	発熱	Y	2014-08-05T12:15/ (1)	2014-08-05T19:54/ (1)	1	RECOVERED/RESOLVED	2	DRUG INTERRUPTED	PROBABLE	N	
Daratumumab 16 mg/kg	810105	M/ 61	ASIAN	FEVER	発熱	Y	2014-10-17/ (3)	2014-10-19/ (5)	3	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	
Daratumumab 16 mg/kg	810205	F/ 47	ASIAN	FEVER	発熱	Y	2014-09-13/ (24)	2014-09-15/ (26)	3	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	
Daratumumab 16 mg/kg	810205	F/ 47	ASIAN	FEVER	発熱	Y	2014-09-20/ (31)	2014-09-23/ (34)	4	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	

LSFAE05: Infusion Related Reactions; All Treated Analysis Population (Study 54767414MMY1002)

Treatment Group	Subject ID	Sex/ Age	Race	Reported Term	Preferred Term[a]	TEAE	Onset Date/ (Study Day)	Outcome Date/ (Study Day)	Duration[b]	Outcome	Toxicity Grade	Action Taken	Causality	Serious Event	DLT Evaluated?
Daratumumab 16 mg/kg	810205	F/ 47	ASIAN	FEVER	発熱	Y	2014-09-28/ (39)	2014-09-29/ (40)	2	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	
Daratumumab 16 mg/kg	810205	F/ 47	ASIAN	FEVER	発熱	Y	2014-10-06/ (47)	2014-10-07/ (48)	2	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	
Daratumumab 16 mg/kg	810205	F/ 47	ASIAN	FEVER	発熱	Y	2014-10-13/ (54)	2014-10-14/ (55)	2	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	
Daratumumab 16 mg/kg	810205	F/ 47	ASIAN	FEVER	発熱	Y	2014-10-26/ (67)	2014-10-27/ (68)	2	RECOVERED/RESOLVED	2	DOSE NOT CHANGED	PROBABLE	N	

[a] Adverse Events are coded using MedDRA 18.0.
[b] Calculated as the number of days between Onset Date and Outcome Date when outcome is Recovered or Recovering.

[LSFAE05.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\lsfae05.sas] 22FEB2016, 11:20

表 2.7.4-付録-111 Time to Onset of Infusion Related Reaction; All Treated Analysis Set - 16 mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

TSFAE20E: Time to Onset of Infusion Related Reaction; All Treated Analysis Set - 16 mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

		Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions
Analysis set: all treated	156			
Total number of subjects with event of infusion related reactions	80	73 (91.3%)	9 (11.3%)	10 (12.5%)
Total number of infusion related reactions	165	135 (81.8%)	13 (7.9%)	17 (10.3%)
Time to onset of infusion related reactions (minutes)				
N[a]	144	128	9	7
Mean (SD)	114.76 (109.128)	102.09 (82.899)	132.11 (93.399)	324.00 (267.927)
Median	90.00	90.00	100.00	495.00[b]
Range	(1.0; 557.0)	(1.0; 540.0)	(60.0; 363.0)	(10.0; 557.0)[b]

[a] Infusion related reactions with no onset time are excluded.
[b] Subject 501031 from GEN 501 Part 1 reported Grade 1 fever for 4 consecutive infusions (4th to 7th infusions) with onset times of 495, 544, 555, and 557 minutes after infusion.
Note: Percentage of the number of infusion related reactions in each event onset sub-group are calculated with the number of 'Total' column in each group as denominator.
Note: Time to onset of infusion related reactions in minutes are calculated as the start of the infusion related reaction minus the start of the latest infusion which is prior to this event.

[TSFAE20E.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae20e.sas] 10APR2015, 09:25

表 2.7.4-付録-112 Infusion Related Reactions by System Organ Class, Preferred Term, Drug Product Formulation and Event Onset Time; All Treated Analysis Set - 16mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

TSFAE20A: Infusion Related Reactions by System Organ Class, Preferred Term, Drug Product Formulation and Event Onset Time; All Treated Analysis Set - 16mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

	Phase 2				Phase 3				Total			
		Event Onset				Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
Analysis set: all treated	64				92				156			
Total number of subjects treated within window	64	64	62	60	92	92	88	86	156	156	150	146
Total number of subjects with event of infusion related reactions	30 (46.9%)	27 (42.2%)	4 (6.5%)	5 (8.3%)	50 (54.3%)	46 (50.0%)	5 (5.7%)	5 (5.8%)	80 (51.3%)	73 (46.8%)	9 (6.0%)	10 (6.8%)
MedDRA system organ class/Preferred term												
呼吸器、胸郭および縦隔障害	21 (32.8%)	21 (32.8%)	0	0	34 (37.0%)	33 (35.9%)	4 (4.5%)	0	55 (35.3%)	54 (34.6%)	4 (2.7%)	0
鼻閉	7 (10.9%)	7 (10.9%)	0	0	10 (10.9%)	10 (10.9%)	1 (1.1%)	0	17 (10.9%)	17 (10.9%)	1 (0.7%)	0
咳嗽	7 (10.9%)	7 (10.9%)	0	0	5 (5.4%)	4 (4.3%)	1 (1.1%)	0	12 (7.7%)	11 (7.1%)	1 (0.7%)	0
アレルギー性鼻炎	6 (9.4%)	6 (9.4%)	0	0	4 (4.3%)	4 (4.3%)	0	0	10 (6.4%)	10 (6.4%)	0	0
咽喉刺激感	3 (4.7%)	3 (4.7%)	0	0	6 (6.5%)	5 (5.4%)	1 (1.1%)	0	9 (5.8%)	8 (5.1%)	1 (0.7%)	0
呼吸困難	2 (3.1%)	2 (3.1%)	0	0	6 (6.5%)	5 (5.4%)	1 (1.1%)	0	8 (5.1%)	7 (4.5%)	1 (0.7%)	0
気管支痙攣	0	0	0	0	4 (4.3%)	4 (4.3%)	0	0	4 (2.6%)	4 (2.6%)	0	0
くしゃみ	2 (3.1%)	2 (3.1%)	0	0	1 (1.1%)	1 (1.1%)	1 (1.1%)	0	3 (1.9%)	3 (1.9%)	1 (0.7%)	0
咽喉絞扼感	0	0	0	0	3 (3.3%)	3 (3.3%)	0	0	3 (1.9%)	3 (1.9%)	0	0
低酸素症	0	0	0	0	2 (2.2%)	2 (2.2%)	0	0	2 (1.3%)	2 (1.3%)	0	0
口腔咽頭痛	0	0	0	0	2 (2.2%)	2 (2.2%)	0	0	2 (1.3%)	2 (1.3%)	0	0
喘鳴	0	0	0	0	2 (2.2%)	2 (2.2%)	0	0	2 (1.3%)	2 (1.3%)	0	0
アレルギー性咳嗽	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
喉頭浮腫	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
アレルギー性喉頭炎	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
鼻部障害	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
一般・全身障害および投与部位の状態	7 (10.9%)	6 (9.4%)	2 (3.2%)	1 (1.7%)	13 (14.1%)	12 (13.0%)	1 (1.1%)	1 (1.2%)	20 (12.8%)	18 (11.5%)	3 (2.0%)	2 (1.4%)
悪寒	2 (3.1%)	2 (3.1%)	0	0	9 (9.8%)	9 (9.8%)	0	0	11 (7.1%)	11 (7.1%)	0	0
発熱	2 (3.1%)	2 (3.1%)	0	1 (1.7%)	3 (3.3%)	2 (2.2%)	1 (1.1%)	1 (1.2%)	5 (3.2%)	4 (2.6%)	1 (0.7%)	2 (1.4%)
胸部不快感	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0
胸痛	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
疲労	1 (1.6%)	1 (1.6%)	1 (1.6%)	0	0	0	0	0	1 (0.6%)	1 (0.6%)	1 (0.7%)	0
インフルエンザ様疾患	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0
注入部位内出血	1 (1.6%)	0	1 (1.6%)	0	0	0	0	0	1 (0.6%)	0	1 (0.7%)	0
疼痛	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0

TSFAE20A: Infusion Related Reactions by System Organ Class, Preferred Term, Drug Product Formulation and Event Onset Time; All Treated Analysis Set - 16mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

	Phase 2				Phase 3				Total			
		Event Onset				Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
胃腸障害	2 (3.1%)	2 (3.1%)	0	0	9 (9.8%)	8 (8.7%)	1 (1.1%)	0	11 (7.1%)	10 (6.4%)	1 (0.7%)	0
悪心	0	0	0	0	8 (8.7%)	7 (7.6%)	1 (1.1%)	0	8 (5.1%)	7 (4.5%)	1 (0.7%)	0
嘔吐	2 (3.1%)	2 (3.1%)	0	0	5 (5.4%)	4 (4.3%)	1 (1.1%)	0	7 (4.5%)	6 (3.8%)	1 (0.7%)	0
上腹部痛	0	0	0	0	1 (1.1%)	0	1 (1.1%)	0	1 (0.6%)	0	1 (0.7%)	0
下痢	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
口の錯感覚	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
皮膚および皮下組織障害	2 (3.1%)	1 (1.6%)	1 (1.6%)	1 (1.7%)	4 (4.3%)	4 (4.3%)	0	0	6 (3.8%)	5 (3.2%)	1 (0.7%)	1 (0.7%)
そう痒症	2 (3.1%)	1 (1.6%)	1 (1.6%)	1 (1.7%)	1 (1.1%)	1 (1.1%)	0	0	3 (1.9%)	2 (1.3%)	1 (0.7%)	1 (0.7%)
発疹	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
斑状皮疹	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
蕁麻疹	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
眼障害	2 (3.1%)	2 (3.1%)	0	0	3 (3.3%)	2 (2.2%)	0	1 (1.2%)	5 (3.2%)	4 (2.6%)	0	1 (0.7%)
眼そう痒症	0	0	0	0	2 (2.2%)	2 (2.2%)	0	0	2 (1.3%)	2 (1.3%)	0	0
霧視	2 (3.1%)	2 (3.1%)	0	0	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0
白内障	0	0	0	0	1 (1.1%)	0	0	1 (1.2%)	1 (0.6%)	0	0	1 (0.7%)
筋骨格系および結合組織障害	1 (1.6%)	0	0	1 (1.7%)	3 (3.3%)	2 (2.2%)	0	1 (1.2%)	4 (2.6%)	2 (1.3%)	0	2 (1.4%)
背部痛	0	0	0	0	2 (2.2%)	2 (2.2%)	0	0	2 (1.3%)	2 (1.3%)	0	0
鼡径部痛	1 (1.6%)	0	0	1 (1.7%)	0	0	0	0	1 (0.6%)	0	0	1 (0.7%)
筋肉痛	0	0	0	0	1 (1.1%)	0	0	1 (1.2%)	1 (0.6%)	0	0	1 (0.7%)
血管障害	1 (1.6%)	1 (1.6%)	1 (1.6%)	0	3 (3.3%)	3 (3.3%)	0	0	4 (2.6%)	4 (2.6%)	1 (0.7%)	0
高血圧	1 (1.6%)	1 (1.6%)	1 (1.6%)	0	2 (2.2%)	2 (2.2%)	0	0	3 (1.9%)	3 (1.9%)	1 (0.7%)	0
潮紅	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
血液およびリンパ系障害	1 (1.6%)	0	0	1 (1.7%)	2 (2.2%)	0	0	2 (2.3%)	3 (1.9%)	0	0	3 (2.1%)
貧血	1 (1.6%)	0	0	1 (1.7%)	1 (1.1%)	0	0	1 (1.2%)	2 (1.3%)	0	0	2 (1.4%)
赤血球凝集	0	0	0	0	1 (1.1%)	0	0	1 (1.2%)	1 (0.6%)	0	0	1 (0.7%)
心臓障害	1 (1.6%)	0	0	1 (1.7%)	2 (2.2%)	2 (2.2%)	0	0	3 (1.9%)	2 (1.3%)	0	1 (0.7%)
動悸	1 (1.6%)	0	0	1 (1.7%)	0	0	0	0	1 (0.6%)	0	0	1 (0.7%)
洞性頻脈	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
頻脈	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
神経系障害	1 (1.6%)	1 (1.6%)	0	0	2 (2.2%)	2 (2.2%)	0	0	3 (1.9%)	3 (1.9%)	0	0
頭痛	1 (1.6%)	1 (1.6%)	0	0	2 (2.2%)	2 (2.2%)	0	0	3 (1.9%)	3 (1.9%)	0	0
精神障害	0	0	0	0	3 (3.3%)	3 (3.3%)	0	0	3 (1.9%)	3 (1.9%)	0	0
不安	0	0	0	0	2 (2.2%)	2 (2.2%)	0	0	2 (1.3%)	2 (1.3%)	0	0
譫妄	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0
免疫系障害	1 (1.6%)	1 (1.6%)	0	0	1 (1.1%)	1 (1.1%)	0	0	2 (1.3%)	2 (1.3%)	0	0
サイトカイン放出症候群	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0

TSFAE20A: Infusion Related Reactions by System Organ Class, Preferred Term, Drug Product Formulation and Event Onset Time; All Treated Analysis Set - 16mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

	Phase 2				Phase 3				Total			
		Event Onset				Event Onset				Event Onset		
	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions	Total	1st Infusion	2nd Infusion	Subsequent Infusions
季節性アレルギー	0	0	0	0	1 (1.1%)	1 (1.1%)	0	0	1 (0.6%)	1 (0.6%)	0	0

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects treated within each window as denominator.

[TSFAE20A.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae20a.sas] 02APR2015, 10:49

表 2.7.4-付録-113 Infusion Related Reactions Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE10A: Infusion Related Reactions Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with IRRs leading to interruption during infusion	3 (13.0%)	3 (13.0%)	27 (49.1%)	27 (49.1%)	59 (37.8%)	56 (35.9%)	2 (66.7%)	2 (66.7%)	91 (38.4%)	88 (37.1%)
MedDRA system organ class/Preferred term										
呼吸器、胸郭および縦隔障害	2 (8.7%)	2 (8.7%)	21 (38.2%)	21 (38.2%)	44 (28.2%)	44 (28.2%)	2 (66.7%)	2 (66.7%)	69 (29.1%)	69 (29.1%)
鼻閉	0	0	3 (5.5%)	3 (5.5%)	12 (7.7%)	12 (7.7%)	1 (33.3%)	1 (33.3%)	16 (6.8%)	16 (6.8%)
アレルギー性鼻炎	0	0	12 (21.8%)	12 (21.8%)	10 (6.4%)	10 (6.4%)	0	0	22 (9.3%)	22 (9.3%)
咳嗽	0	0	2 (3.6%)	2 (3.6%)	9 (5.8%)	9 (5.8%)	1 (33.3%)	1 (33.3%)	12 (5.1%)	12 (5.1%)
呼吸困難	1 (4.3%)	1 (4.3%)	3 (5.5%)	3 (5.5%)	8 (5.1%)	8 (5.1%)	0	0	12 (5.1%)	12 (5.1%)
咽喉刺激感	0	0	0	0	5 (3.2%)	5 (3.2%)	0	0	5 (2.1%)	5 (2.1%)
くしゃみ	0	0	0	0	3 (1.9%)	3 (1.9%)	0	0	3 (1.3%)	3 (1.3%)
咽喉絞扼感	0	0	0	0	3 (1.9%)	3 (1.9%)	0	0	3 (1.3%)	3 (1.3%)
気管支痙攣	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	4 (1.7%)	4 (1.7%)
低酸素症	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
喘鳴	0	0	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	3 (1.3%)	3 (1.3%)
アレルギー性咳嗽	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
喉頭浮腫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
アレルギー性喉頭炎	0	0	3 (5.5%)	3 (5.5%)	1 (0.6%)	1 (0.6%)	0	0	4 (1.7%)	4 (1.7%)
鼻部障害	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
口腔咽頭痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
発声障害	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
一般・全身障害および投与部位の状態	0	0	6 (10.9%)	6 (10.9%)	13 (8.3%)	13 (8.3%)	0	0	19 (8.0%)	19 (8.0%)
悪寒	0	0	3 (5.5%)	3 (5.5%)	11 (7.1%)	11 (7.1%)	0	0	14 (5.9%)	14 (5.9%)
胸部不快感	0	0	2 (3.6%)	2 (3.6%)	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	3 (1.3%)
胸痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
発熱	0	0	2 (3.6%)	2 (3.6%)	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	3 (1.3%)
非心臓性胸痛	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
胃腸障害	1 (4.3%)	1 (4.3%)	6 (10.9%)	6 (10.9%)	8 (5.1%)	8 (5.1%)	1 (33.3%)	1 (33.3%)	16 (6.8%)	16 (6.8%)
悪心	1 (4.3%)	1 (4.3%)	3 (5.5%)	3 (5.5%)	5 (3.2%)	5 (3.2%)	0	0	9 (3.8%)	9 (3.8%)
嘔吐	0	0	4 (7.3%)	4 (7.3%)	5 (3.2%)	5 (3.2%)	1 (33.3%)	1 (33.3%)	10 (4.2%)	10 (4.2%)

TSFAE10A: Infusion Related Reactions Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
上腹部痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
消化不良	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
口唇浮腫	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
心臓障害	1 (4.3%)	1 (4.3%)	0	0	3 (1.9%)	3 (1.9%)	0	0	4 (1.7%)	4 (1.7%)
動悸	1 (4.3%)	1 (4.3%)	0	0	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
洞性頻脈	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
頻脈	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
筋骨格系および結合組織障害	0	0	1 (1.8%)	1 (1.8%)	3 (1.9%)	3 (1.9%)	0	0	4 (1.7%)	4 (1.7%)
背部痛	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
筋肉痛	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
側腹部痛	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
精神障害	0	0	0	0	3 (1.9%)	2 (1.3%)	0	0	3 (1.3%)	2 (0.8%)
不安	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
譫妄	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
血管障害	0	0	3 (5.5%)	3 (5.5%)	3 (1.9%)	2 (1.3%)	0	0	6 (2.5%)	5 (2.1%)
高血圧	0	0	2 (3.6%)	2 (3.6%)	2 (1.3%)	1 (0.6%)	0	0	4 (1.7%)	3 (1.3%)
潮紅	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
眼障害	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
霧視	0	0	0	0	2 (1.3%)	1 (0.6%)	0	0	2 (0.8%)	1 (0.4%)
免疫系障害	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	4 (1.7%)	4 (1.7%)
サイトカイン放出症候群	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
季節性アレルギー	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
過敏症	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
神経系障害	0	0	1 (1.8%)	1 (1.8%)	2 (1.3%)	2 (1.3%)	0	0	3 (1.3%)	3 (1.3%)
頭痛	0	0	0	0	2 (1.3%)	2 (1.3%)	0	0	2 (0.8%)	2 (0.8%)
浮動性めまい	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
皮膚および皮下組織障害	1 (4.3%)	1 (4.3%)	2 (3.6%)	2 (3.6%)	2 (1.3%)	1 (0.6%)	0	0	5 (2.1%)	4 (1.7%)
そう痒症	1 (4.3%)	1 (4.3%)	1 (1.8%)	1 (1.8%)	1 (0.6%)	0	0	0	3 (1.3%)	2 (0.8%)
斑状皮疹	0	0	1 (1.8%)	1 (1.8%)	1 (0.6%)	1 (0.6%)	0	0	2 (0.8%)	2 (0.8%)
発疹	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)
蕁麻疹	0	0	1 (1.8%)	1 (1.8%)	0	0	0	0	1 (0.4%)	1 (0.4%)

TSFAE10A: Infusion Related Reactions Leading to Infusion Interruption During Infusion by System Organ Class, Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related

Keys: IRR = Infusion Related Reactions.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
501P1: ORAEACN="INTERRUPTED".
501P2: ORAEACN="INFUSION TEMPORARILY INTERRUPTED".
2002/1002: Adverse events reported as the reason for action 'infusion interrupted' on the Daratumumab infusion CRF page are summarized.

[TSFAE10A.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae10a.sas] 16MAR2015, 12:04

表 2.7.4-付録-114 Treatment Discontinuation Due to Infusion Related Reactions by Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE07A: Treatment Discontinuation Due to Infusion Related Reactions by Preferred Term and Relationship; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related	Total	Related	Total	Related
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with IRRs leading to treatment discontinuation	3 (13.0%)	3 (13.0%)	0	0	0	0	1 (33.3%)	1 (33.3%)	4 (1.7%)	4 (1.7%)
Preferred term										
気管支痙攣	1 (4.3%)	1 (4.3%)	0	0	0	0	1 (33.3%)	1 (33.3%)	2 (0.8%)	2 (0.8%)
サイトカイン放出症候群	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
潮紅	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)
過敏症	1 (4.3%)	1 (4.3%)	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)

Keys: IRR = Infusion Related Reactions.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events reported as the reason for treatment discontinuation on the end of treatment CRF page are summarized.

[TSFAE07A.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae07a.sas] 16MAR2015, 12:04

表 2.7.4-付録-115 Pre-Infusion Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSICM04: Pre-Infusion Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Analgesics	23 (100%)	55 (100%)	156 (100%)	3 (100%)	237 (100%)
Oxycodone	0	1 (1.8%)	0	0	1 (0.4%)
Paracetamol	23 (100%)	55 (100%)	156 (100%)	3 (100%)	237 (100%)
Procet /01554201/	0	0	1 (0.6%)	0	1 (0.4%)
Antihistamines	23 (100%)	55 (100%)	156 (100%)	3 (100%)	237 (100%)
Cetirizine	12 (52.2%)	8 (14.5%)	12 (7.7%)	0	32 (13.5%)
Clemastine	13 (56.5%)	20 (36.4%)	20 (12.8%)	3 (100%)	56 (23.6%)
Dexchlorpheniramine	0	3 (5.5%)	9 (5.8%)	0	12 (5.1%)
Diphenhydramine	0	25 (45.5%)	113 (72.4%)	0	138 (58.2%)
Fexofenadine	0	0	1 (0.6%)	0	1 (0.4%)
Loratadine	0	0	10 (6.4%)	0	10 (4.2%)
Promethazine	0	0	1 (0.6%)	0	1 (0.4%)
Corticosteroids	23 (100%)	55 (100%)	156 (100%)	3 (100%)	237 (100%)
Intermediate acting	23 (100%)	27 (49.1%)	151 (96.8%)	3 (100%)	204 (86.1%)
Hydrocortisone	3 (13%)	0	0	0	3 (1.3%)
Meprednisone	0	0	8 (5.1%)	0	8 (3.4%)
Methylprednisolone	20 (87%)	27 (49.1%)	143 (91.7%)	3 (100%)	193 (81.4%)
Prednisone	0	0	18 (11.5%)	0	18 (7.6%)
Long acting	0	31 (56.4%)	15 (9.6%)	0	46 (19.4%)
Betamethasone	0	5 (9.1%)	0	0	5 (2.1%)
Dexamethasone	0	26 (47.3%)	15 (9.6%)	0	41 (17.3%)
Other	0	0	19 (12.2%)	0	19 (8%)
Calamine antihistamine	0	0	1 (0.6%)	0	1 (0.4%)
Famotidine	0	0	6 (3.8%)	0	6 (2.5%)
Hydroxyzine	0	0	1 (0.6%)	0	1 (0.4%)
Montelukast	0	0	2 (1.3%)	0	2 (0.8%)
Ondansetron	0	0	10 (6.4%)	0	10 (4.2%)

Percentages are calculated with the number of subjects in each group with available data as denominator.

[TSICM04.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsicm04.sas] 16MAR2015, 12:12

表 2.7.4-付録-116 Summary of Pre- and Post-infusion Medications; All Treated Analysis Population (Study 54767414MMY1002)

TSICM03: Summary of Pre- and Post-infusion Medications; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Number of subjects with any pre-infusion medications	4 (100.0%)	5 (100.0%)	9 (100.0%)
DIPHENHYDRAMINE	4 (100.0%)	5 (100.0%)	9 (100.0%)
METHYLPREDNISOLONE	4 (100.0%)	5 (100.0%)	9 (100.0%)
PARACETAMOL	4 (100.0%)	5 (100.0%)	9 (100.0%)
Number of subjects with any post-infusion medications	4 (100.0%)	5 (100.0%)	9 (100.0%)
METHYLPREDNISOLONE	2 (50.0%)	3 (60.0%)	5 (55.6%)
PREDNISOLONE	2 (50.0%)	2 (40.0%)	4 (44.4%)

Note: Medication is categorized using Anatomical Therapeutic Chemical class and drug preferred term

[TSICM03.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsicm03.sas] 22FEB2016, 11:03

表 2.7.4-付録-117 Post-Infusion Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSICM05: Post-Infusion Medications; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Analgesics	0	2 (3.6%)	3 (1.9%)	0	5 (2.1%)
Oxycodone	0	1 (1.8%)	0	0	1 (0.4%)
Paracetamol	0	2 (3.6%)	2 (1.3%)	0	4 (1.7%)
Pethidine	0	0	2 (1.3%)	0	2 (0.8%)
Antihistamines	0	13 (23.6%)	22 (14.1%)	0	35 (14.8%)
Cetirizine	0	0	2 (1.3%)	0	2 (0.8%)
Clemastine	0	13 (23.6%)	13 (8.3%)	0	26 (11%)
Diphenhydramine	0	0	7 (4.5%)	0	7 (3%)
Loratadine	0	0	1 (0.6%)	0	1 (0.4%)
Corticosteroids	0	52 (94.5%)	150 (96.2%)	0	202 (85.2%)
Intermediate acting	0	22 (40%)	128 (82.1%)	0	150 (63.3%)
Deltison /00201501/	0	0	3 (1.9%)	0	3 (1.3%)
Hydrocortisone	0	0	1 (0.6%)	0	1 (0.4%)
Methylprednisolone	0	15 (27.3%)	59 (37.8%)	0	74 (31.2%)
Prednisolone	0	4 (7.3%)	12 (7.7%)	0	16 (6.8%)
Prednisone	0	6 (10.9%)	65 (41.7%)	0	71 (30%)
Triamcinolone	0	0	1 (0.6%)	0	1 (0.4%)
Long acting	0	34 (61.8%)	28 (17.9%)	0	62 (26.2%)
Betamethasone	0	5 (9.1%)	0	0	5 (2.1%)
Dexamethasone	0	29 (52.7%)	28 (17.9%)	0	57 (24.1%)
Other	0	0	3 (1.9%)	0	3 (1.3%)
Allopurinol	0	0	1 (0.6%)	0	1 (0.4%)
Potassium	0	0	1 (0.6%)	0	1 (0.4%)
Salbutamol	0	0	1 (0.6%)	0	1 (0.4%)
Seretide	0	0	1 (0.6%)	0	1 (0.4%)

Percentages are calculated with the number of subjects in each group with available data as denominator.

[TSICM05.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsicm05.sas] 16MAR2015, 12:12

表 2.7.4-付録-118 Summary of Growth Factor Use with Onset during Study Treatment by Prophylactic Use and by Therapeutic Class, Pharmacologic Class, and Drug;Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSICM05: Summary of Growth Factor Use with Onset during Study Treatment by Prophylactic Use and by Therapeutic Class, Pharmacologic Class, and Drug;Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use
Analysis set: safety	237		243		281		318		103	
Total number of subjects with 1 or more growth factor use	12 (5.1%)	1 (0.4%)	18 (7.4%)	1 (0.4%)	80 (28.5%)	20 (7.1%)	154 (48.4%)	24 (7.5%)	59 (57.3%)	7 (6.8%)
Therapeutic class/pharmacologic class/preferred term										
Immunostimulants	12 (5.1%)	1 (0.4%)	18 (7.4%)	1 (0.4%)	80 (28.5%)	20 (7.1%)	154 (48.4%)	24 (7.5%)	59 (57.3%)	7 (6.8%)
Immunostimulants	12 (5.1%)	1 (0.4%)	18 (7.4%)	1 (0.4%)	80 (28.5%)	20 (7.1%)	154 (48.4%)	24 (7.5%)	59 (57.3%)	7 (6.8%)
Filgrastim	11 (4.6%)	1 (0.4%)	18 (7.4%)	0	66 (23.5%)	15 (5.3%)	116 (36.5%)	15 (4.7%)	50 (48.5%)	6 (5.8%)
Granulocyte colony stimulating factor	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	6 (2.1%)	0	19 (6.0%)	2 (0.6%)	1 (1.0%)	0
Lenograstim	0	0	0	0	8 (2.8%)	3 (1.1%)	18 (5.7%)	4 (1.3%)	5 (4.9%)	1 (1.0%)
Pegfilgrastim	0	0	0	0	2 (0.7%)	1 (0.4%)	12 (3.8%)	4 (1.3%)	13 (12.6%)	0
Lipegfilgrastim	0	0	0	0	2 (0.7%)	2 (0.7%)	1 (0.3%)	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSICM05.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSICM05.SAS] 01JUN2016, 10:47

表 2.7.4-付録-119 Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: safety	237			243			281			318			103		
Total number of subjects with TEAE leading to discontinuation of any study treatment[a]	39 (16.5%)	18 (7.6%)	5 (2.1%)	36 (14.8%)	20 (8.2%)	6 (2.5%)	36 (12.8%)	20 (7.1%)	8 (2.8%)	44 (13.8%)	28 (8.8%)	6 (1.9%)	18 (17.5%)	12 (11.7%)	3 (2.9%)
MedDRA system organ class/Preferred term															
一般・全身障害および投与部位の状態	2 (0.8%)	2 (0.8%)	0	2 (0.8%)	0	0	1 (0.4%)	0	0	11 (3.5%)	7 (2.2%)	1 (0.3%)	0	0	0
疲労	0	0	0	1 (0.4%)	0	0	0	0	0	4 (1.3%)	3 (0.9%)	0	0	0	0
全身健康状態低下	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	3 (0.9%)	2 (0.6%)	0	0	0	0
末梢性浮腫	0	0	0	0	0	0	1 (0.4%)	0	0	2 (0.6%)	1 (0.3%)	0	0	0	0
多臓器不全	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
疼痛	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
無力症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
顔面浮腫	0	0	0	1 (0.4%)	0	0	1 (0.4%)	0	0	0	0	0	0	0	0
全身性浮腫	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0
感染症および寄生虫症	6 (2.5%)	4 (1.7%)	1 (0.4%)	9 (3.7%)	6 (2.5%)	1 (0.4%)	7 (2.5%)	5 (1.8%)	2 (0.7%)	10 (3.1%)	5 (1.6%)	4 (1.3%)	5 (4.9%)	4 (3.9%)	1 (1.0%)
肺炎	1 (0.4%)	1 (0.4%)	0	4 (1.6%)	2 (0.8%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	0	4 (1.3%)	4 (1.3%)	0	1 (1.0%)	1 (1.0%)	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
敗血症性ショック	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (0.4%)	0	1 (0.4%)	3 (0.9%)	1 (0.3%)	2 (0.6%)	0	0	0
細菌性気管支炎	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
ウイルス性肺炎	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
気管支炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
気管支肺炎	0	0	0	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0	0	0	0	0
真菌性食道炎	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0
壊疽	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
胃腸炎	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
乳腺炎	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
壊死性筋膜炎	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
ノカルジア症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
進行性多巣性白質脳症	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
敗血症	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (1.0%)	0	1 (1.0%)
上気道感染	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
尿路感染	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
神経系障害	19 (8.0%)	6 (2.5%)	1 (0.4%)	13 (5.3%)	5 (2.1%)	2 (0.8%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	5 (1.6%)	3 (0.9%)	0	2 (1.9%)	0	1 (1.0%)
平衡障害	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	0	0	0	0
脳梗塞	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0	0	0
脳血管発作	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	1 (0.3%)	0	0	1 (1.0%)	0	1 (1.0%)
認知障害	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
失神	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
自律神経ニューロパチー	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
脳出血	0	0	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
認知症	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
味覚異常	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0
虚血性脳卒中	0	0	0	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0
嗜眠	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
不全単麻痺	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
神経痛	5 (2.1%)	1 (0.4%)	0	2 (0.8%)	0	0	0	0	0	0	0	0	0	0	0
錯感覚	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
末梢性運動ニューロパチー	0	0	0	3 (1.2%)	2 (0.8%)	0	0	0	0	0	0	0	0	0	0
末梢性感覚ニューロパチー	11 (4.6%)	4 (1.7%)	0	5 (2.1%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
失神寸前の状態	0	0	0	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
振戦	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	0	0
胃腸障害	1 (0.4%)	0	0	3 (1.2%)	1 (0.4%)	0	0	0	0	4 (1.3%)	1 (0.3%)	0	0	0	0
下痢	0	0	0	1 (0.4%)	0	0	0	0	0	2 (0.6%)	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
消化不良	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	0	0	0	0
上腹部痛	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
十二指腸潰瘍	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
十二指腸炎	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0
代謝および栄養障害	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	4 (1.3%)	2 (0.6%)	0	0	0	0
高カルシウム血症	0	0	0	0	0	0	0	0	0	2 (0.6%)	1 (0.3%)	0	0	0	0
高血糖	0	0	0	0	0	0	0	0	0	2 (0.6%)	1 (0.3%)	0	0	0	0
体液貯留	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
代謝性アシドーシス	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
精神障害	0	0	0	0	0	0	4 (1.4%)	0	0	4 (1.3%)	2 (0.6%)	0	1 (1.0%)	0	0
うつ病	0	0	0	0	0	0	0	0	0	2 (0.6%)	2 (0.6%)	0	1 (1.0%)	0	0
不眠症	0	0	0	0	0	0	1 (0.4%)	0	0	1 (0.3%)	0	0	0	0	0
気分動揺	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	0	0	0	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
激越	0	0	0	0	0	0	2 (0.7%)	0	0	0	0	0	0	0	0
気分変化	0	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0
睡眠障害	0	0	0	0	0	0	2 (0.7%)	0	0	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (0.4%)	1 (0.4%)	0	4 (1.4%)	2 (0.7%)	2 (0.7%)	3 (0.9%)	3 (0.9%)	0	0	0	0
急性単球性白血病	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
胃腺癌	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
肺腺癌	0	0	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
直腸腺癌	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
移行上皮癌	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	3 (1.3%)	1 (0.4%)	2 (0.8%)	6 (2.5%)	4 (1.6%)	1 (0.4%)	5 (1.8%)	3 (1.1%)	2 (0.7%)	3 (0.9%)	3 (0.9%)	0	5 (4.9%)	4 (3.9%)	1 (1.0%)
喉頭浮腫	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0	0	0
発声障害	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
呼吸困難	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	1 (1.0%)	0
呼吸不全	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (0.3%)	1 (0.3%)	0	1 (1.0%)	0	1 (1.0%)
喘鳴	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
急性呼吸不全	0	0	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
気管支痙攣	0	0	0	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0	0	0	0	0
労作性呼吸困難	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0
しゃっくり	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
胸水症	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
低酸素症	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
間質性肺疾患	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
胸水	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
肺塞栓症	1 (0.4%)	0	1 (0.4%)	0	0	0	3 (1.1%)	3 (1.1%)	0	0	0	0	0	0	0
肺水腫	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
血液およびリンパ系障害	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	0	4 (1.4%)	3 (1.1%)	0	2 (0.6%)	2 (0.6%)	0	1 (1.0%)	1 (1.0%)	0
貧血	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0	0	0
好中球減少症	0	0	0	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0	0	0
鉄芽球性貧血	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
血小板減少症	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	0	2 (0.7%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (1.0%)	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
皮膚および皮下組織障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)	0	0	2 (0.6%)	1 (0.3%)	0	0	0	0
発疹	0	0	0	1 (0.4%)	0	0	0	0	0	1 (0.3%)	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0	0	0
男性型多毛症	0	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0
心臓障害	2 (0.8%)	1 (0.4%)	1 (0.4%)	4 (1.6%)	1 (0.4%)	2 (0.8%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	1 (0.3%)	0	1 (0.3%)	2 (1.9%)	1 (1.0%)	0
心肺不全	0	0	0	0	0	0	0	0	0	1 (0.3%)	0	1 (0.3%)	0	0	0
急性冠動脈症候群	0	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0	0	0	0
急性心筋梗塞	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
狭心症	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	0	0
心房細動	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
心停止	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0	0
うっ血性心不全	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
心筋梗塞	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
腎および尿路障害	0	0	0	0	0	0	4 (1.4%)	4 (1.4%)	0	1 (0.3%)	1 (0.3%)	0	0	0	0
腎不全	0	0	0	0	0	0	2 (0.7%)	2 (0.7%)	0	1 (0.3%)	1 (0.3%)	0	0	0	0
急性腎不全	0	0	0	0	0	0	2 (0.7%)	2 (0.7%)	0	0	0	0	0	0	0
眼障害	0	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
白内障	0	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
脊椎骨折	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
硬膜下血腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
筋骨格系および結合組織障害	3 (1.3%)	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0	3 (1.1%)	1 (0.4%)	0	0	0	0	1 (1.0%)	1 (1.0%)	0
筋力低下	2 (0.8%)	1 (0.4%)	0	0	0	0	2 (0.7%)	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
四肢痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
脊椎痛	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0
血管障害	3 (1.3%)	2 (0.8%)	0	0	0	0	1 (0.4%)	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
大動脈解離	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)	0
循環虚脱	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0
深部静脈血栓症	0	0	0	0	0	0	1 (0.4%)	0	0	0	0	0	0	0	0
起立性低血圧	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0	0	0	0	0	0	0	0

TSFAE13: Number of Subjects who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004						MMY3003+GEN503						MMY1001		
	Vd			DVd			Rd			DRd			DPd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
[a] TEAEs with an action taken of drug withdrawal for any study treatment on the AE CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE13.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE13.SAS] 01JUN2016, 10:39

表 2.7.4-付録-120 Number of Subjects with 1 or More Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Study 54767414MMY1005)

TSFAE19: Number of Subjects with 1 or More Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Study 54767414MMY1005)

		Vd + Daratumumab (16 mg/kg) Toxicity Grade, n (%)				
	Total	1	2	3	4	5
Analysis set: Safety	8					
Total number of subjects with TEAE	8 (100.0%)	0	0	5 (62.5%)	3 (37.5%)	0
MedDRA system organ class/Preferred term						
血液およびリンパ系障害	8 (100.0%)	0	1 (12.5%)	4 (50.0%)	3 (37.5%)	0
血小板減少症	7 (87.5%)	0	1 (12.5%)	3 (37.5%)	3 (37.5%)	0
リンパ球減少症	5 (62.5%)	0	0	4 (50.0%)	1 (12.5%)	0
貧血	3 (37.5%)	2 (25.0%)	1 (12.5%)	0	0	0
白血球減少症	3 (37.5%)	0	1 (12.5%)	2 (25.0%)	0	0
好中球減少症	3 (37.5%)	0	1 (12.5%)	2 (25.0%)	0	0
一般・全身障害および投与部位の状態	5 (62.5%)	2 (25.0%)	2 (25.0%)	1 (12.5%)	0	0
疲労	3 (37.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0	0
悪寒	2 (25.0%)	0	2 (25.0%)	0	0	0
歩行障害	1 (12.5%)	1 (12.5%)	0	0	0	0
末梢性浮腫	1 (12.5%)	0	1 (12.5%)	0	0	0
発熱	1 (12.5%)	0	1 (12.5%)	0	0	0
感染症および寄生虫症	5 (62.5%)	2 (25.0%)	1 (12.5%)	2 (25.0%)	0	0
鼻咽頭炎	2 (25.0%)	1 (12.5%)	0	1 (12.5%)	0	0
気管支炎	1 (12.5%)	0	1 (12.5%)	0	0	0
帯状疱疹	1 (12.5%)	0	0	1 (12.5%)	0	0
インフルエンザ	1 (12.5%)	1 (12.5%)	0	0	0	0
代謝および栄養障害	5 (62.5%)	0	1 (12.5%)	4 (50.0%)	0	0
高血糖	3 (37.5%)	0	1 (12.5%)	2 (25.0%)	0	0
脱水	2 (25.0%)	0	2 (25.0%)	0	0	0
低カリウム血症	2 (25.0%)	0	0	2 (25.0%)	0	0
低リン酸血症	1 (12.5%)	0	1 (12.5%)	0	0	0
神経系障害	5 (62.5%)	3 (37.5%)	2 (25.0%)	0	0	0
異常感覚	3 (37.5%)	3 (37.5%)	0	0	0	0
頭痛	1 (12.5%)	1 (12.5%)	0	0	0	0
神経痛	1 (12.5%)	1 (12.5%)	0	0	0	0
末梢性感覚ニューロパチー	1 (12.5%)	0	1 (12.5%)	0	0	0
ヘルペス後神経痛	1 (12.5%)	0	1 (12.5%)	0	0	0
胃腸障害	4 (50.0%)	1 (12.5%)	3 (37.5%)	0	0	0
便秘	2 (25.0%)	0	2 (25.0%)	0	0	0
下痢	2 (25.0%)	1 (12.5%)	1 (12.5%)	0	0	0
胃炎	2 (25.0%)	0	2 (25.0%)	0	0	0
腹部膨満	1 (12.5%)	0	1 (12.5%)	0	0	0
上腹部痛	1 (12.5%)	1 (12.5%)	0	0	0	0
消化不良	1 (12.5%)	0	1 (12.5%)	0	0	0
悪心	1 (12.5%)	1 (12.5%)	0	0	0	0
胃肉芽腫	1 (12.5%)	1 (12.5%)	0	0	0	0
嘔吐	1 (12.5%)	1 (12.5%)	0	0	0	0
臨床検査	4 (50.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	0	0
血中乳酸脱水素酵素増加	3 (37.5%)	2 (25.0%)	1 (12.5%)	0	0	0
体重減少	3 (37.5%)	2 (25.0%)	1 (12.5%)	0	0	0
アラニンアミノトランスフェラーゼ増加	1 (12.5%)	0	1 (12.5%)	0	0	0

TSFAE19: Number of Subjects with 1 or More Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Study 54767414MMY1005)

		Vd + Daratumumab (16 mg/kg) Toxicity Grade, n (%)				
	Total	1	2	3	4	5
アスパラギン酸アミノトランスフェラーゼ増加	1 (12.5%)	0	0	1 (12.5%)	0	0
血圧上昇	1 (12.5%)	0	1 (12.5%)	0	0	0
血中尿素増加	1 (12.5%)	1 (12.5%)	0	0	0	0
Ｃ－反応性蛋白増加	1 (12.5%)	1 (12.5%)	0	0	0	0
細胞マーカー増加	1 (12.5%)	1 (12.5%)	0	0	0	0
フィブリン分解産物増加	1 (12.5%)	1 (12.5%)	0	0	0	0
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)	0	0	1 (12.5%)	0	0
サーファクタントプロテイン増加	1 (12.5%)	1 (12.5%)	0	0	0	0
呼吸器、胸郭および縦隔障害	4 (50.0%)	0	4 (50.0%)	0	0	0
低酸素症	2 (25.0%)	0	2 (25.0%)	0	0	0
喘鳴	2 (25.0%)	0	2 (25.0%)	0	0	0
発声障害	1 (12.5%)	1 (12.5%)	0	0	0	0
口腔咽頭不快感	1 (12.5%)	1 (12.5%)	0	0	0	0
口腔咽頭痛	1 (12.5%)	0	1 (12.5%)	0	0	0
皮膚および皮下組織障害	4 (50.0%)	2 (25.0%)	2 (25.0%)	0	0	0
皮膚嚢腫	1 (12.5%)	1 (12.5%)	0	0	0	0
皮膚炎	1 (12.5%)	0	1 (12.5%)	0	0	0
紅斑	1 (12.5%)	1 (12.5%)	0	0	0	0
皮下出血	1 (12.5%)	1 (12.5%)	0	0	0	0
全身性皮疹	1 (12.5%)	0	1 (12.5%)	0	0	0
眼障害	2 (25.0%)	2 (25.0%)	0	0	0	0
眼精疲労	1 (12.5%)	1 (12.5%)	0	0	0	0
霧視	1 (12.5%)	1 (12.5%)	0	0	0	0
筋骨格系および結合組織障害	2 (25.0%)	0	2 (25.0%)	0	0	0
筋力低下	1 (12.5%)	0	1 (12.5%)	0	0	0
ミオパチー	1 (12.5%)	0	1 (12.5%)	0	0	0
精神障害	2 (25.0%)	1 (12.5%)	1 (12.5%)	0	0	0
短時間睡眠	1 (12.5%)	0	1 (12.5%)	0	0	0
不眠症	1 (12.5%)	1 (12.5%)	0	0	0	0
耳および迷路障害	1 (12.5%)	1 (12.5%)	0	0	0	0
片耳難聴	1 (12.5%)	1 (12.5%)	0	0	0	0
肝胆道系障害	1 (12.5%)	0	0	1 (12.5%)	0	0
薬物性肝障害	1 (12.5%)	0	0	1 (12.5%)	0	0
傷害、中毒および処置合併症	1 (12.5%)	1 (12.5%)	0	0	0	0
凍瘡	1 (12.5%)	1 (12.5%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)	0	0	1 (12.5%)	0	0
前立腺癌	1 (12.5%)	0	0	1 (12.5%)	0	0
血管障害	1 (12.5%)	0	1 (12.5%)	0	0	0
高血圧	1 (12.5%)	0	1 (12.5%)	0	0	0
低血圧	1 (12.5%)	1 (12.5%)	0	0	0	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages in the total column and toxicity grade columns are calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE19.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE19.SAS] 28SEP2016, 04:20

表 2.7.4-付録-121 Summary of Growth Factor Use; All-treated Analysis Set (Study 54767414MMY1005)

TSICM02: Summary of Growth Factor Use; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Total number of subjects with 1 or more growth factor use	0
Therapeutic class/pharmacologic class/preferred term	
No data to report	

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSICM02.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSICM02.SAS] 28SEP2016, 04:30

表 2.7.4-付録-122 Number of Subjects with TEAE Leading to Treatment Cycle Delays or Dose modifications by System Organ Class, Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE18: Number of Subjects with TEAE Leading to Treatment Cycle Delays or Dose modifications by System Organ Class, Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to treatment cycle delays or dose modifications	8 (100.0%)	8 (100.0%)	0
MedDRA system organ class/Preferred term			
血液およびリンパ系障害	4 (50.0%)	4 (50.0%)	0
血小板減少症	4 (50.0%)	4 (50.0%)	0
代謝および栄養障害	4 (50.0%)	2 (25.0%)	0
脱水	2 (25.0%)	0	0
高血糖	2 (25.0%)	2 (25.0%)	0
感染症および寄生虫症	3 (37.5%)	2 (25.0%)	0
気管支炎	1 (12.5%)	0	0
帯状疱疹	1 (12.5%)	1 (12.5%)	0
鼻咽頭炎	1 (12.5%)	1 (12.5%)	0
神経系障害	3 (37.5%)	0	0
神経痛	1 (12.5%)	0	0
末梢性感覚ニューロパチー	1 (12.5%)	0	0
ヘルペス後神経痛	1 (12.5%)	0	0
胃腸障害	2 (25.0%)	0	0
腹部膨満	1 (12.5%)	0	0
消化不良	1 (12.5%)	0	0
胃炎	1 (12.5%)	0	0
一般・全身障害および投与部位の状態	2 (25.0%)	1 (12.5%)	0
疲労	2 (25.0%)	1 (12.5%)	0
筋骨格系および結合組織障害	2 (25.0%)	0	0
筋力低下	1 (12.5%)	0	0
ミオパチー	1 (12.5%)	0	0
肝胆道系障害	1 (12.5%)	1 (12.5%)	0
薬物性肝障害	1 (12.5%)	1 (12.5%)	0
臨床検査	1 (12.5%)	1 (12.5%)	0
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
[a] Includes adverse events leading to treatment cycle delay or at least 1 of study treatments dose modifications (i.e., dose delays, dose skipping, schedule change or dose reduction) : bortezomib, dexamethasone or daratumumab.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE18.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE18.SAS] 28SEP2016, 04:19

表 2.7.4-付録-123 Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More TEAE by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE05A: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More TEAE by System Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with TEAE leading to discontinuation of any study treatment[a]	1 (12.5%)	1 (12.5%)	0
MedDRA system organ class/Preferred term			
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)	1 (12.5%)	0
前立腺癌	1 (12.5%)	1 (12.5%)	0

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
[a] TEAEs with an action taken of drug withdrawal for any study treatment on the AE CRF page.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE05A.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE05A.SAS] 28SEP2016, 04:14

表 2.7.4-付録-124 Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Total[a]				
Analysis set: safety	281		283	
Total number of subjects with TEAE leading to cycle delays or dose modifications[c]	201 (71.5%)	145 (51.6%)	244 (86.2%)	180 (63.6%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	100 (35.6%)	89 (31.7%)	119 (42.0%)	112 (39.6%)
好中球減少症	81 (28.8%)	74 (26.3%)	107 (37.8%)	105 (37.1%)
血小板減少症	22 (7.8%)	14 (5.0%)	22 (7.8%)	15 (5.3%)
貧血	17 (6.0%)	10 (3.6%)	13 (4.6%)	5 (1.8%)
発熱性好中球減少症	6 (2.1%)	6 (2.1%)	10 (3.5%)	10 (3.5%)
リンパ球減少症	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
白血球減少症	5 (1.8%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
リンパ節症	0	0	1 (0.4%)	0
出血性障害	1 (0.4%)	0	0	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0
血栓性血小板減少性紫斑病	1 (0.4%)	1 (0.4%)	0	0
感染症および寄生虫症	75 (26.7%)	39 (13.9%)	118 (41.7%)	62 (21.9%)
肺炎	19 (6.8%)	12 (4.3%)	21 (7.4%)	16 (5.7%)
上気道感染	13 (4.6%)	1 (0.4%)	20 (7.1%)	3 (1.1%)
気道感染	9 (3.2%)	1 (0.4%)	15 (5.3%)	3 (1.1%)
気管支炎	8 (2.8%)	3 (1.1%)	14 (4.9%)	3 (1.1%)
インフルエンザ	7 (2.5%)	2 (0.7%)	11 (3.9%)	7 (2.5%)
鼻咽頭炎	4 (1.4%)	0	10 (3.5%)	0
下気道感染	4 (1.4%)	2 (0.7%)	9 (3.2%)	3 (1.1%)
インフルエンザ性肺炎	0	0	4 (1.4%)	3 (1.1%)
尿路感染	1 (0.4%)	0	4 (1.4%)	3 (1.1%)
虫垂炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
気管支肺炎	1 (0.4%)	0	2 (0.7%)	2 (0.7%)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
胃腸炎	1 (0.4%)	0	2 (0.7%)	1 (0.4%)
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
感染	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
大葉性肺炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
肺感染	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
耳下腺炎	0	0	2 (0.7%)	0
ＲＳウイルス感染	0	0	2 (0.7%)	1 (0.4%)
鼻炎	0	0	2 (0.7%)	0
急性副鼻腔炎	0	0	1 (0.4%)	0
細菌感染	0	0	1 (0.4%)	1 (0.4%)
細気管支炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	1 (0.4%)	0
蜂巣炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ウイルス性腸炎	0	0	1 (0.4%)	0
喉頭蓋炎	0	0	1 (0.4%)	1 (0.4%)
硬膜外膿瘍	0	0	1 (0.4%)	1 (0.4%)
消化管感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
歯肉炎	0	0	1 (0.4%)	0
Ｈ１Ｎ１インフルエンザ	0	0	1 (0.4%)	1 (0.4%)
リステリア性敗血症	0	0	1 (0.4%)	1 (0.4%)
鼻膿瘍	0	0	1 (0.4%)	1 (0.4%)
好中球減少性敗血症	0	0	1 (0.4%)	1 (0.4%)
口腔真菌感染	0	0	1 (0.4%)	1 (0.4%)
急性中耳炎	0	0	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
咽頭炎	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
細菌性肺炎	1 (0.4%)	0	1 (0.4%)	0
ヘモフィルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
レンサ球菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
サルモネラ性菌血症	0	0	1 (0.4%)	1 (0.4%)
敗血症	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
敗血症性ショック	0	0	1 (0.4%)	1 (0.4%)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
副鼻腔炎	0	0	1 (0.4%)	0
軟部組織感染	0	0	1 (0.4%)	1 (0.4%)
皮下組織膿瘍	0	0	1 (0.4%)	0
歯膿瘍	0	0	1 (0.4%)	0
細菌性上気道感染	0	0	1 (0.4%)	1 (0.4%)
子宮膿瘍	0	0	1 (0.4%)	1 (0.4%)
ウイルス感染	1 (0.4%)	0	1 (0.4%)	0
内臓リーシュマニア症	0	0	1 (0.4%)	1 (0.4%)
創傷感染	0	0	1 (0.4%)	0
四肢膿瘍	1 (0.4%)	1 (0.4%)	0	0
ウイルス性気管支炎	1 (0.4%)	1 (0.4%)	0	0
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0
帯状疱疹	2 (0.7%)	1 (0.4%)	0	0
骨髄炎	1 (0.4%)	1 (0.4%)	0	0
急性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0
水痘	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	1 (0.4%)	0	0
一般・全身障害および投与部位の状態	27 (9.6%)	13 (4.6%)	58 (20.5%)	26 (9.2%)
疲労	11 (3.9%)	5 (1.8%)	29 (10.2%)	14 (4.9%)
発熱	4 (1.4%)	1 (0.4%)	15 (5.3%)	4 (1.4%)
無力症	6 (2.1%)	5 (1.8%)	10 (3.5%)	6 (2.1%)
倦怠感	1 (0.4%)	0	5 (1.8%)	2 (0.7%)
悪寒	0	0	2 (0.7%)	0
薬物不耐性	0	0	2 (0.7%)	0
インフルエンザ様疾患	0	0	2 (0.7%)	0
胸部不快感	0	0	1 (0.4%)	0
脂肪組織増加	0	0	1 (0.4%)	0
歩行障害	0	0	1 (0.4%)	0
全身健康状態低下	0	0	1 (0.4%)	0
粘膜の炎症	0	0	1 (0.4%)	0
全身性炎症反応症候群	0	0	1 (0.4%)	1 (0.4%)
胸痛	1 (0.4%)	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
顔面浮腫	2 (0.7%)	0	0	0
全身性浮腫	1 (0.4%)	0	0	0
末梢性浮腫	5 (1.8%)	2 (0.7%)	0	0
末梢腫脹	1 (0.4%)	0	0	0
胃腸障害	25 (8.9%)	11 (3.9%)	45 (15.9%)	16 (5.7%)
下痢	12 (4.3%)	7 (2.5%)	28 (9.9%)	9 (3.2%)
悪心	0	0	8 (2.8%)	2 (0.7%)
嘔吐	5 (1.8%)	2 (0.7%)	4 (1.4%)	0
便秘	0	0	3 (1.1%)	2 (0.7%)
上腹部痛	1 (0.4%)	0	2 (0.7%)	0
憩室穿孔	0	0	2 (0.7%)	2 (0.7%)
胃腸障害	0	0	2 (0.7%)	1 (0.4%)
腹部不快感	0	0	1 (0.4%)	0
肛門出血	0	0	1 (0.4%)	1 (0.4%)
大腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
嚥下障害	0	0	1 (0.4%)	0
心窩部不快感	0	0	1 (0.4%)	0
胃炎	0	0	1 (0.4%)	0
出血性胃腸管血管異形成	0	0	1 (0.4%)	1 (0.4%)
鼠径ヘルニア	1 (0.4%)	0	1 (0.4%)	0
口腔内潰瘍形成	0	0	1 (0.4%)	0
唾液腺結石	0	0	1 (0.4%)	0
顎下腺腫大	0	0	1 (0.4%)	0
腹痛	2 (0.7%)	0	0	0
口内乾燥	1 (0.4%)	0	0	0
腸閉塞	1 (0.4%)	1 (0.4%)	0	0
下部消化管出血	1 (0.4%)	0	0	0
食道炎	1 (0.4%)	1 (0.4%)	0	0
精神障害	36 (12.8%)	7 (2.5%)	32 (11.3%)	4 (1.4%)
不眠症	13 (4.6%)	1 (0.4%)	11 (3.9%)	1 (0.4%)
うつ病	0	0	5 (1.8%)	1 (0.4%)
激越	4 (1.4%)	1 (0.4%)	4 (1.4%)	0
不安	5 (1.8%)	2 (0.7%)	4 (1.4%)	1 (0.4%)
易刺激性	2 (0.7%)	0	2 (0.7%)	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
精神障害	1 (0.4%)	0	2 (0.7%)	0
気分変化	4 (1.4%)	0	2 (0.7%)	1 (0.4%)
気分動揺	0	0	2 (0.7%)	0
落ち着きのなさ	1 (0.4%)	0	2 (0.7%)	0
睡眠障害	0	0	2 (0.7%)	0
抑うつ気分	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
錯乱状態	1 (0.4%)	1 (0.4%)	0	0
譫妄	1 (0.4%)	1 (0.4%)	0	0
気分変調性障害	1 (0.4%)	0	0	0
神経過敏	5 (1.8%)	1 (0.4%)	0	0
精神病性障害	1 (0.4%)	0	0	0
筋骨格系および結合組織障害	21 (7.5%)	6 (2.1%)	29 (10.2%)	7 (2.5%)
筋力低下	9 (3.2%)	0	14 (4.9%)	0
筋痙縮	8 (2.8%)	3 (1.1%)	7 (2.5%)	2 (0.7%)
背部痛	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
ミオパチー	2 (0.7%)	0	2 (0.7%)	0
筋萎縮症	0	0	1 (0.4%)	1 (0.4%)
関節痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
骨痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
側腹部痛	0	0	1 (0.4%)	0
椎間板突出	0	0	1 (0.4%)	1 (0.4%)
関節腫脹	0	0	1 (0.4%)	0
筋肉痛	0	0	1 (0.4%)	0
四肢痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
顎骨壊死	1 (0.4%)	1 (0.4%)	0	0
脊椎痛	1 (0.4%)	1 (0.4%)	0	0
神経系障害	26 (9.3%)	5 (1.8%)	25 (8.8%)	10 (3.5%)
振戦	7 (2.5%)	0	7 (2.5%)	1 (0.4%)
末梢性ニューロパチー	3 (1.1%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
失神	1 (0.4%)	1 (0.4%)	3 (1.1%)	3 (1.1%)
感覚鈍麻	1 (0.4%)	0	2 (0.7%)	0
錯感覚	0	0	2 (0.7%)	0
脳血管発作	0	0	1 (0.4%)	1 (0.4%)
認知障害	0	0	1 (0.4%)	1 (0.4%)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
浮動性めまい	3 (1.1%)	0	1 (0.4%)	0
体位性めまい	0	0	1 (0.4%)	0
知覚過敏	0	0	1 (0.4%)	0
嗜眠	0	0	1 (0.4%)	1 (0.4%)
神経系障害	0	0	1 (0.4%)	1 (0.4%)
末梢性感覚ニューロパチー	3 (1.1%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
失神寸前の状態	0	0	1 (0.4%)	0
痙攣発作	0	0	1 (0.4%)	0
一過性脳虚血発作	0	0	1 (0.4%)	0
三叉神経障害	0	0	1 (0.4%)	0
脳梗塞	1 (0.4%)	1 (0.4%)	0	0
注意力障害	1 (0.4%)	0	0	0
労作性めまい	1 (0.4%)	0	0	0
頭痛	1 (0.4%)	0	0	0
意識消失	1 (0.4%)	0	0	0
記憶障害	1 (0.4%)	1 (0.4%)	0	0
不随意性筋収縮	1 (0.4%)	0	0	0
精神運動亢進	1 (0.4%)	0	0	0
傾眠	1 (0.4%)	0	0	0
第７脳神経麻痺	1 (0.4%)	0	0	0
代謝および栄養障害	13 (4.6%)	8 (2.8%)	23 (8.1%)	12 (4.2%)
高血糖	8 (2.8%)	5 (1.8%)	13 (4.6%)	8 (2.8%)
脱水	0	0	4 (1.4%)	0
低カルシウム血症	0	0	2 (0.7%)	1 (0.4%)
食欲減退	1 (0.4%)	0	1 (0.4%)	0
糖尿病	0	0	1 (0.4%)	1 (0.4%)
電解質失調	0	0	1 (0.4%)	1 (0.4%)
食物不耐性	0	0	1 (0.4%)	0
低ナトリウム血症	0	0	1 (0.4%)	1 (0.4%)
低リン酸血症	0	0	1 (0.4%)	0
低カリウム血症	4 (1.4%)	3 (1.1%)	0	0
呼吸器、胸郭および縦隔障害	14 (5.0%)	7 (2.5%)	22 (7.8%)	9 (3.2%)
咳嗽	3 (1.1%)	0	5 (1.8%)	0
肺塞栓症	4 (1.4%)	4 (1.4%)	5 (1.8%)	4 (1.4%)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
呼吸困難	5 (1.8%)	0	3 (1.1%)	2 (0.7%)
慢性閉塞性肺疾患	0	0	2 (0.7%)	1 (0.4%)
湿性咳嗽	1 (0.4%)	0	2 (0.7%)	0
肺水腫	0	0	2 (0.7%)	2 (0.7%)
急性肺水腫	0	0	1 (0.4%)	1 (0.4%)
労作性呼吸困難	0	0	1 (0.4%)	0
低酸素症	0	0	1 (0.4%)	0
喉頭浮腫	0	0	1 (0.4%)	0
肺障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
肺臓炎	0	0	1 (0.4%)	0
肺腫瘤	0	0	1 (0.4%)	0
呼吸不全	0	0	1 (0.4%)	1 (0.4%)
急性呼吸不全	1 (0.4%)	1 (0.4%)	0	0
無気肺	1 (0.4%)	1 (0.4%)	0	0
副鼻腔うっ血	1 (0.4%)	0	0	0
腎および尿路障害	12 (4.3%)	4 (1.4%)	19 (6.7%)	1 (0.4%)
腎機能障害	7 (2.5%)	1 (0.4%)	16 (5.7%)	0
急性腎不全	3 (1.1%)	1 (0.4%)	1 (0.4%)	0
慢性腎臓病	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
腎不全	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
臨床検査	13 (4.6%)	2 (0.7%)	18 (6.4%)	9 (3.2%)
アラニンアミノトランスフェラーゼ増加	3 (1.1%)	2 (0.7%)	9 (3.2%)	6 (2.1%)
血中クレアチニン増加	6 (2.1%)	0	6 (2.1%)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	4 (1.4%)	2 (0.7%)
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	0	3 (1.1%)	3 (1.1%)
血中アルカリホスファターゼ増加	1 (0.4%)	0	2 (0.7%)	1 (0.4%)
血中乳酸脱水素酵素増加	0	0	1 (0.4%)	0
血圧低下	0	0	1 (0.4%)	0
腎クレアチニン・クリアランス減少	2 (0.7%)	0	1 (0.4%)	0
好中球中毒性顆粒存在	0	0	1 (0.4%)	1 (0.4%)
糸球体濾過率減少	2 (0.7%)	0	0	0
皮膚および皮下組織障害	10 (3.6%)	0	13 (4.6%)	5 (1.8%)
発疹	3 (1.1%)	0	4 (1.4%)	0
全身性皮疹	0	0	2 (0.7%)	1 (0.4%)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
顔面腫脹	0	0	2 (0.7%)	0
薬疹	0	0	1 (0.4%)	1 (0.4%)
毛髪成長異常	0	0	1 (0.4%)	0
男性型多毛症	0	0	1 (0.4%)	0
多汗症	3 (1.1%)	0	1 (0.4%)	0
点状出血	0	0	1 (0.4%)	0
そう痒症	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
斑状皮疹	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
斑状丘疹状皮疹	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
蕁麻疹	0	0	1 (0.4%)	1 (0.4%)
紅斑	1 (0.4%)	0	0	0
寝汗	1 (0.4%)	0	0	0
壊疽性膿皮症	1 (0.4%)	0	0	0
血管障害	11 (3.9%)	5 (1.8%)	13 (4.6%)	2 (0.7%)
静脈炎	1 (0.4%)	1 (0.4%)	3 (1.1%)	0
潮紅	2 (0.7%)	0	2 (0.7%)	0
低血圧	2 (0.7%)	1 (0.4%)	2 (0.7%)	0
表在性血栓性静脈炎	1 (0.4%)	0	2 (0.7%)	0
血栓症	0	0	2 (0.7%)	1 (0.4%)
深部静脈血栓症	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
塞栓症	0	0	1 (0.4%)	0
血栓性静脈炎	0	0	1 (0.4%)	0
静脈血栓症	0	0	1 (0.4%)	0
高血圧	1 (0.4%)	0	0	0
起立性低血圧	1 (0.4%)	1 (0.4%)	0	0
心臓障害	6 (2.1%)	4 (1.4%)	8 (2.8%)	4 (1.4%)
心房細動	1 (0.4%)	0	2 (0.7%)	0
狭心症	0	0	1 (0.4%)	1 (0.4%)
心房粗動	0	0	1 (0.4%)	0
徐脈	0	0	1 (0.4%)	0
心アミロイドーシス	0	0	1 (0.4%)	0
うっ血性心不全	0	0	1 (0.4%)	1 (0.4%)
洞性不整脈	0	0	1 (0.4%)	1 (0.4%)
洞性頻脈	0	0	1 (0.4%)	1 (0.4%)

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
心筋梗塞	1 (0.4%)	1 (0.4%)	0	0
心嚢液貯留	1 (0.4%)	0	0	0
心膜炎	1 (0.4%)	1 (0.4%)	0	0
上室性頻脈	1 (0.4%)	1 (0.4%)	0	0
眼障害	2 (0.7%)	0	6 (2.1%)	2 (0.7%)
白内障	1 (0.4%)	0	4 (1.4%)	1 (0.4%)
後嚢破裂	0	0	1 (0.4%)	1 (0.4%)
霧視	1 (0.4%)	0	1 (0.4%)	0
水晶体混濁	1 (0.4%)	0	0	0
傷害、中毒および処置合併症	2 (0.7%)	1 (0.4%)	6 (2.1%)	0
脊椎圧迫骨折	0	0	2 (0.7%)	0
腓骨神経損傷	0	0	1 (0.4%)	0
熱傷	0	0	1 (0.4%)	0
各種物質毒性	1 (0.4%)	0	1 (0.4%)	0
手首関節骨折	0	0	1 (0.4%)	0
関節脱臼	1 (0.4%)	1 (0.4%)	0	0
肝胆道系障害	2 (0.7%)	0	4 (1.4%)	3 (1.1%)
肝機能異常	0	0	2 (0.7%)	1 (0.4%)
高ビリルビン血症	1 (0.4%)	0	2 (0.7%)	2 (0.7%)
胆管結石	1 (0.4%)	0	0	0
耳および迷路障害	0	0	3 (1.1%)	0
耳出血	0	0	1 (0.4%)	0
耳鳴	0	0	1 (0.4%)	0
回転性めまい	0	0	1 (0.4%)	0
内分泌障害	3 (1.1%)	1 (0.4%)	2 (0.7%)	0
クッシング様症状	2 (0.7%)	0	1 (0.4%)	0
高コルチコイド症	0	0	1 (0.4%)	0
ステロイド離脱症候群	1 (0.4%)	1 (0.4%)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (1.1%)	0	1 (0.4%)	0
基底細胞癌	0	0	1 (0.4%)	0
肛門直腸の良性新生物	1 (0.4%)	0	0	0
形質細胞性白血病	1 (0.4%)	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
扁平上皮癌	1 (0.4%)	0	0	0
生殖系および乳房障害	1 (0.4%)	0	1 (0.4%)	0
前立腺炎	1 (0.4%)	0	1 (0.4%)	0
Japanese				
Analysis set: safety	15		20	
Total number of subjects with TEAE leading to cycle delays or dose modifications[c]	11 (73.3%)	7 (46.7%)	19 (95.0%)	16 (80.0%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	7 (46.7%)	6 (40.0%)	8 (40.0%)	8 (40.0%)
好中球減少症	4 (26.7%)	3 (20.0%)	7 (35.0%)	7 (35.0%)
血小板減少症	1 (6.7%)	0	1 (5.0%)	1 (5.0%)
貧血	2 (13.3%)	2 (13.3%)	1 (5.0%)	1 (5.0%)
発熱性好中球減少症	0	0	0	0
リンパ球減少症	1 (6.7%)	1 (6.7%)	2 (10.0%)	2 (10.0%)
白血球減少症	1 (6.7%)	0	0	0
リンパ節症	0	0	0	0
出血性障害	0	0	0	0
鉄芽球性貧血	0	0	0	0
血栓性血小板減少性紫斑病	0	0	0	0
感染症および寄生虫症	4 (26.7%)	1 (6.7%)	4 (20.0%)	2 (10.0%)
肺炎	2 (13.3%)	1 (6.7%)	1 (5.0%)	1 (5.0%)
上気道感染	0	0	1 (5.0%)	0
気道感染	0	0	0	0
気管支炎	0	0	0	0
インフルエンザ	0	0	0	0
鼻咽頭炎	0	0	2 (10.0%)	0
下気道感染	0	0	0	0
インフルエンザ性肺炎	0	0	0	0
尿路感染	0	0	0	0
虫垂炎	0	0	0	0
気管支肺炎	1 (6.7%)	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
胃腸炎	0	0	0	0
ウイルス性胃腸炎	0	0	0	0
感染	0	0	0	0
大葉性肺炎	0	0	0	0
肺感染	0	0	0	0
耳下腺炎	0	0	0	0
ＲＳウイルス感染	0	0	0	0
鼻炎	0	0	0	0
急性副鼻腔炎	0	0	0	0
細菌感染	0	0	1 (5.0%)	1 (5.0%)
細気管支炎	0	0	0	0
細菌性気管支炎	0	0	0	0
蜂巣炎	0	0	0	0
ウイルス性腸炎	0	0	1 (5.0%)	0
喉頭蓋炎	0	0	0	0
硬膜外膿瘍	0	0	0	0
消化管感染	0	0	0	0
歯肉炎	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0
リステリア性敗血症	0	0	0	0
鼻膿瘍	0	0	0	0
好中球減少性敗血症	0	0	0	0
口腔真菌感染	0	0	0	0
急性中耳炎	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0
咽頭炎	0	0	0	0
細菌性肺炎	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
レンサ球菌性肺炎	0	0	0	0
サルモネラ性菌血症	0	0	0	0
敗血症	0	0	0	0
敗血症性ショック	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
副鼻腔炎	0	0	0	0
軟部組織感染	0	0	0	0
皮下組織膿瘍	0	0	0	0
歯膿瘍	0	0	0	0
細菌性上気道感染	0	0	0	0
子宮膿瘍	0	0	0	0
ウイルス感染	0	0	0	0
内臓リーシュマニア症	0	0	0	0
創傷感染	0	0	0	0
四肢膿瘍	0	0	0	0
ウイルス性気管支炎	0	0	0	0
感染性小腸結腸炎	0	0	0	0
ヘモフィルス感染	0	0	0	0
帯状疱疹	1 (6.7%)	0	0	0
骨髄炎	0	0	0	0
急性腎盂腎炎	0	0	0	0
尿路性敗血症	0	0	0	0
水痘	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0
一般・全身障害および投与部位の状態	0	0	3 (15.0%)	0
疲労	0	0	1 (5.0%)	0
発熱	0	0	1 (5.0%)	0
無力症	0	0	0	0
倦怠感	0	0	1 (5.0%)	0
悪寒	0	0	0	0
薬物不耐性	0	0	0	0
インフルエンザ様疾患	0	0	0	0
胸部不快感	0	0	0	0
脂肪組織増加	0	0	0	0
歩行障害	0	0	0	0
全身健康状態低下	0	0	0	0
粘膜の炎症	0	0	0	0
全身性炎症反応症候群	0	0	0	0
胸痛	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
顔面浮腫	0	0	0	0
全身性浮腫	0	0	0	0
末梢性浮腫	0	0	0	0
末梢腫脹	0	0	0	0
胃腸障害	1 (6.7%)	0	2 (10.0%)	0
下痢	0	0	0	0
悪心	0	0	2 (10.0%)	0
嘔吐	1 (6.7%)	0	1 (5.0%)	0
便秘	0	0	0	0
上腹部痛	0	0	0	0
憩室穿孔	0	0	0	0
胃腸障害	0	0	0	0
腹部不快感	0	0	0	0
肛門出血	0	0	0	0
大腸炎	0	0	0	0
嚥下障害	0	0	0	0
心窩部不快感	0	0	0	0
胃炎	0	0	0	0
出血性胃腸管血管異形成	0	0	0	0
鼠径ヘルニア	0	0	0	0
口腔内潰瘍形成	0	0	0	0
唾液腺結石	0	0	0	0
顎下腺腫大	0	0	0	0
腹痛	0	0	0	0
口内乾燥	0	0	0	0
腸閉塞	0	0	0	0
下部消化管出血	0	0	0	0
食道炎	0	0	0	0
精神障害	0	0	0	0
不眠症	0	0	0	0
うつ病	0	0	0	0
激越	0	0	0	0
不安	0	0	0	0
易刺激性	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
精神障害	0	0	0	0
気分変化	0	0	0	0
気分動揺	0	0	0	0
落ち着きのなさ	0	0	0	0
睡眠障害	0	0	0	0
抑うつ気分	0	0	0	0
錯乱状態	0	0	0	0
譫妄	0	0	0	0
気分変調性障害	0	0	0	0
神経過敏	0	0	0	0
精神病性障害	0	0	0	0
筋骨格系および結合組織障害	2 (13.3%)	0	0	0
筋力低下	1 (6.7%)	0	0	0
筋痙縮	0	0	0	0
背部痛	0	0	0	0
ミオパチー	1 (6.7%)	0	0	0
筋萎縮症	0	0	0	0
関節痛	0	0	0	0
骨痛	0	0	0	0
側腹部痛	0	0	0	0
椎間板突出	0	0	0	0
関節腫脹	0	0	0	0
筋肉痛	0	0	0	0
四肢痛	0	0	0	0
顎骨壊死	0	0	0	0
脊椎痛	0	0	0	0
神経系障害	1 (6.7%)	0	1 (5.0%)	1 (5.0%)
振戦	0	0	0	0
末梢性ニューロパチー	0	0	1 (5.0%)	1 (5.0%)
失神	0	0	0	0
感覚鈍麻	0	0	0	0
錯感覚	0	0	0	0
脳血管発作	0	0	0	0
認知障害	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
浮動性めまい	0	0	0	0
体位性めまい	0	0	0	0
知覚過敏	0	0	0	0
嗜眠	0	0	0	0
神経系障害	0	0	0	0
末梢性感覚ニューロパチー	0	0	0	0
失神寸前の状態	0	0	0	0
痙攣発作	0	0	0	0
一過性脳虚血発作	0	0	0	0
三叉神経障害	0	0	0	0
脳梗塞	0	0	0	0
注意力障害	0	0	0	0
労作性めまい	0	0	0	0
頭痛	0	0	0	0
意識消失	0	0	0	0
記憶障害	0	0	0	0
不随意性筋収縮	0	0	0	0
精神運動亢進	0	0	0	0
傾眠	0	0	0	0
第７脳神経麻痺	1 (6.7%)	0	0	0
代謝および栄養障害	0	0	3 (15.0%)	2 (10.0%)
高血糖	0	0	2 (10.0%)	2 (10.0%)
脱水	0	0	0	0
低カルシウム血症	0	0	0	0
食欲減退	0	0	1 (5.0%)	0
糖尿病	0	0	0	0
電解質失調	0	0	0	0
食物不耐性	0	0	0	0
低ナトリウム血症	0	0	0	0
低リン酸血症	0	0	0	0
低カリウム血症	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	1 (5.0%)	0
咳嗽	0	0	0	0
肺塞栓症	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
呼吸困難	0	0	0	0
慢性閉塞性肺疾患	0	0	0	0
湿性咳嗽	0	0	0	0
肺水腫	0	0	0	0
急性肺水腫	0	0	0	0
労作性呼吸困難	0	0	0	0
低酸素症	0	0	1 (5.0%)	0
喉頭浮腫	0	0	0	0
肺障害	0	0	0	0
肺臓炎	0	0	0	0
肺腫瘤	0	0	0	0
呼吸不全	0	0	0	0
急性呼吸不全	0	0	0	0
無気肺	0	0	0	0
副鼻腔うっ血	0	0	0	0
腎および尿路障害	1 (6.7%)	1 (6.7%)	2 (10.0%)	0
腎機能障害	0	0	2 (10.0%)	0
急性腎不全	1 (6.7%)	1 (6.7%)	0	0
慢性腎臓病	0	0	0	0
腎不全	0	0	0	0
臨床検査	1 (6.7%)	0	4 (20.0%)	3 (15.0%)
アラニンアミノトランスフェラーゼ増加	0	0	3 (15.0%)	2 (10.0%)
血中クレアチニン増加	1 (6.7%)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (5.0%)	0
γ－グルタミルトランスフェラーゼ増加	0	0	2 (10.0%)	2 (10.0%)
血中アルカリホスファターゼ増加	0	0	1 (5.0%)	0
血中乳酸脱水素酵素増加	0	0	0	0
血圧低下	0	0	1 (5.0%)	0
腎クレアチニン・クリアランス減少	0	0	0	0
好中球中毒性顆粒存在	0	0	0	0
糸球体濾過率減少	0	0	0	0
皮膚および皮下組織障害	1 (6.7%)	0	2 (10.0%)	1 (5.0%)
発疹	1 (6.7%)	0	1 (5.0%)	0
全身性皮疹	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
顔面腫脹	0	0	0	0
薬疹	0	0	1 (5.0%)	1 (5.0%)
毛髪成長異常	0	0	0	0
男性型多毛症	0	0	0	0
多汗症	0	0	0	0
点状出血	0	0	0	0
そう痒症	0	0	0	0
斑状皮疹	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
蕁麻疹	0	0	0	0
紅斑	0	0	0	0
寝汗	0	0	0	0
壊疽性膿皮症	0	0	0	0
血管障害	0	0	2 (10.0%)	0
静脈炎	0	0	0	0
潮紅	0	0	0	0
低血圧	0	0	0	0
表在性血栓性静脈炎	0	0	0	0
血栓症	0	0	1 (5.0%)	0
深部静脈血栓症	0	0	0	0
塞栓症	0	0	1 (5.0%)	0
血栓性静脈炎	0	0	1 (5.0%)	0
静脈血栓症	0	0	0	0
高血圧	0	0	0	0
起立性低血圧	0	0	0	0
心臓障害	0	0	0	0
心房細動	0	0	0	0
狭心症	0	0	0	0
心房粗動	0	0	0	0
徐脈	0	0	0	0
心アミロイドーシス	0	0	0	0
うっ血性心不全	0	0	0	0
洞性不整脈	0	0	0	0
洞性頻脈	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
急性心筋梗塞	0	0	0	0
心筋梗塞	0	0	0	0
心嚢液貯留	0	0	0	0
心膜炎	0	0	0	0
上室性頻脈	0	0	0	0
眼障害	0	0	0	0
白内障	0	0	0	0
後嚢破裂	0	0	0	0
霧視	0	0	0	0
水晶体混濁	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
脊椎圧迫骨折	0	0	0	0
腓骨神経損傷	0	0	0	0
熱傷	0	0	0	0
各種物質毒性	0	0	0	0
手首関節骨折	0	0	0	0
関節脱臼	0	0	0	0
肝胆道系障害	0	0	2 (10.0%)	1 (5.0%)
肝機能異常	0	0	2 (10.0%)	1 (5.0%)
高ビリルビン血症	0	0	0	0
胆管結石	0	0	0	0
耳および迷路障害	0	0	0	0
耳出血	0	0	0	0
耳鳴	0	0	0	0
回転性めまい	0	0	0	0
内分泌障害	0	0	0	0
クッシング様症状	0	0	0	0
高コルチコイド症	0	0	0	0
ステロイド離脱症候群	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0
基底細胞癌	0	0	0	0
肛門直腸の良性新生物	0	0	0	0
形質細胞性白血病	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
扁平上皮癌	0	0	0	0
生殖系および乳房障害	0	0	0	0
前立腺炎	0	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Total number of subjects with TEAE leading to cycle delays or dose modifications[c]	29 (65.9%)	23 (52.3%)	40 (78.4%)	36 (70.6%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	19 (43.2%)	18 (40.9%)	25 (49.0%)	25 (49.0%)
好中球減少症	16 (36.4%)	15 (34.1%)	24 (47.1%)	24 (47.1%)
血小板減少症	1 (2.3%)	0	2 (3.9%)	2 (3.9%)
貧血	3 (6.8%)	3 (6.8%)	2 (3.9%)	2 (3.9%)
発熱性好中球減少症	1 (2.3%)	1 (2.3%)	1 (2.0%)	1 (2.0%)
リンパ球減少症	1 (2.3%)	1 (2.3%)	2 (3.9%)	2 (3.9%)
白血球減少症	1 (2.3%)	0	1 (2.0%)	1 (2.0%)
リンパ節症	0	0	0	0
出血性障害	0	0	0	0
鉄芽球性貧血	0	0	0	0
血栓性血小板減少性紫斑病	0	0	0	0
感染症および寄生虫症	12 (27.3%)	6 (13.6%)	9 (17.6%)	6 (11.8%)
肺炎	4 (9.1%)	2 (4.5%)	1 (2.0%)	1 (2.0%)
上気道感染	1 (2.3%)	0	1 (2.0%)	0
気道感染	0	0	0	0
気管支炎	1 (2.3%)	0	0	0
インフルエンザ	1 (2.3%)	0	0	0
鼻咽頭炎	0	0	2 (3.9%)	0
下気道感染	0	0	0	0
インフルエンザ性肺炎	0	0	0	0
尿路感染	0	0	0	0
虫垂炎	0	0	0	0
気管支肺炎	1 (2.3%)	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
胃腸炎	0	0	0	0
ウイルス性胃腸炎	0	0	0	0
感染	0	0	0	0
大葉性肺炎	0	0	1 (2.0%)	1 (2.0%)
肺感染	0	0	0	0
耳下腺炎	0	0	0	0
ＲＳウイルス感染	0	0	0	0
鼻炎	0	0	0	0
急性副鼻腔炎	0	0	0	0
細菌感染	0	0	1 (2.0%)	1 (2.0%)
細気管支炎	0	0	1 (2.0%)	1 (2.0%)
細菌性気管支炎	0	0	0	0
蜂巣炎	0	0	0	0
ウイルス性腸炎	0	0	1 (2.0%)	0
喉頭蓋炎	0	0	0	0
硬膜外膿瘍	0	0	0	0
消化管感染	0	0	0	0
歯肉炎	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0
リステリア性敗血症	0	0	0	0
鼻膿瘍	0	0	0	0
好中球減少性敗血症	0	0	0	0
口腔真菌感染	0	0	0	0
急性中耳炎	0	0	1 (2.0%)	1 (2.0%)
パラインフルエンザウイルス感染	0	0	0	0
咽頭炎	0	0	0	0
細菌性肺炎	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
レンサ球菌性肺炎	0	0	0	0
サルモネラ性菌血症	0	0	1 (2.0%)	1 (2.0%)
敗血症	1 (2.3%)	1 (2.3%)	0	0
敗血症性ショック	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
副鼻腔炎	0	0	1 (2.0%)	0
軟部組織感染	0	0	0	0
皮下組織膿瘍	0	0	0	0
歯膿瘍	0	0	0	0
細菌性上気道感染	0	0	0	0
子宮膿瘍	0	0	0	0
ウイルス感染	0	0	0	0
内臓リーシュマニア症	0	0	0	0
創傷感染	0	0	0	0
四肢膿瘍	0	0	0	0
ウイルス性気管支炎	0	0	0	0
感染性小腸結腸炎	0	0	0	0
ヘモフィルス感染	0	0	0	0
帯状疱疹	2 (4.5%)	1 (2.3%)	0	0
骨髄炎	1 (2.3%)	1 (2.3%)	0	0
急性腎盂腎炎	1 (2.3%)	1 (2.3%)	0	0
尿路性敗血症	0	0	0	0
水痘	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0
一般・全身障害および投与部位の状態	2 (4.5%)	1 (2.3%)	7 (13.7%)	2 (3.9%)
疲労	1 (2.3%)	0	3 (5.9%)	1 (2.0%)
発熱	0	0	3 (5.9%)	1 (2.0%)
無力症	1 (2.3%)	1 (2.3%)	1 (2.0%)	1 (2.0%)
倦怠感	0	0	1 (2.0%)	0
悪寒	0	0	0	0
薬物不耐性	0	0	0	0
インフルエンザ様疾患	0	0	0	0
胸部不快感	0	0	0	0
脂肪組織増加	0	0	0	0
歩行障害	0	0	0	0
全身健康状態低下	0	0	0	0
粘膜の炎症	0	0	0	0
全身性炎症反応症候群	0	0	0	0
胸痛	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
顔面浮腫	0	0	0	0
全身性浮腫	0	0	0	0
末梢性浮腫	0	0	0	0
末梢腫脹	0	0	0	0
胃腸障害	3 (6.8%)	2 (4.5%)	4 (7.8%)	2 (3.9%)
下痢	1 (2.3%)	1 (2.3%)	2 (3.9%)	2 (3.9%)
悪心	0	0	2 (3.9%)	0
嘔吐	1 (2.3%)	0	1 (2.0%)	0
便秘	0	0	0	0
上腹部痛	0	0	0	0
憩室穿孔	0	0	0	0
胃腸障害	0	0	0	0
腹部不快感	0	0	0	0
肛門出血	0	0	0	0
大腸炎	0	0	0	0
嚥下障害	0	0	0	0
心窩部不快感	0	0	0	0
胃炎	0	0	0	0
出血性胃腸管血管異形成	0	0	0	0
鼠径ヘルニア	0	0	0	0
口腔内潰瘍形成	0	0	0	0
唾液腺結石	0	0	0	0
顎下腺腫大	0	0	0	0
腹痛	0	0	0	0
口内乾燥	0	0	0	0
腸閉塞	0	0	0	0
下部消化管出血	0	0	0	0
食道炎	1 (2.3%)	1 (2.3%)	0	0
精神障害	0	0	0	0
不眠症	0	0	0	0
うつ病	0	0	0	0
激越	0	0	0	0
不安	0	0	0	0
易刺激性	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
精神障害	0	0	0	0
気分変化	0	0	0	0
気分動揺	0	0	0	0
落ち着きのなさ	0	0	0	0
睡眠障害	0	0	0	0
抑うつ気分	0	0	0	0
錯乱状態	0	0	0	0
譫妄	0	0	0	0
気分変調性障害	0	0	0	0
神経過敏	0	0	0	0
精神病性障害	0	0	0	0
筋骨格系および結合組織障害	3 (6.8%)	0	1 (2.0%)	0
筋力低下	2 (4.5%)	0	0	0
筋痙縮	0	0	0	0
背部痛	0	0	0	0
ミオパチー	1 (2.3%)	0	0	0
筋萎縮症	0	0	0	0
関節痛	0	0	0	0
骨痛	0	0	0	0
側腹部痛	0	0	0	0
椎間板突出	0	0	0	0
関節腫脹	0	0	0	0
筋肉痛	0	0	1 (2.0%)	0
四肢痛	0	0	0	0
顎骨壊死	0	0	0	0
脊椎痛	0	0	0	0
神経系障害	2 (4.5%)	0	1 (2.0%)	1 (2.0%)
振戦	0	0	0	0
末梢性ニューロパチー	0	0	1 (2.0%)	1 (2.0%)
失神	0	0	0	0
感覚鈍麻	1 (2.3%)	0	0	0
錯感覚	0	0	0	0
脳血管発作	0	0	0	0
認知障害	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
浮動性めまい	0	0	0	0
体位性めまい	0	0	0	0
知覚過敏	0	0	0	0
嗜眠	0	0	0	0
神経系障害	0	0	0	0
末梢性感覚ニューロパチー	0	0	0	0
失神寸前の状態	0	0	0	0
痙攣発作	0	0	0	0
一過性脳虚血発作	0	0	0	0
三叉神経障害	0	0	0	0
脳梗塞	0	0	0	0
注意力障害	0	0	0	0
労作性めまい	0	0	0	0
頭痛	0	0	0	0
意識消失	0	0	0	0
記憶障害	0	0	0	0
不随意性筋収縮	0	0	0	0
精神運動亢進	0	0	0	0
傾眠	0	0	0	0
第７脳神経麻痺	1 (2.3%)	0	0	0
代謝および栄養障害	0	0	4 (7.8%)	3 (5.9%)
高血糖	0	0	3 (5.9%)	3 (5.9%)
脱水	0	0	0	0
低カルシウム血症	0	0	0	0
食欲減退	0	0	1 (2.0%)	0
糖尿病	0	0	0	0
電解質失調	0	0	0	0
食物不耐性	0	0	0	0
低ナトリウム血症	0	0	0	0
低リン酸血症	0	0	0	0
低カリウム血症	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	3 (5.9%)	0
咳嗽	0	0	2 (3.9%)	0
肺塞栓症	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
呼吸困難	0	0	0	0
慢性閉塞性肺疾患	0	0	0	0
湿性咳嗽	0	0	1 (2.0%)	0
肺水腫	0	0	0	0
急性肺水腫	0	0	0	0
労作性呼吸困難	0	0	0	0
低酸素症	0	0	1 (2.0%)	0
喉頭浮腫	0	0	0	0
肺障害	0	0	0	0
肺臓炎	0	0	1 (2.0%)	0
肺腫瘤	0	0	0	0
呼吸不全	0	0	0	0
急性呼吸不全	0	0	0	0
無気肺	0	0	0	0
副鼻腔うっ血	0	0	0	0
腎および尿路障害	2 (4.5%)	2 (4.5%)	3 (5.9%)	0
腎機能障害	0	0	2 (3.9%)	0
急性腎不全	1 (2.3%)	1 (2.3%)	0	0
慢性腎臓病	1 (2.3%)	1 (2.3%)	1 (2.0%)	0
腎不全	0	0	0	0
臨床検査	2 (4.5%)	1 (2.3%)	4 (7.8%)	3 (5.9%)
アラニンアミノトランスフェラーゼ増加	1 (2.3%)	1 (2.3%)	3 (5.9%)	2 (3.9%)
血中クレアチニン増加	1 (2.3%)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (2.0%)	0
γ－グルタミルトランスフェラーゼ増加	0	0	2 (3.9%)	2 (3.9%)
血中アルカリホスファターゼ増加	0	0	1 (2.0%)	0
血中乳酸脱水素酵素増加	0	0	0	0
血圧低下	0	0	1 (2.0%)	0
腎クレアチニン・クリアランス減少	0	0	0	0
好中球中毒性顆粒存在	0	0	0	0
糸球体濾過率減少	0	0	0	0
皮膚および皮下組織障害	2 (4.5%)	0	3 (5.9%)	2 (3.9%)
発疹	1 (2.3%)	0	1 (2.0%)	0
全身性皮疹	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
顔面腫脹	0	0	0	0
薬疹	0	0	1 (2.0%)	1 (2.0%)
毛髪成長異常	0	0	0	0
男性型多毛症	0	0	0	0
多汗症	0	0	0	0
点状出血	0	0	0	0
そう痒症	0	0	0	0
斑状皮疹	0	0	0	0
斑状丘疹状皮疹	0	0	1 (2.0%)	1 (2.0%)
蕁麻疹	0	0	1 (2.0%)	1 (2.0%)
紅斑	0	0	0	0
寝汗	0	0	0	0
壊疽性膿皮症	1 (2.3%)	0	0	0
血管障害	0	0	2 (3.9%)	0
静脈炎	0	0	0	0
潮紅	0	0	0	0
低血圧	0	0	0	0
表在性血栓性静脈炎	0	0	0	0
血栓症	0	0	1 (2.0%)	0
深部静脈血栓症	0	0	0	0
塞栓症	0	0	1 (2.0%)	0
血栓性静脈炎	0	0	1 (2.0%)	0
静脈血栓症	0	0	0	0
高血圧	0	0	0	0
起立性低血圧	0	0	0	0
心臓障害	0	0	0	0
心房細動	0	0	0	0
狭心症	0	0	0	0
心房粗動	0	0	0	0
徐脈	0	0	0	0
心アミロイドーシス	0	0	0	0
うっ血性心不全	0	0	0	0
洞性不整脈	0	0	0	0
洞性頻脈	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
急性心筋梗塞	0	0	0	0
心筋梗塞	0	0	0	0
心嚢液貯留	0	0	0	0
心膜炎	0	0	0	0
上室性頻脈	0	0	0	0
眼障害	0	0	0	0
白内障	0	0	0	0
後嚢破裂	0	0	0	0
霧視	0	0	0	0
水晶体混濁	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
脊椎圧迫骨折	0	0	0	0
腓骨神経損傷	0	0	0	0
熱傷	0	0	0	0
各種物質毒性	0	0	0	0
手首関節骨折	0	0	0	0
関節脱臼	0	0	0	0
肝胆道系障害	0	0	2 (3.9%)	1 (2.0%)
肝機能異常	0	0	2 (3.9%)	1 (2.0%)
高ビリルビン血症	0	0	0	0
胆管結石	0	0	0	0
耳および迷路障害	0	0	0	0
耳出血	0	0	0	0
耳鳴	0	0	0	0
回転性めまい	0	0	0	0
内分泌障害	1 (2.3%)	0	0	0
クッシング様症状	1 (2.3%)	0	0	0
高コルチコイド症	0	0	0	0
ステロイド離脱症候群	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0
基底細胞癌	0	0	0	0
肛門直腸の良性新生物	0	0	0	0
形質細胞性白血病	0	0	0	0

TSFAE08_3003: Number of Subjects With 1 or More Treatment-emergent Adverse Events Leading to Cycle Delays or Dose Modifications by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
扁平上皮癌	0	0	0	0
生殖系および乳房障害	0	0	0	0
前立腺炎	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes adverse events leading to cycle delays or at least 1 of study treatments dose modifications (i.e., dose delays, dose skipping, or dose reduction) : lenalidomide, dexamethasone or daratumumab.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-125 Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Total[a]						
Analysis set: safety	281			283		
Total number of subjects with TEAE leading to discontinuation of any study treatment[c]	36 (12.8%)	20 (7.1%)	8 (2.8%)	38 (13.4%)	26 (9.2%)	5 (1.8%)
MedDRA system organ class/Preferred term						
一般・全身障害および投与部位の状態	1 (0.4%)	0	0	10 (3.5%)	7 (2.5%)	1 (0.4%)
疲労	0	0	0	4 (1.4%)	3 (1.1%)	0
全身健康状態低下	0	0	0	3 (1.1%)	2 (0.7%)	0
多臓器不全	0	0	0	1 (0.4%)	0	1 (0.4%)
末梢性浮腫	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0
疼痛	0	0	0	1 (0.4%)	1 (0.4%)	0
顔面浮腫	1 (0.4%)	0	0	0	0	0
感染症および寄生虫症	7 (2.5%)	5 (1.8%)	2 (0.7%)	9 (3.2%)	5 (1.8%)	3 (1.1%)
肺炎	2 (0.7%)	2 (0.7%)	0	4 (1.4%)	4 (1.4%)	0
敗血症性ショック	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	1 (0.4%)	2 (0.7%)
細菌性気管支炎	0	0	0	1 (0.4%)	0	0
細菌性肺炎	0	0	0	1 (0.4%)	0	1 (0.4%)
感染	1 (0.4%)	1 (0.4%)	0	0	0	0
真菌性角膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
敗血症	1 (0.4%)	0	1 (0.4%)	0	0	0
神経系障害	3 (1.1%)	2 (0.7%)	1 (0.4%)	4 (1.4%)	3 (1.1%)	0
平衡障害	0	0	0	1 (0.4%)	0	0
脳梗塞	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
認知障害	0	0	0	1 (0.4%)	1 (0.4%)	0
失神	0	0	0	1 (0.4%)	1 (0.4%)	0
脳出血	1 (0.4%)	0	1 (0.4%)	0	0	0
嗜眠	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
精神障害	4 (1.4%)	0	0	4 (1.4%)	2 (0.7%)	0
うつ病	0	0	0	2 (0.7%)	2 (0.7%)	0
不眠症	1 (0.4%)	0	0	1 (0.4%)	0	0
気分動揺	0	0	0	1 (0.4%)	0	0
激越	2 (0.7%)	0	0	0	0	0
気分変化	1 (0.4%)	0	0	0	0	0
睡眠障害	2 (0.7%)	0	0	0	0	0
胃腸障害	0	0	0	3 (1.1%)	1 (0.4%)	0
下痢	0	0	0	1 (0.4%)	0	0
憩室穿孔	0	0	0	1 (0.4%)	1 (0.4%)	0
消化不良	0	0	0	1 (0.4%)	0	0
代謝および栄養障害	0	0	0	3 (1.1%)	2 (0.7%)	0
高カルシウム血症	0	0	0	2 (0.7%)	1 (0.4%)	0
高血糖	0	0	0	1 (0.4%)	1 (0.4%)	0
血液およびリンパ系障害	4 (1.4%)	3 (1.1%)	0	2 (0.7%)	2 (0.7%)	0
貧血	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
好中球減少症	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0	0	0
血小板減少症	2 (0.7%)	1 (0.4%)	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4 (1.4%)	2 (0.7%)	2 (0.7%)	2 (0.7%)	2 (0.7%)	0
急性単球性白血病	0	0	0	1 (0.4%)	1 (0.4%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.4%)	1 (0.4%)	0
肺腺癌	1 (0.4%)	0	1 (0.4%)	0	0	0
形質細胞性白血病	1 (0.4%)	0	1 (0.4%)	0	0	0
前立腺癌	1 (0.4%)	1 (0.4%)	0	0	0	0
直腸腺癌	1 (0.4%)	1 (0.4%)	0	0	0	0
呼吸器、胸郭および縦隔障害	5 (1.8%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	2 (0.7%)	0
発声障害	0	0	0	1 (0.4%)	1 (0.4%)	0
呼吸困難	0	0	0	1 (0.4%)	1 (0.4%)	0
喉頭浮腫	0	0	0	1 (0.4%)	1 (0.4%)	0
呼吸不全	0	0	0	1 (0.4%)	1 (0.4%)	0
喘鳴	0	0	0	1 (0.4%)	1 (0.4%)	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
急性呼吸不全	1 (0.4%)	0	1 (0.4%)	0	0	0
肺塞栓症	3 (1.1%)	3 (1.1%)	0	0	0	0
肺水腫	1 (0.4%)	0	1 (0.4%)	0	0	0
心臓障害	2 (0.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
心肺不全	0	0	0	1 (0.4%)	0	1 (0.4%)
心停止	1 (0.4%)	0	1 (0.4%)	0	0	0
心膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
腎および尿路障害	4 (1.4%)	4 (1.4%)	0	1 (0.4%)	1 (0.4%)	0
腎不全	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	1 (0.4%)	0
急性腎不全	2 (0.7%)	2 (0.7%)	0	0	0	0
皮膚および皮下組織障害	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0
全身性皮疹	0	0	0	1 (0.4%)	1 (0.4%)	0
男性型多毛症	1 (0.4%)	0	0	0	0	0
眼障害	1 (0.4%)	0	0	0	0	0
白内障	1 (0.4%)	0	0	0	0	0
筋骨格系および結合組織障害	3 (1.1%)	1 (0.4%)	0	0	0	0
筋力低下	2 (0.7%)	0	0	0	0	0
脊柱管狭窄症	1 (0.4%)	1 (0.4%)	0	0	0	0
血管障害	1 (0.4%)	0	0	0	0	0
深部静脈血栓症	1 (0.4%)	0	0	0	0	0
Japanese						
Analysis set: safety	15			20		
Total number of subjects with TEAE leading to discontinuation of any study treatment[c]	0	0	0	3 (15.0%)	3 (15.0%)	0
MedDRA system organ class/Preferred term						
一般・全身障害および投与部位の状態	0	0	0	0	0	0
疲労	0	0	0	0	0	0
全身健康状態低下	0	0	0	0	0	0
多臓器不全	0	0	0	0	0	0
末梢性浮腫	0	0	0	0	0	0
疼痛	0	0	0	0	0	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
顔面浮腫	0	0	0	0	0	0
感染症および寄生虫症	0	0	0	1 (5.0%)	1 (5.0%)	0
肺炎	0	0	0	1 (5.0%)	1 (5.0%)	0
敗血症性ショック	0	0	0	0	0	0
細菌性気管支炎	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0
感染	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0
敗血症	0	0	0	0	0	0
神経系障害	0	0	0	1 (5.0%)	1 (5.0%)	0
平衡障害	0	0	0	0	0	0
脳梗塞	0	0	0	1 (5.0%)	1 (5.0%)	0
認知障害	0	0	0	0	0	0
失神	0	0	0	0	0	0
脳出血	0	0	0	0	0	0
嗜眠	0	0	0	0	0	0
精神障害	0	0	0	0	0	0
うつ病	0	0	0	0	0	0
不眠症	0	0	0	0	0	0
気分動揺	0	0	0	0	0	0
激越	0	0	0	0	0	0
気分変化	0	0	0	0	0	0
睡眠障害	0	0	0	0	0	0
胃腸障害	0	0	0	0	0	0
下痢	0	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0
消化不良	0	0	0	0	0	0
代謝および栄養障害	0	0	0	0	0	0
高カルシウム血症	0	0	0	0	0	0
高血糖	0	0	0	0	0	0
血液およびリンパ系障害	0	0	0	0	0	0
貧血	0	0	0	0	0	0
好中球減少症	0	0	0	0	0	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
鉄芽球性貧血	0	0	0	0	0	0
血小板減少症	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (5.0%)	1 (5.0%)	0
急性単球性白血病	0	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (5.0%)	1 (5.0%)	0
肺腺癌	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0
直腸腺癌	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	0	0
発声障害	0	0	0	0	0	0
呼吸困難	0	0	0	0	0	0
喉頭浮腫	0	0	0	0	0	0
呼吸不全	0	0	0	0	0	0
喘鳴	0	0	0	0	0	0
急性呼吸不全	0	0	0	0	0	0
肺塞栓症	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0
心臓障害	0	0	0	0	0	0
心肺不全	0	0	0	0	0	0
心停止	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0
腎および尿路障害	0	0	0	0	0	0
腎不全	0	0	0	0	0	0
急性腎不全	0	0	0	0	0	0
皮膚および皮下組織障害	0	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0
男性型多毛症	0	0	0	0	0	0
眼障害	0	0	0	0	0	0
白内障	0	0	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	0	0
筋力低下	0	0	0	0	0	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
脊柱管狭窄症	0	0	0	0	0	0
血管障害	0	0	0	0	0	0
深部静脈血栓症	0	0	0	0	0	0
East Asian[b]						
Analysis set: safety	44			51		
Total number of subjects with TEAE leading to discontinuation of any study treatment[c]	1 (2.3%)	0	1 (2.3%)	5 (9.8%)	4 (7.8%)	1 (2.0%)
MedDRA system organ class/Preferred term						
一般・全身障害および投与部位の状態	0	0	0	1 (2.0%)	0	1 (2.0%)
疲労	0	0	0	0	0	0
全身健康状態低下	0	0	0	0	0	0
多臓器不全	0	0	0	1 (2.0%)	0	1 (2.0%)
末梢性浮腫	0	0	0	0	0	0
疼痛	0	0	0	0	0	0
顔面浮腫	0	0	0	0	0	0
感染症および寄生虫症	1 (2.3%)	0	1 (2.3%)	2 (3.9%)	2 (3.9%)	0
肺炎	0	0	0	2 (3.9%)	2 (3.9%)	0
敗血症性ショック	0	0	0	0	0	0
細菌性気管支炎	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0
感染	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0
敗血症	1 (2.3%)	0	1 (2.3%)	0	0	0
神経系障害	0	0	0	1 (2.0%)	1 (2.0%)	0
平衡障害	0	0	0	0	0	0
脳梗塞	0	0	0	1 (2.0%)	1 (2.0%)	0
認知障害	0	0	0	0	0	0
失神	0	0	0	0	0	0
脳出血	0	0	0	0	0	0
嗜眠	0	0	0	0	0	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
精神障害	0	0	0	0	0	0
うつ病	0	0	0	0	0	0
不眠症	0	0	0	0	0	0
気分動揺	0	0	0	0	0	0
激越	0	0	0	0	0	0
気分変化	0	0	0	0	0	0
睡眠障害	0	0	0	0	0	0
胃腸障害	0	0	0	0	0	0
下痢	0	0	0	0	0	0
憩室穿孔	0	0	0	0	0	0
消化不良	0	0	0	0	0	0
代謝および栄養障害	0	0	0	0	0	0
高カルシウム血症	0	0	0	0	0	0
高血糖	0	0	0	0	0	0
血液およびリンパ系障害	0	0	0	0	0	0
貧血	0	0	0	0	0	0
好中球減少症	0	0	0	0	0	0
鉄芽球性貧血	0	0	0	0	0	0
血小板減少症	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (2.0%)	1 (2.0%)	0
急性単球性白血病	0	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (2.0%)	1 (2.0%)	0
肺腺癌	0	0	0	0	0	0
形質細胞性白血病	0	0	0	0	0	0
前立腺癌	0	0	0	0	0	0
直腸腺癌	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	0	0	0
発声障害	0	0	0	0	0	0
呼吸困難	0	0	0	0	0	0
喉頭浮腫	0	0	0	0	0	0
呼吸不全	0	0	0	0	0	0
喘鳴	0	0	0	0	0	0

TSFAE13_3003: Number of Subjects Who Discontinued Any Study Treatment Because of 1 or More Treatment-emergent Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd			DRd		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
急性呼吸不全	0	0	0	0	0	0
肺塞栓症	0	0	0	0	0	0
肺水腫	0	0	0	0	0	0
心臓障害	0	0	0	0	0	0
心肺不全	0	0	0	0	0	0
心停止	0	0	0	0	0	0
心膜炎	0	0	0	0	0	0
腎および尿路障害	0	0	0	0	0	0
腎不全	0	0	0	0	0	0
急性腎不全	0	0	0	0	0	0
皮膚および皮下組織障害	0	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0
男性型多毛症	0	0	0	0	0	0
眼障害	0	0	0	0	0	0
白内障	0	0	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	0	0
筋力低下	0	0	0	0	0	0
脊柱管狭窄症	0	0	0	0	0	0
血管障害	0	0	0	0	0	0
深部静脈血栓症	0	0	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] TEAEs with an action taken of drug withdrawal for any study treatment on the AE CRF page.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-126 Summary of Growth Factor Use with Onset during Study Treatment by Prophylactic Use and by Therapeutic Class, Pharmacologic Class, and Drug; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSICM01_MSCS: Summary of Growth Factor Use with Onset during Study Treatment by Prophylactic Use and by Therapeutic Class, Pharmacologic Class, and Drug; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with 1 or more growth factor use	2 (8.7%)	0	1 (1.8%)	1 (1.8%)	24 (15.4%)	3 (1.9%)	0	0	27 (11.4%)	4 (1.7%)
Therapeutic class/pharmacologic class/preferred term										
Immunostimulants	2 (8.7%)	0	1 (1.8%)	1 (1.8%)	24 (15.4%)	3 (1.9%)	0	0	27 (11.4%)	4 (1.7%)
Immunostimulants	2 (8.7%)	0	1 (1.8%)	1 (1.8%)	24 (15.4%)	3 (1.9%)	0	0	27 (11.4%)	4 (1.7%)
Filgrastim	2 (8.7%)	0	0	0	18 (11.5%)	3 (1.9%)	0	0	20 (8.4%)	3 (1.3%)
Granulocyte colony stimulating factor	0	0	1 (1.8%)	1 (1.8%)	2 (1.3%)	0	0	0	3 (1.3%)	1 (0.4%)
Pegfilgrastim	0	0	0	0	3 (1.9%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
Uncoded [GRAN]	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
Uncoded [NEUTROGIN]	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSICM01_MSCS.RTF] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_JAPAN\PROD\TSICM01_MSCS.SAS] 16SEP2016, 09:44

表 2.7.4-付録-127 Summary of Growth Factor Use with Onset during Study Treatment by Prophylactic Use and by Therapeutic Class, Pharmacologic Class, and Drug; All Treated Analysis Population (Study 54767414MMY1002);

TSICM05_J: Summary of Growth Factor Use with Onset during Study Treatment by Prophylactic Use and by Therapeutic Class, Pharmacologic Class, and Drug; All Treated Analysis Population (Study 54767414MMY1002);

	Daratumumab					
	8 mg/kg		16 mg/kg		All groups	
	Total	Prophylactic Use	Total	Prophylactic Use	Total	Prophylactic Use
Analysis set: All Treated Analysis Population	4		5		9	
Total number of subjects with 1 or more growth factor use	0	0	1 (20.0%)	0	1 (11.1%)	0
Therapeutic class/pharmacologic class/preferred term						
Immunostimulants	0	0	1 (20.0%)	0	1 (11.1%)	0
Immunostimulants	0	0	1 (20.0%)	0	1 (11.1%)	0
Filgrastim	0	0	1 (20.0%)	0	1 (11.1%)	0

Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSICM05_J.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_SCS\tsicm05_j.sas] 22JUL2016, 18:00

表 2.7.4-付録-128 Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Analysis set: safety	237		243		281		318		103	
Total number of subjects with infections/infestations	126 (53.2%)	45 (19.0%)	164 (67.5%)	52 (21.4%)	204 (72.6%)	64 (22.8%)	265 (83.3%)	86 (27.0%)	72 (69.9%)	29 (28.2%)
MedDRA system organ class/Preferred term										
感染症および寄生虫症	126 (53.2%)	45 (19.0%)	164 (67.5%)	52 (21.4%)	204 (72.6%)	64 (22.8%)	265 (83.3%)	86 (27.0%)	72 (69.9%)	29 (28.2%)
上気道感染	43 (18.1%)	2 (0.8%)	60 (24.7%)	4 (1.6%)	58 (20.6%)	3 (1.1%)	98 (30.8%)	4 (1.3%)	26 (25.2%)	3 (2.9%)
鼻咽頭炎	9 (3.8%)	0	17 (7.0%)	0	43 (15.3%)	0	76 (23.9%)	0	8 (7.8%)	0
気管支炎	13 (5.5%)	3 (1.3%)	28 (11.5%)	5 (2.1%)	34 (12.1%)	6 (2.1%)	46 (14.5%)	5 (1.6%)	10 (9.7%)	2 (1.9%)
肺炎	28 (11.8%)	23 (9.7%)	29 (11.9%)	20 (8.2%)	37 (13.2%)	23 (8.2%)	41 (12.9%)	23 (7.2%)	11 (10.7%)	8 (7.8%)
気道感染	3 (1.3%)	1 (0.4%)	0	0	22 (7.8%)	2 (0.7%)	33 (10.4%)	5 (1.6%)	0	0
インフルエンザ	7 (3.0%)	2 (0.8%)	8 (3.3%)	1 (0.4%)	13 (4.6%)	2 (0.7%)	23 (7.2%)	8 (2.5%)	5 (4.9%)	3 (2.9%)
鼻炎	2 (0.8%)	0	7 (2.9%)	0	3 (1.1%)	0	20 (6.3%)	0	5 (4.9%)	0
副鼻腔炎	3 (1.3%)	0	10 (4.1%)	3 (1.2%)	10 (3.6%)	0	19 (6.0%)	0	13 (12.6%)	1 (1.0%)
下気道感染	3 (1.3%)	1 (0.4%)	3 (1.2%)	1 (0.4%)	9 (3.2%)	3 (1.1%)	17 (5.3%)	5 (1.6%)	0	0
尿路感染	6 (2.5%)	1 (0.4%)	12 (4.9%)	1 (0.4%)	11 (3.9%)	1 (0.4%)	17 (5.3%)	6 (1.9%)	7 (6.8%)	1 (1.0%)
胃腸炎	4 (1.7%)	3 (1.3%)	5 (2.1%)	2 (0.8%)	4 (1.4%)	0	13 (4.1%)	2 (0.6%)	3 (2.9%)	0
結膜炎	7 (3.0%)	1 (0.4%)	21 (8.6%)	0	3 (1.1%)	0	12 (3.8%)	0	2 (1.9%)	0
帯状疱疹	7 (3.0%)	1 (0.4%)	13 (5.3%)	4 (1.6%)	5 (1.8%)	1 (0.4%)	9 (2.8%)	0	2 (1.9%)	2 (1.9%)
口腔ヘルペス	2 (0.8%)	0	6 (2.5%)	0	2 (0.7%)	0	8 (2.5%)	0	1 (1.0%)	0
咽頭炎	1 (0.4%)	0	5 (2.1%)	0	7 (2.5%)	1 (0.4%)	8 (2.5%)	0	1 (1.0%)	0
感染	3 (1.3%)	0	1 (0.4%)	0	5 (1.8%)	3 (1.1%)	7 (2.2%)	2 (0.6%)	0	0
ウイルス感染	1 (0.4%)	0	0	0	7 (2.5%)	0	7 (2.2%)	0	0	0
蜂巣炎	1 (0.4%)	0	2 (0.8%)	1 (0.4%)	3 (1.1%)	1 (0.4%)	6 (1.9%)	1 (0.3%)	2 (1.9%)	1 (1.0%)
口腔カンジダ症	5 (2.1%)	0	4 (1.6%)	0	4 (1.4%)	0	6 (1.9%)	0	0	0
口腔真菌感染	2 (0.8%)	0	2 (0.8%)	0	5 (1.8%)	0	5 (1.6%)	1 (0.3%)	0	0
皮膚感染	2 (0.8%)	0	1 (0.4%)	0	5 (1.8%)	0	5 (1.6%)	1 (0.3%)	0	0
膀胱炎	0	0	3 (1.2%)	0	7 (2.5%)	0	4 (1.3%)	0	0	0

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
耳感染	0	0	0	0	3 (1.1%)	0	4 (1.3%)	0	1 (1.0%)	0
真菌感染	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	4 (1.3%)	0	0	0
ヘルペスウイルス感染	0	0	0	0	0	0	4 (1.3%)	0	0	0
肺感染	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)	4 (1.3%)	1 (0.3%)	2 (1.9%)	1 (1.0%)
インフルエンザ性肺炎	0	0	0	0	0	0	4 (1.3%)	3 (0.9%)	0	0
気管支肺炎	2 (0.8%)	1 (0.4%)	3 (1.2%)	2 (0.8%)	1 (0.4%)	0	3 (0.9%)	2 (0.6%)	0	0
ウイルス性胃腸炎	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	3 (0.9%)	1 (0.3%)	0	0
消化管感染	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	3 (0.9%)	0	0	0
歯周炎	0	0	0	0	1 (0.4%)	0	3 (0.9%)	0	0	0
ＲＳウイルス感染	0	0	1 (0.4%)	1 (0.4%)	0	0	3 (0.9%)	1 (0.3%)	3 (2.9%)	0
敗血症性ショック	1 (0.4%)	0	0	0	2 (0.7%)	2 (0.7%)	3 (0.9%)	1 (0.3%)	0	0
歯膿瘍	1 (0.4%)	1 (0.4%)	0	0	6 (2.1%)	0	3 (0.9%)	0	1 (1.0%)	0
歯感染	0	0	1 (0.4%)	0	2 (0.7%)	0	3 (0.9%)	0	3 (2.9%)	1 (1.0%)
ウイルス性上気道感染	0	0	2 (0.8%)	0	2 (0.7%)	0	3 (0.9%)	0	0	0
外陰部腟カンジダ症	0	0	0	0	0	0	3 (0.9%)	0	0	0
急性副鼻腔炎	1 (0.4%)	0	0	0	0	0	2 (0.6%)	0	0	0
虫垂炎	0	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	2 (0.6%)	0	0
細気管支炎	0	0	0	0	1 (0.4%)	0	2 (0.6%)	2 (0.6%)	0	0
カンピロバクター胃腸炎	0	0	1 (0.4%)	0	0	0	2 (0.6%)	1 (0.3%)	0	0
丹毒	0	0	2 (0.8%)	0	2 (0.7%)	1 (0.4%)	2 (0.6%)	0	0	0
大腸菌性尿路感染	0	0	0	0	0	0	2 (0.6%)	0	0	0
眼感染	4 (1.7%)	0	0	0	2 (0.7%)	0	2 (0.6%)	0	0	0
毛包炎	0	0	2 (0.8%)	0	1 (0.4%)	0	2 (0.6%)	0	1 (1.0%)	0
皮膚真菌感染	0	0	0	0	1 (0.4%)	0	2 (0.6%)	0	0	0
せつ	1 (0.4%)	0	2 (0.8%)	0	0	0	2 (0.6%)	0	1 (1.0%)	0
歯肉炎	0	0	1 (0.4%)	0	4 (1.4%)	0	2 (0.6%)	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	1 (0.4%)	0	2 (0.6%)	2 (0.6%)	0	0
大葉性肺炎	1 (0.4%)	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	2 (0.6%)	0	0
好中球減少性敗血症	0	0	0	0	0	0	2 (0.6%)	2 (0.6%)	0	0
口腔感染	0	0	0	0	0	0	2 (0.6%)	0	0	0
中耳炎	1 (0.4%)	0	3 (1.2%)	1 (0.4%)	1 (0.4%)	0	2 (0.6%)	0	0	0

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
パラインフルエンザウイルス感染	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	2 (0.6%)	1 (0.3%)	2 (1.9%)	1 (1.0%)
耳下腺炎	0	0	0	0	0	0	2 (0.6%)	0	1 (1.0%)	0
レンサ球菌性咽頭炎	0	0	0	0	1 (0.4%)	0	2 (0.6%)	0	0	0
細菌性肺炎	0	0	0	0	1 (0.4%)	0	2 (0.6%)	1 (0.3%)	0	0
ウイルス性気道感染	3 (1.3%)	0	6 (2.5%)	0	0	0	2 (0.6%)	0	0	0
敗血症	3 (1.3%)	3 (1.3%)	2 (0.8%)	2 (0.8%)	6 (2.1%)	6 (2.1%)	2 (0.6%)	2 (0.6%)	4 (3.9%)	3 (2.9%)
皮下組織膿瘍	0	0	1 (0.4%)	0	0	0	2 (0.6%)	0	0	0
足部白癬	0	0	2 (0.8%)	0	3 (1.1%)	0	2 (0.6%)	0	0	0
細菌性上気道感染	0	0	0	0	0	0	2 (0.6%)	1 (0.3%)	0	0
急性扁桃炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	1 (1.0%)	0
無症候性細菌尿	0	0	0	0	0	0	1 (0.3%)	0	0	0
バチルス感染	0	0	0	0	0	0	1 (0.3%)	0	0	0
細菌感染	1 (0.4%)	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
カンジダ性亀頭炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
細菌性気管支炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
カンピロバクター感染	0	0	0	0	0	0	1 (0.3%)	0	0	0
カンジダ感染	3 (1.3%)	0	2 (0.8%)	0	2 (0.7%)	0	1 (0.3%)	0	0	0
カテーテル留置部位膿瘍	0	0	0	0	0	0	1 (0.3%)	0	0	0
カテーテル留置部位感染	0	0	0	0	0	0	1 (0.3%)	0	0	0
慢性副鼻腔炎	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (0.3%)	0	0	0
ウイルス性結膜炎	0	0	0	0	1 (0.4%)	0	1 (0.3%)	0	0	0
コロナウイルス感染	0	0	0	0	0	0	1 (0.3%)	0	1 (1.0%)	0
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
ウイルス性腸炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
喉頭蓋炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
大腸菌性菌血症	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
硬膜外膿瘍	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
感染性舌炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
感染性脊椎炎	0	0	0	0	0	0	1 (0.3%)	0	0	0

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
注入部位蜂巣炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
ウイルス性喉頭炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
リステリア性敗血症	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
限局性感染	1 (0.4%)	0	0	0	5 (1.8%)	1 (0.4%)	1 (0.3%)	0	0	0
ウイルス性下気道感染	0	0	0	0	1 (0.4%)	0	1 (0.3%)	0	0	0
粘膜感染	2 (0.8%)	0	0	0	3 (1.1%)	0	1 (0.3%)	0	0	0
鼻膿瘍	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
中咽頭カンジダ症	0	0	0	0	0	0	1 (0.3%)	0	0	0
外耳炎	0	0	1 (0.4%)	0	1 (0.4%)	0	1 (0.3%)	0	0	0
急性中耳炎	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0
耳管炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
眼窩周囲蜂巣炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
レジオネラ菌性肺炎	0	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.3%)	1 (0.3%)	0	0
レンサ球菌性肺炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
ウイルス性肺炎	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
前立腺感染	0	0	0	0	0	0	1 (0.3%)	0	0	0
シュードモナス感染	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
腎盂腎炎	0	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.3%)	0	0	0
膿疱性皮疹	0	0	0	0	0	0	1 (0.3%)	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
サルモネラ性菌血症	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
軟部組織感染	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
扁桃炎	1 (0.4%)	0	0	0	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	2 (1.9%)	0
気管炎	0	0	0	0	1 (0.4%)	0	1 (0.3%)	0	0	0
尿道炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
子宮膿瘍	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
腟感染	0	0	2 (0.8%)	0	1 (0.4%)	0	1 (0.3%)	0	0	0
ウイルス性鼻炎	0	0	0	0	0	0	1 (0.3%)	0	0	0
内臓リーシュマニア症	0	0	0	0	0	0	1 (0.3%)	1 (0.3%)	0	0
外陰腟真菌感染	1 (0.4%)	0	0	0	1 (0.4%)	0	1 (0.3%)	0	2 (1.9%)	0
創傷感染	0	0	0	0	3 (1.1%)	0	1 (0.3%)	0	0	0

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
四肢膿瘍	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
頚部膿瘍	0	0	1 (0.4%)	0	0	0	0	0	0	0
アデノウイルス感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
肛門膿瘍	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
体部白癬	1 (0.4%)	0	0	0	0	0	0	0	0	0
脳膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	2 (0.7%)	1 (0.4%)	0	0	0	0
海綿静脈洞血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)
クロストリジウム・ディフィシレ感染	1 (0.4%)	0	1 (0.4%)	0	2 (0.7%)	1 (0.4%)	0	0	1 (1.0%)	1 (1.0%)
細菌性結膜炎	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0
細菌性膀胱炎	1 (0.4%)	0	0	0	0	0	0	0	0	0
大腸菌性膀胱炎	1 (0.4%)	0	0	0	0	0	0	0	0	0
医療機器関連感染	1 (0.4%)	1 (0.4%)	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0
憩室炎	0	0	1 (0.4%)	0	0	0	0	0	2 (1.9%)	1 (1.0%)
赤痢	0	0	1 (0.4%)	0	0	0	0	0	0	0
蓄膿	0	0	0	0	1 (0.4%)	0	0	0	0	0
心内膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
感染性腸炎	0	0	0	0	0	0	0	0	1 (1.0%)	0
感染性小腸結腸炎	0	0	0	0	2 (0.7%)	2 (0.7%)	0	0	0	0
精巣上体炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
伝染性紅斑	0	0	1 (0.4%)	0	0	0	0	0	0	0
大腸菌性敗血症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
真菌性眼感染	0	0	0	0	1 (0.4%)	0	0	0	0	0
眼瞼感染	0	0	1 (0.4%)	0	0	0	0	0	0	0
熱性感染症	0	0	0	0	1 (0.4%)	0	0	0	0	0
真菌性食道炎	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
壊疽	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
サルモネラ菌性胃腸炎	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
陰部ヘルペス	0	0	1 (0.4%)	0	0	0	0	0	2 (1.9%)	0
陰部単純ヘルペス	0	0	0	0	1 (0.4%)	0	0	0	0	0

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
真菌性性器感染	0	0	0	0	1 (0.4%)	0	0	0	0	0
ヘモフィルス感染	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0
単純ヘルペス	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0
麦粒腫	3 (1.3%)	0	4 (1.6%)	0	2 (0.7%)	0	0	0	0	0
咬傷感染	0	0	0	0	1 (0.4%)	0	0	0	0	0
感染性筋炎	0	0	0	0	1 (0.4%)	0	0	0	0	0
真菌性角膜炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
喉頭炎	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	2 (1.9%)	1 (1.0%)
乳腺炎	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)
メタニューモウイルス感染	0	0	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0
爪床感染	1 (0.4%)	0	0	0	0	0	0	0	0	0
爪感染	1 (0.4%)	0	0	0	0	0	0	0	0	0
鼻ヘルペス	0	0	0	0	1 (0.4%)	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
ノカルジア症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
食道カンジダ症	0	0	1 (0.4%)	0	0	0	0	0	0	0
眼部単純ヘルペス	1 (0.4%)	0	0	0	0	0	0	0	0	0
口腔ウイルス感染	0	0	0	0	1 (0.4%)	0	0	0	0	0
骨髄炎	0	0	0	0	2 (0.7%)	2 (0.7%)	0	0	0	0
爪囲炎	1 (0.4%)	0	0	0	1 (0.4%)	0	0	0	0	0
腹膜炎	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
百日咳	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	0	0
ニューモシスチス・イロベチイ肺炎	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
サイトメガロウイルス性肺炎	0	0	2 (0.8%)	2 (0.8%)	0	0	0	0	0	0
肺炎球菌性肺炎	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
進行性多巣性白質脳症	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)
シュードモナス性敗血症	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)
肺敗血症	0	0	2 (0.8%)	1 (0.4%)	0	0	0	0	0	0
肺結核	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE17: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
歯髄炎	0	0	0	0	1 (0.4%)	0	0	0	0	0
穿刺部位感染	1 (0.4%)	0	0	0	0	0	0	0	0	0
急性腎盂腎炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
慢性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
ライノウイルス感染	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
唾液腺炎	0	0	1 (0.4%)	0	0	0	0	0	1 (1.0%)	0
皮膚カンジダ	0	0	0	0	3 (1.1%)	0	0	0	0	0
脊髄感染	0	0	0	0	0	0	0	0	1 (1.0%)	1 (1.0%)
ブドウ球菌性菌血症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
ブドウ球菌感染	0	0	0	0	1 (0.4%)	0	0	0	0	0
ブドウ球菌性咽頭炎	0	0	1 (0.4%)	0	0	0	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0	1 (0.4%)	0	0	0	0	0
ステノトロフォモナス感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
股部白癬	1 (0.4%)	0	0	0	0	0	0	0	0	0
白癬感染	1 (0.4%)	0	0	0	0	0	0	0	0	0
癜風	0	0	0	0	0	0	0	0	1 (1.0%)	0
真菌性舌感染	0	0	1 (0.4%)	0	0	0	0	0	0	0
気管気管支炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0
尿路性敗血症	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
水痘	0	0	0	0	1 (0.4%)	0	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
ウイルス性咽頭炎	1 (0.4%)	0	0	0	0	0	0	0	0	0
ウイルス性ぶどう膜炎	1 (0.4%)	0	0	0	0	0	0	0	0	0
外陰部腟炎	0	0	0	0	1 (0.4%)	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE17.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE17.SAS] 01JUN2016, 10:41

表 2.7.4-付録-129 Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

TSFAE29: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd			DVd		
	n (%)			n (%)		
	Total	<=6 Months	>6 Months	Total	<=6 Months	>6 Months
Analysis set: safety	237			243		
Total number of subjects treated within window[a]	237	237	15	243	243	142
Total number of subjects with treatment-emergent infections and infestations	126 (53.2%)	126 (53.2%)	7 (46.7%)	164 (67.5%)	161 (66.3%)	39 (27.5%)
Preferred term						
上気道感染	43 (18.1%)	42 (17.7%)	2 (13.3%)	60 (24.7%)	55 (22.6%)	17 (12.0%)
肺炎	28 (11.8%)	28 (11.8%)	0	29 (11.9%)	26 (10.7%)	3 (2.1%)
気管支炎	13 (5.5%)	13 (5.5%)	0	28 (11.5%)	24 (9.9%)	5 (3.5%)
結膜炎	7 (3.0%)	7 (3.0%)	0	21 (8.6%)	19 (7.8%)	2 (1.4%)
鼻咽頭炎	9 (3.8%)	9 (3.8%)	1 (6.7%)	17 (7.0%)	15 (6.2%)	2 (1.4%)
帯状疱疹	7 (3.0%)	7 (3.0%)	0	13 (5.3%)	13 (5.3%)	0
尿路感染	6 (2.5%)	6 (2.5%)	0	12 (4.9%)	7 (2.9%)	6 (4.2%)
副鼻腔炎	3 (1.3%)	3 (1.3%)	0	10 (4.1%)	10 (4.1%)	1 (0.7%)
インフルエンザ	7 (3.0%)	7 (3.0%)	0	8 (3.3%)	8 (3.3%)	1 (0.7%)
鼻炎	2 (0.8%)	2 (0.8%)	0	7 (2.9%)	7 (2.9%)	0
口腔ヘルペス	2 (0.8%)	1 (0.4%)	1 (6.7%)	6 (2.5%)	5 (2.1%)	1 (0.7%)
ウイルス性気道感染	3 (1.3%)	3 (1.3%)	0	6 (2.5%)	6 (2.5%)	1 (0.7%)
胃腸炎	4 (1.7%)	4 (1.7%)	0	5 (2.1%)	5 (2.1%)	0
咽頭炎	1 (0.4%)	1 (0.4%)	0	5 (2.1%)	5 (2.1%)	0
麦粒腫	3 (1.3%)	3 (1.3%)	0	4 (1.6%)	4 (1.6%)	0
口腔カンジダ症	5 (2.1%)	5 (2.1%)	0	4 (1.6%)	3 (1.2%)	1 (0.7%)
気管支肺炎	2 (0.8%)	2 (0.8%)	0	3 (1.2%)	3 (1.2%)	0
膀胱炎	0	0	0	3 (1.2%)	3 (1.2%)	0
下気道感染	3 (1.3%)	3 (1.3%)	0	3 (1.2%)	2 (0.8%)	2 (1.4%)
中耳炎	1 (0.4%)	1 (0.4%)	0	3 (1.2%)	3 (1.2%)	0
カンジダ感染	3 (1.3%)	2 (0.8%)	1 (6.7%)	2 (0.8%)	2 (0.8%)	0
蜂巣炎	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	1 (0.7%)

TSFAE29: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd			DVd		
	n (%)			n (%)		
	Total	<=6 Months	>6 Months	Total	<=6 Months	>6 Months
医療機器関連感染	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	0
丹毒	0	0	0	2 (0.8%)	2 (0.8%)	0
毛包炎	0	0	0	2 (0.8%)	2 (0.8%)	0
せつ	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	0
メタニューモウイルス感染	0	0	0	2 (0.8%)	2 (0.8%)	0
口腔真菌感染	2 (0.8%)	2 (0.8%)	0	2 (0.8%)	2 (0.8%)	0
サイトメガロウイルス性肺炎	0	0	0	2 (0.8%)	2 (0.8%)	0
肺敗血症	0	0	0	2 (0.8%)	1 (0.4%)	1 (0.7%)
敗血症	3 (1.3%)	3 (1.3%)	0	2 (0.8%)	2 (0.8%)	0
足部白癬	0	0	0	2 (0.8%)	2 (0.8%)	0
腟感染	0	0	0	2 (0.8%)	2 (0.8%)	0
ウイルス性上気道感染	0	0	0	2 (0.8%)	2 (0.8%)	1 (0.7%)
頚部膿瘍	0	0	0	1 (0.4%)	0	1 (0.7%)
カンピロバクター胃腸炎	0	0	0	1 (0.4%)	1 (0.4%)	0
慢性副鼻腔炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
クロストリジウム・ディフィシレ感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.7%)
細菌性結膜炎	0	0	0	1 (0.4%)	1 (0.4%)	0
憩室炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.7%)
赤痢	0	0	0	1 (0.4%)	1 (0.4%)	0
伝染性紅斑	0	0	0	1 (0.4%)	1 (0.4%)	0
眼瞼感染	0	0	0	1 (0.4%)	1 (0.4%)	0
真菌感染	0	0	0	1 (0.4%)	1 (0.4%)	0
真菌性食道炎	0	0	0	1 (0.4%)	1 (0.4%)	0
サルモネラ菌性胃腸炎	0	0	0	1 (0.4%)	1 (0.4%)	0
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.7%)
消化管感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
陰部ヘルペス	0	0	0	1 (0.4%)	1 (0.4%)	0
歯肉炎	0	0	0	1 (0.4%)	1 (0.4%)	0
ヘモフィルス感染	0	0	0	1 (0.4%)	1 (0.4%)	0
感染	3 (1.3%)	3 (1.3%)	0	1 (0.4%)	1 (0.4%)	0
喉頭炎	0	0	0	1 (0.4%)	1 (0.4%)	0
肺感染	2 (0.8%)	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0

TSFAE29: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd			DVd		
	n (%)			n (%)		
	Total	<=6 Months	>6 Months	Total	<=6 Months	>6 Months
食道カンジダ症	0	0	0	1 (0.4%)	1 (0.4%)	0
外耳炎	0	0	0	1 (0.4%)	1 (0.4%)	0
急性中耳炎	0	0	0	1 (0.4%)	1 (0.4%)	0
パラインフルエンザウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	0
腹膜炎	0	0	0	1 (0.4%)	1 (0.4%)	0
百日咳	0	0	0	1 (0.4%)	1 (0.4%)	0
ニューモシスチス・イロベチイ肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0
肺炎球菌性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0
腎盂腎炎	0	0	0	1 (0.4%)	1 (0.4%)	0
ＲＳウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	0
ライノウイルス感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
唾液腺炎	0	0	0	1 (0.4%)	1 (0.4%)	0
皮膚感染	2 (0.8%)	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0
ブドウ球菌性咽頭炎	0	0	0	1 (0.4%)	1 (0.4%)	0
皮下組織膿瘍	0	0	0	1 (0.4%)	0	1 (0.7%)
真菌性舌感染	0	0	0	1 (0.4%)	0	1 (0.7%)
歯感染	0	0	0	1 (0.4%)	0	1 (0.7%)
気管気管支炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
急性副鼻腔炎	1 (0.4%)	1 (0.4%)	0	0	0	0
細菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0
体部白癬	1 (0.4%)	1 (0.4%)	0	0	0	0
脳膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0
海綿静脈洞血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0
細菌性膀胱炎	1 (0.4%)	1 (0.4%)	0	0	0	0
大腸菌性膀胱炎	1 (0.4%)	1 (0.4%)	0	0	0	0
心内膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
精巣上体炎	1 (0.4%)	1 (0.4%)	0	0	0	0
大腸菌性敗血症	1 (0.4%)	1 (0.4%)	0	0	0	0
眼感染	4 (1.7%)	3 (1.3%)	1 (6.7%)	0	0	0
壊疽	1 (0.4%)	1 (0.4%)	0	0	0	0
単純ヘルペス	1 (0.4%)	1 (0.4%)	0	0	0	0

TSFAE29: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd			DVd		
	n (%)			n (%)		
	Total	<=6 Months	>6 Months	Total	<=6 Months	>6 Months
大葉性肺炎	1 (0.4%)	1 (0.4%)	0	0	0	0
限局性感染	1 (0.4%)	1 (0.4%)	0	0	0	0
粘膜感染	2 (0.8%)	2 (0.8%)	0	0	0	0
爪床感染	1 (0.4%)	1 (0.4%)	0	0	0	0
爪感染	1 (0.4%)	1 (0.4%)	0	0	0	0
ノカルジア症	1 (0.4%)	1 (0.4%)	0	0	0	0
眼部単純ヘルペス	1 (0.4%)	1 (0.4%)	0	0	0	0
爪囲炎	1 (0.4%)	1 (0.4%)	0	0	0	0
穿刺部位感染	1 (0.4%)	0	1 (6.7%)	0	0	0
慢性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0	0	0
気道感染	3 (1.3%)	3 (1.3%)	0	0	0	0
敗血症性ショック	1 (0.4%)	1 (0.4%)	0	0	0	0
ブドウ球菌性菌血症	1 (0.4%)	1 (0.4%)	0	0	0	0
ステノトロフォモナス感染	1 (0.4%)	1 (0.4%)	0	0	0	0
股部白癬	1 (0.4%)	1 (0.4%)	0	0	0	0
白癬感染	1 (0.4%)	1 (0.4%)	0	0	0	0
扁桃炎	1 (0.4%)	1 (0.4%)	0	0	0	0
歯膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0
ウイルス感染	1 (0.4%)	0	1 (6.7%)	0	0	0
ウイルス性咽頭炎	1 (0.4%)	1 (0.4%)	0	0	0	0
ウイルス性ぶどう膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
外陰腟真菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone
Keys: TEAE = treatment-emergent adverse event.
[a] Includes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages in the total column are calculated with the number of treated subjects in each group as denominator. Percentages for months columns are calculated with the number of treated subjects in the months as denominator.

[TSFAE29.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\TSFAE29.SAS] 14JUL2016, 08:52

表 2.7.4-付録-130 Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

TSFAE29A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd			DVd		
	n (%)			n (%)		
	Total	<=6 Months	>6 Months	Total	<=6 Months	>6 Months
Analysis set: safety	237			243		
Total number of subjects treated within window[a]	237	237	9	243	243	141
Total number of subjects with toxicity grade 3 or 4 treatment-emergent infections and infestations	45 (19.0%)	45 (19.0%)	0	52 (21.4%)	51 (21.0%)	1 (0.7%)
Preferred term						
肺炎	23 (9.7%)	23 (9.7%)	0	20 (8.2%)	19 (7.8%)	1 (0.7%)
気管支炎	3 (1.3%)	3 (1.3%)	0	5 (2.1%)	5 (2.1%)	0
帯状疱疹	1 (0.4%)	1 (0.4%)	0	4 (1.6%)	4 (1.6%)	0
上気道感染	2 (0.8%)	2 (0.8%)	0	4 (1.6%)	4 (1.6%)	0
副鼻腔炎	0	0	0	3 (1.2%)	3 (1.2%)	0
気管支肺炎	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	0
医療機器関連感染	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	0
胃腸炎	3 (1.3%)	3 (1.3%)	0	2 (0.8%)	2 (0.8%)	0
サイトメガロウイルス性肺炎	0	0	0	2 (0.8%)	2 (0.8%)	0
敗血症	3 (1.3%)	3 (1.3%)	0	2 (0.8%)	2 (0.8%)	0
蜂巣炎	0	0	0	1 (0.4%)	1 (0.4%)	0
真菌感染	0	0	0	1 (0.4%)	1 (0.4%)	0
真菌性食道炎	0	0	0	1 (0.4%)	1 (0.4%)	0
サルモネラ菌性胃腸炎	0	0	0	1 (0.4%)	1 (0.4%)	0
インフルエンザ	2 (0.8%)	2 (0.8%)	0	1 (0.4%)	1 (0.4%)	0
下気道感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
肺感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
メタニューモウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	0
中耳炎	0	0	0	1 (0.4%)	1 (0.4%)	0
腹膜炎	0	0	0	1 (0.4%)	1 (0.4%)	0
ニューモシスチス・イロベチイ肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0

TSFAE29A: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3004)

	Vd			DVd		
	n (%)			n (%)		
	Total	<=6 Months	>6 Months	Total	<=6 Months	>6 Months
肺炎球菌性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0
肺敗血症	0	0	0	1 (0.4%)	1 (0.4%)	0
腎盂腎炎	0	0	0	1 (0.4%)	1 (0.4%)	0
ＲＳウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	0
ライノウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	0
尿路感染	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0
脳膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0
海綿静脈洞血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0
結膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
心内膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0
精巣上体炎	1 (0.4%)	1 (0.4%)	0	0	0	0
大腸菌性敗血症	1 (0.4%)	1 (0.4%)	0	0	0	0
壊疽	1 (0.4%)	1 (0.4%)	0	0	0	0
ノカルジア症	1 (0.4%)	1 (0.4%)	0	0	0	0
慢性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0	0	0
気道感染	1 (0.4%)	1 (0.4%)	0	0	0	0
ブドウ球菌性菌血症	1 (0.4%)	1 (0.4%)	0	0	0	0
ステノトロフォモナス感染	1 (0.4%)	1 (0.4%)	0	0	0	0
歯膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0
気管気管支炎	1 (0.4%)	1 (0.4%)	0	0	0	0

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone
Keys: TEAE = treatment-emergent adverse event.
[a] Includes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages in the total column are calculated with the number of treated subjects in each group as denominator. Percentages for months columns are calculated with the number of treated subjects in the months as denominator.

[TSFAE29A.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\TSFAE29A.SAS] 14JUL2016, 08:53

表 2.7.4-付録-131 Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
Total[a] Analysis set: safety	281				283			
Total number of subjects treated within window[c]	281	281	216	148	283	283	252	195
Total number of subjects with treatment-emergent infections and infestations	204 (72.6%)	174 (61.9%)	98 (45.4%)	40 (27.0%)	238 (84.1%)	206 (72.8%)	147 (58.3%)	71 (36.4%)
Preferred term								
上気道感染	58 (20.6%)	44 (15.7%)	21 (9.7%)	6 (4.1%)	90 (31.8%)	59 (20.8%)	40 (15.9%)	19 (9.7%)
鼻咽頭炎	43 (15.3%)	28 (10.0%)	19 (8.8%)	7 (4.7%)	68 (24.0%)	49 (17.3%)	34 (13.5%)	9 (4.6%)
肺炎	37 (13.2%)	24 (8.5%)	10 (4.6%)	4 (2.7%)	40 (14.1%)	20 (7.1%)	20 (7.9%)	2 (1.0%)
気管支炎	34 (12.1%)	25 (8.9%)	9 (4.2%)	5 (3.4%)	38 (13.4%)	20 (7.1%)	14 (5.6%)	9 (4.6%)
気道感染	22 (7.8%)	16 (5.7%)	8 (3.7%)	5 (3.4%)	31 (11.0%)	20 (7.1%)	15 (6.0%)	10 (5.1%)
インフルエンザ	13 (4.6%)	9 (3.2%)	2 (0.9%)	3 (2.0%)	21 (7.4%)	10 (3.5%)	8 (3.2%)	4 (2.1%)
副鼻腔炎	10 (3.6%)	7 (2.5%)	2 (0.9%)	2 (1.4%)	18 (6.4%)	9 (3.2%)	4 (1.6%)	6 (3.1%)
下気道感染	9 (3.2%)	5 (1.8%)	6 (2.8%)	3 (2.0%)	17 (6.0%)	11 (3.9%)	12 (4.8%)	1 (0.5%)
鼻炎	3 (1.1%)	3 (1.1%)	0	0	15 (5.3%)	11 (3.9%)	2 (0.8%)	6 (3.1%)
尿路感染	11 (3.9%)	8 (2.8%)	5 (2.3%)	1 (0.7%)	15 (5.3%)	10 (3.5%)	7 (2.8%)	3 (1.5%)
結膜炎	3 (1.1%)	1 (0.4%)	1 (0.5%)	1 (0.7%)	11 (3.9%)	10 (3.5%)	1 (0.4%)	0
胃腸炎	4 (1.4%)	2 (0.7%)	1 (0.5%)	1 (0.7%)	10 (3.5%)	2 (0.7%)	5 (2.0%)	3 (1.5%)
帯状疱疹	5 (1.8%)	5 (1.8%)	0	1 (0.7%)	6 (2.1%)	6 (2.1%)	0	0
口腔カンジダ症	4 (1.4%)	3 (1.1%)	1 (0.5%)	0	6 (2.1%)	5 (1.8%)	1 (0.4%)	0
口腔ヘルペス	2 (0.7%)	2 (0.7%)	0	0	6 (2.1%)	4 (1.4%)	2 (0.8%)	2 (1.0%)
蜂巣炎	3 (1.1%)	3 (1.1%)	1 (0.5%)	0	5 (1.8%)	3 (1.1%)	1 (0.4%)	1 (0.5%)
口腔真菌感染	5 (1.8%)	4 (1.4%)	1 (0.5%)	0	5 (1.8%)	3 (1.1%)	2 (0.8%)	0
皮膚感染	5 (1.8%)	1 (0.4%)	3 (1.4%)	2 (1.4%)	5 (1.8%)	2 (0.7%)	3 (1.2%)	0
ウイルス感染	7 (2.5%)	5 (1.8%)	1 (0.5%)	1 (0.7%)	5 (1.8%)	2 (0.7%)	2 (0.8%)	1 (0.5%)
膀胱炎	7 (2.5%)	6 (2.1%)	1 (0.5%)	0	4 (1.4%)	3 (1.1%)	1 (0.4%)	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
耳感染	3 (1.1%)	2 (0.7%)	1 (0.5%)	0	4 (1.4%)	0	3 (1.2%)	1 (0.5%)
真菌感染	1 (0.4%)	1 (0.4%)	0	0	4 (1.4%)	1 (0.4%)	3 (1.2%)	0
ヘルペスウイルス感染	0	0	0	0	4 (1.4%)	0	2 (0.8%)	2 (1.0%)
感染	5 (1.8%)	3 (1.1%)	2 (0.9%)	0	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.5%)
咽頭炎	7 (2.5%)	4 (1.4%)	2 (0.9%)	1 (0.7%)	4 (1.4%)	4 (1.4%)	0	0
インフルエンザ性肺炎	0	0	0	0	4 (1.4%)	3 (1.1%)	0	1 (0.5%)
気管支肺炎	1 (0.4%)	1 (0.4%)	0	0	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
肺感染	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	3 (1.1%)	2 (0.7%)	2 (0.8%)	0
歯周炎	1 (0.4%)	0	1 (0.5%)	0	3 (1.1%)	1 (0.4%)	2 (0.8%)	0
ＲＳウイルス感染	0	0	0	0	3 (1.1%)	3 (1.1%)	0	0
敗血症性ショック	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	3 (1.1%)	3 (1.1%)	0	0
外陰部腟カンジダ症	0	0	0	0	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
急性副鼻腔炎	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
虫垂炎	1 (0.4%)	0	1 (0.5%)	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
細気管支炎	1 (0.4%)	1 (0.4%)	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
カンピロバクター胃腸炎	0	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
丹毒	2 (0.7%)	2 (0.7%)	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
大腸菌性尿路感染	0	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
眼感染	2 (0.7%)	0	1 (0.5%)	1 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
毛包炎	1 (0.4%)	1 (0.4%)	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
皮膚真菌感染	1 (0.4%)	1 (0.4%)	0	0	2 (0.7%)	2 (0.7%)	0	0
せつ	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
ウイルス性胃腸炎	1 (0.4%)	0	1 (0.5%)	0	2 (0.7%)	0	2 (0.8%)	0
消化管感染	1 (0.4%)	1 (0.4%)	0	0	2 (0.7%)	0	2 (0.8%)	0
歯肉炎	4 (1.4%)	2 (0.7%)	2 (0.9%)	0	2 (0.7%)	2 (0.7%)	0	0
Ｈ１Ｎ１インフルエンザ	1 (0.4%)	1 (0.4%)	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
大葉性肺炎	1 (0.4%)	0	1 (0.5%)	0	2 (0.7%)	2 (0.7%)	0	0
好中球減少性敗血症	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
耳下腺炎	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
細菌性肺炎	1 (0.4%)	1 (0.4%)	0	0	2 (0.7%)	2 (0.7%)	0	0
ウイルス性気道感染	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
敗血症	6 (2.1%)	3 (1.1%)	1 (0.5%)	2 (1.4%)	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
皮下組織膿瘍	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
足部白癬	3 (1.1%)	0	2 (0.9%)	1 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
歯膿瘍	6 (2.1%)	4 (1.4%)	3 (1.4%)	0	2 (0.7%)	2 (0.7%)	2 (0.8%)	0
歯感染	2 (0.7%)	0	2 (0.9%)	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
細菌性上気道感染	0	0	0	0	2 (0.7%)	2 (0.7%)	0	0
急性扁桃炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
無症候性細菌尿	0	0	0	0	1 (0.4%)	0	0	1 (0.5%)
細菌感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
カンジダ性亀頭炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
細菌性気管支炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
カンピロバクター感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
カンジダ感染	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
カテーテル留置部位膿瘍	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
カテーテル留置部位感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
慢性副鼻腔炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性結膜炎	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	0	1 (0.4%)	0
コロナウイルス感染	0	0	0	0	1 (0.4%)	0	0	1 (0.5%)
サイトメガロウイルス感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性腸炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
喉頭蓋炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
大腸菌性菌血症	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
硬膜外膿瘍	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
感染性舌炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
感染性脊椎炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
注入部位蜂巣炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性喉頭炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
リステリア性敗血症	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
限局性感染	5 (1.8%)	2 (0.7%)	3 (1.4%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	0	0
ウイルス性下気道感染	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
粘膜感染	3 (1.1%)	2 (0.7%)	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
鼻膿瘍	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
口腔感染	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
中咽頭カンジダ症	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
外耳炎	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
中耳炎	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	0	1 (0.4%)	0
急性中耳炎	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	0	0	1 (0.5%)
耳管炎	0	0	0	0	1 (0.4%)	0	0	1 (0.5%)
パラインフルエンザウイルス感染	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
眼窩周囲蜂巣炎	0	0	0	0	1 (0.4%)	0	0	1 (0.5%)
レンサ球菌性咽頭炎	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0
ヘモフィルス性肺炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
クレブシエラ菌性肺炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
レジオネラ菌性肺炎	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	0	1 (0.4%)	0
レンサ球菌性肺炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
前立腺感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
シュードモナス感染	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
腎盂腎炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
呼吸器モニリア症	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
サルモネラ性菌血症	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
軟部組織感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
扁桃炎	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
気管炎	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	0	1 (0.4%)	0
尿道炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
子宮膿瘍	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
腟感染	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性鼻炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性上気道感染	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
内臓リーシュマニア症	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
創傷感染	3 (1.1%)	0	1 (0.5%)	2 (1.4%)	1 (0.4%)	0	0	1 (0.5%)
四肢膿瘍	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
アデノウイルス感染	1 (0.4%)	0	0	1 (0.7%)	0	0	0	0
肛門膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
ウイルス性気管支炎	2 (0.7%)	0	1 (0.5%)	1 (0.7%)	0	0	0	0
クロストリジウム・ディフィシレ感染	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	0	0	0	0
細菌性結膜炎	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
蓄膿	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0	0	0	0	0
真菌性眼感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
熱性感染症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
陰部単純ヘルペス	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
真菌性性器感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
単純ヘルペス	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
麦粒腫	2 (0.7%)	2 (0.7%)	0	0	0	0	0	0
咬傷感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
感染性筋炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
真菌性角膜炎	1 (0.4%)	0	0	1 (0.7%)	0	0	0	0
喉頭炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
鼻ヘルペス	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
口腔ウイルス感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
骨髄炎	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	0	0	0	0
爪囲炎	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
百日咳	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
肺結核	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
歯髄炎	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
急性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
皮膚カンジダ	3 (1.1%)	2 (0.7%)	0	1 (0.7%)	0	0	0	0
ブドウ球菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
ブドウ球菌皮膚感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
水痘	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
外陰腟真菌感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
外陰部腟炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
Total number of subjects treated within window[c]	15	15	11	0	20	20	16	1
Total number of subjects with treatment-emergent infections and infestations	13 (86.7%)	10 (66.7%)	6 (54.5%)	0	17 (85.0%)	13 (65.0%)	9 (56.3%)	0
Preferred term								
上気道感染	3 (20.0%)	2 (13.3%)	2 (18.2%)	0	3 (15.0%)	3 (15.0%)	0	0
鼻咽頭炎	4 (26.7%)	3 (20.0%)	2 (18.2%)	0	9 (45.0%)	6 (30.0%)	4 (25.0%)	0
肺炎	3 (20.0%)	2 (13.3%)	1 (9.1%)	0	2 (10.0%)	1 (5.0%)	1 (6.3%)	0
気管支炎	1 (6.7%)	1 (6.7%)	0	0	1 (5.0%)	0	1 (6.3%)	0
気道感染	0	0	0	0	0	0	0	0
インフルエンザ	0	0	0	0	0	0	0	0
副鼻腔炎	0	0	0	0	0	0	0	0
下気道感染	0	0	0	0	0	0	0	0
鼻炎	0	0	0	0	0	0	0	0
尿路感染	0	0	0	0	1 (5.0%)	0	1 (6.3%)	0
結膜炎	0	0	0	0	0	0	0	0
胃腸炎	0	0	0	0	0	0	0	0
帯状疱疹	1 (6.7%)	1 (6.7%)	0	0	0	0	0	0
口腔カンジダ症	0	0	0	0	0	0	0	0
口腔ヘルペス	0	0	0	0	0	0	0	0
蜂巣炎	0	0	0	0	0	0	0	0
口腔真菌感染	0	0	0	0	0	0	0	0
皮膚感染	0	0	0	0	1 (5.0%)	0	1 (6.3%)	0
ウイルス感染	0	0	0	0	0	0	0	0
膀胱炎	1 (6.7%)	1 (6.7%)	0	0	1 (5.0%)	1 (5.0%)	0	0
耳感染	0	0	0	0	0	0	0	0
真菌感染	0	0	0	0	0	0	0	0
ヘルペスウイルス感染	0	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	0	0
咽頭炎	1 (6.7%)	0	1 (9.1%)	0	1 (5.0%)	1 (5.0%)	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
インフルエンザ性肺炎	0	0	0	0	0	0	0	0
気管支肺炎	1 (6.7%)	1 (6.7%)	0	0	0	0	0	0
肺感染	0	0	0	0	0	0	0	0
歯周炎	0	0	0	0	1 (5.0%)	0	1 (6.3%)	0
ＲＳウイルス感染	0	0	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0	0	0
外陰部腟カンジダ症	0	0	0	0	0	0	0	0
急性副鼻腔炎	0	0	0	0	0	0	0	0
虫垂炎	0	0	0	0	0	0	0	0
細気管支炎	0	0	0	0	0	0	0	0
カンピロバクター胃腸炎	0	0	0	0	0	0	0	0
丹毒	0	0	0	0	0	0	0	0
大腸菌性尿路感染	0	0	0	0	0	0	0	0
眼感染	0	0	0	0	0	0	0	0
毛包炎	0	0	0	0	0	0	0	0
皮膚真菌感染	0	0	0	0	0	0	0	0
せつ	0	0	0	0	0	0	0	0
ウイルス性胃腸炎	0	0	0	0	0	0	0	0
消化管感染	0	0	0	0	0	0	0	0
歯肉炎	0	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	0	0	0
大葉性肺炎	0	0	0	0	0	0	0	0
好中球減少性敗血症	0	0	0	0	0	0	0	0
耳下腺炎	0	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0	0
ウイルス性気道感染	0	0	0	0	0	0	0	0
敗血症	0	0	0	0	0	0	0	0
皮下組織膿瘍	0	0	0	0	0	0	0	0
足部白癬	0	0	0	0	0	0	0	0
歯膿瘍	0	0	0	0	0	0	0	0
歯感染	0	0	0	0	0	0	0	0
細菌性上気道感染	0	0	0	0	0	0	0	0
急性扁桃炎	0	0	0	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
無症候性細菌尿	0	0	0	0	0	0	0	0
細菌感染	0	0	0	0	1 (5.0%)	1 (5.0%)	0	0
カンジダ性亀頭炎	0	0	0	0	0	0	0	0
細菌性気管支炎	0	0	0	0	0	0	0	0
カンピロバクター感染	0	0	0	0	0	0	0	0
カンジダ感染	0	0	0	0	0	0	0	0
カテーテル留置部位膿瘍	0	0	0	0	0	0	0	0
カテーテル留置部位感染	0	0	0	0	0	0	0	0
慢性副鼻腔炎	0	0	0	0	0	0	0	0
ウイルス性結膜炎	0	0	0	0	0	0	0	0
コロナウイルス感染	0	0	0	0	0	0	0	0
サイトメガロウイルス感染	0	0	0	0	1 (5.0%)	1 (5.0%)	0	0
ウイルス性腸炎	0	0	0	0	1 (5.0%)	1 (5.0%)	0	0
喉頭蓋炎	0	0	0	0	0	0	0	0
大腸菌性菌血症	0	0	0	0	0	0	0	0
硬膜外膿瘍	0	0	0	0	0	0	0	0
感染性舌炎	0	0	0	0	1 (5.0%)	1 (5.0%)	0	0
感染性脊椎炎	0	0	0	0	0	0	0	0
注入部位蜂巣炎	0	0	0	0	0	0	0	0
ウイルス性喉頭炎	0	0	0	0	0	0	0	0
リステリア性敗血症	0	0	0	0	0	0	0	0
限局性感染	0	0	0	0	0	0	0	0
ウイルス性下気道感染	0	0	0	0	0	0	0	0
粘膜感染	0	0	0	0	0	0	0	0
鼻膿瘍	0	0	0	0	0	0	0	0
口腔感染	0	0	0	0	0	0	0	0
中咽頭カンジダ症	0	0	0	0	0	0	0	0
外耳炎	0	0	0	0	0	0	0	0
中耳炎	1 (6.7%)	1 (6.7%)	0	0	0	0	0	0
急性中耳炎	0	0	0	0	0	0	0	0
耳管炎	0	0	0	0	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
眼窩周囲蜂巣炎	0	0	0	0	0	0	0	0
レンサ球菌性咽頭炎	0	0	0	0	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	0	0	0
レンサ球菌性肺炎	0	0	0	0	0	0	0	0
前立腺感染	0	0	0	0	0	0	0	0
シュードモナス感染	0	0	0	0	0	0	0	0
腎盂腎炎	0	0	0	0	0	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	0	0
サルモネラ性菌血症	0	0	0	0	0	0	0	0
軟部組織感染	0	0	0	0	0	0	0	0
扁桃炎	0	0	0	0	0	0	0	0
気管炎	0	0	0	0	0	0	0	0
尿道炎	0	0	0	0	0	0	0	0
子宮膿瘍	0	0	0	0	0	0	0	0
腟感染	0	0	0	0	0	0	0	0
ウイルス性鼻炎	0	0	0	0	0	0	0	0
ウイルス性上気道感染	0	0	0	0	0	0	0	0
内臓リーシュマニア症	0	0	0	0	0	0	0	0
創傷感染	0	0	0	0	0	0	0	0
四肢膿瘍	0	0	0	0	0	0	0	0
アデノウイルス感染	0	0	0	0	0	0	0	0
肛門膿瘍	0	0	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	0	0
細菌性結膜炎	0	0	0	0	0	0	0	0
蓄膿	1 (6.7%)	1 (6.7%)	0	0	0	0	0	0
感染性小腸結腸炎	0	0	0	0	0	0	0	0
真菌性眼感染	0	0	0	0	0	0	0	0
熱性感染症	0	0	0	0	0	0	0	0
陰部単純ヘルペス	0	0	0	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
真菌性性器感染	0	0	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	0	0	0	0
単純ヘルペス	0	0	0	0	0	0	0	0
麦粒腫	0	0	0	0	0	0	0	0
咬傷感染	0	0	0	0	0	0	0	0
感染性筋炎	0	0	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0	0	0
喉頭炎	0	0	0	0	0	0	0	0
鼻ヘルペス	0	0	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0	0	0
口腔ウイルス感染	0	0	0	0	0	0	0	0
骨髄炎	0	0	0	0	0	0	0	0
爪囲炎	0	0	0	0	0	0	0	0
百日咳	0	0	0	0	0	0	0	0
肺結核	0	0	0	0	0	0	0	0
歯髄炎	0	0	0	0	0	0	0	0
急性腎盂腎炎	0	0	0	0	0	0	0	0
皮膚カンジダ	0	0	0	0	0	0	0	0
ブドウ球菌感染	0	0	0	0	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0	0	0	0	0
尿路性敗血症	0	0	0	0	0	0	0	0
水痘	0	0	0	0	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0	0	0	0	0
外陰腟真菌感染	0	0	0	0	0	0	0	0
外陰部腟炎	0	0	0	0	0	0	0	0
East Asian[b] Analysis set: safety	44				51			
Total number of subjects treated within window[c]	44	44	32	16	51	51	45	23

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
Total number of subjects with treatment-emergent infections and infestations	38 (86.4%)	32 (72.7%)	16 (50.0%)	3 (18.8%)	44 (86.3%)	37 (72.5%)	25 (55.6%)	9 (39.1%)
Preferred term								
上気道感染	18 (40.9%)	14 (31.8%)	7 (21.9%)	1 (6.3%)	22 (43.1%)	19 (37.3%)	9 (20.0%)	8 (34.8%)
鼻咽頭炎	9 (20.5%)	8 (18.2%)	3 (9.4%)	0	17 (33.3%)	10 (19.6%)	8 (17.8%)	1 (4.3%)
肺炎	6 (13.6%)	3 (6.8%)	2 (6.3%)	1 (6.3%)	5 (9.8%)	3 (5.9%)	2 (4.4%)	0
気管支炎	2 (4.5%)	2 (4.5%)	0	0	3 (5.9%)	1 (2.0%)	2 (4.4%)	0
気道感染	0	0	0	0	0	0	0	0
インフルエンザ	1 (2.3%)	0	0	1 (6.3%)	0	0	0	0
副鼻腔炎	2 (4.5%)	1 (2.3%)	1 (3.1%)	0	4 (7.8%)	2 (3.9%)	2 (4.4%)	0
下気道感染	0	0	0	0	0	0	0	0
鼻炎	0	0	0	0	2 (3.9%)	2 (3.9%)	0	0
尿路感染	1 (2.3%)	1 (2.3%)	0	0	2 (3.9%)	1 (2.0%)	1 (2.2%)	0
結膜炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
胃腸炎	0	0	0	0	0	0	0	0
帯状疱疹	4 (9.1%)	4 (9.1%)	0	0	4 (7.8%)	4 (7.8%)	0	0
口腔カンジダ症	0	0	0	0	0	0	0	0
口腔ヘルペス	0	0	0	0	0	0	0	0
蜂巣炎	1 (2.3%)	1 (2.3%)	0	0	1 (2.0%)	0	0	1 (4.3%)
口腔真菌感染	0	0	0	0	0	0	0	0
皮膚感染	0	0	0	0	1 (2.0%)	0	1 (2.2%)	0
ウイルス感染	0	0	0	0	0	0	0	0
膀胱炎	1 (2.3%)	1 (2.3%)	0	0	2 (3.9%)	1 (2.0%)	1 (2.2%)	0
耳感染	0	0	0	0	0	0	0	0
真菌感染	0	0	0	0	0	0	0	0
ヘルペスウイルス感染	0	0	0	0	1 (2.0%)	0	0	1 (4.3%)
感染	0	0	0	0	0	0	0	0
咽頭炎	1 (2.3%)	0	1 (3.1%)	0	1 (2.0%)	1 (2.0%)	0	0
インフルエンザ性肺炎	0	0	0	0	0	0	0	0
気管支肺炎	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
肺感染	0	0	0	0	1 (2.0%)	0	1 (2.2%)	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
歯周炎	0	0	0	0	3 (5.9%)	1 (2.0%)	2 (4.4%)	0
ＲＳウイルス感染	0	0	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0	0	0
外陰部腟カンジダ症	0	0	0	0	0	0	0	0
急性副鼻腔炎	0	0	0	0	0	0	0	0
虫垂炎	0	0	0	0	0	0	0	0
細気管支炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
カンピロバクター胃腸炎	0	0	0	0	0	0	0	0
丹毒	0	0	0	0	0	0	0	0
大腸菌性尿路感染	0	0	0	0	0	0	0	0
眼感染	0	0	0	0	0	0	0	0
毛包炎	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
皮膚真菌感染	0	0	0	0	0	0	0	0
せつ	0	0	0	0	0	0	0	0
ウイルス性胃腸炎	0	0	0	0	0	0	0	0
消化管感染	0	0	0	0	0	0	0	0
歯肉炎	0	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
大葉性肺炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
好中球減少性敗血症	0	0	0	0	0	0	0	0
耳下腺炎	0	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0	0
ウイルス性気道感染	0	0	0	0	0	0	0	0
敗血症	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
皮下組織膿瘍	0	0	0	0	0	0	0	0
足部白癬	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
歯膿瘍	0	0	0	0	0	0	0	0
歯感染	0	0	0	0	0	0	0	0
細菌性上気道感染	0	0	0	0	0	0	0	0
急性扁桃炎	0	0	0	0	0	0	0	0
無症候性細菌尿	0	0	0	0	0	0	0	0
細菌感染	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
カンジダ性亀頭炎	0	0	0	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
細菌性気管支炎	0	0	0	0	0	0	0	0
カンピロバクター感染	0	0	0	0	0	0	0	0
カンジダ感染	0	0	0	0	0	0	0	0
カテーテル留置部位膿瘍	0	0	0	0	0	0	0	0
カテーテル留置部位感染	0	0	0	0	0	0	0	0
慢性副鼻腔炎	0	0	0	0	0	0	0	0
ウイルス性結膜炎	0	0	0	0	0	0	0	0
コロナウイルス感染	0	0	0	0	0	0	0	0
サイトメガロウイルス感染	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
ウイルス性腸炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
喉頭蓋炎	0	0	0	0	0	0	0	0
大腸菌性菌血症	0	0	0	0	0	0	0	0
硬膜外膿瘍	0	0	0	0	0	0	0	0
感染性舌炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
感染性脊椎炎	0	0	0	0	0	0	0	0
注入部位蜂巣炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
ウイルス性喉頭炎	0	0	0	0	0	0	0	0
リステリア性敗血症	0	0	0	0	0	0	0	0
限局性感染	0	0	0	0	0	0	0	0
ウイルス性下気道感染	0	0	0	0	0	0	0	0
粘膜感染	0	0	0	0	0	0	0	0
鼻膿瘍	0	0	0	0	0	0	0	0
口腔感染	0	0	0	0	0	0	0	0
中咽頭カンジダ症	0	0	0	0	0	0	0	0
外耳炎	0	0	0	0	0	0	0	0
中耳炎	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
急性中耳炎	0	0	0	0	1 (2.0%)	0	0	1 (4.3%)
耳管炎	0	0	0	0	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0	0	0	0	0
レンサ球菌性咽頭炎	0	0	0	0	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
クレブシエラ菌性肺炎	0	0	0	0	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	0	0	0
レンサ球菌性肺炎	0	0	0	0	0	0	0	0
前立腺感染	0	0	0	0	0	0	0	0
シュードモナス感染	0	0	0	0	0	0	0	0
腎盂腎炎	0	0	0	0	0	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	0	0
サルモネラ性菌血症	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
軟部組織感染	0	0	0	0	0	0	0	0
扁桃炎	0	0	0	0	0	0	0	0
気管炎	0	0	0	0	0	0	0	0
尿道炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
子宮膿瘍	0	0	0	0	0	0	0	0
腟感染	0	0	0	0	0	0	0	0
ウイルス性鼻炎	0	0	0	0	0	0	0	0
ウイルス性上気道感染	0	0	0	0	0	0	0	0
内臓リーシュマニア症	0	0	0	0	0	0	0	0
創傷感染	0	0	0	0	0	0	0	0
四肢膿瘍	0	0	0	0	0	0	0	0
アデノウイルス感染	0	0	0	0	0	0	0	0
肛門膿瘍	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	0	0
細菌性結膜炎	0	0	0	0	0	0	0	0
蓄膿	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
感染性小腸結腸炎	0	0	0	0	0	0	0	0
真菌性眼感染	0	0	0	0	0	0	0	0
熱性感染症	0	0	0	0	0	0	0	0
陰部単純ヘルペス	0	0	0	0	0	0	0	0
真菌性性器感染	0	0	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	0	0	0	0
単純ヘルペス	1 (2.3%)	0	1 (3.1%)	0	0	0	0	0

TSFAE26_3003: Number of Subjects With 1 or More Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
麦粒腫	0	0	0	0	0	0	0	0
咬傷感染	0	0	0	0	0	0	0	0
感染性筋炎	0	0	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0	0	0
喉頭炎	0	0	0	0	0	0	0	0
鼻ヘルペス	0	0	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0	0	0
口腔ウイルス感染	0	0	0	0	0	0	0	0
骨髄炎	2 (4.5%)	1 (2.3%)	1 (3.1%)	0	0	0	0	0
爪囲炎	0	0	0	0	0	0	0	0
百日咳	0	0	0	0	0	0	0	0
肺結核	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
歯髄炎	0	0	0	0	0	0	0	0
急性腎盂腎炎	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
皮膚カンジダ	0	0	0	0	0	0	0	0
ブドウ球菌感染	0	0	0	0	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0	0	0	0	0
尿路性敗血症	0	0	0	0	0	0	0	0
水痘	0	0	0	0	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0	0	0	0	0
外陰腟真菌感染	0	0	0	0	0	0	0	0
外陰部腟炎	0	0	0	0	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages in the total column are calculated with the number of treated subjects in each group as denominator. Percentages for months columns are calculated with the number of treated subjects in the months as denominator.
Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event.

表 2.7.4-付録-132 Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
Total[a] Analysis set: safety	281				283			
Total number of subjects treated within window[c]	281	281	216	148	283	283	251	195
Total number of subjects with toxicity grade 3 or 4 treatment-emergent infections and infestations	64 (22.8%)	39 (13.9%)	21 (9.7%)	9 (6.1%)	80 (28.3%)	52 (18.4%)	32 (12.7%)	9 (4.6%)
Preferred term								
肺炎	23 (8.2%)	15 (5.3%)	6 (2.8%)	3 (2.0%)	22 (7.8%)	11 (3.9%)	10 (4.0%)	2 (1.0%)
インフルエンザ	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	8 (2.8%)	6 (2.1%)	2 (0.8%)	0
下気道感染	3 (1.1%)	1 (0.4%)	3 (1.4%)	0	5 (1.8%)	4 (1.4%)	2 (0.8%)	0
気道感染	2 (0.7%)	2 (0.7%)	0	0	5 (1.8%)	2 (0.7%)	3 (1.2%)	1 (0.5%)
尿路感染	1 (0.4%)	1 (0.4%)	0	0	5 (1.8%)	3 (1.1%)	2 (0.8%)	0
気管支炎	6 (2.1%)	3 (1.1%)	1 (0.5%)	2 (1.4%)	4 (1.4%)	2 (0.7%)	2 (0.8%)	0
インフルエンザ性肺炎	0	0	0	0	3 (1.1%)	2 (0.7%)	0	1 (0.5%)
上気道感染	3 (1.1%)	3 (1.1%)	0	0	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
虫垂炎	1 (0.4%)	0	1 (0.5%)	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
細気管支炎	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
気管支肺炎	0	0	0	0	2 (0.7%)	2 (0.7%)	0	0
Ｈ１Ｎ１インフルエンザ感染	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
大葉性肺炎	3 (1.1%)	3 (1.1%)	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
好中球減少性敗血症	1 (0.4%)	0	1 (0.5%)	0	2 (0.7%)	2 (0.7%)	0	0
敗血症	0	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
急性扁桃炎	6 (2.1%)	3 (1.1%)	1 (0.5%)	2 (1.4%)	2 (0.7%)	1 (0.4%)	0	1 (0.5%)
細菌感染	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
カンピロバクター胃腸炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
蜂巣炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
サイトメガロウイルス感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
喉頭蓋炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
大腸菌性菌血症	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
硬膜外膿瘍	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
胃腸炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性胃腸炎	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	0	1 (0.4%)	0
リステリア性敗血症	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
肺感染	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0
鼻膿瘍	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
口腔真菌感染	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
急性中耳炎	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	0	0	1 (0.5%)
パラインフルエンザウイルス感染	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
眼窩周囲蜂巣炎	0	0	0	0	1 (0.4%)	0	0	1 (0.5%)
細菌性肺炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ヘモフィルス性肺炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
クレブシエラ菌性肺炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
レジオネラ菌性肺炎	1 (0.4%)	0	1 (0.5%)	0	1 (0.4%)	0	1 (0.4%)	0
レンサ球菌性肺炎	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
シュードモナス感染	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
呼吸器モニリア症	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ＲＳウイルス感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
サルモネラ性菌血症	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
敗血症性ショック	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	1 (0.4%)	1 (0.4%)	0	0
皮膚感染	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
軟部組織感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
扁桃炎	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
細菌性上気道感染	0	0	0	0	1 (0.4%)	1 (0.4%)	0	0
子宮膿瘍	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
内臓リーシュマニア症	0	0	0	0	1 (0.4%)	0	1 (0.4%)	0
四肢膿瘍	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
アデノウイルス感染	1 (0.4%)	0	0	1 (0.7%)	0	0	0	0
肛門膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
ウイルス性気管支炎	1 (0.4%)	0	0	1 (0.7%)	0	0	0	0
クロストリジウム・ディフィシレ感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0	0	0	0	0
丹毒	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
消化管感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
帯状疱疹	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
真菌性角膜炎	1 (0.4%)	0	0	1 (0.7%)	0	0	0	0
限局性感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
骨髄炎	2 (0.7%)	1 (0.4%)	1 (0.5%)	0	0	0	0	0
咽頭炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
肺結核	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
急性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	0	1 (0.5%)	0	0	0	0	0
Japanese Analysis set: safety	15				20			
Total number of subjects treated within window[c]	15	15	11	0	20	20	16	1
Total number of subjects with toxicity grade 3 or 4 treatment-emergent infections and infestations	2 (13.3%)	1 (6.7%)	1 (9.1%)	0	5 (25.0%)	2 (10.0%)	3 (18.8%)	0
Preferred term								
肺炎	2 (13.3%)	1 (6.7%)	1 (9.1%)	0	2 (10.0%)	0	2 (12.5%)	0
インフルエンザ	0	0	0	0	0	0	0	0
下気道感染	0	0	0	0	0	0	0	0
気道感染	0	0	0	0	0	0	0	0
尿路感染	0	0	0	0	1 (5.0%)	0	1 (6.3%)	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
気管支炎	0	0	0	0	0	0	0	0
インフルエンザ性肺炎	0	0	0	0	0	0	0	0
上気道感染	0	0	0	0	0	0	0	0
虫垂炎	0	0	0	0	0	0	0	0
細気管支炎	0	0	0	0	0	0	0	0
気管支肺炎	0	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	0	0
大葉性肺炎	0	0	0	0	0	0	0	0
好中球減少性敗血症	0	0	0	0	0	0	0	0
敗血症	0	0	0	0	0	0	0	0
急性扁桃炎	0	0	0	0	0	0	0	0
細菌感染	0	0	0	0	1 (5.0%)	1 (5.0%)	0	0
カンピロバクター胃腸炎	0	0	0	0	0	0	0	0
蜂巣炎	0	0	0	0	0	0	0	0
サイトメガロウイルス感染	0	0	0	0	1 (5.0%)	1 (5.0%)	0	0
喉頭蓋炎	0	0	0	0	0	0	0	0
大腸菌性菌血症	0	0	0	0	0	0	0	0
硬膜外膿瘍	0	0	0	0	0	0	0	0
胃腸炎	0	0	0	0	0	0	0	0
ウイルス性胃腸炎	0	0	0	0	0	0	0	0
リステリア性敗血症	0	0	0	0	0	0	0	0
肺感染	0	0	0	0	0	0	0	0
鼻膿瘍	0	0	0	0	0	0	0	0
口腔真菌感染	0	0	0	0	0	0	0	0
急性中耳炎	0	0	0	0	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	0	0	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
レンサ球菌性肺炎	0	0	0	0	0	0	0	0
シュードモナス感染	0	0	0	0	0	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	0	0
ＲＳウイルス感染	0	0	0	0	0	0	0	0
サルモネラ性菌血症	0	0	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0	0	0
皮膚感染	0	0	0	0	0	0	0	0
軟部組織感染	0	0	0	0	0	0	0	0
扁桃炎	0	0	0	0	0	0	0	0
細菌性上気道感染	0	0	0	0	0	0	0	0
子宮膿瘍	0	0	0	0	0	0	0	0
内臓リーシュマニア症	0	0	0	0	0	0	0	0
四肢膿瘍	0	0	0	0	0	0	0	0
アデノウイルス感染	0	0	0	0	0	0	0	0
肛門膿瘍	0	0	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	0	0
感染性小腸結腸炎	0	0	0	0	0	0	0	0
丹毒	0	0	0	0	0	0	0	0
消化管感染	0	0	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	0	0	0	0
帯状疱疹	0	0	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0	0	0
限局性感染	0	0	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0	0	0
骨髄炎	0	0	0	0	0	0	0	0
咽頭炎	0	0	0	0	0	0	0	0
肺結核	0	0	0	0	0	0	0	0
急性腎盂腎炎	0	0	0	0	0	0	0	0
尿路性敗血症	0	0	0	0	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0	0	0	0	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
East Asian[b] Analysis set: safety	44				51			
Total number of subjects treated within window[c]	44	44	32	16	51	51	45	23
Total number of subjects with toxicity grade 3 or 4 treatment-emergent infections and infestations	11 (25.0%)	8 (18.2%)	2 (6.3%)	1 (6.3%)	10 (19.6%)	6 (11.8%)	3 (6.7%)	1 (4.3%)
Preferred term								
肺炎	4 (9.1%)	2 (4.5%)	1 (3.1%)	1 (6.3%)	3 (5.9%)	1 (2.0%)	2 (4.4%)	0
インフルエンザ	0	0	0	0	0	0	0	0
下気道感染	0	0	0	0	0	0	0	0
気道感染	0	0	0	0	0	0	0	0
尿路感染	1 (2.3%)	1 (2.3%)	0	0	1 (2.0%)	0	1 (2.2%)	0
気管支炎	0	0	0	0	0	0	0	0
インフルエンザ性肺炎	0	0	0	0	0	0	0	0
上気道感染	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
虫垂炎	0	0	0	0	0	0	0	0
細気管支炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
気管支肺炎	0	0	0	0	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0	0	0	0	0
感染	0	0	0	0	0	0	0	0
大葉性肺炎	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
好中球減少性敗血症	0	0	0	0	0	0	0	0
敗血症	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
急性扁桃炎	0	0	0	0	0	0	0	0
細菌感染	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
カンピロバクター胃腸炎	0	0	0	0	0	0	0	0
蜂巣炎	0	0	0	0	0	0	0	0
サイトメガロウイルス感染	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
喉頭蓋炎	0	0	0	0	0	0	0	0
大腸菌性菌血症	0	0	0	0	0	0	0	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
硬膜外膿瘍	0	0	0	0	0	0	0	0
胃腸炎	0	0	0	0	0	0	0	0
ウイルス性胃腸炎	0	0	0	0	0	0	0	0
リステリア性敗血症	0	0	0	0	0	0	0	0
肺感染	0	0	0	0	0	0	0	0
鼻膿瘍	0	0	0	0	0	0	0	0
口腔真菌感染	0	0	0	0	0	0	0	0
急性中耳炎	0	0	0	0	1 (2.0%)	0	0	1 (4.3%)
パラインフルエンザウイルス感染	0	0	0	0	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0	0	0	0	0
細菌性肺炎	0	0	0	0	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0	0	0	0	0
レンサ球菌性肺炎	0	0	0	0	0	0	0	0
シュードモナス感染	0	0	0	0	0	0	0	0
呼吸器モニリア症	0	0	0	0	0	0	0	0
ＲＳウイルス感染	0	0	0	0	0	0	0	0
サルモネラ性菌血症	0	0	0	0	1 (2.0%)	1 (2.0%)	0	0
敗血症性ショック	0	0	0	0	0	0	0	0
皮膚感染	0	0	0	0	0	0	0	0
軟部組織感染	0	0	0	0	0	0	0	0
扁桃炎	0	0	0	0	0	0	0	0
細菌性上気道感染	0	0	0	0	0	0	0	0
子宮膿瘍	0	0	0	0	0	0	0	0
内臓リーシュマニア症	0	0	0	0	0	0	0	0
四肢膿瘍	0	0	0	0	0	0	0	0
アデノウイルス感染	0	0	0	0	0	0	0	0
肛門膿瘍	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
ウイルス性気管支炎	0	0	0	0	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	0	0

TSFAE26A_3003: Number of Subjects With 1 or More Toxicity Grade 3 or 4 Treatment Emergent Adverse Events of Infections/Infestations by months (New Onsets) and MedDRA Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd n (%)				DRd n (%)			
	Total	0-<=6 Months	6-<=12 Months	12+ Months	Total	0-<=6 Months	6-<=12 Months	12+ Months
感染性小腸結腸炎	0	0	0	0	0	0	0	0
丹毒	0	0	0	0	0	0	0	0
消化管感染	0	0	0	0	0	0	0	0
ヘモフィルス感染	0	0	0	0	0	0	0	0
帯状疱疹	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
真菌性角膜炎	0	0	0	0	0	0	0	0
限局性感染	0	0	0	0	0	0	0	0
壊死性筋膜炎	0	0	0	0	0	0	0	0
骨髄炎	2 (4.5%)	1 (2.3%)	1 (3.1%)	0	0	0	0	0
咽頭炎	0	0	0	0	0	0	0	0
肺結核	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
急性腎盂腎炎	1 (2.3%)	1 (2.3%)	0	0	0	0	0	0
尿路性敗血症	0	0	0	0	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
[c] Includes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages in the total column are calculated with the number of treated subjects in each group as denominator. Percentages for months columns are calculated with the number of treated subjects in the months as denominator.
Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event.

[TSFAE26A_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE26A_3003.SAS] 04AUG2016, 08:56

表 2.7.4-付録-133 Number of Subjects with 1 or More Toxicity Grade 3 or 4 Treatment-emergent Infections and Infestations by Treatment Cycle (New Onset) and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE16A: Number of Subjects with 1 or More Toxicity Grade 3 or 4 Treatment-emergent Infections and Infestations by Treatment Cycle (New Onset) and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)				
	n (%)				
	Total	Cycles 1-3	Cycles 4-8	Cycles 9+	Cycles 1-8
Analysis set: Safety	8	8	8	3	8
Total number of subjects with grade 3 or 4 treatment emergent infections and infestations	2 (25.0%)	1 (12.5%)	1 (12.5%)	0	2 (25.0%)
Preferred term					
帯状疱疹	1 (12.5%)	0	1 (12.5%)	0	1 (12.5%)
鼻咽頭炎	1 (12.5%)	1 (12.5%)	0	0	1 (12.5%)

Key: Vd = bortezomib-dexamethasone.
Note: Percentages in the total column are calculated with the number of subjects in safety population as denominator. Percentages for cycle columns are calculated with the number of treated subjects in the cycles as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE16A.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE16A.SAS] 28SEP2016, 04:18

表 2.7.4-付録-134 Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Total[a] Analysis set: safety	281		283	
Total number of subjects with infections/infestations	204 (72.6%)	64 (22.8%)	238 (84.1%)	80 (28.3%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	204 (72.6%)	64 (22.8%)	238 (84.1%)	80 (28.3%)
上気道感染	58 (20.6%)	3 (1.1%)	90 (31.8%)	3 (1.1%)
鼻咽頭炎	43 (15.3%)	0	68 (24.0%)	0
肺炎	37 (13.2%)	23 (8.2%)	40 (14.1%)	22 (7.8%)
気管支炎	34 (12.1%)	6 (2.1%)	38 (13.4%)	4 (1.4%)
気道感染	22 (7.8%)	2 (0.7%)	31 (11.0%)	5 (1.8%)
インフルエンザ	13 (4.6%)	2 (0.7%)	21 (7.4%)	8 (2.8%)
副鼻腔炎	10 (3.6%)	0	18 (6.4%)	0
下気道感染	9 (3.2%)	3 (1.1%)	17 (6.0%)	5 (1.8%)
鼻炎	3 (1.1%)	0	15 (5.3%)	0
尿路感染	11 (3.9%)	1 (0.4%)	15 (5.3%)	5 (1.8%)
結膜炎	3 (1.1%)	0	11 (3.9%)	0
胃腸炎	4 (1.4%)	0	10 (3.5%)	1 (0.4%)
帯状疱疹	5 (1.8%)	1 (0.4%)	6 (2.1%)	0
口腔カンジダ症	4 (1.4%)	0	6 (2.1%)	0
口腔ヘルペス	2 (0.7%)	0	6 (2.1%)	0
蜂巣炎	3 (1.1%)	1 (0.4%)	5 (1.8%)	1 (0.4%)
口腔真菌感染	5 (1.8%)	0	5 (1.8%)	1 (0.4%)
皮膚感染	5 (1.8%)	0	5 (1.8%)	1 (0.4%)
ウイルス感染	7 (2.5%)	0	5 (1.8%)	0
膀胱炎	7 (2.5%)	0	4 (1.4%)	0
耳感染	3 (1.1%)	0	4 (1.4%)	0
真菌感染	1 (0.4%)	0	4 (1.4%)	0
ヘルペスウイルス感染	0	0	4 (1.4%)	0
感染	5 (1.8%)	3 (1.1%)	4 (1.4%)	2 (0.7%)
咽頭炎	7 (2.5%)	1 (0.4%)	4 (1.4%)	0
インフルエンザ性肺炎	0	0	4 (1.4%)	3 (1.1%)
気管支肺炎	1 (0.4%)	0	3 (1.1%)	2 (0.7%)
肺感染	2 (0.7%)	1 (0.4%)	3 (1.1%)	1 (0.4%)
歯周炎	1 (0.4%)	0	3 (1.1%)	0
ＲＳウイルス感染	0	0	3 (1.1%)	1 (0.4%)
敗血症性ショック	2 (0.7%)	2 (0.7%)	3 (1.1%)	1 (0.4%)
外陰部腟カンジダ症	0	0	3 (1.1%)	0
急性副鼻腔炎	0	0	2 (0.7%)	0
虫垂炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
細気管支炎	1 (0.4%)	0	2 (0.7%)	2 (0.7%)
カンピロバクター胃腸炎	0	0	2 (0.7%)	1 (0.4%)
丹毒	2 (0.7%)	1 (0.4%)	2 (0.7%)	0
大腸菌性尿路感染	0	0	2 (0.7%)	0
眼感染	2 (0.7%)	0	2 (0.7%)	0
毛包炎	1 (0.4%)	0	2 (0.7%)	0
皮膚真菌感染	1 (0.4%)	0	2 (0.7%)	0
せつ	0	0	2 (0.7%)	0
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
消化管感染	1 (0.4%)	1 (0.4%)	2 (0.7%)	0

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
歯肉炎	4 (1.4%)	0	2 (0.7%)	0
Ｈ１Ｎ１インフルエンザ	1 (0.4%)	0	2 (0.7%)	2 (0.7%)
大葉性肺炎	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
好中球減少性敗血症	0	0	2 (0.7%)	2 (0.7%)
耳下腺炎	0	0	2 (0.7%)	0
細菌性肺炎	1 (0.4%)	0	2 (0.7%)	1 (0.4%)
ウイルス性気道感染	0	0	2 (0.7%)	0
敗血症	6 (2.1%)	6 (2.1%)	2 (0.7%)	2 (0.7%)
皮下組織膿瘍	0	0	2 (0.7%)	0
足部白癬	3 (1.1%)	0	2 (0.7%)	0
歯膿瘍	6 (2.1%)	0	2 (0.7%)	0
歯感染	2 (0.7%)	0	2 (0.7%)	0
細菌性上気道感染	0	0	2 (0.7%)	1 (0.4%)
急性扁桃炎	0	0	1 (0.4%)	1 (0.4%)
無症候性細菌尿	0	0	1 (0.4%)	0
細菌感染	0	0	1 (0.4%)	1 (0.4%)
カンジダ性亀頭炎	0	0	1 (0.4%)	0
細菌性気管支炎	0	0	1 (0.4%)	0
カンピロバクター感染	0	0	1 (0.4%)	0
カンジダ感染	2 (0.7%)	0	1 (0.4%)	0
カテーテル留置部位膿瘍	0	0	1 (0.4%)	0
カテーテル留置部位感染	0	0	1 (0.4%)	0
慢性副鼻腔炎	0	0	1 (0.4%)	0
ウイルス性結膜炎	1 (0.4%)	0	1 (0.4%)	0
コロナウイルス感染	0	0	1 (0.4%)	0
サイトメガロウイルス感染	0	0	1 (0.4%)	1 (0.4%)
ウイルス性腸炎	0	0	1 (0.4%)	0
喉頭蓋炎	0	0	1 (0.4%)	1 (0.4%)
大腸菌性菌血症	0	0	1 (0.4%)	1 (0.4%)
硬膜外膿瘍	0	0	1 (0.4%)	1 (0.4%)
感染性舌炎	0	0	1 (0.4%)	0
感染性脊椎炎	0	0	1 (0.4%)	0
注入部位蜂巣炎	0	0	1 (0.4%)	0
ウイルス性喉頭炎	0	0	1 (0.4%)	0
リステリア性敗血症	0	0	1 (0.4%)	1 (0.4%)
限局性感染	5 (1.8%)	1 (0.4%)	1 (0.4%)	0
ウイルス性下気道感染	1 (0.4%)	0	1 (0.4%)	0
粘膜感染	3 (1.1%)	0	1 (0.4%)	0
鼻膿瘍	0	0	1 (0.4%)	1 (0.4%)
口腔感染	0	0	1 (0.4%)	0
中咽頭カンジダ症	0	0	1 (0.4%)	0
外耳炎	1 (0.4%)	0	1 (0.4%)	0
中耳炎	1 (0.4%)	0	1 (0.4%)	0
急性中耳炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
耳管炎	0	0	1 (0.4%)	0
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
眼窩周囲蜂巣炎	0	0	1 (0.4%)	1 (0.4%)
レンサ球菌性咽頭炎	1 (0.4%)	0	1 (0.4%)	0
ヘモフィルス性肺炎	0	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
レンサ球菌性肺炎	0	0	1 (0.4%)	1 (0.4%)
前立腺感染	0	0	1 (0.4%)	0
シュードモナス感染	0	0	1 (0.4%)	1 (0.4%)
腎盂腎炎	0	0	1 (0.4%)	0
呼吸器モニリア症	0	0	1 (0.4%)	1 (0.4%)

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
サルモネラ性菌血症	0	0	1 (0.4%)	1 (0.4%)
軟部組織感染	0	0	1 (0.4%)	1 (0.4%)
扁桃炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
気管炎	1 (0.4%)	0	1 (0.4%)	0
尿道炎	0	0	1 (0.4%)	0
子宮膿瘍	0	0	1 (0.4%)	1 (0.4%)
腟感染	1 (0.4%)	0	1 (0.4%)	0
ウイルス性鼻炎	0	0	1 (0.4%)	0
ウイルス性上気道感染	2 (0.7%)	0	1 (0.4%)	0
内臓リーシュマニア症	0	0	1 (0.4%)	1 (0.4%)
創傷感染	3 (1.1%)	0	1 (0.4%)	0
四肢膿瘍	1 (0.4%)	1 (0.4%)	0	0
アデノウイルス感染	1 (0.4%)	1 (0.4%)	0	0
肛門膿瘍	1 (0.4%)	1 (0.4%)	0	0
ウイルス性気管支炎	2 (0.7%)	1 (0.4%)	0	0
クロストリジウム・ディフィシレ感染	2 (0.7%)	1 (0.4%)	0	0
細菌性結膜炎	1 (0.4%)	0	0	0
蓄膿	1 (0.4%)	0	0	0
感染性小腸結腸炎	2 (0.7%)	2 (0.7%)	0	0
真菌性眼感染	1 (0.4%)	0	0	0
熱性感染症	1 (0.4%)	0	0	0
陰部単純ヘルペス	1 (0.4%)	0	0	0
真菌性性器感染	1 (0.4%)	0	0	0
ヘモフィルス感染	1 (0.4%)	1 (0.4%)	0	0
単純ヘルペス	1 (0.4%)	0	0	0
麦粒腫	2 (0.7%)	0	0	0
咬傷感染	1 (0.4%)	0	0	0
感染性筋炎	1 (0.4%)	0	0	0
真菌性角膜炎	1 (0.4%)	1 (0.4%)	0	0
喉頭炎	1 (0.4%)	0	0	0
鼻ヘルペス	1 (0.4%)	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	0	0
口腔ウイルス感染	1 (0.4%)	0	0	0
骨髄炎	2 (0.7%)	2 (0.7%)	0	0
爪囲炎	1 (0.4%)	0	0	0
百日咳	1 (0.4%)	0	0	0
肺結核	1 (0.4%)	1 (0.4%)	0	0
歯髄炎	1 (0.4%)	0	0	0
急性腎盂腎炎	1 (0.4%)	1 (0.4%)	0	0
皮膚カンジダ	3 (1.1%)	0	0	0
ブドウ球菌感染	1 (0.4%)	0	0	0
ブドウ球菌皮膚感染	1 (0.4%)	0	0	0
尿路性敗血症	1 (0.4%)	1 (0.4%)	0	0
水痘	1 (0.4%)	0	0	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	1 (0.4%)	0	0
外陰腟真菌感染	1 (0.4%)	0	0	0
外陰部腟炎	1 (0.4%)	0	0	0
Japanese Analysis set: safety	15		20	
Total number of subjects with infections/infestations	13 (86.7%)	2 (13.3%)	17 (85.0%)	5 (25.0%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	13 (86.7%)	2 (13.3%)	17 (85.0%)	5 (25.0%)
上気道感染	3 (20.0%)	0	3 (15.0%)	0

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
鼻咽頭炎	4 (26.7%)	0	9 (45.0%)	0
肺炎	3 (20.0%)	2 (13.3%)	2 (10.0%)	2 (10.0%)
気管支炎	1 (6.7%)	0	1 (5.0%)	0
気道感染	0	0	0	0
インフルエンザ	0	0	0	0
副鼻腔炎	0	0	0	0
下気道感染	0	0	0	0
鼻炎	0	0	0	0
尿路感染	0	0	1 (5.0%)	1 (5.0%)
結膜炎	0	0	0	0
胃腸炎	0	0	0	0
帯状疱疹	1 (6.7%)	0	0	0
口腔カンジダ症	0	0	0	0
口腔ヘルペス	0	0	0	0
蜂巣炎	0	0	0	0
口腔真菌感染	0	0	0	0
皮膚感染	0	0	1 (5.0%)	0
ウイルス感染	0	0	0	0
膀胱炎	1 (6.7%)	0	1 (5.0%)	0
耳感染	0	0	0	0
真菌感染	0	0	0	0
ヘルペスウイルス感染	0	0	0	0
感染	0	0	0	0
咽頭炎	1 (6.7%)	0	1 (5.0%)	0
インフルエンザ性肺炎	0	0	0	0
気管支肺炎	1 (6.7%)	0	0	0
肺感染	0	0	0	0
歯周炎	0	0	1 (5.0%)	0
ＲＳウイルス感染	0	0	0	0
敗血症性ショック	0	0	0	0
外陰部腟カンジダ症	0	0	0	0
急性副鼻腔炎	0	0	0	0
虫垂炎	0	0	0	0
細気管支炎	0	0	0	0
カンピロバクター胃腸炎	0	0	0	0
丹毒	0	0	0	0
大腸菌性尿路感染	0	0	0	0
眼感染	0	0	0	0
毛包炎	0	0	0	0
皮膚真菌感染	0	0	0	0
せつ	0	0	0	0
ウイルス性胃腸炎	0	0	0	0
消化管感染	0	0	0	0
歯肉炎	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	0
大葉性肺炎	0	0	0	0
好中球減少性敗血症	0	0	0	0
耳下腺炎	0	0	0	0
細菌性肺炎	0	0	0	0
ウイルス性気道感染	0	0	0	0
敗血症	0	0	0	0
皮下組織膿瘍	0	0	0	0
足部白癬	0	0	0	0
歯膿瘍	0	0	0	0
歯感染	0	0	0	0
細菌性上気道感染	0	0	0	0

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
急性扁桃炎	0	0	0	0
無症候性細菌尿	0	0	0	0
細菌感染	0	0	1 (5.0%)	1 (5.0%)
カンジダ性亀頭炎	0	0	0	0
細菌性気管支炎	0	0	0	0
カンピロバクター感染	0	0	0	0
カンジダ感染	0	0	0	0
カテーテル留置部位膿瘍	0	0	0	0
カテーテル留置部位感染	0	0	0	0
慢性副鼻腔炎	0	0	0	0
ウイルス性結膜炎	0	0	0	0
コロナウイルス感染	0	0	0	0
サイトメガロウイルス感染	0	0	1 (5.0%)	1 (5.0%)
ウイルス性腸炎	0	0	1 (5.0%)	0
喉頭蓋炎	0	0	0	0
大腸菌性菌血症	0	0	0	0
硬膜外膿瘍	0	0	0	0
感染性舌炎	0	0	1 (5.0%)	0
感染性脊椎炎	0	0	0	0
注入部位蜂巣炎	0	0	0	0
ウイルス性喉頭炎	0	0	0	0
リステリア性敗血症	0	0	0	0
限局性感染	0	0	0	0
ウイルス性下気道感染	0	0	0	0
粘膜感染	0	0	0	0
鼻膿瘍	0	0	0	0
口腔感染	0	0	0	0
中咽頭カンジダ症	0	0	0	0
外耳炎	0	0	0	0
中耳炎	1 (6.7%)	0	0	0
急性中耳炎	0	0	0	0
耳管炎	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0
レンサ球菌性咽頭炎	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
レンサ球菌性肺炎	0	0	0	0
前立腺感染	0	0	0	0
シュードモナス感染	0	0	0	0
腎盂腎炎	0	0	0	0
呼吸器モニリア症	0	0	0	0
サルモネラ性菌血症	0	0	0	0
軟部組織感染	0	0	0	0
扁桃炎	0	0	0	0
気管炎	0	0	0	0
尿道炎	0	0	0	0
子宮膿瘍	0	0	0	0
腟感染	0	0	0	0
ウイルス性鼻炎	0	0	0	0
ウイルス性上気道感染	0	0	0	0
内臓リーシュマニア症	0	0	0	0
創傷感染	0	0	0	0
四肢膿瘍	0	0	0	0
アデノウイルス感染	0	0	0	0

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
肛門膿瘍	0	0	0	0
ウイルス性気管支炎	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0
細菌性結膜炎	0	0	0	0
蓄膿	1 (6.7%)	0	0	0
感染性小腸結腸炎	0	0	0	0
真菌性眼感染	0	0	0	0
熱性感染症	0	0	0	0
陰部単純ヘルペス	0	0	0	0
真菌性性器感染	0	0	0	0
ヘモフィルス感染	0	0	0	0
単純ヘルペス	0	0	0	0
麦粒腫	0	0	0	0
咬傷感染	0	0	0	0
感染性筋炎	0	0	0	0
真菌性角膜炎	0	0	0	0
喉頭炎	0	0	0	0
鼻ヘルペス	0	0	0	0
壊死性筋膜炎	0	0	0	0
口腔ウイルス感染	0	0	0	0
骨髄炎	0	0	0	0
爪囲炎	0	0	0	0
百日咳	0	0	0	0
肺結核	0	0	0	0
歯髄炎	0	0	0	0
急性腎盂腎炎	0	0	0	0
皮膚カンジダ	0	0	0	0
ブドウ球菌感染	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0
尿路性敗血症	0	0	0	0
水痘	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0
外陰腟真菌感染	0	0	0	0
外陰部腟炎	0	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Total number of subjects with infections/infestations	38 (86.4%)	11 (25.0%)	44 (86.3%)	10 (19.6%)
MedDRA system organ class/Preferred term				
感染症および寄生虫症	38 (86.4%)	11 (25.0%)	44 (86.3%)	10 (19.6%)
上気道感染	18 (40.9%)	1 (2.3%)	22 (43.1%)	0
鼻咽頭炎	9 (20.5%)	0	17 (33.3%)	0
肺炎	6 (13.6%)	4 (9.1%)	5 (9.8%)	3 (5.9%)
気管支炎	2 (4.5%)	0	3 (5.9%)	0
気道感染	0	0	0	0
インフルエンザ	1 (2.3%)	0	0	0
副鼻腔炎	2 (4.5%)	0	4 (7.8%)	0
下気道感染	0	0	0	0
鼻炎	0	0	2 (3.9%)	0
尿路感染	1 (2.3%)	1 (2.3%)	2 (3.9%)	1 (2.0%)
結膜炎	0	0	1 (2.0%)	0
胃腸炎	0	0	0	0
帯状疱疹	4 (9.1%)	1 (2.3%)	4 (7.8%)	0
口腔カンジダ症	0	0	0	0

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
口腔ヘルペス	0	0	0	0
蜂巣炎	1 (2.3%)	0	1 (2.0%)	0
口腔真菌感染	0	0	0	0
皮膚感染	0	0	1 (2.0%)	0
ウイルス感染	0	0	0	0
膀胱炎	1 (2.3%)	0	2 (3.9%)	0
耳感染	0	0	0	0
真菌感染	0	0	0	0
ヘルペスウイルス感染	0	0	1 (2.0%)	0
感染	0	0	0	0
咽頭炎	1 (2.3%)	0	1 (2.0%)	0
インフルエンザ性肺炎	0	0	0	0
気管支肺炎	1 (2.3%)	0	0	0
肺感染	0	0	1 (2.0%)	0
歯周炎	0	0	3 (5.9%)	0
ＲＳウイルス感染	0	0	0	0
敗血症性ショック	0	0	0	0
外陰部腟カンジダ症	0	0	0	0
急性副鼻腔炎	0	0	0	0
虫垂炎	0	0	0	0
細気管支炎	0	0	1 (2.0%)	1 (2.0%)
カンピロバクター胃腸炎	0	0	0	0
丹毒	0	0	0	0
大腸菌性尿路感染	0	0	0	0
眼感染	0	0	0	0
毛包炎	1 (2.3%)	0	0	0
皮膚真菌感染	0	0	0	0
せつ	0	0	0	0
ウイルス性胃腸炎	0	0	0	0
消化管感染	0	0	0	0
歯肉炎	0	0	0	0
Ｈ１Ｎ１インフルエンザ	1 (2.3%)	0	0	0
大葉性肺炎	0	0	1 (2.0%)	1 (2.0%)
好中球減少性敗血症	0	0	0	0
耳下腺炎	0	0	0	0
細菌性肺炎	0	0	0	0
ウイルス性気道感染	0	0	0	0
敗血症	1 (2.3%)	1 (2.3%)	0	0
皮下組織膿瘍	0	0	0	0
足部白癬	0	0	1 (2.0%)	0
歯膿瘍	0	0	0	0
歯感染	0	0	0	0
細菌性上気道感染	0	0	0	0
急性扁桃炎	0	0	0	0
無症候性細菌尿	0	0	0	0
細菌感染	0	0	1 (2.0%)	1 (2.0%)
カンジダ性亀頭炎	0	0	0	0
細菌性気管支炎	0	0	0	0
カンピロバクター感染	0	0	0	0
カンジダ感染	0	0	0	0
カテーテル留置部位膿瘍	0	0	0	0
カテーテル留置部位感染	0	0	0	0
慢性副鼻腔炎	0	0	0	0
ウイルス性結膜炎	0	0	0	0
コロナウイルス感染	0	0	0	0
サイトメガロウイルス感染	0	0	1 (2.0%)	1 (2.0%)

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
ウイルス性腸炎	0	0	1 (2.0%)	0
喉頭蓋炎	0	0	0	0
大腸菌性菌血症	0	0	0	0
硬膜外膿瘍	0	0	0	0
感染性舌炎	0	0	1 (2.0%)	0
感染性脊椎炎	0	0	0	0
注入部位蜂巣炎	0	0	1 (2.0%)	0
ウイルス性喉頭炎	0	0	0	0
リステリア性敗血症	0	0	0	0
限局性感染	0	0	0	0
ウイルス性下気道感染	0	0	0	0
粘膜感染	0	0	0	0
鼻膿瘍	0	0	0	0
口腔感染	0	0	0	0
中咽頭カンジダ症	0	0	0	0
外耳炎	0	0	0	0
中耳炎	1 (2.3%)	0	0	0
急性中耳炎	0	0	1 (2.0%)	1 (2.0%)
耳管炎	0	0	0	0
パラインフルエンザウイルス感染	0	0	0	0
眼窩周囲蜂巣炎	0	0	0	0
レンサ球菌性咽頭炎	0	0	0	0
ヘモフィルス性肺炎	0	0	0	0
クレブシエラ菌性肺炎	0	0	0	0
レジオネラ菌性肺炎	0	0	0	0
レンサ球菌性肺炎	0	0	0	0
前立腺感染	0	0	0	0
シュードモナス感染	0	0	0	0
腎盂腎炎	0	0	0	0
呼吸器モニリア症	0	0	0	0
サルモネラ性菌血症	0	0	1 (2.0%)	1 (2.0%)
軟部組織感染	0	0	0	0
扁桃炎	0	0	0	0
気管炎	0	0	0	0
尿道炎	0	0	1 (2.0%)	0
子宮膿瘍	0	0	0	0
腟感染	0	0	0	0
ウイルス性鼻炎	0	0	0	0
ウイルス性上気道感染	0	0	0	0
内臓リーシュマニア症	0	0	0	0
創傷感染	0	0	0	0
四肢膿瘍	0	0	0	0
アデノウイルス感染	0	0	0	0
肛門膿瘍	1 (2.3%)	1 (2.3%)	0	0
ウイルス性気管支炎	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	0
細菌性結膜炎	0	0	0	0
蓄膿	1 (2.3%)	0	0	0
感染性小腸結腸炎	0	0	0	0
真菌性眼感染	0	0	0	0
熱性感染症	0	0	0	0
陰部単純ヘルペス	0	0	0	0
真菌性性器感染	0	0	0	0
ヘモフィルス感染	0	0	0	0
単純ヘルペス	1 (2.3%)	0	0	0
麦粒腫	0	0	0	0

TSFAE_J05_3003: Number of Subjects With 1 or More Treatment-emergent Infections and Infestations by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
咬傷感染	0	0	0	0
感染性筋炎	0	0	0	0
真菌性角膜炎	0	0	0	0
喉頭炎	0	0	0	0
鼻ヘルペス	0	0	0	0
壊死性筋膜炎	0	0	0	0
口腔ウイルス感染	0	0	0	0
骨髄炎	2 (4.5%)	2 (4.5%)	0	0
爪囲炎	0	0	0	0
百日咳	0	0	0	0
肺結核	1 (2.3%)	1 (2.3%)	0	0
歯髄炎	0	0	0	0
急性腎盂腎炎	1 (2.3%)	1 (2.3%)	0	0
皮膚カンジダ	0	0	0	0
ブドウ球菌感染	0	0	0	0
ブドウ球菌皮膚感染	0	0	0	0
尿路性敗血症	0	0	0	0
水痘	0	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0	0
外陰腟真菌感染	0	0	0	0
外陰部腟炎	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Key: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events are reported using MedDRA version 18.0.

[TSFAE_J05_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE_J05_3003.SAS] 13JUL2016, 09:12

表 2.7.4-付録-135 Number of Subjects with 1 or More Treatment-emergent Herpes Zoster Reactivation by MedDRA High Level Term and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE21: Number of Subjects with 1 or More Treatment-emergent Herpes Zoster Reactivation by MedDRA High Level Term and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with treatment emergent herpes zoster reactivation	1 (12.5%)	1 (12.5%)	0
MedDRA high level term/Preferred term			
ヘルペスウイルス感染	1 (12.5%)	1 (12.5%)	0
帯状疱疹	1 (12.5%)	1 (12.5%)	0

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE21.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE21.SAS] 28SEP2016, 04:21

表 2.7.4-付録-136 Incidence of Treatment-emergent Herpes Zoster by Prophylactic Use of Antivirals of Herpes Infection; Safety Analysis Set (Study 54767414MMY1005)

TSFAE21A: Incidence of Treatment-emergent Herpes Zoster by Prophylactic Use of Antivirals of Herpes Infection; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
		Prophylaxis	
	Total	No	Yes
Analysis set: Safety	8	1	7
Herpes zoster			
No	7 (87.5%)	1 (100.0%)	6 (85.7%)
Yes	1 (12.5%)	0	1 (14.3%)

Key: Vd = bortezomib-dexamethasone.
Note: Percentages in Total column for each group calculated with the number of subjects as denominator. Percentages of prophylaxis sub-groups calculated with number of subjects per sub-group as denominator. Incidence is based on the number of subjects experiencing at least one adverse event, not the number of events. A subject is only counted once based on worst occurrence (i.e. event=yes, medication=yes). A subject is counted as event=yes and prophylaxis=yes if the initial start date of event is after medication start and within 14 days of medication end (for medications that were stopped); A subject experiencing an event prior to the start of medication is counted as an event=yes, prophylaxis=no; A subject with event more than 14 days after the stop of medication is also counted as an event=yes, prophylaxis=no.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE21A.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE21A.SAS] 28SEP2016, 04:21

表 2.7.4-付録-137 Number of Subjects with 1 or More Treatment-emergent Herpes Zoster Reactivation by MedDRA High Level Term and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE19_3003: Number of Subjects with 1 or More Treatment-emergent Herpes Zoster Reactivation by MedDRA High Level Term and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Total[a]				
Analysis set: safety	281		283	
Total number of subjects with treatment emergent herpes zoster reactivation	5 (1.8%)	1 (0.4%)	6 (2.1%)	0
MedDRA high level term/Preferred term				
ヘルペスウイルス感染	5 (1.8%)	1 (0.4%)	6 (2.1%)	0
帯状疱疹	5 (1.8%)	1 (0.4%)	6 (2.1%)	0
Japanese				
Analysis set: safety	15		20	
Total number of subjects with treatment emergent herpes zoster reactivation	1 (6.7%)	0	0	0
MedDRA high level term/Preferred term				
ヘルペスウイルス感染	1 (6.7%)	0	0	0
帯状疱疹	1 (6.7%)	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Total number of subjects with treatment emergent herpes zoster reactivation	4 (9.1%)	1 (2.3%)	4 (7.8%)	0
MedDRA high level term/Preferred term				
ヘルペスウイルス感染	4 (9.1%)	1 (2.3%)	4 (7.8%)	0
帯状疱疹	4 (9.1%)	1 (2.3%)	4 (7.8%)	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE19_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSFAE19_3003.SAS] 05JUL2016, 08:52

表 2.7.4-付録-138 Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE22PART1OF2: Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
Analysis set: all treated	23			55			156		
Total number of subjects treated within window [a]	23	23	0	55	55	11	156	156	52
Total number of subjects with TEAE of infections/infestations	7 (30.4%)	7 (30.4%)	-	32 (58.2%)	31 (56.4%)	4 (36.4%)	85 (54.5%)	79 (50.6%)	20 (38.5%)
上気道感染	0	0	-	12 (21.8%)	12 (21.8%)	0	27 (17.3%)	23 (14.7%)	9 (17.3%)
鼻咽頭炎	2 (8.7%)	2 (8.7%)	-	9 (16.4%)	8 (14.5%)	2 (18.2%)	18 (11.5%)	16 (10.3%)	3 (5.8%)
肺炎	1 (4.3%)	1 (4.3%)	-	4 (7.3%)	4 (7.3%)	0	13 (8.3%)	10 (6.4%)	3 (5.8%)
副鼻腔炎	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	1 (1.8%)	0	9 (5.8%)	9 (5.8%)	1 (1.9%)
尿路感染	0	0	-	2 (3.6%)	2 (3.6%)	0	7 (4.5%)	4 (2.6%)	3 (5.8%)
気管支炎	0	0	-	0	0	0	5 (3.2%)	4 (2.6%)	2 (3.8%)
結膜炎	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
帯状疱疹	1 (4.3%)	1 (4.3%)	-	4 (7.3%)	4 (7.3%)	0	3 (1.9%)	2 (1.3%)	1 (1.9%)
大葉性肺炎	0	0	-	0	0	0	3 (1.9%)	3 (1.9%)	0
口腔カンジダ症	0	0	-	3 (5.5%)	3 (5.5%)	0	3 (1.9%)	3 (1.9%)	0
カンジダ感染	0	0	-	2 (3.6%)	1 (1.8%)	1 (9.1%)	2 (1.3%)	2 (1.3%)	0
単純ヘルペス	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
感染	0	0	-	1 (1.8%)	1 (1.8%)	0	2 (1.3%)	2 (1.3%)	0
インフルエンザ	0	0	-	3 (5.5%)	2 (3.6%)	1 (9.1%)	2 (1.3%)	2 (1.3%)	0
パラインフルエンザウイルス感染	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
咽頭炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
鼻炎	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
軟部組織感染	0	0	-	0	0	0	2 (1.3%)	2 (1.3%)	0
水痘	0	0	-	0	0	0	2 (1.3%)	1 (0.6%)	1 (1.9%)
蜂巣炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
膀胱炎	0	0	-	1 (1.8%)	1 (1.8%)	0	1 (0.6%)	0	1 (1.9%)
サイトメガロウイルス性脈絡網膜炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
医療機器関連感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0

TSFAE22PART1OF2: Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months
耳感染	0	0	-	1 (1.8%)	0	1 (9.1%)	1 (0.6%)	1 (0.6%)	0
胃腸炎	1 (4.3%)	1 (4.3%)	-	1 (1.8%)	0	1 (9.1%)	1 (0.6%)	0	1 (1.9%)
ウイルス性胃腸炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
性器感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
Ｈ１Ｎ１インフルエンザ	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
麦粒腫	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
下気道感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
粘膜感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
眼部単純ヘルペス	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口腔真菌感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
口腔ヘルペス	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
爪囲炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	1 (1.9%)
レンサ球菌性肺炎	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
腎盂腎炎	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
気道感染	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
敗血症	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
レンサ球菌感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
歯感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
ウイルス性上気道感染	0	0	-	0	0	0	1 (0.6%)	0	1 (1.9%)
外陰腟真菌感染	0	0	-	0	0	0	1 (0.6%)	1 (0.6%)	0
菌血症	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
真菌感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
真菌性消化管感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
肺感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
メタニューモウイルス感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
ＲＳウイルス感染	0	0	-	2 (3.6%)	2 (3.6%)	0	0	0	0
細菌性尿路感染	0	0	-	1 (1.8%)	1 (1.8%)	0	0	0	0
ウイルス感染	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0
外陰部腟カンジダ症	1 (4.3%)	1 (4.3%)	-	0	0	0	0	0	0

TSFAE22PART1OF2: Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg			8 mg/kg			16 mg/kg		
		Event Onset Within			Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months	Total	≤6 months	>6 months

Keys: TEAE = treatment-emergent adverse event.
[a]Includes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects treated within each window as denominator.

[TSFAE22PART1OF2.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae22.sas] 16MAR2015, 16:20

TSFAE22PART2OF2: Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
Analysis set: all treated	3			237		
Total number of subjects treated within window [a]	3	3	0	237	237	63
Total number of subjects with TEAE of infections/infestations	1 (33.3%)	1 (33.3%)	-	125 (52.7%)	118 (49.8%)	24 (38.1%)
上気道感染	0	0	-	39 (16.5%)	35 (14.8%)	9 (14.3%)
鼻咽頭炎	1 (33.3%)	1 (33.3%)	-	30 (12.7%)	27 (11.4%)	5 (7.9%)
肺炎	0	0	-	18 (7.6%)	15 (6.3%)	3 (4.8%)
副鼻腔炎	0	0	-	11 (4.6%)	11 (4.6%)	1 (1.6%)
尿路感染	1 (33.3%)	1 (33.3%)	-	10 (4.2%)	7 (3.0%)	3 (4.8%)
気管支炎	0	0	-	5 (2.1%)	4 (1.7%)	2 (3.2%)
結膜炎	0	0	-	3 (1.3%)	3 (1.3%)	0
帯状疱疹	0	0	-	8 (3.4%)	7 (3.0%)	1 (1.6%)
大葉性肺炎	0	0	-	3 (1.3%)	3 (1.3%)	0
口腔カンジダ症	0	0	-	6 (2.5%)	6 (2.5%)	0
カンジダ感染	0	0	-	4 (1.7%)	3 (1.3%)	1 (1.6%)
単純ヘルペス	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
感染	0	0	-	3 (1.3%)	3 (1.3%)	0
インフルエンザ	0	0	-	5 (2.1%)	4 (1.7%)	1 (1.6%)
パラインフルエンザウイルス感染	0	0	-	2 (0.8%)	2 (0.8%)	0
咽頭炎	0	0	-	2 (0.8%)	2 (0.8%)	0
鼻炎	0	0	-	2 (0.8%)	2 (0.8%)	0
軟部組織感染	0	0	-	2 (0.8%)	2 (0.8%)	0
水痘	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
蜂巣炎	0	0	-	1 (0.4%)	1 (0.4%)	0
膀胱炎	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
サイトメガロウイルス性脈絡網膜炎	0	0	-	1 (0.4%)	1 (0.4%)	0
医療機器関連感染	0	0	-	1 (0.4%)	1 (0.4%)	0
耳感染	0	0	-	2 (0.8%)	1 (0.4%)	1 (1.6%)
胃腸炎	0	0	-	3 (1.3%)	1 (0.4%)	2 (3.2%)
ウイルス性胃腸炎	0	0	-	1 (0.4%)	1 (0.4%)	0

TSFAE22PART2OF2: Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months
性器感染	0	0	-	1 (0.4%)	1 (0.4%)	0
Ｈ１Ｎ１インフルエンザ	0	0	-	1 (0.4%)	1 (0.4%)	0
麦粒腫	0	0	-	1 (0.4%)	1 (0.4%)	0
下気道感染	0	0	-	1 (0.4%)	1 (0.4%)	0
粘膜感染	0	0	-	1 (0.4%)	1 (0.4%)	0
眼部単純ヘルペス	0	0	-	1 (0.4%)	1 (0.4%)	0
口腔真菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
口腔ヘルペス	0	0	-	1 (0.4%)	1 (0.4%)	0
爪囲炎	0	0	-	1 (0.4%)	1 (0.4%)	1 (1.6%)
レンサ球菌性肺炎	0	0	-	1 (0.4%)	1 (0.4%)	0
腎盂腎炎	0	0	-	1 (0.4%)	0	1 (1.6%)
気道感染	0	0	-	1 (0.4%)	0	1 (1.6%)
敗血症	0	0	-	1 (0.4%)	1 (0.4%)	0
レンサ球菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
歯感染	0	0	-	1 (0.4%)	1 (0.4%)	0
ウイルス性上気道感染	0	0	-	1 (0.4%)	0	1 (1.6%)
外陰腟真菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
菌血症	0	0	-	1 (0.4%)	1 (0.4%)	0
真菌感染	0	0	-	1 (0.4%)	1 (0.4%)	0
真菌性消化管感染	0	0	-	1 (0.4%)	1 (0.4%)	0
肺感染	0	0	-	1 (0.4%)	1 (0.4%)	0
メタニューモウイルス感染	0	0	-	1 (0.4%)	1 (0.4%)	0
ＲＳウイルス感染	0	0	-	2 (0.8%)	2 (0.8%)	0
細菌性尿路感染	0	0	-	1 (0.4%)	1 (0.4%)	0
ウイルス感染	0	0	-	1 (0.4%)	1 (0.4%)	0
外陰部腟カンジダ症	0	0	-	1 (0.4%)	1 (0.4%)	0

Keys: TEAE = treatment-emergent adverse event.
[a]Includes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects treated within each window as denominator.

TSFAE22PART2OF2: Treatment Emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	24 mg/kg			Total		
		Event Onset Within			Event Onset Within	
	Total	≤6 months	>6 months	Total	≤6 months	>6 months

[TSFAE22PART2OF2.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae22.sas] 16MAR2015, 16:20

表 2.7.4-付録-139 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maiximum Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE25: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maiximum Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Analysis set: safety	237		243		281		318		103	
Total number of subjects with Bleeding TEAE	9 (3.8%)	2 (0.8%)	17 (7.0%)	3 (1.2%)	11 (3.9%)	1 (0.4%)	15 (4.7%)	1 (0.3%)	7 (6.8%)	1 (1.0%)
MedDRA system organ class/Preferred term										
血管障害	3 (1.3%)	0	5 (2.1%)	0	5 (1.8%)	0	5 (1.6%)	0	1 (1.0%)	1 (1.0%)
血腫	3 (1.3%)	0	5 (2.1%)	0	5 (1.8%)	0	5 (1.6%)	0	1 (1.0%)	1 (1.0%)
腎および尿路障害	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	4 (1.3%)	0	3 (2.9%)	0
血尿	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	4 (1.3%)	0	3 (2.9%)	0
眼障害	0	0	3 (1.2%)	0	1 (0.4%)	0	2 (0.6%)	0	1 (1.0%)	0
結膜出血	0	0	3 (1.2%)	0	1 (0.4%)	0	2 (0.6%)	0	1 (1.0%)	0
筋骨格系および結合組織障害	0	0	1 (0.4%)	0	0	0	2 (0.6%)	0	0	0
出血性関節症	0	0	1 (0.4%)	0	0	0	2 (0.6%)	0	0	0
胃腸障害	1 (0.4%)	0	2 (0.8%)	0	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0
肛門出血	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0
痔出血	0	0	1 (0.4%)	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	1 (0.4%)	0	4 (1.6%)	1 (0.4%)	2 (0.7%)	0	1 (0.3%)	0	2 (1.9%)	0
喀血	1 (0.4%)	0	3 (1.2%)	0	2 (0.7%)	0	1 (0.3%)	0	2 (1.9%)	0
肺胞出血	1 (0.4%)	0	0	0	0	0	0	0	0	0
肺出血	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
硬膜下血腫	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
神経系障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
くも膜下出血	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0
生殖系および乳房障害	1 (0.4%)	0	0	0	0	0	0	0	0	0

TSFAE25: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maiximum Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
子宮出血	1 (0.4%)	0	0	0	0	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE25.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE25.SAS] 30JUN2016, 10:04

表 2.7.4-付録-140 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE25: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Analysis set: safety	237		243		281		318		103	
Total number of subjects with Bleeding TEAE	21 (8.9%)	2 (0.8%)	27 (11.1%)	4 (1.6%)	27 (9.6%)	1 (0.4%)	38 (11.9%)	2 (0.6%)	16 (15.5%)	1 (1.0%)
MedDRA system organ class/Preferred term										
呼吸器、胸郭および縦隔障害	13 (5.5%)	1 (0.4%)	15 (6.2%)	1 (0.4%)	16 (5.7%)	0	12 (3.8%)	0	7 (6.8%)	0
鼻出血	12 (5.1%)	1 (0.4%)	13 (5.3%)	1 (0.4%)	14 (5.0%)	0	10 (3.1%)	0	5 (4.9%)	0
喀血	1 (0.4%)	0	3 (1.2%)	0	2 (0.7%)	0	2 (0.6%)	0	2 (1.9%)	0
肺胞出血	1 (0.4%)	0	0	0	0	0	0	0	0	0
肺出血	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
胃腸障害	1 (0.4%)	0	4 (1.6%)	0	5 (1.8%)	0	8 (2.5%)	1 (0.3%)	5 (4.9%)	0
直腸出血	0	0	0	0	1 (0.4%)	0	5 (1.6%)	0	4 (3.9%)	0
肛門出血	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0	1 (0.3%)	1 (0.3%)	0	0
血便排泄	0	0	1 (0.4%)	0	0	0	1 (0.3%)	0	0	0
痔出血	0	0	1 (0.4%)	0	0	0	1 (0.3%)	0	0	0
歯肉出血	0	0	0	0	1 (0.4%)	0	0	0	0	0
下部消化管出血	0	0	0	0	1 (0.4%)	0	0	0	0	0
口腔内出血	0	0	1 (0.4%)	0	1 (0.4%)	0	0	0	1 (1.0%)	0
腎および尿路障害	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	6 (1.9%)	1 (0.3%)	3 (2.9%)	0
血尿	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	6 (1.9%)	1 (0.3%)	3 (2.9%)	0
血管障害	3 (1.3%)	0	5 (2.1%)	0	6 (2.1%)	0	6 (1.9%)	0	1 (1.0%)	1 (1.0%)
血腫	3 (1.3%)	0	5 (2.1%)	0	6 (2.1%)	0	6 (1.9%)	0	1 (1.0%)	1 (1.0%)
眼障害	0	0	3 (1.2%)	0	1 (0.4%)	0	3 (0.9%)	0	1 (1.0%)	0
結膜出血	0	0	3 (1.2%)	0	1 (0.4%)	0	3 (0.9%)	0	1 (1.0%)	0
皮膚および皮下組織障害	3 (1.3%)	0	0	0	0	0	3 (0.9%)	0	1 (1.0%)	0
点状出血	2 (0.8%)	0	0	0	0	0	3 (0.9%)	0	1 (1.0%)	0
皮膚出血	1 (0.4%)	0	0	0	0	0	0	0	0	0

TSFAE25: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004				MMY3003+GEN503				MMY1001	
	Vd		DVd		Rd		DRd		DPd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
筋骨格系および結合組織障害	0	0	1 (0.4%)	0	0	0	2 (0.6%)	0	0	0
出血性関節症	0	0	1 (0.4%)	0	0	0	2 (0.6%)	0	0	0
生殖系および乳房障害	1 (0.4%)	0	0	0	2 (0.7%)	0	1 (0.3%)	0	0	0
腟出血	0	0	0	0	2 (0.7%)	0	1 (0.3%)	0	0	0
子宮出血	1 (0.4%)	0	0	0	0	0	0	0	0	0
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
硬膜下血腫	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0
硬膜下出血	0	0	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0
神経系障害	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)	0	0	0	0	0
脳出血	0	0	0	0	1 (0.4%)	0	0	0	0	0
くも膜下出血	1 (0.4%)	1 (0.4%)	0	0	0	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: Anal haemorrhage, Cerebral haemorrhage, Conjunctival haemorrhage, Epistaxis, Gingival bleeding, Haemarthrosis, Haematochezia, Haematoma, Haematuria, Haemoptysis, Haemorrhage subcutaneous, Haemorrhoidal haemorrhage, Lip haemorrhage, Lower gastrointestinal haemorrhage, Mouth haemorrhage, Petechiae, Pulmonary alveolar haemorrhage, Pulmonary haemorrhage, Rectal haemorrhage, Skin haemorrhage, Subarachnoid haemorrhage, Subdural haematoma, Subdural haemorrhage, Urinary bladder haemorrhage, Uterine haemorrhage, Vaginal haemorrhage; the subject is counted only once regardless of the number of events or the number of occurrences.

[TSFAE25.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016_4MSU\RE_MMY_RR_2016_4MSU\PROD\TSFAE25.SAS] 28SEP2016, 08:19

表 2.7.4-付録-141 Summary of Transfusions; All-treated Analysis Set (Study 54767414MMY1005)

TSICM06: Summary of Transfusions; All-treated Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: All-treated	8
Transfusion during treatment	1 (12.5%)
Type of transfusion	
Platelets	1 (12.5%)

Key: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in all-treated population as denominator.

[TSICM06.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSICM06.SAS] 28SEP2016, 04:31

表 2.7.4-付録-142 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE28: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg)		
	All Grades n (%)	Grade 3 or 4 n (%)	Grade 5 n (%)
Analysis set: Safety	8		
Total number of subjects with Treatment-emergent Bleeding Adverse Events	1 (12.5%)	0	0
MedDRA system organ class/Preferred term			
皮膚および皮下組織障害	1 (12.5%)	0	0
皮下出血	1 (12.5%)	0	0

Keys: Vd = bortezomib-dexamethasone.
Note: Percentages calculated with the number of subjects in safety population in 'All Grades' column as denominator.
Note: Adverse events are coded using MedDRA version 18.0.
Note: Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: Anal haemorrhage, Cerebral haemorrhage, Conjunctival haemorrhage, Epistaxis, Gingival bleeding, Haemarthrosis, Haematochezia, Haematoma, Haematuria, Haemoptysis, Haemorrhage subcutaneous, Haemorrhoidal haemorrhage, Lip haemorrhage, Lower gastrointestinal haemorrhage, Mouth haemorrhage, Petechiae, Pulmonary alveolar haemorrhage, Pulmonary haemorrhage, Rectal haemorrhage, Skin haemorrhage, Subarachnoid haemorrhage, Subdural haematoma, Subdural haemorrhage, Urinary bladder haemorrhage, Uterine haemorrhage, Vaginal haemorrhage; the subject is counted only once regardless of the number of events or the number of occurrences.

[TSFAE28.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE28.SAS] 28SEP2016, 04:22

表 2.7.4-付録-143 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class, Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Study 54767414MMY1005)

TSFAE29: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class, Preferred Term and Maximum Toxicity Grade; Safety Analysis Set (Study 54767414MMY1005)

		Vd + Daratumumab (16 mg/kg) Toxicity Grade, n (%)				
	Total	1	2	3	4	5
Analysis set: Safety	8					
Total number of subjects with Treatment-emergent Bleeding Adverse Events	1 (12.5%)	1 (12.5%)	0	0	0	0
MedDRA system organ class/Preferred term						
皮膚および皮下組織障害	1 (12.5%)	1 (12.5%)	0	0	0	0
皮下出血	1 (12.5%)	1 (12.5%)	0	0	0	0

Keys: Vd = bortezomib-dexamethasone.
Note: Percentages in the total column and toxicity grade columns are calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.
Note: Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: Anal haemorrhage, Cerebral haemorrhage, Conjunctival haemorrhage, Epistaxis, Gingival bleeding, Haemarthrosis, Haematochezia, Haematoma, Haematuria, Haemoptysis, Haemorrhage subcutaneous, Haemorrhoidal haemorrhage, Lip haemorrhage, Lower gastrointestinal haemorrhage, Mouth haemorrhage, Petechiae, Pulmonary alveolar haemorrhage, Pulmonary haemorrhage, Rectal haemorrhage, Skin haemorrhage, Subarachnoid haemorrhage, Subdural haematoma, Subdural haemorrhage, Urinary bladder haemorrhage, Uterine haemorrhage, Vaginal haemorrhage; the subject is counted only once regardless of the number of events or the number of occurrences.

[TSFAE29.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE29.SAS] 28SEP2016, 04:23

表 2.7.4-付録-144 Summary of On-study Transfusion; Safety Analysis Set (Study 54767414MMY3003)

TSITRSF01_3003: Summary of On-study Transfusion; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	Number of Subjects	Number of Transfusions	Number of Subjects	Number of Transfusions
Total[a]				
Analysis set: safety	281		283	
Subjects with transfusions	64 (22.8%)	246	54 (19.1%)	172
Type of transfusions				
Whole Blood	1 (0.4%)	2	0	0
Packed Red Blood Cells	63 (22.4%)	189	47 (16.6%)	127
Fresh Frozen Plasma	2 (0.7%)	5	2 (0.7%)	4
Platelets	23 (8.2%)	50	20 (7.1%)	40
Other	0	0	1 (0.4%)	1
Japanese				
Analysis set: safety	15		20	
Subjects with transfusions	2 (13.3%)	8	1 (5.0%)	6
Type of transfusions				
Whole Blood	0	0	0	0
Packed Red Blood Cells	2 (13.3%)	6	1 (5.0%)	6
Fresh Frozen Plasma	0	0	0	0
Platelets	1 (6.7%)	2	0	0
Other	0	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Subjects with transfusions	11 (25.0%)	55	5 (9.8%)	36
Type of transfusions				
Whole Blood	0	0	0	0
Packed Red Blood Cells	11 (25.0%)	46	4 (7.8%)	19
Fresh Frozen Plasma	1 (2.3%)	2	0	0
Platelets	5 (11.4%)	7	3 (5.9%)	17
Other	0	0	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Percentages calculated with the number of subjects in each treatment group as denominator.

[TSITRSF01_3003.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\TSITRSF01_3003.SAS] 30JUN2016, 23:56

表 2.7.4-付録-145 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

TSFAE25_3003: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Total[a]				
Analysis set: safety	281		283	
Total number of subjects with bleeding events	27 (9.6%)	1 (0.4%)	34 (12.0%)	2 (0.7%)
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	16 (5.7%)	0	11 (3.9%)	0
鼻出血	14 (5.0%)	0	9 (3.2%)	0
喀血	2 (0.7%)	0	2 (0.7%)	0
胃腸障害	5 (1.8%)	0	8 (2.8%)	1 (0.4%)
直腸出血	1 (0.4%)	0	5 (1.8%)	0
肛門出血	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
血便排泄	0	0	1 (0.4%)	0
痔出血	0	0	1 (0.4%)	0
歯肉出血	1 (0.4%)	0	0	0
下部消化管出血	1 (0.4%)	0	0	0
口腔内出血	1 (0.4%)	0	0	0
腎および尿路障害	1 (0.4%)	0	5 (1.8%)	1 (0.4%)
血尿	1 (0.4%)	0	5 (1.8%)	1 (0.4%)
血管障害	6 (2.1%)	0	5 (1.8%)	0
血腫	6 (2.1%)	0	5 (1.8%)	0
皮膚および皮下組織障害	0	0	3 (1.1%)	0
点状出血	0	0	3 (1.1%)	0
眼障害	1 (0.4%)	0	2 (0.7%)	0
結膜出血	1 (0.4%)	0	2 (0.7%)	0
筋骨格系および結合組織障害	0	0	2 (0.7%)	0
出血性関節症	0	0	2 (0.7%)	0
生殖系および乳房障害	2 (0.7%)	0	1 (0.4%)	0
腟出血	2 (0.7%)	0	1 (0.4%)	0
傷害、中毒および処置合併症	1 (0.4%)	1 (0.4%)	0	0
硬膜下血腫	1 (0.4%)	1 (0.4%)	0	0
神経系障害	1 (0.4%)	0	0	0
脳出血	1 (0.4%)	0	0	0
Japanese				
Analysis set: safety	15		20	
Total number of subjects with bleeding events	0	0	0	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	0	0	0	0
鼻出血	0	0	0	0
喀血	0	0	0	0
胃腸障害	0	0	0	0
直腸出血	0	0	0	0
肛門出血	0	0	0	0
血便排泄	0	0	0	0
痔出血	0	0	0	0
歯肉出血	0	0	0	0
下部消化管出血	0	0	0	0
口腔内出血	0	0	0	0
腎および尿路障害	0	0	0	0
血尿	0	0	0	0

TSFAE25_3003: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
血管障害	0	0	0	0
血腫	0	0	0	0
皮膚および皮下組織障害	0	0	0	0
点状出血	0	0	0	0
眼障害	0	0	0	0
結膜出血	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0
出血性関節症	0	0	0	0
生殖系および乳房障害	0	0	0	0
腟出血	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
硬膜下血腫	0	0	0	0
神経系障害	0	0	0	0
脳出血	0	0	0	0
East Asian[b]				
Analysis set: safety	44		51	
Total number of subjects with bleeding events	4 (9.1%)	0	3 (5.9%)	0
MedDRA system organ class/Preferred term				
呼吸器、胸郭および縦隔障害	2 (4.5%)	0	3 (5.9%)	0
鼻出血	2 (4.5%)	0	1 (2.0%)	0
喀血	0	0	2 (3.9%)	0
胃腸障害	2 (4.5%)	0	0	0
直腸出血	0	0	0	0
肛門出血	1 (2.3%)	0	0	0
血便排泄	0	0	0	0
痔出血	0	0	0	0
歯肉出血	0	0	0	0
下部消化管出血	0	0	0	0
口腔内出血	1 (2.3%)	0	0	0
腎および尿路障害	0	0	0	0
血尿	0	0	0	0
血管障害	0	0	0	0
血腫	0	0	0	0
皮膚および皮下組織障害	0	0	0	0
点状出血	0	0	0	0
眼障害	1 (2.3%)	0	0	0
結膜出血	1 (2.3%)	0	0	0
筋骨格系および結合組織障害	0	0	0	0
出血性関節症	0	0	0	0
生殖系および乳房障害	0	0	0	0
腟出血	0	0	0	0
傷害、中毒および処置合併症	0	0	0	0
硬膜下血腫	0	0	0	0
神経系障害	0	0	0	0
脳出血	0	0	0	0

TSFAE25_3003: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY3003)

	Rd		DRd	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Key: TEAE = treatment-emergent adverse event.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event.
Note: Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events are reported using MedDRA version 18.0.
Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: Anal haemorrhage, Cerebral haemorrhage, Conjunctival haemorrhage, Epistaxis, Gingival bleeding, Haemarthrosis, Haematochezia, Haematoma, Haematuria, Haemoptysis, Haemorrhage subcutaneous, Haemorrhoidal haemorrhage, Lip haemorrhage, Lower gastrointestinal haemorrhage, Mouth haemorrhage, Petechiae, Pulmonary alveolar haemorrhage, Pulmonary haemorrhage, Rectal haemorrhage, Skin haemorrhage, Subarachnoid haemorrhage, Subdural haematoma, Subdural haemorrhage, Urinary bladder haemorrhage, Uterine haemorrhage, Vaginal haemorrhage; the subject is counted only once regardless of the number of events or the number of occurrences.

[TSFAE25_3003.RTF] [JNJ-54767414\MMY3003\DBR_SBLA_2016_4MSU\RE_JAPAN\PROD\TSFAE25_3003.SAS] 21OCT2016, 23:11

表 2.7.4-付録-146 Transfusions During Treatment; All Treated Analysis Set (Studies MMY2002, GEN501 and MMY1002)

TSFTRNF01: Transfusions During Treatment; All Treated Analysis Set (Studies MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	Number of Transfusions	Number(%) of Subjects	Number of Transfusions	Number(%) of Subjects	Number of Transfusions	Number(%) of Subjects	Number of Transfusions	Number(%) of Subjects	Number of Transfusions	Number(%) of Subjects
Analysis set: all treated		23		55		156		3		237
Transfusions during treatment	5	3 (13.0%)	55	13 (23.6%)	208	48 (30.8%)	2	1 (33.3%)	270	65 (27.4%)
Type of Transfusion										
Red Blood Cells[a]	5	3 (13.0%)	28	8 (14.5%)	134	45 (28.8%)	2	1 (33.3%)	169	57 (24.1%)
Platelets	0	0	26	7 (12.7%)	73	15 (9.6%)	0	0	99	22 (9.3%)
Blood, Whole	0	0	1	1 (1.8%)	1	1 (0.6%)	0	0	2	2 (0.8%)

[a]Red blood cells may include concentrated or packed RBC and erythrocytes.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFTRNF01.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsftrnf01.sas] 09APR2015, 09:49

表 2.7.4-付録-147 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE01_MSCS: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Analysis set: all treated	23		55		156		3		237	
Total number of subjects with Bleeding TEAE	0	0	5 (9.1%)	0	18 (11.5%)	2 (1.3%)	0	0	23 (9.7%)	2 (0.8%)
MedDRA system organ class/Preferred term										
呼吸器、胸郭および縦隔障害	0	0	2 (3.6%)	0	8 (5.1%)	0	0	0	10 (4.2%)	0
鼻出血	0	0	2 (3.6%)	0	8 (5.1%)	0	0	0	10 (4.2%)	0
胃腸障害	0	0	0	0	4 (2.6%)	0	0	0	4 (1.7%)	0
歯肉出血	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
血便排泄	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
口唇出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
血管障害	0	0	1 (1.8%)	0	4 (2.6%)	0	0	0	5 (2.1%)	0
血腫	0	0	1 (1.8%)	0	4 (2.6%)	0	0	0	5 (2.1%)	0
皮膚および皮下組織障害	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
点状出血	0	0	0	0	2 (1.3%)	0	0	0	2 (0.8%)	0
眼障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
結膜出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
傷害、中毒および処置合併症	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
硬膜下血腫	0	0	0	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.4%)	1 (0.4%)
腎および尿路障害	0	0	2 (3.6%)	0	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
血尿	0	0	2 (3.6%)	0	1 (0.6%)	1 (0.6%)	0	0	3 (1.3%)	1 (0.4%)
生殖系および乳房障害	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0
腟出血	0	0	0	0	1 (0.6%)	0	0	0	1 (0.4%)	0

TSFAE01_MSCS: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term and Maximum Toxicity Grade; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg		8 mg/kg		16 mg/kg		24 mg/kg		Total	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4

Keys: TEAE = treatment-emergent adverse event.
Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: Anal haemorrhage, Cerebral haemorrhage, Conjunctival haemorrhage, Epistaxis, Gingival bleeding, Haemarthrosis, Haematochezia, Haematoma, Haematuria, Haemoptysis, Haemorrhage subcutaneous, Haemorrhoidal haemorrhage, Lip haemorrhage, Lower gastrointestinal haemorrhage, Mouth haemorrhage, Petechiae, Pulmonary alveolar haemorrhage, Pulmonary haemorrhage, Rectal haemorrhage, Skin haemorrhage, Subarachnoid haemorrhage, Subdural haematoma, Subdural haemorrhage, Urinary bladder haemorrhage, Uterine haemorrhage, Vaginal haemorrhage; the subject is counted only once regardless of the number of events or the number of occurrences.
Note: Adverse events are reported using MedDRA version 17.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE01_MSCS.RTF] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_JAPAN\PROD\TSFAE01_MSCS.SAS] 04OCT2016, 17:48

表 2.7.4-付録-148 Transfusions During Treatment; All Treated Analysis Population (Study 54767414MMY1002)

TSICM05: Transfusions During Treatment; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab					
	8 mg/kg		16 mg/kg		All groups	
	Number of Transfusions	Number (%) of Subjects	Number of Transfusions	Number (%) of Subjects	Number of Transfusions	Number (%) of Subjects
Analysis set: All Treated Analysis Population		4		5		9
Transfusions during treatment	1	1 (25.0%)	8	1 (20.0%)	9	2 (22.2%)
Type of transfusion						
Packed Red Blood Cells	0	0	2	1 (20.0%)	2	1 (11.1%)
Platelets	1	1 (25.0%)	6	1 (20.0%)	7	2 (22.2%)

Percentages are calculated with the number of subjects in each group as denominator.

[TSICM05.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_CSR\tsicm05.sas] 22FEB2016, 11:04

表 2.7.4-付録-149 Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE25_J: Number of Subjects with 1 or More Treatment-emergent Bleeding Adverse Events by MedDRA System-Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Total number of subjects with Bleeding TEAE	0	0	0

Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE25_J.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_SCS\tsfae25_j.sas] 22JUL2016, 17:57

表 2.7.4-付録-150 Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFAE22A: Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with TEAE with Potential Link to QT Prolongation	7 (3.0%)	4 (1.6%)	5 (1.8%)	17 (5.3%)	4 (3.9%)
MedDRA system organ class / Preferred term					
神経系障害	6 (2.5%)	1 (0.4%)	3 (1.1%)	11 (3.5%)	4 (3.9%)
失神	6 (2.5%)	1 (0.4%)	2 (0.7%)	11 (3.5%)	3 (2.9%)
意識消失	0	0	1 (0.4%)	0	1 (1.0%)
臨床検査	0	1 (0.4%)	1 (0.4%)	6 (1.9%)	0
心電図ＱＴ延長	0	0	1 (0.4%)	6 (1.9%)	0
心電図ＱＴ間隔異常	0	1 (0.4%)	0	0	0
心臓障害	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0
心停止	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
心室性不整脈	0	1 (0.4%)	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Key: TEAE = treatment-emergent adverse event.
Rd is only from MMY3003.
Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: ECG QT Interval Abnormal, ECG QT prolonged, Long QT syndrome, Long QT syndrome congenital, Torsade de pointes, Ventricular tachycardia, Cardiac arrest, Cardiac death, Cardiac fibrillation, Cardio-respiratory arrest, ECG repolarisation abnormality, ECG U-WAVE abnormality, Loss of consciousness, Sudden cardiac death, Sudden death, Syncope, Ventricular arrhythmia, Ventricular fibrillation, Ventricular flutter, Ventricular tachyarrhythmia; the subject is counted only once regardless of the number of events or the number of occurrences.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE22A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFAE22A.SAS] 01JUL2016, 14:47

表 2.7.4-付録-151 Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

TSFAE26A: Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Study 54767414MMY1005)

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: Safety	8
Total number of subjects with TEAE with Potential Link to QT Prolongation	0
MedDRA system organ class / Preferred term	
No data to report	

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: ECG QT Interval Abnormal, ECG QT prolonged, Long QT syndrome, Long QT syndrome congenital, Torsade de pointes, Ventricular tachycardia, Cardiac arrest, Cardiac death, Cardiac fibrillation, Cardio-respiratory arrest, ECG repolarisation abnormality, ECG U-WAVE abnormality, Loss of consciousness, Sudden cardiac death, Sudden death, Syncope, Ventricular arrhythmia, Ventricular fibrillation, Ventricular flutter, Ventricular tachyarrhythmia; the subject is counted only once regardless of the number of events or the number of occurrences.
Note: Percentages calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE26A.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE26A.SAS] 28SEP2016, 04:22

表 2.7.4-付録-152 Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFAE02_MSCS: Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg	8 mg/kg	16 mg/kg	24 mg/kg	Total
Analysis set: all treated	23	55	156	3	237
Total number of subjects with TEAE with Potential Link to QT Prolongation	5 (21.7%)	1 (1.8%)	3 (1.9%)	0	9 (3.8%)
MedDRA system organ class / Preferred term					
臨床検査	5 (21.7%)	0	1 (0.6%)	0	6 (2.5%)
心電図ＱＴ延長	5 (21.7%)	0	1 (0.6%)	0	6 (2.5%)
神経系障害	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
失神	0	1 (1.8%)	1 (0.6%)	0	2 (0.8%)
心臓障害	0	0	1 (0.6%)	0	1 (0.4%)
心肺停止	0	0	1 (0.6%)	0	1 (0.4%)

Keys: TEAE = treatment-emergent adverse event.
Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: ECG QT Interval Abnormal, ECG QT prolonged, Long QT syndrome, Long QT syndrome congenital, Torsade de pointes, Ventricular tachycardia, Cardiac arrest, Cardiac death, Cardiac fibrillation, Cardio-respiratory arrest, ECG repolarisation abnormality, ECG U-WAVE abnormality, Loss of consciousness, Sudden cardiac death, Sudden death, Syncope, Ventricular arrhythmia, Ventricular fibrillation, Ventricular flutter, Ventricular tachyarrhythmia; the subject is counted only once regardless of the number of events or the number of occurrences.
Note: Adverse events are reported using MedDRA version 17.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02_MSCS.RTF] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_JAPAN\PROD\TSFAE02_MSCS.SAS] 16SEP2016, 09:44

表 2.7.4-付録-153 Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

TSFAE22A_J: Number of Subjects with 1 or More Treatment-emergent Adverse Events with Potential Link to QT Prolongation by MedDRA System-Organ Class and Preferred Term; All Treated Analysis Population (Study 54767414MMY1002)

	Daratumumab		
	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9
Total number of subjects with TEAE with Potential Link to QT Prolongation	0	0	0

Note: Includes all subjects who had one or more occurrences of an adverse event that coded to one of the following MedDRA preferred terms: ECG QT Interval Abnormal, ECG QT prolonged, Long QT syndrome, Long QT syndrome congenital, Torsade de pointes, Ventricular tachycardia, Cardiac arrest, Cardiac death, Cardiac fibrillation, Cardio-respiratory arrest, ECG repolarisation abnormality, ECG U-WAVE abnormality, Loss of consciousness, Sudden cardiac death, Sudden death, Syncope, Ventricular arrhythmia, Ventricular fibrillation, Ventricular flutter, Ventricular tachyarrhythmia; the subject is counted only once regardless of the number of events or the number of occurrences.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE22A_J.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_SCS\tsfae22a_j.sas] 22JUL2016, 17:57

表 2.7.4-付録-154 Summary of Secondary Primary Malignancies; Safety Analysis Set
(Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFSPM01: Summary of Secondary Primary Malignancies; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004		MMY3003+GEN503		MMY1001
	Vd	DVd	Rd	DRd	DPd
Analysis set: safety	237	243	281	318	103
Total number of subjects with second primary malignancies	1 (0.4%)	6 (2.5%)	10 (3.6%)	10 (3.1%)	0
Cancer Type/Dictionary-derived Term					
Cutaneous/non-invasive	0	1 (0.4%)	5 (1.8%)	6 (1.9%)	0
基底細胞癌	0	0	2 (0.7%)	2 (0.6%)	0
ボーエン病	0	0	0	1 (0.3%)	0
扁平上皮癌	0	0	3 (1.1%)	2 (0.6%)	0
皮膚有棘細胞癌	0	1 (0.4%)	0	1 (0.3%)	0
Non-cutaneous/invasive	1 (0.4%)	5 (2.1%)	4 (1.4%)	2 (0.6%)	0
胃腺癌	0	0	0	1 (0.3%)	0
結腸腺癌	0	1 (0.4%)	0	0	0
膀胱移行上皮癌	0	0	1 (0.4%)	0	0
乳癌	1 (0.4%)	1 (0.4%)	0	0	0
腸管腺癌	0	0	1 (0.4%)	0	0
乳管内増殖性病変	0	1 (0.4%)	0	0	0
脂肪肉腫	0	1 (0.4%)	0	0	0
肺腺癌	0	0	1 (0.4%)	0	0
皮膚転移	0	0	0	1 (0.3%)	0
前立腺癌	0	0	1 (0.4%)	0	0
移行上皮癌	0	1 (0.4%)	0	0	0
Hematologic malignancies	0	0	1 (0.4%)	2 (0.6%)	0
急性単球性白血病	0	0	0	1 (0.3%)	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.3%)	0
鉄芽球性貧血	0	0	1 (0.4%)	0	0

For studies MMY1001 and GEN503, information on second primary malignancies is captured on the adverse event CRF page and only collected during the adverse event collection period.
Cutaneous/non-invasive includes Squamous cell carcinoma of skin, Squamous cell carcinoma, Basal cell carcinoma, Bowen's disease.
Non-cutaneous/invasive includes Breast cancer, Adenocarcinoma of colon, Transitional cell carcinoma, Intraductal proliferative breast lesion, Liposarcoma, Bladder transitional cell carcinoma, Intestinal adenocarcinoma, Lung adenocarcinoma, Prostate cancer, Adenocarcinoma gastric, Metastases to skin.
Hematologic malignancies includes Sideroblastic anaemia, Acute monocytic leukaemia, Epstein-Barr virus associated lymphoproliferative disorder.

[TSFSPM01.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFSPM01.SAS] 06JUL2016, 09:22

表 2.7.4-付録-155 List of Subjects with Second Primary Malignancies; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

LSFSPM01A: List of Subjects with Second Primary Malignancies; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

					Prior MM Therapy[a]					
Treatment Group	Unique Subject ID	Dictionary-derived Term	Existing Malignancy (Initiation Diagnosis Date)?	Study Day of Diagnosis	PI	IMid	ALKY	ASCT	Treatment	Survival Status at Cut-off
Vd	54767414MMY3004-460016	乳癌	Y(2011)	100	Y	N	Y	N	Surgery	Alive
DVd	54767414MMY3004-360003	結腸腺癌	N	196	Y	Y	Y	Y	Surgery	Alive
	54767414MMY3004-390050	皮膚有棘細胞癌	N	135	Y	Y	Y	Y	Surgery	Alive
	54767414MMY3004-480013	移行上皮癌	N	61	Y	Y	Y	N	Radiotherapy	Alive
	54767414MMY3004-610004	乳管内増殖性病変	N	347	Y	Y	Y	Y	Surgery	Alive
	54767414MMY3004-700019	脂肪肉腫	N	172	Y	N	Y	N	Surgery	Alive
	54767414MMY3004-700028	乳癌	N	32	Y	Y	Y	N	Surgery,Systemic therapy	Alive
Rd	54767414MMY3003-100018	扁平上皮癌	N	396	Y	Y	Y	Y	Surgery	Alive
	54767414MMY3003-320016	膀胱移行上皮癌	N	217	N	Y	Y	Y	Surgery	Alive
	54767414MMY3003-330032	腸管腺癌	N	429	Y	Y	Y	Y	Systemic therapy	Alive
	54767414MMY3003-330046	鉄芽球性貧血	N	115	Y	N	Y	Y		Alive
	54767414MMY3003-340009	肺腺癌	N	109	Y	N	Y	Y	Palliative supportive care	Dead
	54767414MMY3003-440005	扁平上皮癌	N	320	Y	Y	Y	Y	Surgery	Alive
	54767414MMY3003-440051	基底細胞癌	N	3	Y	Y	N	N	Surgery	Alive
	54767414MMY3003-460011	基底細胞癌	N	471	Y	N	Y	Y	Surgery	Alive
	54767414MMY3003-480019	前立腺癌	N	309	Y	Y	Y	Y		Alive
	54767414MMY3003-610003	扁平上皮癌	N	396	Y	Y	Y	Y		Dead
DRd	54767414MMY3003-100006	皮膚有棘細胞癌	Y(2014-05)	154	Y	N	Y	N	Surgery	Alive
			Y(2014-05)	154	Y	N	Y	N	Surgery	Alive
			Y(2014-05)	357	Y	N	Y	N	Surgery	Alive
	54767414MMY3003-100015	基底細胞癌	Y(2016-01-15)	459	Y	Y	Y	Y	Surgery,Radiotherapy	Alive
	54767414MMY3003-100023	基底細胞癌	N	140	Y	Y	Y	N	Surgery	Alive
	54767414MMY3003-101002	急性単球性白血病	N	106	Y	N	Y	Y	Palliative supportive care	Dead
	54767414MMY3003-440014	扁平上皮癌	N	392	Y	Y	Y	Y	Surgery	Alive
	54767414MMY3003-810011	ボーエン病	Y(2005)	179	Y	N	N	N	Surgery	Alive
	54767414MMY3003-810037	エプスタイン・バーウイルス関連リンパ増殖性障害	N	139	N	N	Y	Y	Systemic therapy	Alive
	54767414MMY3003-820002	皮膚転移	N	182	Y	N	Y	N		Dead
	JNJ54767414GEN503-FR01005	胃腺癌		122	Y	N	Y	Y		Alive

LSFSPM01A: List of Subjects with Second Primary Malignancies; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Treatment Group	Unique Subject ID	Dictionary-derived Term	Existing Malignancy (Initiation Diagnosis Date)?	Study Day of Diagnosis	Prior MM Therapy[a]				Treatment	Survival Status at Cut-off
					PI	IMid	ALKY	ASCT		
	JNJ54767414GEN503-US01002	扁平上皮癌		176	Y	Y	N	N		Alive
				316	Y	Y	N	N		Alive

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
[a]PI = proteasome inhibitor; IMid = Immunomodulatory agent; ALKY = alkylating agents; ASCT = autologous stem cell transplant.
For studies MMY1001 and GEN503, information on second primary malignancies is captured on the adverse event CRF page and only collected during the adverse event collection period.

[LSFSPM01A.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\LSFSPM01A.SAS] 13JUN2016, 12:34

表 2.7.4-付録-156 Secondary Primary Malignancy; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

LSFAE01: Secondary Primary Malignancy; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

Study ID	Dose Level	Subject ID	AE Onset Date/ AE End Date	Dictionary-Derived Term (Reported Term for the Adverse Event)	Study Day of Start of AE/ Duration (Days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Therapy Given; Outcome of AE
GEN501	16 mg/kg	501245	2014-01-17/2014-01-23	皮膚癌 (SKIN CARCINOMA)	29/ 7	No/ 2	Not Related/ Dose Not Changed	Not Reported; Recovered/Resolved

[LSFAE01.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\lsfae01.sas] 03APR2015, 12:27

表 2.7.4-付録-157 Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFLAB02PART1OF3: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Vd						DVd					
	Toxicity Grade						Toxicity Grade					
	Total	0	1	2	3	4	Total	0	1	2	3	4
Analysis set: safety	237						243					
Hematology												
WBC low	237	79	107	37			241	27	98	81	31	
(Leukopenia)	(100.0%)	(33.3%)	(45.1%)	(15.6%)	14 (5.9%)	0	(99.2%)	(11.2%)	(40.7%)	(33.6%)	(12.9%)	4 (1.7%)
Hemoglobin low	237		119	71	37		241		119	77	40	
(Anemia)	(100.0%)	10 (4.2%)	(50.2%)	(30.0%)	(15.6%)	0	(99.2%)	5 (2.1%)	(49.4%)	(32.0%)	(16.6%)	0
Platelets low	237		91	39	53	32	240		75	33	69	47
(Thrombocytopenia)	(100.0%)	22 (9.3%)	(38.4%)	(16.5%)	(22.4%)	(13.5%)	(98.8%)	16 (6.7%)	(31.3%)	(13.8%)	(28.8%)	(19.6%)
Neutrophils low	237	85	107	31			241	44	117	41	31	
(Neutropenia)	(100.0%)	(35.9%)	(45.1%)	(13.1%)	13 (5.5%)	1 (0.4%)	(99.2%)	(18.3%)	(48.5%)	(17.0%)	(12.9%)	8 (3.3%)
Lymphocytes low	235		72	82	62		238		45	68	105	
(Lymphopenia)	(99.2%)	11 (4.7%)	(30.6%)	(34.9%)	(26.4%)	8 (3.4%)	(97.9%)	4 (1.7%)	(18.9%)	(28.6%)	(44.1%)	16 (6.7%)
Biochemistry												
ALT high	234	167	62				240	150	79			
	(98.7%)	(71.4%)	(26.5%)	3 (1.3%)	1 (0.4%)	1 (0.4%)	(98.8%)	(62.5%)	(32.9%)	5 (2.1%)	5 (2.1%)	1 (0.4%)
AST high	233	182	47				238	178	55			
	(98.3%)	(78.1%)	(20.2%)	3 (1.3%)	0	1 (0.4%)	(97.9%)	(74.8%)	(23.1%)	2 (0.8%)	2 (0.8%)	1 (0.4%)
Creatinine high	233	135	66	27			240	150	65			
	(98.3%)	(57.9%)	(28.3%)	(11.6%)	3 (1.3%)	2 (0.9%)	(98.8%)	(62.5%)	(27.1%)	20 (8.3%)	4 (1.7%)	1 (0.4%)
Sodium high	233	205					240	196	33			
(Hypernatremia)	(98.3%)	(88.0%)	19 (8.2%)	8 (3.4%)	1 (0.4%)	0	(98.8%)	(81.7%)	(13.8%)	6 (2.5%)	4 (1.7%)	1 (0.4%)
Sodium low	233	169	48				240	157	71			
(Hyponatremia)	(98.3%)	(72.5%)	(20.6%)	0	13 (5.6%)	3 (1.3%)	(98.8%)	(65.4%)	(29.6%)	0	12 (5.0%)	0
Potassium high	232	201					240	205	25			
(Hyperkalemia)	(97.9%)	(86.6%)	21 (9.1%)	9 (3.9%)	1 (0.4%)	0	(98.8%)	(85.4%)	(10.4%)	9 (3.8%)	1 (0.4%)	0
Potassium low	232	198		25			240	171		55		
(Hypokalemia)	(97.9%)	(85.3%)	0	(10.8%)	8 (3.4%)	1 (0.4%)	(98.8%)	(71.3%)	0	(22.9%)	10 (4.2%)	4 (1.7%)
Bilirubin high	233	207					240	203	29			
	(98.3%)	(88.8%)	17 (7.3%)	8 (3.4%)	1 (0.4%)	0	(98.8%)	(84.6%)	(12.1%)	8 (3.3%)	0	0
Alkaline phosphatase high	231	186	43				240	161	73			
	(97.5%)	(80.5%)	(18.6%)	2 (0.9%)	0	0	(98.8%)	(67.1%)	(30.4%)	5 (2.1%)	1 (0.4%)	0

TSFLAB02PART1OF3: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Vd						DVd					
	Toxicity Grade						Toxicity Grade					
	Total	0	1	2	3	4	Total	0	1	2	3	4
Urate high (Hyperuricemia)	230 (97.0%)	167 (72.6%)	53 (23.0%)	0	0	10 (4.3%)	240 (98.8%)	183 (76.3%)	52 (21.7%)	0	0	5 (2.1%)
Corrected calcium high (Hypercalcemia)	235 (99.2%)	161 (68.5%)	58 (24.7%)	8 (3.4%)	5 (2.1%)	3 (1.3%)	241 (99.2%)	178 (73.9%)	40 (16.6%)	11 (4.6%)	3 (1.2%)	9 (3.7%)
Corrected calcium low (Hypocalcemia)	235 (99.2%)	132 (56.2%)	92 (39.1%)	8 (3.4%)	1 (0.4%)	2 (0.9%)	241 (99.2%)	89 (36.9%)	122 (50.6%)	21 (8.7%)	4 (1.7%)	5 (2.1%)
Phosphates low (Hypophosphatemia)	212 (89.5%)	142 (67.0%)	14 (6.6%)	45 (21.2%)	11 (5.2%)	0	234 (96.3%)	138 (59.0%)	15 (6.4%)	59 (25.2%)	22 (9.4%)	0
Magnesium high (Hypermagnesemia)	0	0	0	0	0	0	0	0	0	0	0	0
Magnesium low (Hypomagmesemia)	0	0	0	0	0	0	0	0	0	0	0	0
Albumin low (Hypoalbuminemia)	235 (99.2%)	106 (45.1%)	68 (28.9%)	53 (22.6%)	8 (3.4%)	0	241 (99.2%)	96 (39.8%)	75 (31.1%)	62 (25.7%)	8 (3.3%)	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: WBC = White Blood Cell.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade did not worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLAB02PART1OF3.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFLAB02.SAS] 01JUN2016, 10:43

TSFLAB02PART2OF3: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Rd						DRd					
	Toxicity Grade						Toxicity Grade					
	Total	0	1	2	3	4	Total	0	1	2	3	4
Analysis set: safety	281						318					
Hematology												
WBC low	280		89	97	63		317		60	111	118	
(Leukopenia)	(99.6%)	25 (8.9%)	(31.8%)	(34.6%)	(22.5%)	6 (2.1%)	(99.7%)	10 (3.2%)	(18.9%)	(35.0%)	(37.2%)	18 (5.7%)
Hemoglobin low	281		125	88	58		317		149	115	43	
(Anemia)	(100.0%)	10 (3.6%)	(44.5%)	(31.3%)	(20.6%)	0	(99.7%)	10 (3.2%)	(47.0%)	(36.3%)	(13.6%)	0
Platelets low	280	67	137	32	29		317	49	179	46		
(Thrombocytopenia)	(99.6%)	(23.9%)	(48.9%)	(11.4%)	(10.4%)	15 (5.4%)	(99.7%)	(15.5%)	(56.5%)	(14.5%)	25 (7.9%)	18 (5.7%)
Neutrophils low	280		76	75	91		317		41	94	123	51
(Neutropenia)	(99.6%)	15 (5.4%)	(27.1%)	(26.8%)	(32.5%)	23 (8.2%)	(99.7%)	8 (2.5%)	(12.9%)	(29.7%)	(38.8%)	(16.1%)
Lymphocytes low	279		65	95	94		317		50	92	138	
(Lymphopenia)	(99.3%)	7 (2.5%)	(23.3%)	(34.1%)	(33.7%)	18 (6.5%)	(99.7%)	6 (1.9%)	(15.8%)	(29.0%)	(43.5%)	31 (9.8%)
Biochemistry												
ALT high	276	200	67				314	209	88			
	(98.2%)	(72.5%)	(24.3%)	4 (1.4%)	5 (1.8%)	0	(98.7%)	(66.6%)	(28.0%)	9 (2.9%)	8 (2.5%)	0
AST high	266	216	49				310	244	62			
	(94.7%)	(81.2%)	(18.4%)	1 (0.4%)	0	0	(97.5%)	(78.7%)	(20.0%)	1 (0.3%)	3 (1.0%)	0
Creatinine high	277	175	74				315	203	81			
	(98.6%)	(63.2%)	(26.7%)	20 (7.2%)	4 (1.4%)	4 (1.4%)	(99.1%)	(64.4%)	(25.7%)	28 (8.9%)	3 (1.0%)	0
Sodium high	275	256					315	288				
(Hypernatremia)	(97.9%)	(93.1%)	15 (5.5%)	4 (1.5%)	0	0	(99.1%)	(91.4%)	23 (7.3%)	2 (0.6%)	0	2 (0.6%)
Sodium low	275	211	56				315	236	67			
(Hyponatremia)	(97.9%)	(76.7%)	(20.4%)	0	5 (1.8%)	3 (1.1%)	(99.1%)	(74.9%)	(21.3%)	0	12 (3.8%)	0
Potassium high	275	216	42				315	255	35			
(Hyperkalemia)	(97.9%)	(78.5%)	(15.3%)	15 (5.5%)	1 (0.4%)	1 (0.4%)	(99.1%)	(81.0%)	(11.1%)	13 (4.1%)	8 (2.5%)	4 (1.3%)
Potassium low	275	191		72			315	228		68		
(Hypokalemia)	(97.9%)	(69.5%)	0	(26.2%)	9 (3.3%)	3 (1.1%)	(99.1%)	(72.4%)	0	(21.6%)	17 (5.4%)	2 (0.6%)
Bilirubin high	276	245					313	277				
	(98.2%)	(88.8%)	24 (8.7%)	6 (2.2%)	1 (0.4%)	0	(98.4%)	(88.5%)	25 (8.0%)	9 (2.9%)	2 (0.6%)	0
Alkaline phosphatase high	276	216	52				314	213	90			
	(98.2%)	(78.3%)	(18.8%)	8 (2.9%)	0	0	(98.7%)	(67.8%)	(28.7%)	10 (3.2%)	1 (0.3%)	0
Urate high	268	214	46				309	256	45			
(Hyperuricemia)	(95.4%)	(79.9%)	(17.2%)	0	0	8 (3.0%)	(97.2%)	(82.8%)	(14.6%)	0	0	8 (2.6%)
Corrected calcium high	277	203	64				317	246	61			
(Hypercalcemia)	(98.6%)	(73.3%)	(23.1%)	5 (1.8%)	1 (0.4%)	4 (1.4%)	(99.7%)	(77.6%)	(19.2%)	4 (1.3%)	2 (0.6%)	4 (1.3%)

TSFLAB02PART2OF3: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Rd						DRd					
	Toxicity Grade						Toxicity Grade					
	Total	0	1	2	3	4	Total	0	1	2	3	4
Corrected calcium low (Hypocalcemia)	277 (98.6%)	103 (37.2%)	138 (49.8%)	25 (9.0%)	8 (2.9%)	3 (1.1%)	317 (99.7%)	86 (27.1%)	196 (61.8%)	23 (7.3%)	6 (1.9%)	6 (1.9%)
Phosphates low (Hypophosphatemia)	258 (91.8%)	139 (53.9%)	9 (3.5%)	82 (31.8%)	28 (10.9%)	0	264 (83.0%)	132 (50.0%)	12 (4.5%)	89 (33.7%)	31 (11.7%)	0
Magnesium high (Hypermagnesemia)	0	0	0	0	0	0	0	0	0	0	0	0
Magnesium low (Hypomagmesemia)	0	0	0	0	0	0	0	0	0	0	0	0
Albumin low (Hypoalbuminemia)	277 (98.6%)	118 (42.6%)	97 (35.0%)	58 (20.9%)	4 (1.4%)	0	317 (99.7%)	135 (42.6%)	101 (31.9%)	78 (24.6%)	3 (0.9%)	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: WBC = White Blood Cell.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade did not worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLAB02PART2OF3.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFLAB02.SAS] 01JUN2016, 10:43

TSFLAB02PART3OF3: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd					
		Toxicity Grade				
	Total	0	1	2	3	4
Analysis set: safety	103					
Hematology						
WBC low (Leukopenia)	102 (99.0%)	2 (2.0%)	8 (7.8%)	25 (24.5%)	47 (46.1%)	20 (19.6%)
Hemoglobin low (Anemia)	102 (99.0%)	0	31 (30.4%)	38 (37.3%)	33 (32.4%)	0
Platelets low (Thrombocytopenia)	102 (99.0%)	13 (12.7%)	50 (49.0%)	19 (18.6%)	10 (9.8%)	10 (9.8%)
Neutrophils low (Neutropenia)	102 (99.0%)	1 (1.0%)	7 (6.9%)	10 (9.8%)	37 (36.3%)	47 (46.1%)
Lymphocytes low (Lymphopenia)	102 (99.0%)	1 (1.0%)	12 (11.8%)	15 (14.7%)	47 (46.1%)	27 (26.5%)
Biochemistry						
ALT high	98 (95.1%)	75 (76.5%)	16 (16.3%)	4 (4.1%)	3 (3.1%)	0
AST high	98 (95.1%)	76 (77.6%)	17 (17.3%)	2 (2.0%)	3 (3.1%)	0
Creatinine high	98 (95.1%)	64 (65.3%)	21 (21.4%)	12 (12.2%)	1 (1.0%)	0
Sodium high (Hypernatremia)	98 (95.1%)	94 (95.9%)	4 (4.1%)	0	0	0
Sodium low (Hyponatremia)	98 (95.1%)	57 (58.2%)	30 (30.6%)	0	11 (11.2%)	0
Potassium high (Hyperkalemia)	97 (94.2%)	85 (87.6%)	11 (11.3%)	1 (1.0%)	0	0
Potassium low (Hypokalemia)	97 (94.2%)	71 (73.2%)	0	24 (24.7%)	2 (2.1%)	0
Bilirubin high	98 (95.1%)	84 (85.7%)	8 (8.2%)	4 (4.1%)	2 (2.0%)	0
Alkaline phosphatase high	98 (95.1%)	70 (71.4%)	23 (23.5%)	4 (4.1%)	1 (1.0%)	0
Urate high (Hyperuricemia)	96 (93.2%)	79 (82.3%)	13 (13.5%)	0	0	4 (4.2%)
Corrected calcium high (Hypercalcemia)	98 (95.1%)	67 (68.4%)	19 (19.4%)	2 (2.0%)	1 (1.0%)	9 (9.2%)
Corrected calcium low (Hypocalcemia)	98 (95.1%)	36 (36.7%)	58 (59.2%)	0	3 (3.1%)	1 (1.0%)
Phosphates low (Hypophosphatemia)	97 (94.2%)	63 (64.9%)	3 (3.1%)	21 (21.6%)	10 (10.3%)	0
Magnesium high (Hypermagnesemia)	98 (95.1%)	95 (96.9%)	2 (2.0%)	0	1 (1.0%)	0

TSFLAB02PART3OF3: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001 DPd Toxicity Grade					
	Total	0	1	2	3	4
Magnesium low (Hypomagmesemia)	98 (95.1%)	74 (75.5%)	21 (21.4%)	3 (3.1%)	0	0
Albumin low (Hypoalbuminemia)	98 (95.1%)	42 (42.9%)	32 (32.7%)	22 (22.4%)	2 (2.0%)	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone;
Keys: WBC = White Blood Cell.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade did not worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

表 2.7.4-付録-158 Summary of Worst Toxicity Grade during Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY1005)

TSFLAB02: Summary of Worst Toxicity Grade during Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY1005)

		Vd + Daratumumab (16 mg/kg) Toxicity Grade, n (%)				
	Total	0	1	2	3	4
Analysis set: Safety	8					
Hematology						
WBC low (Leukopenia)	8 (100.0%)	3 (37.5%)	1 (12.5%)	2 (25.0%)	2 (25.0%)	0
Hemoglobin low (Anemia)	8 (100.0%)	0	5 (62.5%)	3 (37.5%)	0	0
Platelets low (Thrombocytopenia)	8 (100.0%)	0	1 (12.5%)	1 (12.5%)	3 (37.5%)	3 (37.5%)
Neutrophils low (Neutropenia)	8 (100.0%)	4 (50.0%)	0	2 (25.0%)	2 (25.0%)	0
Lymphocytes low (Lymphopenia)	8 (100.0%)	1 (12.5%)	0	1 (12.5%)	5 (62.5%)	1 (12.5%)
Biochemistry						
ALT high	8 (100.0%)	5 (62.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
AST high	8 (100.0%)	4 (50.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	0
Creatinine high	8 (100.0%)	6 (75.0%)	2 (25.0%)	0	0	0
Sodium high (Hypernatremia)	8 (100.0%)	7 (87.5%)	1 (12.5%)	0	0	0
Sodium low (Hyponatremia)	8 (100.0%)	4 (50.0%)	4 (50.0%)	0	0	0
Potassium high (Hyperkalemia)	8 (100.0%)	6 (75.0%)	2 (25.0%)	0	0	0
Potassium low (Hypokalemia)	8 (100.0%)	6 (75.0%)	0	0	2 (25.0%)	0
Bilirubin high	8 (100.0%)	6 (75.0%)	1 (12.5%)	1 (12.5%)	0	0
Alkaline phosphatase high	8 (100.0%)	5 (62.5%)	3 (37.5%)	0	0	0
Uric acid high (Hyperuricemia)	8 (100.0%)	8 (100.0%)	0	0	0	0
Corrected calcium high (Hypercalcemia)	8 (100.0%)	8 (100.0%)	0	0	0	0
Corrected calcium low (Hypocalcemia)	8 (100.0%)	2 (25.0%)	6 (75.0%)	0	0	0
Phosphates low (Hypophosphatemia)	8 (100.0%)	5 (62.5%)	0	3 (37.5%)	0	0
Albumin low (Hypoalbuminemia)	8 (100.0%)	2 (25.0%)	6 (75.0%)	0	0	0

Keys: Vd = bortezomib-dexamethasone; WBC = White Blood Cell; AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade did not worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLAB02.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFLAB02.SAS] 28SEP2016, 04:29

表 2.7.4-付録-159 Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY3003)

TSFLAB02_3003: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY3003)

	Rd						DRd					
		Toxicity Grade, n (%)						Toxicity Grade, n (%)				
	Total	0	1	2	3	4	Total	0	1	2	3	4
Total[a]												
Analysis set: safety	281						283					
Hematology												
WBC low	280		89	97	63		282		55	101	102	
(Leukopenia)	(99.6%)	25 (8.9%)	(31.8%)	(34.6%)	(22.5%)	6 (2.1%)	(99.6%)	7 (2.5%)	(19.5%)	(35.8%)	(36.2%)	17 (6.0%)
Hemoglobin low	281		125	88	58		282		133	99	40	
(Anemia)	(100.0%)	10 (3.6%)	(44.5%)	(31.3%)	(20.6%)	0	(99.6%)	10 (3.5%)	(47.2%)	(35.1%)	(14.2%)	0
Platelets low	280	67	137	32	29		282	45	156	42		
(Thrombocytopenia)	(99.6%)	(23.9%)	(48.9%)	(11.4%)	(10.4%)	15 (5.4%)	(99.6%)	(16.0%)	(55.3%)	(14.9%)	22 (7.8%)	17 (6.0%)
Neutrophils low	280		76	75	91		282		38	85	103	49
(Neutropenia)	(99.6%)	15 (5.4%)	(27.1%)	(26.8%)	(32.5%)	23 (8.2%)	(99.6%)	7 (2.5%)	(13.5%)	(30.1%)	(36.5%)	(17.4%)
Lymphocytes low	279		65	95	94		282		47	80	124	
(Lymphopenia)	(99.3%)	7 (2.5%)	(23.3%)	(34.1%)	(33.7%)	18 (6.5%)	(99.6%)	3 (1.1%)	(16.7%)	(28.4%)	(44.0%)	28 (9.9%)
Biochemistry												
ALT high	276	200	67				279	196	69			
	(98.2%)	(72.5%)	(24.3%)	4 (1.4%)	5 (1.8%)	0	(98.6%)	(70.3%)	(24.7%)	7 (2.5%)	7 (2.5%)	0
AST high	266	216	49				275	228	44			
	(94.7%)	(81.2%)	(18.4%)	1 (0.4%)	0	0	(97.2%)	(82.9%)	(16.0%)	1 (0.4%)	2 (0.7%)	0
Creatinine high	277	175	74				280	183	69			
	(98.6%)	(63.2%)	(26.7%)	20 (7.2%)	4 (1.4%)	4 (1.4%)	(98.9%)	(65.4%)	(24.6%)	25 (8.9%)	3 (1.1%)	0
Sodium high	275	256					280	255				
(Hypernatremia)	(97.9%)	(93.1%)	15 (5.5%)	4 (1.5%)	0	0	(98.9%)	(91.1%)	22 (7.9%)	2 (0.7%)	0	1 (0.4%)
Sodium low	275	211	56				280	205	64			
(Hyponatremia)	(97.9%)	(76.7%)	(20.4%)	0	5 (1.8%)	3 (1.1%)	(98.9%)	(73.2%)	(22.9%)	0	11 (3.9%)	0
Potassium high	275	216	42				280	234	34			
(Hyperkalemia)	(97.9%)	(78.5%)	(15.3%)	15 (5.5%)	1 (0.4%)	1 (0.4%)	(98.9%)	(83.6%)	(12.1%)	12 (4.3%)	0	0
Potassium low	275	191		72			280	203		62		
(Hypokalemia)	(97.9%)	(69.5%)	0	(26.2%)	9 (3.3%)	3 (1.1%)	(98.9%)	(72.5%)	0	(22.1%)	14 (5.0%)	1 (0.4%)
Bilirubin high	276	245					278	243				
	(98.2%)	(88.8%)	24 (8.7%)	6 (2.2%)	1 (0.4%)	0	(98.2%)	(87.4%)	25 (9.0%)	8 (2.9%)	2 (0.7%)	0
Alkaline phosphatase	276	216	52				279	193	77			
high	(98.2%)	(78.3%)	(18.8%)	8 (2.9%)	0	0	(98.6%)	(69.2%)	(27.6%)	8 (2.9%)	1 (0.4%)	0

TSFLAB02_3003: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY3003)

	Rd Toxicity Grade, n (%)						DRd Toxicity Grade, n (%)					
	Total	0	1	2	3	4	Total	0	1	2	3	4
Uric acid high (Hyperuricemia)	268 (95.4%)	214 (79.9%)	46 (17.2%)	0	0	8 (3.0%)	274 (96.8%)	228 (83.2%)	38 (13.9%)	0	0	8 (2.9%)
Corrected calcium high (Hypercalcemia)	277 (98.6%)	203 (73.3%)	64 (23.1%)	5 (1.8%)	1 (0.4%)	4 (1.4%)	282 (99.6%)	217 (77.0%)	55 (19.5%)	4 (1.4%)	2 (0.7%)	4 (1.4%)
Corrected calcium low (Hypocalcemia)	277 (98.6%)	103 (37.2%)	138 (49.8%)	25 (9.0%)	8 (2.9%)	3 (1.1%)	282 (99.6%)	82 (29.1%)	168 (59.6%)	22 (7.8%)	5 (1.8%)	5 (1.8%)
Phosphates low (Hypophosphatemia)	258 (91.8%)	139 (53.9%)	9 (3.5%)	82 (31.8%)	28 (10.9%)	0	264 (93.3%)	132 (50.0%)	12 (4.5%)	89 (33.7%)	31 (11.7%)	0
Albumin low (Hypoalbuminemia)	277 (98.6%)	118 (42.6%)	97 (35.0%)	58 (20.9%)	4 (1.4%)	0	282 (99.6%)	122 (43.3%)	86 (30.5%)	72 (25.5%)	2 (0.7%)	0
Japanese												
Analysis set: safety	15						20					
Hematology												
WBC low (Leukopenia)	15 (100.0%)	2 (13.3%)	2 (13.3%)	8 (53.3%)	3 (20.0%)	0	20 (100.0%)	0	2 (10.0%)	11 (55.0%)	6 (30.0%)	1 (5.0%)
Hemoglobin low (Anemia)	15 (100.0%)	1 (6.7%)	5 (33.3%)	7 (46.7%)	2 (13.3%)	0	20 (100.0%)	1 (5.0%)	13 (65.0%)	5 (25.0%)	1 (5.0%)	0
Platelets low (Thrombocytopenia)	15 (100.0%)	3 (20.0%)	8 (53.3%)	2 (13.3%)	1 (6.7%)	1 (6.7%)	20 (100.0%)	5 (25.0%)	11 (55.0%)	3 (15.0%)	0	1 (5.0%)
Neutrophils low (Neutropenia)	15 (100.0%)	1 (6.7%)	4 (26.7%)	6 (40.0%)	2 (13.3%)	2 (13.3%)	20 (100.0%)	0	4 (20.0%)	5 (25.0%)	7 (35.0%)	4 (20.0%)
Lymphocytes low (Lymphopenia)	15 (100.0%)	1 (6.7%)	3 (20.0%)	3 (20.0%)	6 (40.0%)	2 (13.3%)	20 (100.0%)	0	5 (25.0%)	3 (15.0%)	8 (40.0%)	4 (20.0%)
Biochemistry												
ALT high	15 (100.0%)	12 (80.0%)	3 (20.0%)	0	0	0	20 (100.0%)	13 (65.0%)	1 (5.0%)	3 (15.0%)	3 (15.0%)	0
AST high	15 (100.0%)	13 (86.7%)	2 (13.3%)	0	0	0	20 (100.0%)	14 (70.0%)	4 (20.0%)	1 (5.0%)	1 (5.0%)	0
Creatinine high	15 (100.0%)	12 (80.0%)	2 (13.3%)	0	0	1 (6.7%)	20 (100.0%)	13 (65.0%)	6 (30.0%)	1 (5.0%)	0	0
Sodium high (Hypernatremia)	15 (100.0%)	15 (100.0%)	0	0	0	0	20 (100.0%)	20 (100.0%)	0	0	0	0
Sodium low (Hyponatremia)	15 (100.0%)	11 (73.3%)	4 (26.7%)	0	0	0	20 (100.0%)	14 (70.0%)	6 (30.0%)	0	0	0

TSFLAB02_3003: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY3003)

	Rd Toxicity Grade, n (%)						DRd Toxicity Grade, n (%)					
	Total	0	1	2	3	4	Total	0	1	2	3	4
Potassium high (Hyperkalemia)	15 (100.0%)	14 (93.3%)	1 (6.7%)	0	0	0	20 (100.0%)	16 (80.0%)	3 (15.0%)	1 (5.0%)	0	0
Potassium low (Hypokalemia)	15 (100.0%)	12 (80.0%)	0	3 (20.0%)	0	0	20 (100.0%)	15 (75.0%)	0	5 (25.0%)	0	0
Bilirubin high	15 (100.0%)	14 (93.3%)	0	1 (6.7%)	0	0	20 (100.0%)	20 (100.0%)	0	0	0	0
Alkaline phosphatase high	15 (100.0%)	12 (80.0%)	3 (20.0%)	0	0	0	20 (100.0%)	13 (65.0%)	6 (30.0%)	1 (5.0%)	0	0
Uric acid high (Hyperuricemia)	15 (100.0%)	12 (80.0%)	3 (20.0%)	0	0	0	20 (100.0%)	19 (95.0%)	1 (5.0%)	0	0	0
Corrected calcium high (Hypercalcemia)	15 (100.0%)	13 (86.7%)	1 (6.7%)	0	0	1 (6.7%)	20 (100.0%)	18 (90.0%)	1 (5.0%)	0	0	1 (5.0%)
Corrected calcium low (Hypocalcemia)	15 (100.0%)	11 (73.3%)	4 (26.7%)	0	0	0	20 (100.0%)	17 (85.0%)	3 (15.0%)	0	0	0
Phosphates low (Hypophosphatemia)	15 (100.0%)	10 (66.7%)	1 (6.7%)	2 (13.3%)	2 (13.3%)	0	20 (100.0%)	9 (45.0%)	2 (10.0%)	7 (35.0%)	2 (10.0%)	0
Albumin low (Hypoalbuminemia)	15 (100.0%)	8 (53.3%)	5 (33.3%)	2 (13.3%)	0	0	20 (100.0%)	11 (55.0%)	5 (25.0%)	4 (20.0%)	0	0
East Asian[b]												
Analysis set: safety	44						51					
Hematology												
WBC low (Leukopenia)	44 (100.0%)	4 (9.1%)	12 (27.3%)	16 (36.4%)	12 (27.3%)	0	51 (100.0%)	0	9 (17.6%)	20 (39.2%)	18 (35.3%)	4 (7.8%)
Hemoglobin low (Anemia)	44 (100.0%)	2 (4.5%)	15 (34.1%)	16 (36.4%)	11 (25.0%)	0	51 (100.0%)	1 (2.0%)	29 (56.9%)	16 (31.4%)	5 (9.8%)	0
Platelets low (Thrombocytopenia)	44 (100.0%)	6 (13.6%)	23 (52.3%)	6 (13.6%)	7 (15.9%)	2 (4.5%)	51 (100.0%)	10 (19.6%)	29 (56.9%)	7 (13.7%)	2 (3.9%)	3 (5.9%)
Neutrophils low (Neutropenia)	44 (100.0%)	1 (2.3%)	10 (22.7%)	12 (27.3%)	16 (36.4%)	5 (11.4%)	51 (100.0%)	0	7 (13.7%)	12 (23.5%)	22 (43.1%)	10 (19.6%)
Lymphocytes low (Lymphopenia)	44 (100.0%)	4 (9.1%)	9 (20.5%)	16 (36.4%)	10 (22.7%)	5 (11.4%)	51 (100.0%)	1 (2.0%)	11 (21.6%)	14 (27.5%)	18 (35.3%)	7 (13.7%)
Biochemistry												
ALT high	43 (97.7%)	36 (83.7%)	6 (14.0%)	0	1 (2.3%)	0	51 (100.0%)	33 (64.7%)	12 (23.5%)	3 (5.9%)	3 (5.9%)	0

TSFLAB02_3003: Summary of Worst Toxicity Grade During Treatment in Hematology and Biochemistry; Safety Analysis Set (Study 54767414MMY3003)

	Rd Toxicity Grade, n (%)						DRd Toxicity Grade, n (%)					
	Total	0	1	2	3	4	Total	0	1	2	3	4
AST high	43 (97.7%)	38 (88.4%)	5 (11.6%)	0	0	0	51 (100.0%)	36 (70.6%)	13 (25.5%)	1 (2.0%)	1 (2.0%)	0
Creatinine high	43 (97.7%)	34 (79.1%)	7 (16.3%)	1 (2.3%)	0	1 (2.3%)	51 (100.0%)	39 (76.5%)	10 (19.6%)	2 (3.9%)	0	0
Sodium high (Hypernatremia)	43 (97.7%)	42 (97.7%)	1 (2.3%)	0	0	0	51 (100.0%)	47 (92.2%)	4 (7.8%)	0	0	0
Sodium low (Hyponatremia)	43 (97.7%)	30 (69.8%)	11 (25.6%)	0	2 (4.7%)	0	51 (100.0%)	42 (82.4%)	7 (13.7%)	0	2 (3.9%)	0
Potassium high (Hyperkalemia)	43 (97.7%)	41 (95.3%)	2 (4.7%)	0	0	0	51 (100.0%)	46 (90.2%)	4 (7.8%)	1 (2.0%)	0	0
Potassium low (Hypokalemia)	43 (97.7%)	28 (65.1%)	0	15 (34.9%)	0	0	51 (100.0%)	37 (72.5%)	0	12 (23.5%)	2 (3.9%)	0
Bilirubin high	43 (97.7%)	37 (86.0%)	4 (9.3%)	2 (4.7%)	0	0	51 (100.0%)	50 (98.0%)	1 (2.0%)	0	0	0
Alkaline phosphatase high	43 (97.7%)	32 (74.4%)	9 (20.9%)	2 (4.7%)	0	0	51 (100.0%)	37 (72.5%)	12 (23.5%)	2 (3.9%)	0	0
Uric acid high (Hyperuricemia)	42 (95.5%)	36 (85.7%)	6 (14.3%)	0	0	0	51 (100.0%)	47 (92.2%)	3 (5.9%)	0	0	1 (2.0%)
Corrected calcium high (Hypercalcemia)	43 (97.7%)	37 (86.0%)	4 (9.3%)	1 (2.3%)	0	1 (2.3%)	51 (100.0%)	45 (88.2%)	4 (7.8%)	0	0	2 (3.9%)
Corrected calcium low (Hypocalcemia)	43 (97.7%)	20 (46.5%)	21 (48.8%)	2 (4.7%)	0	0	51 (100.0%)	23 (45.1%)	25 (49.0%)	2 (3.9%)	1 (2.0%)	0
Phosphates low (Hypophosphatemia)	42 (95.5%)	25 (59.5%)	2 (4.8%)	13 (31.0%)	2 (4.8%)	0	50 (98.0%)	27 (54.0%)	3 (6.0%)	15 (30.0%)	5 (10.0%)	0
Albumin low (Hypoalbuminemia)	43 (97.7%)	23 (53.5%)	11 (25.6%)	8 (18.6%)	1 (2.3%)	0	51 (100.0%)	29 (56.9%)	11 (21.6%)	11 (21.6%)	0	0

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: WBC = White Blood Cell.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade did not worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. Percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

表 2.7.4-付録-160 Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFLAB03APART1OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Analysis set: safety						237						243
WBC low (Leukopenia)												
Postbaseline												
0	68	10	1	0	0	79	24	3	0	0	0	27
1	71	31	5	0	0	107	70	26	2	0	0	98
2	8	23	6	0	0	37	35	35	11	0	0	81
3	4	5	3	2	0	14	10	13	7	1	0	31
4	0	0	0	0	0	0	0	4	0	0	0	4
Total	151	69	15	2	0	237	139	81	20	1	0	241
Hemoglobin low (Anemia)												
Postbaseline												
0	9	1	0	0	0	10	5	0	0	0	0	5
1	49	65	5	0	0	119	37	75	7	0	0	119
2	5	46	19	1	0	71	4	43	28	2	0	77
3	2	8	23	4	0	37	0	10	22	8	0	40
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	65	120	47	5	0	237	46	128	57	10	0	241
Platelets low (Thrombocytopenia)												
Postbaseline												
0	22	0	0	0	0	22	16	0	0	0	0	16
1	80	11	0	0	0	91	70	5	0	0	0	75
2	30	9	0	0	0	39	27	6	0	0	0	33
3	29	20	3	1	0	53	47	22	0	0	0	69
4	9	18	3	1	1	32	8	30	6	2	1	47
Total	170	58	6	2	1	237	168	63	6	2	1	240
Neutrophils low (Neutropenia)												
Postbaseline												
0	69	14	2	0	0	85	37	7	0	0	0	44
1	58	41	8	0	0	107	70	40	7	0	0	117
2	5	17	8	1	0	31	19	15	7	0	0	41

TSFLAB03APART1OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
3	6	5	2	0	0	13	7	13	9	2	0	31
4	1	0	0	0	0	1	2	4	2	0	0	8
Total	139	77	20	1	0	237	135	79	25	2	0	241
Lymphocytes low (Lymphopenia)												
Postbaseline												
0	11	0	0	0	0	11	4	0	0	0	0	4
1	50	20	1	1	0	72	34	11	0	0	0	45
2	39	38	4	1	0	82	38	29	1	0	0	68
3	16	31	10	5	0	62	32	56	11	6	0	105
4	0	2	5	1	0	8	1	8	5	2	0	16
Total	116	91	20	8	0	235	109	104	17	8	0	238
Leukocytosis												
Postbaseline												
0	237	0	0	0	0	237	241	0	0	0	0	241
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	237	0	0	0	0	237	241	0	0	0	0	241
Hemoglobin increased												
Postbaseline												
0	236	0	0	0	0	236	238	0	0	0	0	238
1	1	0	0	0	0	1	3	0	0	0	0	3
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	237	0	0	0	0	237	241	0	0	0	0	241
Lymphocytes count increased												
Postbaseline												
0	213	0	2	0	0	215	218	0	1	0	0	219
1	0	0	0	0	0	0	0	0	0	0	0	0
2	16	0	4	0	0	20	18	0	1	0	0	19
3	0	0	0	0	0	0	0	0	0	0	0	0

TSFLAB03APART1OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	229	0	6	0	0	235	236	0	2	0	0	238

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: WBC = White Blood Cell.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: Repeat for Platelets low (Thrombocytopenia), Neutrophils low (Neutropenia) and Lymphocytes low (Lymphopenia).

TSFLAB03APART2OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Analysis set: safety						281						318
WBC low (Leukopenia)												
Postbaseline												
0	25	0	0	0	0	25	9	1	0	0	0	10
1	68	18	3	0	0	89	48	12	0	0	0	60
2	47	45	5	0	0	97	76	34	1	0	0	111
3	20	31	12	0	0	63	60	44	13	1	0	118
4	5	0	1	0	0	6	8	7	3	0	0	18
Total	165	94	21	0	0	280	201	98	17	1	0	317
Hemoglobin low (Anemia)												
Postbaseline												
0	10	0	0	0	0	10	9	1	0	0	0	10
1	49	73	3	0	0	125	49	97	3	0	0	149
2	11	49	27	1	0	88	8	73	30	4	0	115
3	3	19	30	6	0	58	2	20	17	4	0	43
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	73	141	60	7	0	281	68	191	50	8	0	317
Platelets low (Thrombocytopenia)												
Postbaseline												
0	65	2	0	0	0	67	49	0	0	0	0	49
1	113	24	0	0	0	137	143	36	0	0	0	179
2	7	24	1	0	0	32	21	24	1	0	0	46
3	10	16	2	1	0	29	9	10	5	1	0	25
4	4	9	2	0	0	15	9	8	0	1	0	18
Total	199	75	5	1	0	280	231	78	6	2	0	317
Neutrophils low (Neutropenia)												
Postbaseline												
0	15	0	0	0	0	15	6	2	0	0	0	8
1	58	17	0	1	0	76	32	8	1	0	0	41
2	40	34	1	0	0	75	64	25	5	0	0	94
3	36	44	10	1	0	91	74	38	8	2	1	123
4	12	9	2	0	0	23	23	22	4	2	0	51
Total	161	104	13	2	0	280	199	95	18	4	1	317

TSFLAB03APART2OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Lymphocytes low (Lymphopenia)												
Postbaseline												
0	7	0	0	0	0	7	6	0	0	0	0	6
1	45	18	2	0	0	65	44	6	0	0	0	50
2	47	44	3	1	0	95	59	31	2	0	0	92
3	22	55	13	4	0	94	33	82	19	4	0	138
4	5	5	6	2	0	18	2	11	8	9	1	31
Total	126	122	24	7	0	279	144	130	29	13	1	317
Leukocytosis												
Postbaseline												
0	280	0	0	0	0	280	317	0	0	0	0	317
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	280	0	0	0	0	280	317	0	0	0	0	317
Hemoglobin increased												
Postbaseline												
0	280	0	0	0	0	280	317	0	0	0	0	317
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	1	0	0	0	0	1	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	281	0	0	0	0	281	317	0	0	0	0	317
Lymphocytes count increased												
Postbaseline												
0	272	0	2	0	0	274	305	0	1	0	0	306
1	0	0	0	0	0	0	0	0	0	0	0	0
2	3	0	2	0	0	5	11	0	0	0	0	11
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	275	0	4	0	0	279	316	0	1	0	0	317

TSFLAB03APART2OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Keys: WBC = White Blood Cell.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: Repeat for Platelets low (Thrombocytopenia), Neutrophils low (Neutropenia) and Lymphocytes low (Lymphopenia).

TSFLAB03APART3OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
Analysis set: safety						103
WBC low (Leukopenia)						
Postbaseline						
0	2	0	0	0	0	2
1	7	1	0	0	0	8
2	12	13	0	0	0	25
3	22	20	5	0	0	47
4	7	9	4	0	0	20
Total	50	43	9	0	0	102
Hemoglobin low (Anemia)						
Postbaseline						
0	0	0	0	0	0	0
1	10	20	1	0	0	31
2	2	16	19	1	0	38
3	0	6	25	2	0	33
4	0	0	0	0	0	0
Total	12	42	45	3	0	102
Platelets low (Thrombocytopenia)						
Postbaseline						
0	12	1	0	0	0	13
1	38	11	1	0	0	50
2	7	12	0	0	0	19
3	1	6	3	0	0	10
4	1	4	3	2	0	10
Total	59	34	7	2	0	102
Neutrophils low (Neutropenia)						
Postbaseline						
0	1	0	0	0	0	1
1	5	2	0	0	0	7
2	5	4	1	0	0	10
3	22	13	2	0	0	37
4	24	17	6	0	0	47
Total	57	36	9	0	0	102

TSFLAB03APART3OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
Lymphocytes low (Lymphopenia)						
Postbaseline						
0	1	0	0	0	0	1
1	10	2	0	0	0	12
2	9	5	0	0	1	15
3	4	26	16	1	0	47
4	1	6	11	9	0	27
Total	25	39	27	10	1	102
Leukocytosis						
Postbaseline						
0	102	0	0	0	0	102
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	102	0	0	0	0	102
Hemoglobin increased						
Postbaseline						
0	102	0	0	0	0	102
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	102	0	0	0	0	102
Lymphocytes count increased						
Postbaseline						
0	92	0	2	0	0	94
1	0	0	0	0	0	0
2	7	0	0	0	0	7
3	1	0	0	0	0	1
4	0	0	0	0	0	0
Total	100	0	2	0	0	102

TSFLAB03APART3OF3: Shift table of baseline versus worst toxicity grade during treatment in hematological test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone;
Keys: WBC = White Blood Cell.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.
Note: Repeat for Platelets low (Thrombocytopenia), Neutrophils low (Neutropenia) and Lymphocytes low (Lymphopenia).

表 2.7.4-付録-161 Shift Table of Baseline versus Worst Toxicity Grade during Treatment; Safety Analysis Set (Study 54767414MMY1005)

TSFLAB01: Shift Table of Baseline versus Worst Toxicity Grade during Treatment; Safety Analysis Set (Study 54767414MMY1005)

	Treatment Group and Evaluation at Baseline					
	Vd + Daratumumab (16 mg/kg)					
	n					
	0	1	2	3	4	Total
WBC low (Leukopenia)						
Postbaseline						
0	3	0	0	0	0	3
1	1	0	0	0	0	1
2	1	1	0	0	0	2
3	1	0	1	0	0	2
4	0	0	0	0	0	0
Total	6	1	1	0	0	8
Hemoglobin low (Anemia)						
Postbaseline						
0	0	0	0	0	0	0
1	4	1	0	0	0	5
2	0	2	1	0	0	3
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	4	3	1	0	0	8
Platelets low (Thrombocytopenia)						
Postbaseline						
0	0	0	0	0	0	0
1	1	0	0	0	0	1
2	1	0	0	0	0	1
3	3	0	0	0	0	3
4	2	1	0	0	0	3
Total	7	1	0	0	0	8
Neutrophils low (Neutropenia)						
Postbaseline						
0	4	0	0	0	0	4
1	0	0	0	0	0	0
2	2	0	0	0	0	2
3	1	1	0	0	0	2
4	0	0	0	0	0	0

TSFLAB01: Shift Table of Baseline versus Worst Toxicity Grade during Treatment; Safety Analysis Set (Study 54767414MMY1005)

	Treatment Group and Evaluation at Baseline					
	Vd + Daratumumab (16 mg/kg)					
	n					
	0	1	2	3	4	Total
Total	7	1	0	0	0	8
Lymphocytes low (Lymphopenia)						
Postbaseline						
0	1	0	0	0	0	1
1	0	0	0	0	0	0
2	1	0	0	0	0	1
3	5	0	0	0	0	5
4	0	1	0	0	0	1
Total	7	1	0	0	0	8
ALT high						
Postbaseline						
0	5	0	0	0	0	5
1	1	0	0	0	0	1
2	1	0	0	0	0	1
3	0	1	0	0	0	1
4	0	0	0	0	0	0
Total	7	1	0	0	0	8
AST high						
Postbaseline						
0	4	0	0	0	0	4
1	2	0	0	0	0	2
2	1	0	0	0	0	1
3	0	1	0	0	0	1
4	0	0	0	0	0	0
Total	7	1	0	0	0	8
Creatinine high						
Postbaseline						
0	6	0	0	0	0	6
1	1	1	0	0	0	2
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	7	1	0	0	0	8

TSFLAB01: Shift Table of Baseline versus Worst Toxicity Grade during Treatment; Safety Analysis Set (Study 54767414MMY1005)

	Treatment Group and Evaluation at Baseline					
	Vd + Daratumumab (16 mg/kg)					
	n					
	0	1	2	3	4	Total
Sodium high (Hypernatremia)						
Postbaseline						
0	7	0	0	0	0	7
1	1	0	0	0	0	1
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	8	0	0	0	0	8
Sodium low (Hyponatremia)						
Postbaseline						
0	4	0	0	0	0	4
1	3	1	0	0	0	4
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	7	1	0	0	0	8
Potassium high (Hyperkalemia)						
Postbaseline						
0	6	0	0	0	0	6
1	2	0	0	0	0	2
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	8	0	0	0	0	8
Potassium low (Hypokalemia)						
Postbaseline						
0	6	0	0	0	0	6
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	1	0	1	0	0	2

TSFLAB01: Shift Table of Baseline versus Worst Toxicity Grade during Treatment; Safety Analysis Set (Study 54767414MMY1005)

	Treatment Group and Evaluation at Baseline					
	Vd + Daratumumab (16 mg/kg)					
	n					
	0	1	2	3	4	Total
4	0	0	0	0	0	0
Total	7	0	1	0	0	8
Bilirubin high						
Postbaseline						
0	6	0	0	0	0	6
1	1	0	0	0	0	1
2	0	0	1	0	0	1
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	7	0	1	0	0	8
Alkaline phosphatase high						
Postbaseline						
0	5	0	0	0	0	5
1	1	2	0	0	0	3
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	6	2	0	0	0	8
Uric acid high (Hyperuricemia)						
Postbaseline						
0	8	0	0	0	0	8
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	8	0	0	0	0	8
Corrected calcium high (Hypercalcemia)						
Postbaseline						
0	8	0	0	0	0	8
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0

TSFLAB01: Shift Table of Baseline versus Worst Toxicity Grade during Treatment; Safety Analysis Set (Study 54767414MMY1005)

	Treatment Group and Evaluation at Baseline					
	Vd + Daratumumab (16 mg/kg)					
	n					
	0	1	2	3	4	Total
4	0	0	0	0	0	0
Total	8	0	0	0	0	8
Corrected calcium low (Hypocalcemia)						
Postbaseline						
0	2	0	0	0	0	2
1	5	1	0	0	0	6
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	7	1	0	0	0	8
Phosphates low (Hypophosphatemia)						
Postbaseline						
0	5	0	0	0	0	5
1	0	0	0	0	0	0
2	2	0	1	0	0	3
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	7	0	1	0	0	8
Albumin low (Hypoalbuminemia)						
Postbaseline						
0	2	0	0	0	0	2
1	5	1	0	0	0	6
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	7	1	0	0	0	8

Keys: Vd = bortezomib-dexamethasone; WBC = White Blood Cell; AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.

表 2.7.4-付録-162 Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Hematological Test; Safety Analysis Set (Study 54767414MMY3003)

TSFLAB03A_3003:Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Hematological Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Total[a]												
WBC low (Leukopenia)												
Postbaseline												
0	25	0	0	0	0	25	6	1	0	0	0	7
1	68	18	3	0	0	89	43	12	0	0	0	55
2	47	45	5	0	0	97	69	31	1	0	0	101
3	20	31	12	0	0	63	48	42	11	1	0	102
4	5	0	1	0	0	6	7	7	3	0	0	17
Total	165	94	21	0	0	280	173	93	15	1	0	282
Hemoglobin low (Anemia)												
Postbaseline												
0	10	0	0	0	0	10	9	1	0	0	0	10
1	49	73	3	0	0	125	40	91	2	0	0	133
2	11	49	27	1	0	88	6	65	24	4	0	99
3	3	19	30	6	0	58	2	20	15	3	0	40
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	73	141	60	7	0	281	57	177	41	7	0	282
Platelets low (Thrombocytopenia)												
Postbaseline												
0	65	2	0	0	0	67	45	0	0	0	0	45
1	113	24	0	0	0	137	127	29	0	0	0	156
2	7	24	1	0	0	32	19	22	1	0	0	42
3	10	16	2	1	0	29	8	8	5	1	0	22
4	4	9	2	0	0	15	9	7	0	1	0	17
Total	199	75	5	1	0	280	208	66	6	2	0	282
Neutrophils low (Neutropenia)												
Postbaseline												
0	15	0	0	0	0	15	5	2	0	0	0	7
1	58	17	0	1	0	76	29	8	1	0	0	38
2	40	34	1	0	0	75	57	23	5	0	0	85
3	36	44	10	1	0	91	59	36	7	0	1	103
4	12	9	2	0	0	23	21	22	4	2	0	49
Total	161	104	13	2	0	280	171	91	17	2	1	282

TSFLAB03A_3003:Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Hematological Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Lymphocytes low (Lymphopenia)												
Postbaseline												
0	7	0	0	0	0	7	3	0	0	0	0	3
1	45	18	2	0	0	65	42	5	0	0	0	47
2	47	44	3	1	0	95	48	31	1	0	0	80
3	22	55	13	4	0	94	25	79	16	4	0	124
4	5	5	6	2	0	18	2	11	7	7	1	28
Total	126	122	24	7	0	279	120	126	24	11	1	282
Japanese												
WBC low (Leukopenia)												
Postbaseline												
0	2	0	0	0	0	2	0	0	0	0	0	0
1	2	0	0	0	0	2	0	2	0	0	0	2
2	1	5	2	0	0	8	6	4	1	0	0	11
3	1	0	2	0	0	3	1	2	3	0	0	6
4	0	0	0	0	0	0	0	0	1	0	0	1
Total	6	5	4	0	0	15	7	8	5	0	0	20
Hemoglobin low (Anemia)												
Postbaseline												
0	1	0	0	0	0	1	1	0	0	0	0	1
1	2	3	0	0	0	5	3	9	1	0	0	13
2	0	3	4	0	0	7	0	4	1	0	0	5
3	0	1	1	0	0	2	0	1	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	3	7	5	0	0	15	4	14	2	0	0	20
Platelets low (Thrombocytopenia)												
Postbaseline												
0	3	0	0	0	0	3	5	0	0	0	0	5
1	5	3	0	0	0	8	8	3	0	0	0	11
2	0	2	0	0	0	2	0	3	0	0	0	3
3	0	1	0	0	0	1	0	0	0	0	0	0
4	1	0	0	0	0	1	0	1	0	0	0	1
Total	9	6	0	0	0	15	13	7	0	0	0	20
Neutrophils low (Neutropenia)												
Postbaseline												
0	1	0	0	0	0	1	0	0	0	0	0	0

TSFLAB03A_3003:Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Hematological Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
1	2	2	0	0	0	4	1	3	0	0	0	4
2	1	5	0	0	0	6	3	1	1	0	0	5
3	0	0	2	0	0	2	4	2	1	0	0	7
4	1	0	1	0	0	2	1	1	2	0	0	4
Total	5	7	3	0	0	15	9	7	4	0	0	20
Lymphocytes low (Lymphopenia)												
Postbaseline												
0	1	0	0	0	0	1	0	0	0	0	0	0
1	2	1	0	0	0	3	5	0	0	0	0	5
2	1	2	0	0	0	3	1	1	1	0	0	3
3	1	5	0	0	0	6	0	7	1	0	0	8
4	0	0	2	0	0	2	0	3	1	0	0	4
Total	5	8	2	0	0	15	6	11	3	0	0	20
East Asian[b]												
WBC low (Leukopenia)												
Postbaseline												
0	4	0	0	0	0	4	0	0	0	0	0	0
1	10	2	0	0	0	12	6	3	0	0	0	9
2	5	9	2	0	0	16	13	6	1	0	0	20
3	4	5	3	0	0	12	7	6	5	0	0	18
4	0	0	0	0	0	0	1	1	2	0	0	4
Total	23	16	5	0	0	44	27	16	8	0	0	51
Hemoglobin low (Anemia)												
Postbaseline												
0	2	0	0	0	0	2	1	0	0	0	0	1
1	5	10	0	0	0	15	4	24	1	0	0	29
2	0	6	10	0	0	16	0	8	8	0	0	16
3	0	3	6	2	0	11	0	2	2	1	0	5
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	7	19	16	2	0	44	5	34	11	1	0	51
Platelets low (Thrombocytopenia)												
Postbaseline												
0	5	1	0	0	0	6	10	0	0	0	0	10
1	15	8	0	0	0	23	24	5	0	0	0	29
2	0	6	0	0	0	6	1	6	0	0	0	7
3	2	4	0	1	0	7	1	0	1	0	0	2

TSFLAB03A_3003:Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Hematological Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
4	1	0	1	0	0	2	0	3	0	0	0	3
Total	23	19	1	1	0	44	36	14	1	0	0	51
Neutrophils low (Neutropenia)												
Postbaseline												
0	1	0	0	0	0	1	0	0	0	0	0	0
1	7	3	0	0	0	10	2	5	0	0	0	7
2	5	7	0	0	0	12	8	3	1	0	0	12
3	5	8	2	1	0	16	11	8	3	0	0	22
4	2	1	2	0	0	5	4	4	2	0	0	10
Total	20	19	4	1	0	44	25	20	6	0	0	51
Lymphocytes low (Lymphopenia)												
Postbaseline												
0	4	0	0	0	0	4	1	0	0	0	0	1
1	6	2	1	0	0	9	10	1	0	0	0	11
2	11	5	0	0	0	16	10	3	1	0	0	14
3	1	8	1	0	0	10	3	12	3	0	0	18
4	1	0	4	0	0	5	0	5	2	0	0	7
Total	23	15	6	0	0	44	24	21	6	0	0	51

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.

表 2.7.4-付録-163 Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

TSFLAB03BPART1OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Analysis set: safety						237						243
ALT high												
Postbaseline												
0	161	6	0	0	0	167	147	3	0	0	0	150
1	50	12	0	0	0	62	61	18	0	0	0	79
2	2	1	0	0	0	3	3	2	0	0	0	5
3	0	1	0	0	0	1	4	1	0	0	0	5
4	1	0	0	0	0	1	1	0	0	0	0	1
Total	214	20	0	0	0	234	216	24	0	0	0	240
AST high												
Postbaseline												
0	178	4	0	0	0	182	168	10	0	0	0	178
1	36	11	0	0	0	47	38	17	0	0	0	55
2	1	2	0	0	0	3	0	2	0	0	0	2
3	0	0	0	0	0	0	2	0	0	0	0	2
4	1	0	0	0	0	1	1	0	0	0	0	1
Total	216	17	0	0	0	233	209	29	0	0	0	238
Creatinine high												
Postbaseline												
0	130	5	0	0	0	135	144	4	2	0	0	150
1	33	30	3	0	0	66	29	34	2	0	0	65
2	5	9	13	0	0	27	5	8	7	0	0	20
3	0	1	1	1	0	3	1	0	3	0	0	4
4	2	0	0	0	0	2	0	0	1	0	0	1
Total	170	45	17	1	0	233	179	46	15	0	0	240
Sodium high (Hypernatremia)												
Postbaseline												
0	202	3	0	0	0	205	191	5	0	0	0	196
1	18	1	0	0	0	19	28	5	0	0	0	33
2	7	1	0	0	0	8	6	0	0	0	0	6

TSFLAB03BPART1OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
3	1	0	0	0	0	1	4	0	0	0	0	4
4	0	0	0	0	0	0	1	0	0	0	0	1
Total	228	5	0	0	0	233	230	10	0	0	0	240
Sodium low (Hyponatremia)												
Postbaseline												
0	159	10	0	0	0	169	148	8	0	1	0	157
1	35	11	0	2	0	48	52	17	0	2	0	71
2	0	0	0	0	0	0	0	0	0	0	0	0
3	7	5	0	1	0	13	6	6	0	0	0	12
4	2	1	0	0	0	3	0	0	0	0	0	0
Total	203	27	0	3	0	233	206	31	0	3	0	240
Potassium high (Hyperkalemia)												
Postbaseline												
0	196	4	1	0	0	201	203	2	0	0	0	205
1	18	3	0	0	0	21	22	3	0	0	0	25
2	8	1	0	0	0	9	8	1	0	0	0	9
3	1	0	0	0	0	1	1	0	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	223	8	1	0	0	232	234	6	0	0	0	240
Potassium low (Hypokalemia)												
Postbaseline												
0	197	0	1	0	0	198	169	0	2	0	0	171
1	0	0	0	0	0	0	0	0	0	0	0	0
2	18	0	7	0	0	25	50	0	5	0	0	55
3	5	0	3	0	0	8	8	0	2	0	0	10
4	1	0	0	0	0	1	3	0	1	0	0	4
Total	221	0	11	0	0	232	230	0	10	0	0	240
Glucose low (Hypoglycemia)												
Postbaseline												
0	210	3	0	0	0	213	200	1	1	0	0	202
1	17	2	0	0	0	19	33	1	0	0	0	34
2	3	0	0	0	0	3	1	0	0	0	0	1
3	0	0	0	0	0	0	0	0	0	0	0	0

TSFLAB03BPART1OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	230	5	0	0	0	235	234	2	1	0	0	237
Bilirubin high												
Postbaseline												
0	204	3	0	0	0	207	198	3	1	1	0	203
1	15	1	1	0	0	17	25	4	0	0	0	29
2	5	1	2	0	0	8	6	2	0	0	0	8
3	1	0	0	0	0	1	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	225	5	3	0	0	233	229	9	1	1	0	240
Alkaline phosphatase high												
Postbaseline												
0	184	2	0	0	0	186	157	4	0	0	0	161
1	36	7	0	0	0	43	64	9	0	0	0	73
2	1	1	0	0	0	2	2	3	0	0	0	5
3	0	0	0	0	0	0	0	1	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	221	10	0	0	0	231	223	17	0	0	0	240
Uric acid high (Hyperuricemia)												
Postbaseline												
0	142	24	0	0	1	167	148	32	0	0	3	183
1	26	27	0	0	0	53	25	24	0	0	3	52
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	3	5	0	0	2	10	1	3	0	0	1	5
Total	171	56	0	0	3	230	174	59	0	0	7	240
Corrected calcium high (Hypercalcemia)												
Postbaseline												
0	157	4	0	0	0	161	178	0	0	0	0	178
1	47	10	0	1	0	58	27	11	0	2	0	40
2	3	3	1	1	0	8	7	2	2	0	0	11
3	2	1	1	1	0	5	1	1	0	1	0	3

TSFLAB03BPART1OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
4	2	1	0	0	0	3	6	2	1	0	0	9
Total	211	19	2	3	0	235	219	16	3	3	0	241
Corrected calcium low (Hypocalcemia)												
Postbaseline												
0	131	1	0	0	0	132	87	0	2	0	0	89
1	85	6	1	0	0	92	119	3	0	0	0	122
2	8	0	0	0	0	8	19	2	0	0	0	21
3	1	0	0	0	0	1	2	2	0	0	0	4
4	2	0	0	0	0	2	4	1	0	0	0	5
Total	227	7	1	0	0	235	231	8	2	0	0	241
Phosphates low (Hypophosphatemia)												
Postbaseline												
0	134	3	4	1	0	142	131	4	3	0	0	138
1	11	0	3	0	0	14	14	1	0	0	0	15
2	39	1	3	2	0	45	55	1	3	0	0	59
3	8	0	2	1	0	11	17	0	3	2	0	22
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	192	4	12	4	0	212	217	6	9	2	0	234
Magnesium high (Hypermagnesemia)												
Postbaseline												
0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0	0	0
Magnesium low (Hypomagmesemia)												
Postbaseline												
0	0	0	0	0	0	0	0	0	0	0	0	0

TSFLAB03BPART1OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3004											
	Treatment Group and Evaluation at Baseline											
	Vd						DVd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0	0	0
Albumin low (Hypoalbuminemia)												
Postbaseline												
0	104	0	2	0	0	106	94	0	2	0	0	96
1	58	8	2	0	0	68	59	13	3	0	0	75
2	37	9	7	0	0	53	33	18	11	0	0	62
3	4	1	3	0	0	8	4	1	1	2	0	8
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	203	18	14	0	0	235	190	32	17	2	0	241
Cpk Increased												
Postbaseline												
0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.

TSFLAB03BPART2OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Analysis set: safety						281						318
ALT high												
Postbaseline												
0	194	6	0	0	0	200	203	5	1	0	0	209
1	53	14	0	0	0	67	79	6	3	0	0	88
2	4	0	0	0	0	4	8	1	0	0	0	9
3	5	0	0	0	0	5	6	1	0	1	0	8
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	256	20	0	0	0	276	296	13	4	1	0	314
AST high												
Postbaseline												
0	196	20	0	0	0	216	231	13	0	0	0	244
1	41	8	0	0	0	49	53	7	1	1	0	62
2	1	0	0	0	0	1	1	0	0	0	0	1
3	0	0	0	0	0	0	2	1	0	0	0	3
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	238	28	0	0	0	266	287	21	1	1	0	310
Creatinine high												
Postbaseline												
0	170	5	0	0	0	175	190	13	0	0	0	203
1	45	25	4	0	0	74	48	32	1	0	0	81
2	6	9	5	0	0	20	5	14	9	0	0	28
3	2	0	2	0	0	4	0	2	1	0	0	3
4	2	2	0	0	0	4	0	0	0	0	0	0
Total	225	41	11	0	0	277	243	61	11	0	0	315
Sodium high (Hypernatremia)												
Postbaseline												
0	256	0	0	0	0	256	286	2	0	0	0	288
1	14	1	0	0	0	15	22	1	0	0	0	23
2	4	0	0	0	0	4	1	1	0	0	0	2
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	2	0	0	0	0	2
Total	274	1	0	0	0	275	311	4	0	0	0	315

TSFLAB03BPART2OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Sodium low (Hyponatremia)												
Postbaseline												
0	198	12	0	1	0	211	222	12	0	2	0	236
1	41	11	0	4	0	56	49	16	0	2	0	67
2	0	0	0	0	0	0	0	0	0	0	0	0
3	4	0	0	1	0	5	5	6	0	1	0	12
4	2	0	0	1	0	3	0	0	0	0	0	0
Total	245	23	0	7	0	275	276	34	0	5	0	315
Potassium high (Hyperkalemia)												
Postbaseline												
0	216	0	0	0	0	216	251	2	2	0	0	255
1	34	7	0	1	0	42	30	5	0	0	0	35
2	13	1	1	0	0	15	9	3	1	0	0	13
3	1	0	0	0	0	1	7	0	0	0	1	8
4	1	0	0	0	0	1	2	0	0	1	1	4
Total	265	8	1	1	0	275	299	10	3	1	2	315
Potassium low (Hypokalemia)												
Postbaseline												
0	190	0	0	1	0	191	227	0	1	0	0	228
1	0	0	0	0	0	0	0	0	0	0	0	0
2	62	0	10	0	0	72	57	0	10	1	0	68
3	7	0	2	0	0	9	14	0	3	0	0	17
4	3	0	0	0	0	3	2	0	0	0	0	2
Total	262	0	12	1	0	275	300	0	14	1	0	315
Glucose low (Hypoglycemia)												
Postbaseline												
0	231	3	0	0	0	234	263	1	0	1	0	265
1	22	4	0	0	0	26	36	2	0	0	0	38
2	1	1	0	0	0	2	3	1	0	0	0	4
3	0	0	0	0	0	0	0	1	0	0	0	1
4	0	0	0	0	0	0	1	0	0	0	0	1
Total	254	8	0	0	0	262	303	5	0	1	0	309
Bilirubin high												

TSFLAB03BPART2OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Postbaseline												
0	245	0	0	0	0	245	277	0	0	0	0	277
1	23	1	0	0	0	24	24	1	0	0	0	25
2	5	1	0	0	0	6	6	2	1	0	0	9
3	1	0	0	0	0	1	2	0	0	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	274	2	0	0	0	276	309	3	1	0	0	313
Alkaline phosphatase high												
Postbaseline												
0	212	4	0	0	0	216	210	3	0	0	0	213
1	46	5	1	0	0	52	80	10	0	0	0	90
2	5	3	0	0	0	8	6	4	0	0	0	10
3	0	0	0	0	0	0	1	0	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	263	12	1	0	0	276	297	17	0	0	0	314
Uric acid high (Hyperuricemia)												
Postbaseline												
0	189	23	0	0	2	214	233	22	0	0	1	256
1	27	17	0	0	2	46	16	28	0	0	1	45
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	5	1	0	0	2	8	2	4	0	0	2	8
Total	221	41	0	0	6	268	251	54	0	0	4	309
Corrected calcium high (Hypercalcemia)												
Postbaseline												
0	196	5	1	1	0	203	236	7	3	0	0	246
1	54	10	0	0	0	64	51	7	2	1	0	61
2	2	0	3	0	0	5	2	2	0	0	0	4
3	1	0	0	0	0	1	1	0	0	1	0	2
4	3	0	0	0	1	4	2	2	0	0	0	4
Total	256	15	4	1	1	277	292	18	5	2	0	317

TSFLAB03BPART2OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Corrected calcium low (Hypocalcemia)												
Postbaseline												
0	102	1	0	0	0	103	86	0	0	0	0	86
1	135	3	0	0	0	138	192	4	0	0	0	196
2	25	0	0	0	0	25	20	2	1	0	0	23
3	8	0	0	0	0	8	5	0	0	1	0	6
4	3	0	0	0	0	3	3	2	0	0	1	6
Total	273	4	0	0	0	277	306	8	1	1	1	317
Phosphates low (Hypophosphatemia)												
Postbaseline												
0	134	0	5	0	0	139	132	0	0	0	0	132
1	8	1	0	0	0	9	11	0	1	0	0	12
2	73	2	7	0	0	82	83	1	4	1	0	89
3	24	0	4	0	0	28	25	0	4	2	0	31
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	239	3	16	0	0	258	251	1	9	3	0	264
Magnesium high (Hypermagnesemia)												
Postbaseline												
0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0	0	0
Magnesium low (Hypomagmesemia)												
Postbaseline												
0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0

TSFLAB03BPART2OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY3003+GEN503											
	Treatment Group and Evaluation at Baseline											
	Rd						DRd					
	0	1	2	3	4	Total	0	1	2	3	4	Total
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0	0	0
Albumin low (Hypoalbuminemia)												
Postbaseline												
0	117	1	0	0	0	118	127	7	1	0	0	135
1	90	4	3	0	0	97	84	11	5	1	0	101
2	34	11	13	0	0	58	52	13	12	1	0	78
3	2	0	2	0	0	4	2	0	1	0	0	3
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	243	16	18	0	0	277	265	31	19	2	0	317
Cpk Increased												
Postbaseline												
0	0	0	0	0	0	0	32	0	0	0	0	32
1	0	0	0	0	0	0	2	1	0	0	0	3
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	34	1	0	0	0	35

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.

TSFLAB03BPART3OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
Analysis set: safety						103
ALT high						
Postbaseline						
0	72	3	0	0	0	75
1	12	4	0	0	0	16
2	1	3	0	0	0	4
3	3	0	0	0	0	3
4	0	0	0	0	0	0
Total	88	10	0	0	0	98
AST high						
Postbaseline						
0	72	4	0	0	0	76
1	10	7	0	0	0	17
2	1	1	0	0	0	2
3	3	0	0	0	0	3
4	0	0	0	0	0	0
Total	86	12	0	0	0	98
Creatinine high						
Postbaseline						
0	52	12	0	0	0	64
1	6	14	1	0	0	21
2	3	5	4	0	0	12
3	0	0	0	0	1	1
4	0	0	0	0	0	0
Total	61	31	5	0	1	98
Sodium high (Hypernatremia)						
Postbaseline						
0	94	0	0	0	0	94
1	3	1	0	0	0	4
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	97	1	0	0	0	98

TSFLAB03BPART3OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
Sodium low (Hyponatremia)						
Postbaseline						
0	51	5	0	1	0	57
1	23	7	0	0	0	30
2	0	0	0	0	0	0
3	2	5	0	4	0	11
4	0	0	0	0	0	0
Total	76	17	0	5	0	98
Potassium high (Hyperkalemia)						
Postbaseline						
0	84	1	0	0	0	85
1	10	1	0	0	0	11
2	1	0	0	0	0	1
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	95	2	0	0	0	97
Potassium low (Hypokalemia)						
Postbaseline						
0	70	0	1	0	0	71
1	0	0	0	0	0	0
2	21	0	3	0	0	24
3	0	0	2	0	0	2
4	0	0	0	0	0	0
Total	91	0	6	0	0	97
Glucose low (Hypoglycemia)						
Postbaseline						
0	84	1	0	0	0	85
1	10	1	1	0	0	12
2	1	0	0	0	0	1
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	95	2	1	0	0	98
Bilirubin high						

TSFLAB03BPART3OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
Postbaseline						
0	83	1	0	0	0	84
1	7	1	0	0	0	8
2	0	3	1	0	0	4
3	2	0	0	0	0	2
4	0	0	0	0	0	0
Total	92	5	1	0	0	98
Alkaline phosphatase high						
Postbaseline						
0	69	1	0	0	0	70
1	20	3	0	0	0	23
2	3	1	0	0	0	4
3	0	1	0	0	0	1
4	0	0	0	0	0	0
Total	92	6	0	0	0	98
Uric acid high (Hyperuricemia)						
Postbaseline						
0	70	7	0	0	2	79
1	7	5	0	0	1	13
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	1	1	0	0	2	4
Total	78	13	0	0	5	96
Corrected calcium high (Hypercalcemia)						
Postbaseline						
0	62	3	1	1	0	67
1	16	2	1	0	0	19
2	2	0	0	0	0	2
3	0	0	0	1	0	1
4	2	2	0	1	4	9
Total	82	7	2	3	4	98

TSFLAB03BPART3OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
Corrected calcium low (Hypocalcemia)						
Postbaseline						
0	33	2	0	0	1	36
1	43	13	1	1	0	58
2	0	0	0	0	0	0
3	1	1	0	0	1	3
4	0	0	0	0	1	1
Total	77	16	1	1	3	98
Phosphates low (Hypophosphatemia)						
Postbaseline						
0	62	0	1	0	0	63
1	2	1	0	0	0	3
2	19	1	1	0	0	21
3	9	0	1	0	0	10
4	0	0	0	0	0	0
Total	92	2	3	0	0	97
Magnesium high (Hypermagnesemia)						
Postbaseline						
0	93	2	0	0	0	95
1	1	1	0	0	0	2
2	0	0	0	0	0	0
3	1	0	0	0	0	1
4	0	0	0	0	0	0
Total	95	3	0	0	0	98
Magnesium low (Hypomagmesemia)						
Postbaseline						
0	70	3	1	0	0	74
1	15	5	1	0	0	21
2	1	2	0	0	0	3
3	0	0	0	0	0	0

TSFLAB03BPART3OF3: Shift table of baseline versus worst toxicity grade during treatment in biochemistry test; Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

	MMY1001					
	Treatment Group and Evaluation at Baseline					
	DPd					
	0	1	2	3	4	Total
4	0	0	0	0	0	0
Total	86	10	2	0	0	98
Albumin low (Hypoalbuminemia)						
Postbaseline						
0	39	1	2	0	0	42
1	22	10	0	0	0	32
2	6	5	11	0	0	22
3	1	1	0	0	0	2
4	0	0	0	0	0	0
Total	68	17	13	0	0	98
Cpk Increased						
Postbaseline						
0	0	0	0	0	0	0
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
Total	0	0	0	0	0	0

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Rd is only from MMY3003.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.

[TSFLAB03BPART3OF3.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\TSFLAB03B.SAS] 01JUN2016, 10:45

表 2.7.4-付録-164 Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Total[a]												
ALT high												
Postbaseline												
0	194	6	0	0	0	200	190	5	1	0	0	196
1	53	14	0	0	0	67	64	5	0	0	0	69
2	4	0	0	0	0	4	6	1	0	0	0	7
3	5	0	0	0	0	5	6	0	0	1	0	7
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	256	20	0	0	0	276	266	11	1	1	0	279
AST high												
Postbaseline												
0	196	20	0	0	0	216	218	10	0	0	0	228
1	41	8	0	0	0	49	37	5	1	1	0	44
2	1	0	0	0	0	1	1	0	0	0	0	1
3	0	0	0	0	0	0	2	0	0	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	238	28	0	0	0	266	258	15	1	1	0	275
Creatinine high												
Postbaseline												
0	170	5	0	0	0	175	170	13	0	0	0	183
1	45	25	4	0	0	74	41	27	1	0	0	69
2	6	9	5	0	0	20	5	12	8	0	0	25
3	2	0	2	0	0	4	0	2	1	0	0	3
4	2	2	0	0	0	4	0	0	0	0	0	0
Total	225	41	11	0	0	277	216	54	10	0	0	280
Sodium high (Hypernatremia)												
Postbaseline												
0	256	0	0	0	0	256	253	2	0	0	0	255
1	14	1	0	0	0	15	21	1	0	0	0	22
2	4	0	0	0	0	4	1	1	0	0	0	2
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	1	0	0	0	0	1
Total	274	1	0	0	0	275	276	4	0	0	0	280

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Sodium low (Hyponatremia)												
Postbaseline												
0	198	12	0	1	0	211	192	11	0	2	0	205
1	41	11	0	4	0	56	46	16	0	2	0	64
2	0	0	0	0	0	0	0	0	0	0	0	0
3	4	0	0	1	0	5	5	5	0	1	0	11
4	2	0	0	1	0	3	0	0	0	0	0	0
Total	245	23	0	7	0	275	243	32	0	5	0	280
Potassium high (Hyperkalemia)												
Postbaseline												
0	216	0	0	0	0	216	232	1	1	0	0	234
1	34	7	0	1	0	42	29	5	0	0	0	34
2	13	1	1	0	0	15	9	3	0	0	0	12
3	1	0	0	0	0	1	0	0	0	0	0	0
4	1	0	0	0	0	1	0	0	0	0	0	0
Total	265	8	1	1	0	275	270	9	1	0	0	280
Potassium low (Hypokalemia)												
Postbaseline												
0	190	0	0	1	0	191	202	0	1	0	0	203
1	0	0	0	0	0	0	0	0	0	0	0	0
2	62	0	10	0	0	72	52	0	9	1	0	62
3	7	0	2	0	0	9	12	0	2	0	0	14
4	3	0	0	0	0	3	1	0	0	0	0	1
Total	262	0	12	1	0	275	267	0	12	1	0	280
Bilirubin high												
Postbaseline												
0	245	0	0	0	0	245	243	0	0	0	0	243
1	23	1	0	0	0	24	24	1	0	0	0	25
2	5	1	0	0	0	6	5	2	1	0	0	8
3	1	0	0	0	0	1	2	0	0	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	274	2	0	0	0	276	274	3	1	0	0	278
Alkaline phosphatase high												
Postbaseline												
0	212	4	0	0	0	216	190	3	0	0	0	193
1	46	5	1	0	0	52	67	10	0	0	0	77
2	5	3	0	0	0	8	4	4	0	0	0	8

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
3	0	0	0	0	0	0	1	0	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	263	12	1	0	0	276	262	17	0	0	0	279
Uric acid high (Hyperuricemia)												
Postbaseline												
0	189	23	0	0	2	214	206	21	0	0	1	228
1	27	17	0	0	2	46	15	22	0	0	1	38
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	5	1	0	0	2	8	2	4	0	0	2	8
Total	221	41	0	0	6	268	223	47	0	0	4	274
Corrected calcium high (Hypercalcemia)												
Postbaseline												
0	196	5	1	1	0	203	207	7	3	0	0	217
1	54	10	0	0	0	64	48	5	2	0	0	55
2	2	0	3	0	0	5	2	2	0	0	0	4
3	1	0	0	0	0	1	1	0	0	1	0	2
4	3	0	0	0	1	4	2	2	0	0	0	4
Total	256	15	4	1	1	277	260	16	5	1	0	282
Corrected calcium low (Hypocalcemia)												
Postbaseline												
0	102	1	0	0	0	103	82	0	0	0	0	82
1	135	3	0	0	0	138	166	2	0	0	0	168
2	25	0	0	0	0	25	20	1	1	0	0	22
3	8	0	0	0	0	8	4	0	0	1	0	5
4	3	0	0	0	0	3	3	1	0	0	1	5
Total	273	4	0	0	0	277	275	4	1	1	1	282
Phosphates low (Hypophosphatemia)												
Postbaseline												
0	134	0	5	0	0	139	132	0	0	0	0	132
1	8	1	0	0	0	9	11	0	1	0	0	12
2	73	2	7	0	0	82	83	1	4	1	0	89
3	24	0	4	0	0	28	25	0	4	2	0	31
4	0	0	0	0	0	0	0	0	0	0	0	0

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Total	239	3	16	0	0	258	251	1	9	3	0	264
Albumin low (Hypoalbuminemia)												
Postbaseline												
0	117	1	0	0	0	118	115	6	1	0	0	122
1	90	4	3	0	0	97	76	5	5	0	0	86
2	34	11	13	0	0	58	51	12	8	1	0	72
3	2	0	2	0	0	4	1	0	1	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	243	16	18	0	0	277	243	23	15	1	0	282
Japanese												
ALT high												
Postbaseline												
0	12	0	0	0	0	12	13	0	0	0	0	13
1	2	1	0	0	0	3	1	0	0	0	0	1
2	0	0	0	0	0	0	3	0	0	0	0	3
3	0	0	0	0	0	0	3	0	0	0	0	3
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	14	1	0	0	0	15	20	0	0	0	0	20
AST high												
Postbaseline												
0	11	2	0	0	0	13	13	1	0	0	0	14
1	2	0	0	0	0	2	4	0	0	0	0	4
2	0	0	0	0	0	0	1	0	0	0	0	1
3	0	0	0	0	0	0	1	0	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	13	2	0	0	0	15	19	1	0	0	0	20
Creatinine high												
Postbaseline												
0	11	1	0	0	0	12	12	1	0	0	0	13
1	2	0	0	0	0	2	3	3	0	0	0	6
2	0	0	0	0	0	0	0	0	1	0	0	1
3	0	0	0	0	0	0	0	0	0	0	0	0
4	1	0	0	0	0	1	0	0	0	0	0	0
Total	14	1	0	0	0	15	15	4	1	0	0	20
Sodium high (Hypernatremia)												
Postbaseline												

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
0	15	0	0	0	0	15	20	0	0	0	0	20
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	15	0	0	0	0	15	20	0	0	0	0	20
Sodium low (Hyponatremia)												
Postbaseline												
0	10	1	0	0	0	11	13	1	0	0	0	14
1	3	1	0	0	0	4	5	1	0	0	0	6
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	13	2	0	0	0	15	18	2	0	0	0	20
Potassium high (Hyperkalemia)												
Postbaseline												
0	14	0	0	0	0	14	16	0	0	0	0	16
1	1	0	0	0	0	1	3	0	0	0	0	3
2	0	0	0	0	0	0	0	1	0	0	0	1
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	15	0	0	0	0	15	19	1	0	0	0	20
Potassium low (Hypokalemia)												
Postbaseline												
0	12	0	0	0	0	12	15	0	0	0	0	15
1	0	0	0	0	0	0	0	0	0	0	0	0
2	3	0	0	0	0	3	5	0	0	0	0	5
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	15	0	0	0	0	15	20	0	0	0	0	20
Bilirubin high												
Postbaseline												
0	14	0	0	0	0	14	20	0	0	0	0	20
1	0	0	0	0	0	0	0	0	0	0	0	0
2	1	0	0	0	0	1	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Total	15	0	0	0	0	15	20	0	0	0	0	20
Alkaline phosphatase high												
Postbaseline												
0	12	0	0	0	0	12	13	0	0	0	0	13
1	2	1	0	0	0	3	6	0	0	0	0	6
2	0	0	0	0	0	0	1	0	0	0	0	1
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	14	1	0	0	0	15	20	0	0	0	0	20
Uric acid high (Hyperuricemia)												
Postbaseline												
0	10	2	0	0	0	12	16	3	0	0	0	19
1	3	0	0	0	0	3	0	1	0	0	0	1
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	13	2	0	0	0	15	16	4	0	0	0	20
Corrected calcium high (Hypercalcemia)												
Postbaseline												
0	12	0	1	0	0	13	16	2	0	0	0	18
1	1	0	0	0	0	1	0	1	0	0	0	1
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	1	0	0	0	0	1	1	0	0	0	0	1
Total	14	0	1	0	0	15	17	3	0	0	0	20
Corrected calcium low (Hypocalcemia)												
Postbaseline												
0	11	0	0	0	0	11	17	0	0	0	0	17
1	4	0	0	0	0	4	3	0	0	0	0	3
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	15	0	0	0	0	15	20	0	0	0	0	20
Phosphates low (Hypophosphatemia)												

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Postbaseline												
0	10	0	0	0	0	10	9	0	0	0	0	9
1	1	0	0	0	0	1	2	0	0	0	0	2
2	2	0	0	0	0	2	5	0	2	0	0	7
3	2	0	0	0	0	2	1	0	1	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	15	0	0	0	0	15	17	0	3	0	0	20
Albumin low (Hypoalbuminemia)												
Postbaseline												
0	8	0	0	0	0	8	11	0	0	0	0	11
1	5	0	0	0	0	5	4	0	1	0	0	5
2	2	0	0	0	0	2	2	1	1	0	0	4
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	15	0	0	0	0	15	17	1	2	0	0	20
East Asian[b]												
ALT high												
Postbaseline												
0	35	1	0	0	0	36	33	0	0	0	0	33
1	5	1	0	0	0	6	12	0	0	0	0	12
2	0	0	0	0	0	0	3	0	0	0	0	3
3	1	0	0	0	0	1	3	0	0	0	0	3
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	41	2	0	0	0	43	51	0	0	0	0	51
AST high												
Postbaseline												
0	33	5	0	0	0	38	34	2	0	0	0	36
1	4	1	0	0	0	5	12	1	0	0	0	13
2	0	0	0	0	0	0	1	0	0	0	0	1
3	0	0	0	0	0	0	1	0	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	37	6	0	0	0	43	48	3	0	0	0	51
Creatinine high												
Postbaseline												
0	33	1	0	0	0	34	38	1	0	0	0	39
1	5	2	0	0	0	7	5	5	0	0	0	10

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
2	1	0	0	0	0	1	1	0	1	0	0	2
3	0	0	0	0	0	0	0	0	0	0	0	0
4	1	0	0	0	0	1	0	0	0	0	0	0
Total	40	3	0	0	0	43	44	6	1	0	0	51
Sodium high (Hypernatremia)												
Postbaseline												
0	42	0	0	0	0	42	47	0	0	0	0	47
1	1	0	0	0	0	1	4	0	0	0	0	4
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	43	0	0	0	0	43	51	0	0	0	0	51
Sodium low (Hyponatremia)												
Postbaseline												
0	26	4	0	0	0	30	38	4	0	0	0	42
1	8	2	0	1	0	11	6	1	0	0	0	7
2	0	0	0	0	0	0	0	0	0	0	0	0
3	1	0	0	1	0	2	1	1	0	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	35	6	0	2	0	43	45	6	0	0	0	51
Potassium high (Hyperkalemia)												
Postbaseline												
0	41	0	0	0	0	41	46	0	0	0	0	46
1	2	0	0	0	0	2	4	0	0	0	0	4
2	0	0	0	0	0	0	0	1	0	0	0	1
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	43	0	0	0	0	43	50	1	0	0	0	51
Potassium low (Hypokalemia)												
Postbaseline												
0	28	0	0	0	0	28	37	0	0	0	0	37
1	0	0	0	0	0	0	0	0	0	0	0	0
2	14	0	1	0	0	15	10	0	2	0	0	12
3	0	0	0	0	0	0	2	0	0	0	0	2
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	42	0	1	0	0	43	49	0	2	0	0	51
Bilirubin high												

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
Postbaseline												
0	37	0	0	0	0	37	50	0	0	0	0	50
1	4	0	0	0	0	4	1	0	0	0	0	1
2	1	1	0	0	0	2	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	42	1	0	0	0	43	51	0	0	0	0	51
Alkaline phosphatase high												
Postbaseline												
0	32	0	0	0	0	32	37	0	0	0	0	37
1	8	1	0	0	0	9	11	1	0	0	0	12
2	1	1	0	0	0	2	2	0	0	0	0	2
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	41	2	0	0	0	43	50	1	0	0	0	51
Uric acid high (Hyperuricemia)												
Postbaseline												
0	29	6	0	0	1	36	43	4	0	0	0	47
1	5	1	0	0	0	6	1	2	0	0	0	3
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	1	0	0	0	1
Total	34	7	0	0	1	42	44	7	0	0	0	51
Corrected calcium high (Hypercalcemia)												
Postbaseline												
0	35	1	1	0	0	37	43	2	0	0	0	45
1	3	1	0	0	0	4	2	1	1	0	0	4
2	1	0	0	0	0	1	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	1	0	0	0	0	1	2	0	0	0	0	2
Total	40	2	1	0	0	43	47	3	1	0	0	51
Corrected calcium low (Hypocalcemia)												
Postbaseline												
0	20	0	0	0	0	20	23	0	0	0	0	23
1	21	0	0	0	0	21	25	0	0	0	0	25

TSFLAB03B_3003: Shift Table of Baseline versus Worst Toxicity Grade During Treatment in Biochemistry Test; Safety Analysis Set (Study 54767414MMY3003)

	Treatment Group and Evaluation at Baseline											
	Rd n						DRd n					
	0	1	2	3	4	Total	0	1	2	3	4	Total
2	2	0	0	0	0	2	2	0	0	0	0	2
3	0	0	0	0	0	0	1	0	0	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	43	0	0	0	0	43	51	0	0	0	0	51
Phosphates low (Hypophosphatemia) Postbaseline												
0	25	0	0	0	0	25	27	0	0	0	0	27
1	2	0	0	0	0	2	3	0	0	0	0	3
2	12	1	0	0	0	13	13	0	2	0	0	15
3	2	0	0	0	0	2	4	0	1	0	0	5
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	41	1	0	0	0	42	47	0	3	0	0	50
Albumin low (Hypoalbuminemia) Postbaseline												
0	22	1	0	0	0	23	29	0	0	0	0	29
1	11	0	0	0	0	11	9	1	1	0	0	11
2	5	0	3	0	0	8	3	5	3	0	0	11
3	1	0	0	0	0	1	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
Total	39	1	3	0	0	43	41	6	4	0	0	51

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
[a] Total summary include all subjects of the group.
[b] East Asian: Japan, Korea and Taiwan.

表 2.7.4-付録-165 Hematology: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFLB01APART1OF3: Hematology: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg					8 mg/kg				
		Toxicity Grade					Toxicity Grade			
	Total	1	2	3	4	Total	1	2	3	4
Analysis set: all treated	23					55				
WBC low (Leukopenia)	23 (100.0%)	2 (8.7%)	6 (26.1%)	2 (8.7%)	0	55 (100.0%)	8 (14.5%)	11 (20.0%)	8 (14.5%)	2 (3.6%)
Hemoglobin low (Anemia)	23 (100.0%)	5 (21.7%)	8 (34.8%)	2 (8.7%)	0	55 (100.0%)	2 (3.6%)	11 (20.0%)	11 (20.0%)	0
Platelets low (Thrombocytopenia)	23 (100.0%)	4 (17.4%)	3 (13.0%)	2 (8.7%)	0	55 (100.0%)	13 (23.6%)	4 (7.3%)	6 (10.9%)	8 (14.5%)
Neutrophils low (Neutropenia)	22 (95.7%)	1 (4.5%)	5 (22.7%)	1 (4.5%)	0	55 (100.0%)	7 (12.7%)	11 (20.0%)	4 (7.3%)	4 (7.3%)
Lymphocytes low (Lymphopenia)	22 (95.7%)	1 (4.5%)	2 (9.1%)	9 (40.9%)	4 (18.2%)	55 (100.0%)	4 (7.3%)	8 (14.5%)	11 (20.0%)	16 (29.1%)

Keys: WBC = White Blood Cell

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0.3

Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade didn't worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLB01APART1OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb01a.sas] 16MAR2015, 16:19

TSFLB01APART2OF3: Hematology: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg					24 mg/kg				
		Toxicity Grade					Toxicity Grade			
	Total	1	2	3	4	Total	1	2	3	4
Analysis set: all treated	156					3				
WBC low (Leukopenia)	156 (100.0%)	27 (17.3%)	33 (21.2%)	26 (16.7%)	3 (1.9%)	3 (100.0%)	1 (33.3%)	1 (33.3%)	0	-
Hemoglobin low (Anemia)	156 (100.0%)	10 (6.4%)	28 (17.9%)	30 (19.2%)	0	3 (100.0%)	0	0	0	-
Platelets low (Thrombocytopenia)	155 (99.4%)	29 (18.7%)	17 (11.0%)	15 (9.7%)	13 (8.4%)	3 (100.0%)	0	0	0	-
Neutrophils low (Neutropenia)	156 (100.0%)	26 (16.7%)	34 (21.8%)	25 (16.0%)	7 (4.5%)	3 (100.0%)	2 (66.7%)	0	0	-
Lymphocytes low (Lymphopenia)	156 (100.0%)	16 (10.3%)	35 (22.4%)	46 (29.5%)	15 (9.6%)	3 (100.0%)	0	1 (33.3%)	1 (33.3%)	-

Keys: WBC = White Blood Cell
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0.3
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade didn't worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLB01APART2OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb01a.sas] 16MAR2015, 16:19

TSFLB01APART3OF3: Hematology: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total				
		Toxicity Grade			
	Total	1	2	3	4
Analysis set: all treated	237				
WBC low (Leukopenia)	237 (100.0%)	38 (16.0%)	51 (21.5%)	36 (15.2%)	5 (2.1%)
Hemoglobin low (Anemia)	237 (100.0%)	17 (7.2%)	47 (19.8%)	43 (18.1%)	0
Platelets low (Thrombocytopenia)	236 (99.6%)	46 (19.5%)	24 (10.2%)	23 (9.7%)	21 (8.9%)
Neutrophils low (Neutropenia)	236 (99.6%)	36 (15.3%)	50 (21.2%)	30 (12.7%)	11 (4.7%)
Lymphocytes low (Lymphopenia)	236 (99.6%)	21 (8.9%)	46 (19.5%)	67 (28.4%)	35 (14.8%)

Keys: WBC = White Blood Cell
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0.3
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade didn't worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLB01APART3OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb01a.sas] 16MAR2015, 16:19

表 2.7.4-付録-166 Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Creatinine (umol/L)							
Daratumumab 8 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	4 (100.0%)	0	0	0	0	0	4
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	4 (80.0%)	0	0	0	0	0	4
Grade 2	0	0	1 (20.0%)	0	0	0	1
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	1	0	0	0	5
Hemoglobin (g/L)							
Daratumumab 8 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0
Grade 2	0	2 (50.0%)	1 (25.0%)	0	0	0	3
Grade 3	0	1 (25.0%)	0	0	0	0	1
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	0	3	1	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0
Grade 2	1 (20.0%)	1 (20.0%)	2 (40.0%)	0	0	0	4
Grade 3	0	1 (20.0%)	0	0	0	0	1
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	1	2	2	0	0	0	5

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Platelets (x10E9/L)							
Daratumumab 8 mg/kg							
Grade 0	3 (75.0%)	0	0	0	0	0	3
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	1 (25.0%)	0	0	0	0	1
Unknown	0	0	0	0	0	0	0
Total	3	1	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	2 (40.0%)	0	0	0	0	0	2
Grade 1	0	2 (40.0%)	0	0	0	0	2
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	1 (20.0%)	0	0	0	0	1
Unknown	0	0	0	0	0	0	0
Total	2	3	0	0	0	0	5
Leukocytes (x10E9/L)							
Daratumumab 8 mg/kg							
Grade 0	2 (50.0%)	0	0	0	0	0	2
Grade 1	0	0	0	0	0	0	0
Grade 2	1 (25.0%)	0	1 (25.0%)	0	0	0	2
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	3	0	1	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0
Grade 2	1 (20.0%)	0	0	0	0	0	1
Grade 3	2 (40.0%)	0	1 (20.0%)	1 (20.0%)	0	0	4
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	3	0	1	1	0	0	5
Neutrophils (x10E9/L)							
Daratumumab 8 mg/kg							

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Grade 0	1 (25.0%)	0	0	0	0	0	1
Grade 1	0	0	0	0	0	0	0
Grade 2	2 (50.0%)	0	0	1 (25.0%)	0	0	3
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	3	0	0	1	0	0	4
Daratumumab 16 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0
Grade 2	0	1 (20.0%)	0	0	0	0	1
Grade 3	3 (60.0%)	0	1 (20.0%)	0	0	0	4
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	3	1	1	0	0	0	5
Lymphocytes (x10E9/L) Increase							
Daratumumab 8 mg/kg							
Grade 0	3 (75.0%)	0	0	0	0	0	3
Grade 1	0	0	0	0	0	0	0
Grade 2	1 (25.0%)	0	0	0	0	0	1
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	5 (100.0%)	0	0	0	0	0	5
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5
Lymphocytes (x10E9/L) Decrease							
Daratumumab 8 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Grade 2	2 (50.0%)	0	0	0	0	0	2
Grade 3	0	0	0	0	0	0	0
Grade 4	1 (25.0%)	0	0	1 (25.0%)	0	0	2
Unknown	0	0	0	0	0	0	0
Total	3	0	0	1	0	0	4
Daratumumab 16 mg/kg							
Grade 0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	2 (40.0%)	0	0	0	0	0	2
Grade 4	1 (20.0%)	1 (20.0%)	1 (20.0%)	0	0	0	3
Unknown	0	0	0	0	0	0	0
Total	3	1	1	0	0	0	5
Alanine Aminotransferase (U/L)							
Daratumumab 8 mg/kg							
Grade 0	3 (75.0%)	0	0	0	0	0	3
Grade 1	1 (25.0%)	0	0	0	0	0	1
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	4 (80.0%)	0	0	0	0	0	4
Grade 1	1 (20.0%)	0	0	0	0	0	1
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5
Aspartate Aminotransferase (U/L)							
Daratumumab 8 mg/kg							
Grade 0	2 (50.0%)	0	0	0	0	0	2
Grade 1	0	2 (50.0%)	0	0	0	0	2
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	2	2	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	3 (60.0%)	0	0	0	0	0	3
Grade 1	2 (40.0%)	0	0	0	0	0	2
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5
Bilirubin High							
Daratumumab 8 mg/kg							
Grade 0	4 (100.0%)	0	0	0	0	0	4
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	5 (100.0%)	0	0	0	0	0	5
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5
Urate High							
Daratumumab 8 mg/kg							
Grade 0	4 (100.0%)	0	0	0	0	0	4
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Total	4	0	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	4 (80.0%)	0	0	0	0	0	4
Grade 1	1 (20.0%)	0	0	0	0	0	1
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5
Corrected Calcium High							
Daratumumab 8 mg/kg							
Grade 0	4 (100.0%)	0	0	0	0	0	4
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	0	0	0	0	4
Daratumumab 16 mg/kg							
Grade 0	5 (100.0%)	0	0	0	0	0	5
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5
Corrected Calcium Low							
Daratumumab 8 mg/kg							
Grade 0	2 (50.0%)	0	0	0	0	0	2
Grade 1	2 (50.0%)	0	0	0	0	0	2
Grade 2	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	4	0	0	0	0	0	4

TSFLAB01_J: Shifts in Laboratory: Baseline Versus Worst Grade; All Treated Analysis Population (Study 54767414MMY1002)

	Baseline Toxicity Grade						
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Unknown	Total
Daratumumab 16 mg/kg							
Grade 0	2 (40.0%)	0	0	0	0	0	2
Grade 1	2 (40.0%)	0	0	0	0	0	2
Grade 2	1 (20.0%)	0	0	0	0	0	1
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Total	5	0	0	0	0	0	5

[TSFLAB01_J.rtf] [JNJ-54767414\54767414MMY1002\DBR_CSR\RE_SCS\tsflab01_j.sas] 27JUL2016, 18:28

表 2.7.4-付録-167 Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFLB04PART1OF3: Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Analysis set: all treated						23						55
Worst grade during treatment												
WBC low (Leukopenia)												
Grade 0	11	1	0	-	-	12	10	2	1	-	-	13
Grade 1	2	0	0	-	-	2	8	9	0	-	-	17
Grade 2	3	3	1	-	-	7	7	4	4	-	-	15
Grade 3	0	0	2	-	-	2	2	4	2	-	-	8
Grade 4	0	0	0	-	-	0	1	1	0	-	-	2
Total	16	4	3	-	-	23	28	20	7	-	-	55
Hemoglobin low (Anemia)												
Grade 0	0	0	0	-	-	0	2	0	0	0	-	2
Grade 1	5	2	0	-	-	7	2	15	1	0	-	18
Grade 2	1	7	6	-	-	14	1	10	11	1	-	23
Grade 3	0	2	0	-	-	2	0	4	7	1	-	12
Grade 4	0	0	0	-	-	0	0	0	0	0	-	0
Total	6	11	6	-	-	23	5	29	19	2	-	55
Platelets low (Thrombocytopenia)												
Grade 0	5	0	-	-	-	5	14	0	0	0	-	14
Grade 1	4	9	-	-	-	13	13	8	0	0	-	21
Grade 2	1	2	-	-	-	3	1	3	2	0	-	6
Grade 3	1	1	-	-	-	2	1	1	4	0	-	6
Grade 4	0	0	-	-	-	0	0	3	3	2	-	8
Total	11	12	-	-	-	23	29	15	9	2	-	55
Neutrophils low (Neutropenia)												
Grade 0	10	1	1	-	-	12	12	2	1	0	-	15
Grade 1	1	3	0	-	-	4	7	8	1	0	-	16
Grade 2	1	4	0	-	-	5	6	5	2	2	-	15
Grade 3	0	0	1	-	-	1	3	1	0	1	-	5
Grade 4	0	0	0	-	-	0	3	1	0	0	-	4
Total	12	8	2	-	-	22	31	17	4	3	-	55
Lymphocytes low (Lymphopenia)												
Grade 0	4	0	0	0	-	4	3	0	0	0	0	3
Grade 1	1	0	0	0	-	1	4	1	0	0	0	5
Grade 2	1	1	1	0	-	3	7	1	6	1	0	15

TSFLB04PART1OF3: Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 3	2	3	4	1	-	10	2	4	5	4	0	15
Grade 4	0	0	1	3	-	4	2	3	7	4	1	17
Total	8	4	6	4	-	22	18	9	18	9	1	55
Leukocytosis												
Grade 0	23	-	-	-	-	23	55	-	-	-	-	55
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	23	-	-	-	-	23	55	-	-	-	-	55
Hemoglobin increased												
Grade 0	23	-	-	-	-	23	55	-	-	-	-	55
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	23	-	-	-	-	23	55	-	-	-	-	55
Lymphocytes count increased												
Grade 0	22	-	-	-	-	22	52	-	-	-	-	52
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	3	-	-	-	-	3
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	22	-	-	-	-	22	55	-	-	-	-	55

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0. Grade 0 means normal.
For each parameter, a subject is included if both baseline and post-baseline values are available.

[TSFLB04PART1OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb04.sas] 16MAR2015, 16:19

TSFLB04PART2OF3: Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Analysis set: all treated						156						3
Worst grade during treatment												
WBC low (Leukopenia)												
Grade 0	27	3	1	0	-	31	1	0	-	-	-	1
Grade 1	27	19	4	0	-	50	1	0	-	-	-	1
Grade 2	13	20	11	1	-	45	0	1	-	-	-	1
Grade 3	7	14	5	1	-	27	0	0	-	-	-	0
Grade 4	2	1	0	0	-	3	0	0	-	-	-	0
Total	76	57	21	2	-	156	2	1	-	-	-	3
Hemoglobin low (Anemia)												
Grade 0	6	0	0	0	-	6	-	0	0	-	-	0
Grade 1	10	36	3	0	-	49	-	2	0	-	-	2
Grade 2	1	27	35	2	-	65	-	0	1	-	-	1
Grade 3	0	7	23	6	-	36	-	0	0	-	-	0
Grade 4	0	0	0	0	-	0	-	0	0	-	-	0
Total	17	70	61	8	-	156	-	2	1	-	-	3
Platelets low (Thrombocytopenia)												
Grade 0	50	0	0	0	-	50	2	0	-	-	-	2
Grade 1	29	29	0	0	-	58	0	1	-	-	-	1
Grade 2	3	14	1	0	-	18	0	0	-	-	-	0
Grade 3	2	9	4	1	-	16	0	0	-	-	-	0
Grade 4	2	8	2	1	-	13	0	0	-	-	-	0
Total	86	60	7	2	-	155	2	1	-	-	-	3
Neutrophils low (Neutropenia)												
Grade 0	31	6	0	0	-	37	1	-	-	-	-	1
Grade 1	26	16	4	0	-	46	2	-	-	-	-	2
Grade 2	18	16	7	0	-	41	0	-	-	-	-	0
Grade 3	13	9	3	0	-	25	0	-	-	-	-	0
Grade 4	1	3	2	1	-	7	0	-	-	-	-	0
Total	89	50	16	1	-	156	3	-	-	-	-	3
Lymphocytes low (Lymphopenia)												
Grade 0	12	0	0	0	-	12	-	0	0	0	-	0
Grade 1	16	12	0	0	-	28	-	0	0	0	-	0
Grade 2	13	22	11	1	-	47	-	1	0	0	-	1
Grade 3	5	15	26	8	-	54	-	0	1	1	-	2
Grade 4	2	1	3	9	-	15	-	0	0	0	-	0
Total	48	50	40	18	-	156	-	1	1	1	-	3
Leukocytosis												

TSFLB04PART2OF3: Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 0	156	-	-	-	-	156	3	-	-	-	-	3
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	156	-	-	-	-	156	3	-	-	-	-	3
Hemoglobin increased												
Grade 0	156	-	-	-	-	156	3	-	-	-	-	3
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	156	-	-	-	-	156	3	-	-	-	-	3
Lymphocytes count increased												
Grade 0	152	-	-	-	-	152	3	-	-	-	-	3
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	3	-	-	-	-	3	0	-	-	-	-	0
Grade 3	1	-	-	-	-	1	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	156	-	-	-	-	156	3	-	-	-	-	3

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0. Grade 0 means normal.
For each parameter, a subject is included if both baseline and post-baseline values are available.

[TSFLB04PART2OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb04.sas] 16MAR2015, 16:19

TSFLB04PART3OF3: Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Analysis set: all treated						237
Worst grade during treatment						
WBC low (Leukopenia)						
Grade 0	49	6	2	0	-	57
Grade 1	38	28	4	0	-	70
Grade 2	23	28	16	1	-	68
Grade 3	9	18	9	1	-	37
Grade 4	3	2	0	0	-	5
Total	122	82	31	2	-	237
Hemoglobin low (Anemia)						
Grade 0	8	0	0	0	-	8
Grade 1	17	55	4	0	-	76
Grade 2	3	44	53	3	-	103
Grade 3	0	13	30	7	-	50
Grade 4	0	0	0	0	-	0
Total	28	112	87	10	-	237
Platelets low (Thrombocytopenia)						
Grade 0	71	0	0	0	-	71
Grade 1	46	47	0	0	-	93
Grade 2	5	19	3	0	-	27
Grade 3	4	11	8	1	-	24
Grade 4	2	11	5	3	-	21
Total	128	88	16	4	-	236
Neutrophils low (Neutropenia)						
Grade 0	54	9	2	0	-	65
Grade 1	36	27	5	0	-	68
Grade 2	25	25	9	2	-	61
Grade 3	16	10	4	1	-	31
Grade 4	4	4	2	1	-	11
Total	135	75	22	4	-	236
Lymphocytes low (Lymphopenia)						
Grade 0	19	0	0	0	0	19
Grade 1	21	13	0	0	0	34
Grade 2	21	25	18	2	0	66
Grade 3	9	22	36	14	0	81
Grade 4	4	4	11	16	1	36
Total	74	64	65	32	1	236
Leukocytosis						

TSFLB04PART3OF3: Hematology: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 0	237	-	-	-	-	237
Grade 1	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0
Total	237	-	-	-	-	237
Hemoglobin increased						
Grade 0	237	-	-	-	-	237
Grade 1	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0
Total	237	-	-	-	-	237
Lymphocytes count increased						
Grade 0	229	-	-	-	-	229
Grade 1	0	-	-	-	-	0
Grade 2	6	-	-	-	-	6
Grade 3	1	-	-	-	-	1
Grade 4	0	-	-	-	-	0
Total	236	-	-	-	-	236

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0. Grade 0 means normal.
For each parameter, a subject is included if both baseline and post-baseline values are available.

[TSFLB04PART3OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb04.sas] 16MAR2015, 16:19

表 2.7.4-付録-168 Chemistry: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFLB01BPART1OF3: Chemistry: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg					8 mg/kg				
		Toxicity Grade					Toxicity Grade			
	Total	1	2	3	4	Total	1	2	3	4
Analysis set: all treated	23					55				
ALT high	23 (100.0%)	5 (21.7%)	1 (4.3%)	0	0	55 (100.0%)	10 (18.2%)	3 (5.5%)	0	0
AST high	23 (100.0%)	7 (30.4%)	0	0	0	55 (100.0%)	14 (25.5%)	0	1 (1.8%)	0
Creatinine high	23 (100.0%)	5 (21.7%)	2 (8.7%)	0	0	55 (100.0%)	9 (16.4%)	6 (10.9%)	0	0
Sodium high (Hypernatremia)	23 (100.0%)	5 (21.7%)	1 (4.3%)	0	0	55 (100.0%)	2 (3.6%)	0	0	0
Sodium low (Hyponatremia)	23 (100.0%)	1 (4.3%)	0	0	0	55 (100.0%)	7 (12.7%)	0	6 (10.9%)	1 (1.8%)
Potassium high (Hyperkalemia)	23 (100.0%)	0	0	0	0	55 (100.0%)	3 (5.5%)	3 (5.5%)	4 (7.3%)	2 (3.6%)
Potassium low (Hypokalemia)	23 (100.0%)	0	3 (13.0%)	0	0	55 (100.0%)	0	4 (7.3%)	2 (3.6%)	1 (1.8%)
Bilirubin high	22 (95.7%)	1 (4.5%)	0	1 (4.5%)	0	55 (100.0%)	2 (3.6%)	1 (1.8%)	0	0
Alkaline phosphatase high	23 (100.0%)	0	0	0	0	55 (100.0%)	6 (10.9%)	1 (1.8%)	0	0
Urate high (Hyperuricemia)	23 (100.0%)	6 (26.1%)	0	0	1 (4.3%)	52 (94.5%)	10 (19.2%)	0	0	2 (3.8%)
Corrected calcium high (Hypercalcemia)	23 (100.0%)	0	0	0	2 (8.7%)	55 (100.0%)	10 (18.2%)	0	2 (3.6%)	1 (1.8%)
Corrected calcium low (Hypocalcemia)	23 (100.0%)	0	0	1 (4.3%)	0	55 (100.0%)	19 (34.5%)	0	1 (1.8%)	1 (1.8%)
Phosphates low (Hypophosphatemia)	0	0	0	0	0	19 (34.5%)	0	4 (21.1%)	1 (5.3%)	0
Magnesium high (Hypermagnesemia)	0	0	0	0	0	18 (32.7%)	1 (5.6%)	0	0	0
Magnesium low (Hypomagmesemia)	0	0	0	0	0	18 (32.7%)	3 (16.7%)	0	0	0
Albumin low (Hypoalbuminemia)	23 (100.0%)	7 (30.4%)	1 (4.3%)	0	0	55 (100.0%)	15 (27.3%)	8 (14.5%)	2 (3.6%)	0

TSFLB01BPART1OF3: Chemistry: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg					8 mg/kg				
		Toxicity Grade					Toxicity Grade			
	Total	1	2	3	4	Total	1	2	3	4

Keys: AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0.3
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade didn't worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

[TSFLB01BPART1OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb01b.sas] 16MAR2015, 16:19

TSFLB01BPART2OF3: Chemistry: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg					24 mg/kg				
		Toxicity Grade					Toxicity Grade			
	Total	1	2	3	4	Total	1	2	3	4
Analysis set: all treated	156					3				
ALT high	150 (96.2%)	19 (12.7%)	1 (0.7%)	0	0	3 (100.0%)	0	0	-	-
AST high	149 (95.5%)	25 (16.8%)	3 (2.0%)	2 (1.3%)	0	3 (100.0%)	0	0	-	-
Creatinine high	151 (96.8%)	18 (11.9%)	11 (7.3%)	3 (2.0%)	0	3 (100.0%)	1 (33.3%)	0	-	-
Sodium high (Hypernatremia)	151 (96.8%)	6 (4.0%)	2 (1.3%)	0	0	3 (100.0%)	0	0	-	-
Sodium low (Hyponatremia)	151 (96.8%)	38 (25.2%)	0	6 (4.0%)	0	3 (100.0%)	0	0	-	-
Potassium high (Hyperkalemia)	151 (96.8%)	6 (4.0%)	3 (2.0%)	3 (2.0%)	1 (0.7%)	3 (100.0%)	0	0	-	-
Potassium low (Hypokalemia)	151 (96.8%)	0	23 (15.2%)	4 (2.6%)	0	3 (100.0%)	0	1 (33.3%)	-	-
Bilirubin high	151 (96.8%)	7 (4.6%)	1 (0.7%)	2 (1.3%)	0	3 (100.0%)	0	0	-	-
Alkaline phosphatase high	150 (96.2%)	18 (12.0%)	0	1 (0.7%)	0	3 (100.0%)	0	0	-	-
Urate high (Hyperuricemia)	142 (91.0%)	20 (14.1%)	0	0	6 (4.2%)	3 (100.0%)	1 (33.3%)	0	-	-
Corrected calcium high (Hypercalcemia)	152 (97.4%)	30 (19.7%)	8 (5.3%)	6 (3.9%)	4 (2.6%)	3 (100.0%)	0	0	-	-
Corrected calcium low (Hypocalcemia)	152 (97.4%)	43 (28.3%)	5 (3.3%)	0	0	3 (100.0%)	1 (33.3%)	0	-	-
Phosphates low (Hypophosphatemia)	102 (65.4%)	0	10 (9.8%)	6 (5.9%)	0	0	0	0	-	-
Magnesium high (Hypermagnesemia)	100 (64.1%)	4 (4.0%)	0	1 (1.0%)	0	0	0	0	-	-
Magnesium low (Hypomagmesemia)	100 (64.1%)	14 (14.0%)	2 (2.0%)	0	0	0	0	0	-	-
Albumin low (Hypoalbuminemia)	152 (97.4%)	29 (19.1%)	28 (18.4%)	5 (3.3%)	0	3 (100.0%)	0	0	-	-

TSFLB01BPART2OF3: Chemistry: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg					24 mg/kg				
		Toxicity Grade					Toxicity Grade			
	Total	1	2	3	4	Total	1	2	3	4

Keys: AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0.3
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade didn't worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

TSFLB01BPART3OF3: Chemistry: Treatment-emergent Worsening Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total				
		Toxicity Grade			
	Total	1	2	3	4
Analysis set: all treated	237				
ALT high	231 (97.5%)	34 (14.7%)	5 (2.2%)	0	0
AST high	230 (97.0%)	46 (20.0%)	3 (1.3%)	3 (1.3%)	0
Creatinine high	232 (97.9%)	33 (14.2%)	19 (8.2%)	3 (1.3%)	0
Sodium high (Hypernatremia)	232 (97.9%)	13 (5.6%)	3 (1.3%)	0	0
Sodium low (Hyponatremia)	232 (97.9%)	46 (19.8%)	0	12 (5.2%)	1 (0.4%)
Potassium high (Hyperkalemia)	232 (97.9%)	9 (3.9%)	6 (2.6%)	7 (3.0%)	3 (1.3%)
Potassium low (Hypokalemia)	232 (97.9%)	0	31 (13.4%)	6 (2.6%)	1 (0.4%)
Bilirubin high	231 (97.5%)	10 (4.3%)	2 (0.9%)	3 (1.3%)	0
Alkaline phosphatase high	231 (97.5%)	24 (10.4%)	1 (0.4%)	1 (0.4%)	0
Urate high (Hyperuricemia)	220 (92.8%)	37 (16.8%)	0	0	9 (4.1%)
Corrected calcium high (Hypercalcemia)	233 (98.3%)	40 (17.2%)	8 (3.4%)	8 (3.4%)	7 (3.0%)
Corrected calcium low (Hypocalcemia)	233 (98.3%)	63 (27.0%)	5 (2.1%)	2 (0.9%)	1 (0.4%)
Phosphates low (Hypophosphatemia)	121 (51.1%)	0	14 (11.6%)	7 (5.8%)	0
Magnesium high (Hypermagnesemia)	118 (49.8%)	5 (4.2%)	0	1 (0.8%)	0
Magnesium low (Hypomagmesemia)	118 (49.8%)	17 (14.4%)	2 (1.7%)	0	0
Albumin low (Hypoalbuminemia)	233 (98.3%)	51 (21.9%)	37 (15.9%)	7 (3.0%)	0

Keys: AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase.
Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0.3
Note: For each parameter, the total column includes all subjects with available data at both baseline and post-baseline, including those whose toxicity grade didn't worsen during treatment; percentages in the total column are calculated with the number of treated subjects in each group as denominator. For each parameter, the toxicity grade columns only include subjects whose toxicity grade worsened during treatment; percentages for toxicity grade columns are calculated with the number of subjects in the total column as denominator. For each subject and each parameter, the worst toxicity grade is selected.

表 2.7.4-付録-169 Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

TSFLB05PART1OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Analysis set: all treated						23						55
Worst grade during treatment												
ALT high												
Grade 0	14	0	-	-	-	14	37	0	-	-	-	37
Grade 1	5	3	-	-	-	8	10	5	-	-	-	15
Grade 2	1	0	-	-	-	1	0	3	-	-	-	3
Grade 3	0	0	-	-	-	0	0	0	-	-	-	0
Grade 4	0	0	-	-	-	0	0	0	-	-	-	0
Total	20	3	-	-	-	23	47	8	-	-	-	55
AST high												
Grade 0	8	2	-	-	-	10	32	0	-	-	-	32
Grade 1	7	6	-	-	-	13	14	8	-	-	-	22
Grade 2	0	0	-	-	-	0	0	0	-	-	-	0
Grade 3	0	0	-	-	-	0	0	1	-	-	-	1
Grade 4	0	0	-	-	-	0	0	0	-	-	-	0
Total	15	8	-	-	-	23	46	9	-	-	-	55
Creatinine high												
Grade 0	12	0	0	-	-	12	27	1	0	0	-	28
Grade 1	5	2	0	-	-	7	9	6	0	0	-	15
Grade 2	2	0	2	-	-	4	1	5	5	0	-	11
Grade 3	0	0	0	-	-	0	0	0	0	1	-	1
Grade 4	0	0	0	-	-	0	0	0	0	0	-	0
Total	19	2	2	-	-	23	37	12	5	1	-	55
Sodium high (Hypernatremia)												
Grade 0	17	-	-	-	-	17	53	-	-	-	-	53
Grade 1	5	-	-	-	-	5	2	-	-	-	-	2
Grade 2	1	-	-	-	-	1	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	23	-	-	-	-	23	55	-	-	-	-	55
Sodium low (Hyponatremia)												
Grade 0	22	-	-	-	-	22	38	0	-	0	-	38
Grade 1	1	-	-	-	-	1	7	2	-	0	-	9
Grade 2	0	-	-	-	-	0	0	0	-	0	-	0

TSFLB05PART1OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 3	0	-	-	-	-	0	4	2	-	1	-	7
Grade 4	0	-	-	-	-	0	1	0	-	0	-	1
Total	23	-	-	-	-	23	50	4	-	1	-	55
Potassium high (Hyperkalemia)												
Grade 0	22	-	-	1	-	23	41	2	-	-	-	43
Grade 1	0	-	-	0	-	0	3	0	-	-	-	3
Grade 2	0	-	-	0	-	0	3	0	-	-	-	3
Grade 3	0	-	-	0	-	0	4	0	-	-	-	4
Grade 4	0	-	-	0	-	0	2	0	-	-	-	2
Total	22	-	-	1	-	23	53	2	-	-	-	55
Potassium low (Hypokalemia)												
Grade 0	18	-	0	-	-	18	46	-	0	-	-	46
Grade 1	0	-	0	-	-	0	0	-	0	-	-	0
Grade 2	3	-	2	-	-	5	4	-	2	-	-	6
Grade 3	0	-	0	-	-	0	2	-	0	-	-	2
Grade 4	0	-	0	-	-	0	0	-	1	-	-	1
Total	21	-	2	-	-	23	52	-	3	-	-	55
Glucose high (Hyperglycemia)												
Grade 0	-	-	-	-	-	-	5	0	0	-	-	5
Grade 1	-	-	-	-	-	-	4	1	0	-	-	5
Grade 2	-	-	-	-	-	-	0	1	0	-	-	1
Grade 3	-	-	-	-	-	-	0	0	1	-	-	1
Grade 4	-	-	-	-	-	-	0	1	0	-	-	1
Total	-	-	-	-	-	-	9	3	1	-	-	13
Glucose low (Hypoglycemia)												
Grade 0	21	-	-	-	-	21	50	-	-	-	-	50
Grade 1	2	-	-	-	-	2	4	-	-	-	-	4
Grade 2	0	-	-	-	-	0	1	-	-	-	-	1
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	23	-	-	-	-	23	55	-	-	-	-	55
Bilirubin high												
Grade 0	20	-	-	-	-	20	51	0	-	-	-	51
Grade 1	1	-	-	-	-	1	2	1	-	-	-	3
Grade 2	0	-	-	-	-	0	1	0	-	-	-	1
Grade 3	1	-	-	-	-	1	0	0	-	-	-	0
Grade 4	0	-	-	-	-	0	0	0	-	-	-	0
Total	22	-	-	-	-	22	54	1	-	-	-	55

TSFLB05PART1OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Alkaline phosphatase high												
Grade 0	21	0	-	-	-	21	46	0	-	-	-	46
Grade 1	0	2	-	-	-	2	6	2	-	-	-	8
Grade 2	0	0	-	-	-	0	0	1	-	-	-	1
Grade 3	0	0	-	-	-	0	0	0	-	-	-	0
Grade 4	0	0	-	-	-	0	0	0	-	-	-	0
Total	21	2	-	-	-	23	52	3	-	-	-	55
Uric acid high (Hyperuricemia)												
Grade 0	15	0	-	-	-	15	33	0	-	-	1	34
Grade 1	6	1	-	-	-	7	10	6	-	-	0	16
Grade 2	0	0	-	-	-	0	0	0	-	-	0	0
Grade 3	0	0	-	-	-	0	0	0	-	-	0	0
Grade 4	0	1	-	-	-	1	1	1	-	-	0	2
Total	21	2	-	-	-	23	44	7	-	-	1	52
Corrected calcium high (Hypercalcemia)												
Grade 0	21	-	-	-	-	21	34	1	-	0	-	35
Grade 1	0	-	-	-	-	0	10	6	-	0	-	16
Grade 2	0	-	-	-	-	0	0	0	-	0	-	0
Grade 3	0	-	-	-	-	0	1	1	-	1	-	3
Grade 4	2	-	-	-	-	2	1	0	-	0	-	1
Total	23	-	-	-	-	23	46	8	-	1	-	55
Corrected calcium low (Hypocalcemia)												
Grade 0	22	-	-	-	-	22	28	0	-	-	-	28
Grade 1	0	-	-	-	-	0	19	6	-	-	-	25
Grade 2	0	-	-	-	-	0	0	0	-	-	-	0
Grade 3	1	-	-	-	-	1	1	0	-	-	-	1
Grade 4	0	-	-	-	-	0	1	0	-	-	-	1
Total	23	-	-	-	-	23	49	6	-	-	-	55
Phosphates low (Hypophosphatemia)												
Grade 0	-	-	-	-	-	-	14	-	-	-	-	14
Grade 1	-	-	-	-	-	-	0	-	-	-	-	0
Grade 2	-	-	-	-	-	-	4	-	-	-	-	4
Grade 3	-	-	-	-	-	-	1	-	-	-	-	1
Grade 4	-	-	-	-	-	-	0	-	-	-	-	0
Total	-	-	-	-	-	-	19	-	-	-	-	19

TSFLB05PART1OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Magnesium high (Hypermagnesemia)												
Grade 0	-	-	-	-	-	-	17	-	-	-	-	17
Grade 1	-	-	-	-	-	-	1	-	-	-	-	1
Grade 2	-	-	-	-	-	-	0	-	-	-	-	0
Grade 3	-	-	-	-	-	-	0	-	-	-	-	0
Grade 4	-	-	-	-	-	-	0	-	-	-	-	0
Total	-	-	-	-	-	-	18	-	-	-	-	18
Magnesium low (Hypomagmesemia)												
Grade 0	-	-	-	-	-	-	10	1	-	-	-	11
Grade 1	-	-	-	-	-	-	3	4	-	-	-	7
Grade 2	-	-	-	-	-	-	0	0	-	-	-	0
Grade 3	-	-	-	-	-	-	0	0	-	-	-	0
Grade 4	-	-	-	-	-	-	0	0	-	-	-	0
Total	-	-	-	-	-	-	13	5	-	-	-	18
Albumin low (Hypoalbuminemia)												
Grade 0	14	0	-	-	-	14	18	1	0	-	-	19
Grade 1	7	1	-	-	-	8	15	8	0	-	-	23
Grade 2	1	0	-	-	-	1	4	4	3	-	-	11
Grade 3	0	0	-	-	-	0	0	1	1	-	-	2
Grade 4	0	0	-	-	-	0	0	0	0	-	-	0
Total	22	1	-	-	-	23	37	14	4	-	-	55
Cholesterol High												
Grade 0	-	-	-	-	-	-	3	0	-	-	-	3
Grade 1	-	-	-	-	-	-	0	1	-	-	-	1
Grade 2	-	-	-	-	-	-	0	0	-	-	-	0
Grade 3	-	-	-	-	-	-	0	0	-	-	-	0
Grade 4	-	-	-	-	-	-	0	0	-	-	-	0
Total	-	-	-	-	-	-	3	1	-	-	-	4
Cpk Increased												
Grade 0	19	1	-	-	-	20	35	-	-	-	-	35
Grade 1	0	1	-	-	-	1	2	-	-	-	-	2
Grade 2	0	0	-	-	-	0	0	-	-	-	-	0
Grade 3	1	1	-	-	-	2	0	-	-	-	-	0
Grade 4	0	0	-	-	-	0	0	-	-	-	-	0
Total	20	3	-	-	-	23	37	-	-	-	-	37
Haptoglobin Decreased												

TSFLB05PART1OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	<=4 mg/kg						8 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 0	19	0	-	-	-	19	2	-	-	-	-	2
Grade 1	0	3	-	-	-	3	1	-	-	-	-	1
Grade 2	0	0	-	-	-	0	0	-	-	-	-	0
Grade 3	0	0	-	-	-	0	0	-	-	-	-	0
Grade 4	0	0	-	-	-	0	0	-	-	-	-	0
Total	19	3	-	-	-	22	3	-	-	-	-	3
Hypoalbumine-Mia												
Grade 0	-	-	-	-	-	-	9	1	0	-	-	10
Grade 1	-	-	-	-	-	-	6	2	0	-	-	8
Grade 2	-	-	-	-	-	-	3	2	5	-	-	10
Grade 3	-	-	-	-	-	-	0	0	0	-	-	0
Grade 4	-	-	-	-	-	-	0	0	0	-	-	0
Total	-	-	-	-	-	-	18	5	5	-	-	28
Hypertriglycer-Idemia												
Grade 0	-	-	-	-	-	-	1	0	-	-	-	1
Grade 1	-	-	-	-	-	-	2	1	-	-	-	3
Grade 2	-	-	-	-	-	-	0	0	-	-	-	0
Grade 3	-	-	-	-	-	-	0	0	-	-	-	0
Grade 4	-	-	-	-	-	-	0	0	-	-	-	0
Total	-	-	-	-	-	-	3	1	-	-	-	4
Proteinuria												
Grade 0	5	-	-	-	-	5	2	-	-	-	-	2
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	5	-	-	-	-	5	2	-	-	-	-	2

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0. Grade 0 means normal.
For each parameter, a subject is included if both baseline and post-baseline values are available.

[TSFLB05PART1OF3.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsflb05.sas] 16MAR2015, 16:19

TSFLB05PART2OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Analysis set: all treated						156						3
Worst grade during treatment												
ALT high												
Grade 0	123	2	-	-	-	125	3	-	-	-	-	3
Grade 1	19	5	-	-	-	24	0	-	-	-	-	0
Grade 2	0	1	-	-	-	1	0	-	-	-	-	0
Grade 3	0	0	-	-	-	0	0	-	-	-	-	0
Grade 4	0	0	-	-	-	0	0	-	-	-	-	0
Total	142	8	-	-	-	150	3	-	-	-	-	3
AST high												
Grade 0	103	6	0	-	-	109	3	-	-	-	-	3
Grade 1	25	10	0	-	-	35	0	-	-	-	-	0
Grade 2	1	2	0	-	-	3	0	-	-	-	-	0
Grade 3	1	0	1	-	-	2	0	-	-	-	-	0
Grade 4	0	0	0	-	-	0	0	-	-	-	-	0
Total	130	18	1	-	-	149	3	-	-	-	-	3
Creatinine high												
Grade 0	73	2	0	0	-	75	2	-	-	-	-	2
Grade 1	18	30	0	0	-	48	1	-	-	-	-	1
Grade 2	2	9	13	0	-	24	0	-	-	-	-	0
Grade 3	1	2	0	1	-	4	0	-	-	-	-	0
Grade 4	0	0	0	0	-	0	0	-	-	-	-	0
Total	94	43	13	1	-	151	3	-	-	-	-	3
Sodium high (Hypernatremia)												
Grade 0	139	4	-	-	-	143	3	-	-	-	-	3
Grade 1	6	0	-	-	-	6	0	-	-	-	-	0
Grade 2	2	0	-	-	-	2	0	-	-	-	-	0
Grade 3	0	0	-	-	-	0	0	-	-	-	-	0
Grade 4	0	0	-	-	-	0	0	-	-	-	-	0
Total	147	4	-	-	-	151	3	-	-	-	-	3
Sodium low (Hyponatremia)												
Grade 0	96	3	-	0	-	99	3	-	-	-	-	3
Grade 1	38	7	-	1	-	46	0	-	-	-	-	0
Grade 2	0	0	-	0	-	0	0	-	-	-	-	0
Grade 3	2	4	-	0	-	6	0	-	-	-	-	0
Grade 4	0	0	-	0	-	0	0	-	-	-	-	0
Total	136	14	-	1	-	151	3	-	-	-	-	3
Potassium high (Hyperkalemia)												

TSFLB05PART2OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 0	136	1	1	-	-	138	3	-	-	-	-	3
Grade 1	6	0	0	-	-	6	0	-	-	-	-	0
Grade 2	3	0	0	-	-	3	0	-	-	-	-	0
Grade 3	3	0	0	-	-	3	0	-	-	-	-	0
Grade 4	1	0	0	-	-	1	0	-	-	-	-	0
Total	149	1	1	-	-	151	3	-	-	-	-	3
Potassium low (Hypokalemia)												
Grade 0	115	-	5	0	-	120	2	-	-	-	-	2
Grade 1	0	-	0	0	-	0	0	-	-	-	-	0
Grade 2	23	-	3	0	-	26	1	-	-	-	-	1
Grade 3	3	-	1	1	-	5	0	-	-	-	-	0
Grade 4	0	-	0	0	-	0	0	-	-	-	-	0
Total	141	-	9	1	-	151	3	-	-	-	-	3
Glucose high (Hyperglycemia)												
Grade 0	17	0	-	0	-	17	-	-	-	-	-	-
Grade 1	8	3	-	1	-	12	-	-	-	-	-	-
Grade 2	0	1	-	0	-	1	-	-	-	-	-	-
Grade 3	0	0	-	0	-	0	-	-	-	-	-	-
Grade 4	0	0	-	0	-	0	-	-	-	-	-	-
Total	25	4	-	1	-	30	-	-	-	-	-	-
Glucose low (Hypoglycemia)												
Grade 0	127	2	-	-	-	129	2	-	-	-	-	2
Grade 1	13	4	-	-	-	17	1	-	-	-	-	1
Grade 2	2	1	-	-	-	3	0	-	-	-	-	0
Grade 3	1	0	-	-	-	1	0	-	-	-	-	0
Grade 4	0	0	-	-	-	0	0	-	-	-	-	0
Total	143	7	-	-	-	150	3	-	-	-	-	3
Bilirubin high												
Grade 0	141	-	-	-	-	141	3	-	-	-	-	3
Grade 1	7	-	-	-	-	7	0	-	-	-	-	0
Grade 2	1	-	-	-	-	1	0	-	-	-	-	0
Grade 3	2	-	-	-	-	2	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	151	-	-	-	-	151	3	-	-	-	-	3
Alkaline phosphatase high												
Grade 0	120	1	0	-	-	121	3	-	-	-	-	3
Grade 1	18	9	0	-	-	27	0	-	-	-	-	0
Grade 2	0	0	1	-	-	1	0	-	-	-	-	0

TSFLB05PART2OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 3	0	1	0	-	-	1	0	-	-	-	-	0
Grade 4	0	0	0	-	-	0	0	-	-	-	-	0
Total	138	11	1	-	-	150	3	-	-	-	-	3
Uric acid high (Hyperuricemia)												
Grade 0	88	7	-	-	2	97	1	1	-	-	-	2
Grade 1	20	16	-	-	2	38	1	0	-	-	-	1
Grade 2	0	0	-	-	0	0	0	0	-	-	-	0
Grade 3	0	0	-	-	0	0	0	0	-	-	-	0
Grade 4	3	3	-	-	1	7	0	0	-	-	-	0
Total	111	26	-	-	5	142	2	1	-	-	-	3
Corrected calcium high (Hypercalcemia)												
Grade 0	77	9	1	0	1	88	3	-	-	-	-	3
Grade 1	30	9	2	0	0	41	0	-	-	-	-	0
Grade 2	4	4	1	1	1	11	0	-	-	-	-	0
Grade 3	1	3	2	1	0	7	0	-	-	-	-	0
Grade 4	1	1	2	0	1	5	0	-	-	-	-	0
Total	113	26	8	2	3	152	3	-	-	-	-	3
Corrected calcium low (Hypocalcemia)												
Grade 0	88	5	1	-	-	94	2	-	-	-	-	2
Grade 1	43	9	0	-	-	52	1	-	-	-	-	1
Grade 2	5	0	1	-	-	6	0	-	-	-	-	0
Grade 3	0	0	0	-	-	0	0	-	-	-	-	0
Grade 4	0	0	0	-	-	0	0	-	-	-	-	0
Total	136	14	2	-	-	152	3	-	-	-	-	3
Phosphates low (Hypophosphatemia)												
Grade 0	83	-	1	0	-	84	-	-	-	-	-	-
Grade 1	0	-	0	0	-	0	-	-	-	-	-	-
Grade 2	10	-	1	1	-	12	-	-	-	-	-	-
Grade 3	3	-	3	0	-	6	-	-	-	-	-	-
Grade 4	0	-	0	0	-	0	-	-	-	-	-	-
Total	96	-	5	1	-	102	-	-	-	-	-	-
Magnesium high (Hypermagnesemia)												
Grade 0	95	-	-	-	-	95	-	-	-	-	-	-
Grade 1	4	-	-	-	-	4	-	-	-	-	-	-

TSFLB05PART2OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 2	0	-	-	-	-	0	-	-	-	-	-	-
Grade 3	1	-	-	-	-	1	-	-	-	-	-	-
Grade 4	0	-	-	-	-	0	-	-	-	-	-	-
Total	100	-	-	-	-	100	-	-	-	-	-	-
Magnesium low (Hypomagmesemia)												
Grade 0	68	6	0	-	-	74	-	-	-	-	-	-
Grade 1	14	9	0	-	-	23	-	-	-	-	-	-
Grade 2	1	1	1	-	-	3	-	-	-	-	-	-
Grade 3	0	0	0	-	-	0	-	-	-	-	-	-
Grade 4	0	0	0	-	-	0	-	-	-	-	-	-
Total	83	16	1	-	-	100	-	-	-	-	-	-
Albumin low (Hypoalbuminemia)												
Grade 0	59	4	0	0	-	63	2	0	-	-	-	2
Grade 1	29	7	2	0	-	38	0	1	-	-	-	1
Grade 2	11	17	17	1	-	46	0	0	-	-	-	0
Grade 3	1	1	3	0	-	5	0	0	-	-	-	0
Grade 4	0	0	0	0	-	0	0	0	-	-	-	0
Total	100	29	22	1	-	152	2	1	-	-	-	3
Cholesterol High												
Grade 0	2	0	-	-	-	2	-	-	-	-	-	-
Grade 1	2	0	-	-	-	2	-	-	-	-	-	-
Grade 2	0	1	-	-	-	1	-	-	-	-	-	-
Grade 3	0	0	-	-	-	0	-	-	-	-	-	-
Grade 4	0	0	-	-	-	0	-	-	-	-	-	-
Total	4	1	-	-	-	5	-	-	-	-	-	-
Cpk Increased												
Grade 0	44	0	-	-	-	44	3	-	-	-	-	3
Grade 1	3	1	-	-	-	4	0	-	-	-	-	0
Grade 2	0	0	-	-	-	0	0	-	-	-	-	0
Grade 3	2	0	-	-	-	2	0	-	-	-	-	0
Grade 4	0	0	-	-	-	0	0	-	-	-	-	0
Total	49	1	-	-	-	50	3	-	-	-	-	3
Haptoglobin Decreased												
Grade 0	3	-	-	-	-	3	3	-	-	-	-	3
Grade 1	0	-	-	-	-	0	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0	0	-	-	-	-	0

TSFLB05PART2OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	16 mg/kg						24 mg/kg					
	Baseline Grade						Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 4	0	-	-	-	-	0	0	-	-	-	-	0
Total	3	-	-	-	-	3	3	-	-	-	-	3
Hypoalbumine-Mia												
Grade 0	23	1	0	-	-	24	-	-	-	-	-	-
Grade 1	8	4	0	-	-	12	-	-	-	-	-	-
Grade 2	1	2	2	-	-	5	-	-	-	-	-	-
Grade 3	0	0	0	-	-	0	-	-	-	-	-	-
Grade 4	0	0	0	-	-	0	-	-	-	-	-	-
Total	32	7	2	-	-	41	-	-	-	-	-	-
Hypertriglycer-Idemia												
Grade 0	2	0	-	-	-	2	-	-	-	-	-	-
Grade 1	0	2	-	-	-	2	-	-	-	-	-	-
Grade 2	0	1	-	-	-	1	-	-	-	-	-	-
Grade 3	0	0	-	-	-	0	-	-	-	-	-	-
Grade 4	0	0	-	-	-	0	-	-	-	-	-	-
Total	2	3	-	-	-	5	-	-	-	-	-	-
Proteinuria												
Grade 0	-	-	-	-	-	-	2	-	-	-	-	2
Grade 1	-	-	-	-	-	-	0	-	-	-	-	0
Grade 2	-	-	-	-	-	-	0	-	-	-	-	0
Grade 3	-	-	-	-	-	-	0	-	-	-	-	0
Grade 4	-	-	-	-	-	-	0	-	-	-	-	0
Total	-	-	-	-	-	-	2	-	-	-	-	2

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0. Grade 0 means normal.
For each parameter, a subject is included if both baseline and post-baseline values are available.

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TSFLB05PART3OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Analysis set: all treated						237
Worst grade during treatment						
ALT high						
Grade 0	177	2	-	-	-	179
Grade 1	34	13	-	-	-	47
Grade 2	1	4	-	-	-	5
Grade 3	0	0	-	-	-	0
Grade 4	0	0	-	-	-	0
Total	212	19	-	-	-	231
AST high						
Grade 0	146	8	0	-	-	154
Grade 1	46	24	0	-	-	70
Grade 2	1	2	0	-	-	3
Grade 3	1	1	1	-	-	3
Grade 4	0	0	0	-	-	0
Total	194	35	1	-	-	230
Creatinine high						
Grade 0	114	3	0	0	-	117
Grade 1	33	38	0	0	-	71
Grade 2	5	14	20	0	-	39
Grade 3	1	2	0	2	-	5
Grade 4	0	0	0	0	-	0
Total	153	57	20	2	-	232
Sodium high (Hypernatremia)						
Grade 0	212	4	-	-	-	216
Grade 1	13	0	-	-	-	13
Grade 2	3	0	-	-	-	3
Grade 3	0	0	-	-	-	0
Grade 4	0	0	-	-	-	0
Total	228	4	-	-	-	232
Sodium low (Hyponatremia)						
Grade 0	159	3	-	0	-	162
Grade 1	46	9	-	1	-	56
Grade 2	0	0	-	0	-	0
Grade 3	6	6	-	1	-	13
Grade 4	1	0	-	0	-	1
Total	212	18	-	2	-	232
Potassium high (Hyperkalemia)						

TSFLB05PART3OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 0	202	3	1	1	-	207
Grade 1	9	0	0	0	-	9
Grade 2	6	0	0	0	-	6
Grade 3	7	0	0	0	-	7
Grade 4	3	0	0	0	-	3
Total	227	3	1	1	-	232
Potassium low (Hypokalemia)						
Grade 0	181	-	5	0	-	186
Grade 1	0	-	0	0	-	0
Grade 2	31	-	7	0	-	38
Grade 3	5	-	1	1	-	7
Grade 4	0	-	1	0	-	1
Total	217	-	14	1	-	232
Glucose high (Hyperglycemia)						
Grade 0	22	0	0	0	-	22
Grade 1	12	4	0	1	-	17
Grade 2	0	2	0	0	-	2
Grade 3	0	0	1	0	-	1
Grade 4	0	1	0	0	-	1
Total	34	7	1	1	-	43
Glucose low (Hypoglycemia)						
Grade 0	200	2	-	-	-	202
Grade 1	20	4	-	-	-	24
Grade 2	3	1	-	-	-	4
Grade 3	1	0	-	-	-	1
Grade 4	0	0	-	-	-	0
Total	224	7	-	-	-	231
Bilirubin high						
Grade 0	215	0	-	-	-	215
Grade 1	10	1	-	-	-	11
Grade 2	2	0	-	-	-	2
Grade 3	3	0	-	-	-	3
Grade 4	0	0	-	-	-	0
Total	230	1	-	-	-	231
Alkaline phosphatase high						
Grade 0	190	1	0	-	-	191
Grade 1	24	13	0	-	-	37
Grade 2	0	1	1	-	-	2

TSFLB05PART3OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 3	0	1	0	-	-	1
Grade 4	0	0	0	-	-	0
Total	214	16	1	-	-	231
Uric acid high (Hyperuricemia)						
Grade 0	137	8	-	-	3	148
Grade 1	37	23	-	-	2	62
Grade 2	0	0	-	-	0	0
Grade 3	0	0	-	-	0	0
Grade 4	4	5	-	-	1	10
Total	178	36	-	-	6	220
Corrected calcium high (Hypercalcemia)						
Grade 0	135	10	1	0	1	147
Grade 1	40	15	2	0	0	57
Grade 2	4	4	1	1	1	11
Grade 3	2	4	2	2	0	10
Grade 4	4	1	2	0	1	8
Total	185	34	8	3	3	233
Corrected calcium low (Hypocalcemia)						
Grade 0	140	5	1	-	-	146
Grade 1	63	15	0	-	-	78
Grade 2	5	0	1	-	-	6
Grade 3	2	0	0	-	-	2
Grade 4	1	0	0	-	-	1
Total	211	20	2	-	-	233
Phosphates low (Hypophosphatemia)						
Grade 0	97	-	1	0	-	98
Grade 1	0	-	0	0	-	0
Grade 2	14	-	1	1	-	16
Grade 3	4	-	3	0	-	7
Grade 4	0	-	0	0	-	0
Total	115	-	5	1	-	121
Magnesium high (Hypermagnesemia)						
Grade 0	112	-	-	-	-	112
Grade 1	5	-	-	-	-	5

TSFLB05PART3OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 2	0	-	-	-	-	0
Grade 3	1	-	-	-	-	1
Grade 4	0	-	-	-	-	0
Total	118	-	-	-	-	118
Magnesium low (Hypomagmesemia)						
Grade 0	78	7	0	-	-	85
Grade 1	17	13	0	-	-	30
Grade 2	1	1	1	-	-	3
Grade 3	0	0	0	-	-	0
Grade 4	0	0	0	-	-	0
Total	96	21	1	-	-	118
Albumin low (Hypoalbuminemia)						
Grade 0	93	5	0	0	-	98
Grade 1	51	17	2	0	-	70
Grade 2	16	21	20	1	-	58
Grade 3	1	2	4	0	-	7
Grade 4	0	0	0	0	-	0
Total	161	45	26	1	-	233
Cholesterol High						
Grade 0	5	0	-	-	-	5
Grade 1	2	1	-	-	-	3
Grade 2	0	1	-	-	-	1
Grade 3	0	0	-	-	-	0
Grade 4	0	0	-	-	-	0
Total	7	2	-	-	-	9
Cpk Increased						
Grade 0	101	1	-	-	-	102
Grade 1	5	2	-	-	-	7
Grade 2	0	0	-	-	-	0
Grade 3	3	1	-	-	-	4
Grade 4	0	0	-	-	-	0
Total	109	4	-	-	-	113
Haptoglobin Decreased						
Grade 0	27	0	-	-	-	27
Grade 1	1	3	-	-	-	4
Grade 2	0	0	-	-	-	0
Grade 3	0	0	-	-	-	0

TSFLB05PART3OF3: Chemistry: Shifts from Baseline Toxicity Grade to Worst Toxicity Grade During Treatment; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

	Total					
	Baseline Grade					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Grade 4	0	0	-	-	-	0
Total	28	3	-	-	-	31
Hypoalbumine-Mia						
Grade 0	32	2	0	-	-	34
Grade 1	14	6	0	-	-	20
Grade 2	4	4	7	-	-	15
Grade 3	0	0	0	-	-	0
Grade 4	0	0	0	-	-	0
Total	50	12	7	-	-	69
Hypertriglycer-Idemia						
Grade 0	3	0	-	-	-	3
Grade 1	2	3	-	-	-	5
Grade 2	0	1	-	-	-	1
Grade 3	0	0	-	-	-	0
Grade 4	0	0	-	-	-	0
Total	5	4	-	-	-	9
Proteinuria						
Grade 0	9	-	-	-	-	9
Grade 1	0	-	-	-	-	0
Grade 2	0	-	-	-	-	0
Grade 3	0	-	-	-	-	0
Grade 4	0	-	-	-	-	0
Total	9	-	-	-	-	9

Note: The laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.0. Grade 0 means normal.
For each parameter, a subject is included if both baseline and post-baseline values are available.

表 2.7.4-付録-170 List of Possible Subjects Meeting Hy's Law Criteria; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

LSFLAB01: List of Possible Subjects Meeting Hy's Law Criteria; All Treated Analysis Set (Studies: MMY2002, GEN501 and MMY1002)

Study ID	Treatment Group	Enrollment No.	Dose number where ALT ≥ 3xULN	Dose number where AST ≥ 3xULN	Dose number where bilirubin ≥ 2xULN	Baseline ALP ≤ 2xULN	Other clinical explanation
GEN501 Part 1	<=4 mg/kg	501015	3			Yes	
	8 mg/kg	501026	2, 5			Yes	
GEN501 Part 2	8 mg/kg	501224	2			No	
	16 mg/kg	501242	5	2, 5, 6, 7, 13		Yes	
MMY2002	8 mg/kg	100014	1	1, 3		Yes	
	16 mg/kg	100008		5		Yes	
		100059		6	6	Yes	
		100084		1		Yes	
		100138		11		Yes	

[LSFLAB01.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\lsflab01.sas] 03APR2015, 17:37

表 2.7.4-付録-171 Subgroup Analyses on Overview of Treatment-Emergent Adverse Events; All Treated Analysis Set - 16 mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

TSFAE01S: Subgroup Analyses on Overview of Treatment-Emergent Adverse Events; All Treated Analysis Set - 16 mg/kg Group (Studies: MMY2002, GEN501 and MMY1002)

		16 mg/kg					
		N	TEAE	Serious TEAE	Grade 3 or Higher TEAE	TD due to TEAE[a]	Death due to TEAE[b]
All subjects		156	154 (98.7%)	50 (32.1%)	88 (56.4%)	6 (3.8%)	3 (1.9%)
Age:	18 to <65 years	86	86 (100.0%)	26 (30.2%)	45 (52.3%)	3 (3.5%)	1 (1.2%)
	65 to <75 years	54	52 (96.3%)	20 (37.0%)	35 (64.8%)	1 (1.9%)	0
	>=75 years	16	16 (100.0%)	4 (25.0%)	8 (50.0%)	2 (12.5%)	2 (12.5%)
Sex:	Male	84	82 (97.6%)	24 (28.6%)	42 (50.0%)	2 (2.4%)	2 (2.4%)
	Female	72	72 (100.0%)	26 (36.1%)	46 (63.9%)	4 (5.6%)	1 (1.4%)
Race:	White	119	117 (98.3%)	40 (33.6%)	64 (53.8%)	6 (5.0%)	3 (2.5%)
	Other	37	37 (100.0%)	10 (27.0%)	24 (64.9%)	0	0
Renal Impairment (Creatinine Clearance)	>=60 ml/min	95	94 (98.9%)	29 (30.5%)	48 (50.5%)	2 (2.1%)	2 (2.1%)
	30– <60 ml/min	56	56 (100.0%)	19 (33.9%)	37 (66.1%)	4 (7.1%)	1 (1.8%)
	<30 ml/min	5	4 (80.0%)	2 (40.0%)	3 (60.0%)	0	0
Hepatic Function[c]	Normal	134	132 (98.5%)	40 (29.9%)	72 (53.7%)	2 (1.5%)	1 (0.7%)
	Mildly Impaired	21	21 (100.0%)	9 (42.9%)	15 (71.4%)	4 (19.0%)	2 (9.5%)
Geographic Region:	EU	40	39 (97.5%)	15 (37.5%)	12 (30.0%)	3 (7.5%)	1 (2.5%)
	North America + Japan	116	115 (99.1%)	35 (30.2%)	76 (65.5%)	3 (2.6%)	2 (1.7%)
Drug Products:	Phase 2 Product	64	63 (98.4%)	17 (26.6%)	34 (53.1%)	1 (1.6%)	1 (1.6%)
	Phase 3 Product	92	91 (98.9%)	33 (35.9%)	54 (58.7%)	5 (5.4%)	2 (2.2%)

Keys: TEAE = treatment-emergent adverse event. TD = treatment discontinuation.
Note: Percentages are calculated with the number of subjects in each subgroup as denominator.
[a]Treatment discontinuation due to adverse event on the end of treatment CRF page.
[b]Death due to adverse event on the death CRF page.
[c]Hepatic function is classified into 4 levels per NCI Organ Dysfunction criteria: Normal: total bilirubin ≤ ULN and AST ≤ ULN; Mildly Impaired: (total bilirubin ≤ ULN and AST > ULN) or (ULN < total bilirubin ≤ 1.5×ULN); Moderately Impaired: 1.5×ULN < total bilirubin ≤ 3×ULN; and Severely Impaired: total bilirubin > 3×ULN.

[TSFAE01S.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2014\RE_SCS_2014\tsfae01s.sas] 16MAR2015, 16:21

表 2.7.4-付録-172 Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

TSFAE01A_J: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
Analysis set: all treated	42	106	148	283	243	674			
Total number of subjects with TEAE related to study treatment	33 (78.6%)	81 (76.4%)	114 (77.0%)	215 (76.0%)	182 (74.9%)	511 (75.8%)			
MedDRA system organ class / Preferred term									
呼吸器、胸郭および縦隔障害	26 (61.9%)	34 (32.1%)	60 (40.5%)	103 (36.4%)	96 (39.5%)	259 (38.4%)	10038738		
咳嗽	6 (14.3%)	9 (8.5%)	15 (10.1%)	32 (11.3%)	27 (11.1%)	74 (11.0%)	10011224		
呼吸困難	2 (4.8%)	8 (7.5%)	10 (6.8%)	32 (11.3%)	32 (13.2%)	74 (11.0%)	10013968		
気管支痙攣	0	4 (3.8%)	4 (2.7%)	13 (4.6%)	22 (9.1%)	39 (5.8%)	10006482		
鼻閉	4 (9.5%)	13 (12.3%)	17 (11.5%)	8 (2.8%)	11 (4.5%)	36 (5.3%)	10028735		
咽喉刺激感	2 (4.8%)	7 (6.6%)	9 (6.1%)	8 (2.8%)	12 (4.9%)	29 (4.3%)	10043521		
アレルギー性鼻炎	10 (23.8%)	0	10 (6.8%)	8 (2.8%)	3 (1.2%)	21 (3.1%)	10039085		
喘鳴	0	3 (2.8%)	3 (2.0%)	7 (2.5%)	5 (2.1%)	15 (2.2%)	10047924		
鼻漏	0	1 (0.9%)	1 (0.7%)	8 (2.8%)	4 (1.6%)	13 (1.9%)	10039101		
労作性呼吸困難	0	2 (1.9%)	2 (1.4%)	4 (1.4%)	3 (1.2%)	9 (1.3%)	10013971		
喉頭浮腫	0	1 (0.9%)	1 (0.7%)	6 (2.1%)	2 (0.8%)	9 (1.3%)	10023845		
湿性咳嗽	0	2 (1.9%)	2 (1.4%)	5 (1.8%)	1 (0.4%)	8 (1.2%)	10036790		
咽喉絞扼感	3 (7.1%)	0	3 (2.0%)	1 (0.4%)	4 (1.6%)	8 (1.2%)	10043528		
低酸素症	1 (2.4%)	0	1 (0.7%)	6 (2.1%)	0	7 (1.0%)	10021143		
口腔咽頭痛	0	2 (1.9%)	2 (1.4%)	1 (0.4%)	2 (0.8%)	5 (0.7%)	10068319		
くしゃみ	1 (2.4%)	2 (1.9%)	3 (2.0%)	2 (0.7%)	0	5 (0.7%)	10041232		
発声障害	0	0	0	3 (1.1%)	1 (0.4%)	4 (0.6%)	10013952		
アレルギー性咳嗽	1 (2.4%)	0	1 (0.7%)	0	2 (0.8%)	3 (0.4%)	10053779		
鼻出血	0	0	0	0	3 (1.2%)	3 (0.4%)	10015090		
鼻閉塞	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10028748		
アレルギー性呼吸器症状	0	0	0	2 (0.7%)	0	2 (0.3%)	10063527		
肺臓炎	0	0	0	2 (0.7%)	0	2 (0.3%)	10035742		
窒息	0	0	0	1 (0.4%)	0	1 (0.1%)	10003497		
喘息	0	0	0	0	1 (0.4%)	1 (0.1%)	10003553		

TSFAE01A_J: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
気管支拡張症	0	0	0	1 (0.4%)	0	1 (0.1%)	10006445		
しゃっくり	0	0	0	1 (0.4%)	0	1 (0.1%)	10020039		
胸水症	0	0	0	0	1 (0.4%)	1 (0.1%)	10048612		
喉頭不快感	0	0	0	1 (0.4%)	0	1 (0.1%)	10054115		
喉頭狭窄	0	0	0	1 (0.4%)	0	1 (0.1%)	10023862		
アレルギー性喉頭炎	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10064866		
喉頭刺激感	0	0	0	1 (0.4%)	0	1 (0.1%)	10058670		
鼻部不快感	0	0	0	1 (0.4%)	0	1 (0.1%)	10052437		
鼻部障害	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10062209		
器質化肺炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10067472		
口腔咽頭不快感	0	0	0	0	1 (0.4%)	1 (0.1%)	10068318		
口腔咽頭腫脹	0	0	0	0	1 (0.4%)	1 (0.1%)	10031118		
咽頭浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10034829		
誤嚥性肺炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10035669		
呼気延長	0	0	0	1 (0.4%)	0	1 (0.1%)	10059411		
肺動脈血栓症	0	0	0	0	1 (0.4%)	1 (0.1%)	10037340		
肺塞栓症	0	0	0	1 (0.4%)	0	1 (0.1%)	10037377		
肺水腫	0	0	0	1 (0.4%)	0	1 (0.1%)	10037423		
気道うっ血	0	0	0	0	1 (0.4%)	1 (0.1%)	10052251		
低音性連続性ラ音	0	0	0	0	1 (0.4%)	1 (0.1%)	10039109		
副鼻腔障害	0	0	0	1 (0.4%)	0	1 (0.1%)	10062244		
上気道性喘鳴	0	0	0	1 (0.4%)	0	1 (0.1%)	10042241		
窒息感	0	0	0	1 (0.4%)	0	1 (0.1%)	10042444		
上気道咳症候群	0	0	0	0	1 (0.4%)	1 (0.1%)	10070488		
一般・全身障害および投与部位の状態	11 (26.2%)	42 (39.6%)	53 (35.8%)	81 (28.6%)	59 (24.3%)	193 (28.6%)	10018065		
疲労	6 (14.3%)	24 (22.6%)	30 (20.3%)	35 (12.4%)	27 (11.1%)	92 (13.6%)	10016256		
発熱	1 (2.4%)	4 (3.8%)	5 (3.4%)	23 (8.1%)	17 (7.0%)	45 (6.7%)	10037660		
悪寒	4 (9.5%)	8 (7.5%)	12 (8.1%)	14 (4.9%)	10 (4.1%)	36 (5.3%)	10008531		
無力症	0	4 (3.8%)	4 (2.7%)	8 (2.8%)	6 (2.5%)	18 (2.7%)	10003549		
インフルエンザ様疾患	0	4 (3.8%)	4 (2.7%)	4 (1.4%)	3 (1.2%)	11 (1.6%)	10022004		
胸部不快感	0	2 (1.9%)	2 (1.4%)	5 (1.8%)	2 (0.8%)	9 (1.3%)	10008469		

TSFAE01A_J: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
倦怠感	0	2 (1.9%)	2 (1.4%)	2 (0.7%)	2 (0.8%)	6 (0.9%)	10025482		
末梢性浮腫	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	4 (1.6%)	6 (0.9%)	10030124		
冷感	0	0	0	5 (1.8%)	0	5 (0.7%)	10016326		
疼痛	0	1 (0.9%)	1 (0.7%)	0	4 (1.6%)	5 (0.7%)	10033371		
末梢腫脹	1 (2.4%)	0	1 (0.7%)	2 (0.7%)	0	3 (0.4%)	10048959		
胸痛	1 (2.4%)	1 (0.9%)	2 (1.4%)	0	0	2 (0.3%)	10008479		
顔面浮腫	0	0	0	0	2 (0.8%)	2 (0.3%)	10016029		
全身健康状態低下	0	0	0	2 (0.7%)	0	2 (0.3%)	10049438		
非心臓性胸痛	0	0	0	2 (0.7%)	0	2 (0.3%)	10062501		
浮腫	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10030095		
腋窩痛	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10048750		
溢出	0	0	0	1 (0.4%)	0	1 (0.1%)	10015866		
高熱	0	0	0	1 (0.4%)	0	1 (0.1%)	10020843		
注入部位内出血	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10059203		
注入部位そう痒感	0	0	0	0	1 (0.4%)	1 (0.1%)	10053664		
注入部位発疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10059830		
注射部位内出血	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10022052		
注射部位反応	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10022095		
多臓器不全	0	0	0	1 (0.4%)	0	1 (0.1%)	10028154		
粘膜浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10030111		
分泌物分泌	0	0	0	1 (0.4%)	0	1 (0.1%)	10053459		
苦悶感	0	0	0	1 (0.4%)	0	1 (0.1%)	10040007		
血液およびリンパ系障害	2 (4.8%)	33 (31.1%)	35 (23.6%)	61 (21.6%)	95 (39.1%)	191 (28.3%)	10005329		
血小板減少症	0	16 (15.1%)	16 (10.8%)	23 (8.1%)	73 (30.0%)	112 (16.6%)	10043554		
好中球減少症	1 (2.4%)	11 (10.4%)	12 (8.1%)	43 (15.2%)	17 (7.0%)	72 (10.7%)	10029354		
貧血	0	18 (17.0%)	18 (12.2%)	13 (4.6%)	22 (9.1%)	53 (7.9%)	10002034		
リンパ球減少症	0	4 (3.8%)	4 (2.7%)	7 (2.5%)	26 (10.7%)	37 (5.5%)	10025327		
白血球減少症	2 (4.8%)	5 (4.7%)	7 (4.7%)	11 (3.9%)	10 (4.1%)	28 (4.2%)	10024384		
発熱性好中球減少症	0	0	0	4 (1.4%)	2 (0.8%)	6 (0.9%)	10016288		
血液障害	0	0	0	0	1 (0.4%)	1 (0.1%)	10061590		
リンパ節症	0	0	0	1 (0.4%)	0	1 (0.1%)	10025197		
赤血球凝集	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10049190		

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	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
胃腸障害	6 (14.3%)	28 (26.4%)	34 (23.0%)	74 (26.1%)	50 (20.6%)	158 (23.4%)	10017947		
悪心	5 (11.9%)	17 (16.0%)	22 (14.9%)	25 (8.8%)	16 (6.6%)	63 (9.3%)	10028813		
下痢	1 (2.4%)	6 (5.7%)	7 (4.7%)	28 (9.9%)	19 (7.8%)	54 (8.0%)	10012735		
嘔吐	1 (2.4%)	10 (9.4%)	11 (7.4%)	22 (7.8%)	12 (4.9%)	45 (6.7%)	10047700		
便秘	0	7 (6.6%)	7 (4.7%)	12 (4.2%)	9 (3.7%)	28 (4.2%)	10010774		
口内炎	0	1 (0.9%)	1 (0.7%)	6 (2.1%)	1 (0.4%)	8 (1.2%)	10042128		
腹痛	0	0	0	5 (1.8%)	0	5 (0.7%)	10000081		
上腹部痛	1 (2.4%)	0	1 (0.7%)	3 (1.1%)	1 (0.4%)	5 (0.7%)	10000087		
腹部不快感	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	3 (0.4%)	10000059		
腹部膨満	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	3 (0.4%)	10000060		
消化不良	0	0	0	1 (0.4%)	2 (0.8%)	3 (0.4%)	10013946		
放屁	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	3 (0.4%)	10016766		
口の錯感覚	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	0	3 (0.4%)	10057372		
口内乾燥	0	0	0	2 (0.7%)	0	2 (0.3%)	10013781		
嚥下障害	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10013950		
胃食道逆流性疾患	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10017885		
口唇腫脹	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10024570		
裂肛	0	0	0	1 (0.4%)	0	1 (0.1%)	10002153		
肛門出血	0	0	0	0	1 (0.4%)	1 (0.1%)	10049555		
憩室穿孔	0	0	0	0	1 (0.4%)	1 (0.1%)	10061820		
おくび	0	0	0	1 (0.4%)	0	1 (0.1%)	10015137		
胃炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10017853		
胃腸障害	0	0	0	1 (0.4%)	0	1 (0.1%)	10017944		
口の感覚鈍麻	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10057371		
口唇そう痒症	0	0	0	1 (0.4%)	0	1 (0.1%)	10070721		
非感染性歯肉炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10074863		
嚥下痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10030094		
口腔内不快感	0	0	0	0	1 (0.4%)	1 (0.1%)	10030973		
口腔障害	0	0	0	0	1 (0.4%)	1 (0.1%)	10067621		
口蓋浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10056998		
舌そう痒症	0	0	0	0	1 (0.4%)	1 (0.1%)	10070072		
感染症および寄生虫症	5 (11.9%)	15 (14.2%)	20 (13.5%)	72 (25.4%)	41 (16.9%)	133 (19.7%)	10021881		

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	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
上気道感染	1 (2.4%)	3 (2.8%)	4 (2.7%)	25 (8.8%)	15 (6.2%)	44 (6.5%)	10046306		
肺炎	1 (2.4%)	4 (3.8%)	5 (3.4%)	12 (4.2%)	11 (4.5%)	28 (4.2%)	10035664		
気管支炎	0	0	0	8 (2.8%)	7 (2.9%)	15 (2.2%)	10006451		
帯状疱疹	2 (4.8%)	1 (0.9%)	3 (2.0%)	4 (1.4%)	4 (1.6%)	11 (1.6%)	10019974		
結膜炎	0	0	0	3 (1.1%)	4 (1.6%)	7 (1.0%)	10010741		
鼻咽頭炎	0	1 (0.9%)	1 (0.7%)	5 (1.8%)	1 (0.4%)	7 (1.0%)	10028810		
気道感染	0	0	0	7 (2.5%)	0	7 (1.0%)	10062352		
副鼻腔炎	0	3 (2.8%)	3 (2.0%)	2 (0.7%)	2 (0.8%)	7 (1.0%)	10040753		
インフルエンザ	0	0	0	3 (1.1%)	1 (0.4%)	4 (0.6%)	10022000		
敗血症	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	2 (0.8%)	4 (0.6%)	10040047		
カンジダ感染	1 (2.4%)	1 (0.9%)	2 (1.4%)	0	1 (0.4%)	3 (0.4%)	10074170		
大葉性肺炎	0	2 (1.9%)	2 (1.4%)	1 (0.4%)	0	3 (0.4%)	10024738		
下気道感染	0	0	0	3 (1.1%)	0	3 (0.4%)	10024968		
鼻炎	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10039083		
尿路感染	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10046571		
気管支肺炎	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10006469		
真菌感染	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10017533		
ヘルペスウイルス感染	0	0	0	2 (0.7%)	0	2 (0.3%)	10019973		
感染	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10021789		
口腔真菌感染	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10061324		
口腔ヘルペス	0	0	0	2 (0.7%)	0	2 (0.3%)	10067152		
細菌性肺炎	0	0	0	2 (0.7%)	0	2 (0.3%)	10060946		
ＲＳウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10061603		
急性扁桃炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10001093		
細菌感染	0	0	0	1 (0.4%)	0	1 (0.1%)	10060945		
細気管支炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10006448		
細菌性気管支炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10061736		
カンピロバクター胃腸炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10007048		
細菌性結膜炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10061784		
コロナウイルス感染	0	0	0	1 (0.4%)	0	1 (0.1%)	10053983		
サイトメガロウイルス感染	0	0	0	1 (0.4%)	0	1 (0.1%)	10011831		
丹毒	0	0	0	1 (0.4%)	0	1 (0.1%)	10015145		

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	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
大腸菌性菌血症	0	0	0	1 (0.4%)	0	1 (0.1%)	10054258		
毛包炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10016936		
消化管感染	0	0	0	0	1 (0.4%)	1 (0.1%)	10017964		
陰部ヘルペス	0	0	0	0	1 (0.4%)	1 (0.1%)	10018150		
Ｈ１Ｎ１インフルエンザ	0	0	0	1 (0.4%)	0	1 (0.1%)	10069767		
注入部位蜂巣炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10065455		
口腔カンジダ症	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10030963		
急性中耳炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10033079		
パラインフルエンザウイルス感染	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10061907		
眼窩周囲蜂巣炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10057182		
腹膜炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10034674		
百日咳	0	0	0	0	1 (0.4%)	1 (0.1%)	10034738		
咽頭炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10034835		
サイトメガロウイルス性肺炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10035676		
インフルエンザ性肺炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10035714		
レジオネラ菌性肺炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10035718		
肺炎球菌性肺炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10035728		
肺敗血症	0	0	0	0	1 (0.4%)	1 (0.1%)	10051739		
腎盂腎炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10037596		
ウイルス性気道感染	0	0	0	0	1 (0.4%)	1 (0.1%)	10062106		
敗血症性ショック	0	0	0	1 (0.4%)	0	1 (0.1%)	10040070		
皮膚感染	0	0	0	1 (0.4%)	0	1 (0.1%)	10040872		
ブドウ球菌性咽頭炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10061554		
皮下組織膿瘍	0	0	0	1 (0.4%)	0	1 (0.1%)	10042343		
足部白癬	0	0	0	0	1 (0.4%)	1 (0.1%)	10043873		
真菌性舌感染	0	0	0	0	1 (0.4%)	1 (0.1%)	10075845		
腟感染	0	0	0	0	1 (0.4%)	1 (0.1%)	10046914		
水痘	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10046980		
ウイルス感染	0	0	0	1 (0.4%)	0	1 (0.1%)	10047461		
外陰部腟カンジダ症	0	0	0	1 (0.4%)	0	1 (0.1%)	10047784		
皮膚および皮下組織障害	2 (4.8%)	6 (5.7%)	8 (5.4%)	49 (17.3%)	20 (8.2%)	77 (11.4%)	10040785		

TSFAE01A_J: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
そう痒症	0	1 (0.9%)	1 (0.7%)	18 (6.4%)	3 (1.2%)	22 (3.3%)	10037087		
多汗症	1 (2.4%)	0	1 (0.7%)	11 (3.9%)	1 (0.4%)	13 (1.9%)	10020642		
発疹	0	0	0	7 (2.5%)	4 (1.6%)	11 (1.6%)	10037844		
斑状丘疹状皮疹	0	1 (0.9%)	1 (0.7%)	4 (1.4%)	3 (1.2%)	8 (1.2%)	10037868		
蕁麻疹	0	1 (0.9%)	1 (0.7%)	5 (1.8%)	1 (0.4%)	7 (1.0%)	10046735		
紅斑	0	0	0	3 (1.1%)	2 (0.8%)	5 (0.7%)	10015150		
手掌・足底発赤知覚不全症候群	0	1 (0.9%)	1 (0.7%)	0	2 (0.8%)	3 (0.4%)	10033553		
ざ瘡様皮膚炎	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10012432		
アレルギー性皮膚炎	0	0	0	0	2 (0.8%)	2 (0.3%)	10012434		
日光角化症	0	0	0	1 (0.4%)	0	1 (0.1%)	10000614		
脱毛症	0	0	0	1 (0.4%)	0	1 (0.1%)	10001760		
冷汗	0	0	0	1 (0.4%)	0	1 (0.1%)	10009866		
皮膚炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10012431		
接触性皮膚炎	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10012442		
薬疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10013687		
皮膚乾燥	0	0	0	1 (0.4%)	0	1 (0.1%)	10013786		
湿疹	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10014184		
全身紅斑	0	0	0	1 (0.4%)	0	1 (0.1%)	10051576		
手皮膚炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10058898		
寝汗	0	0	0	0	1 (0.4%)	1 (0.1%)	10029410		
皮膚疼痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10033474		
アレルギー性そう痒症	0	0	0	1 (0.4%)	0	1 (0.1%)	10063438		
全身性そう痒症	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10052576		
紅斑性皮疹	0	0	0	0	1 (0.4%)	1 (0.1%)	10037855		
全身性皮疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10037858		
斑状皮疹	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10037867		
丘疹性皮疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10037876		
そう痒性皮疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10037884		
皮膚剥脱	0	0	0	0	1 (0.4%)	1 (0.1%)	10040844		
皮膚色素過剰	0	0	0	1 (0.4%)	0	1 (0.1%)	10040865		
皮膚潰瘍	0	0	0	1 (0.4%)	0	1 (0.1%)	10040943		

TSFAE01A_J: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
顔面腫脹	0	0	0	0	1 (0.4%)	1 (0.1%)	10042682		
神経系障害	2 (4.8%)	12 (11.3%)	14 (9.5%)	33 (11.7%)	24 (9.9%)	71 (10.5%)	10029205		
頭痛	1 (2.4%)	4 (3.8%)	5 (3.4%)	13 (4.6%)	5 (2.1%)	23 (3.4%)	10019211		
浮動性めまい	0	3 (2.8%)	3 (2.0%)	6 (2.1%)	4 (1.6%)	13 (1.9%)	10013573		
末梢性感覚ニューロパチー	0	2 (1.9%)	2 (1.4%)	2 (0.7%)	7 (2.9%)	11 (1.6%)	10034620		
味覚異常	0	2 (1.9%)	2 (1.4%)	4 (1.4%)	2 (0.8%)	8 (1.2%)	10013911		
錯感覚	0	0	0	2 (0.7%)	3 (1.2%)	5 (0.7%)	10033775		
振戦	0	1 (0.9%)	1 (0.7%)	4 (1.4%)	0	5 (0.7%)	10044565		
注意力障害	0	0	0	2 (0.7%)	2 (0.8%)	4 (0.6%)	10013496		
嗜眠	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	0	3 (0.4%)	10024264		
記憶障害	0	0	0	1 (0.4%)	2 (0.8%)	3 (0.4%)	10027175		
失神寸前の状態	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10036653		
失神	0	0	0	2 (0.7%)	0	2 (0.3%)	10042772		
味覚消失	0	0	0	1 (0.4%)	0	1 (0.1%)	10001480		
平衡障害	0	0	0	1 (0.4%)	0	1 (0.1%)	10049848		
異常感覚	0	0	0	1 (0.4%)	0	1 (0.1%)	10013886		
頭部不快感	0	0	0	0	1 (0.4%)	1 (0.1%)	10019194		
知覚過敏	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10020568		
神経痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10029223		
末梢性ニューロパチー	0	0	0	1 (0.4%)	0	1 (0.1%)	10029331		
下肢静止不能症候群	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10058920		
一過性脳虚血発作	0	0	0	0	1 (0.4%)	1 (0.1%)	10044390		
視野欠損	0	0	0	1 (0.4%)	0	1 (0.1%)	10047555		
筋骨格系および結合組織障害	3 (7.1%)	14 (13.2%)	17 (11.5%)	27 (9.5%)	12 (4.9%)	56 (8.3%)	10028395		
筋痙縮	1 (2.4%)	4 (3.8%)	5 (3.4%)	11 (3.9%)	1 (0.4%)	17 (2.5%)	10028334		
背部痛	1 (2.4%)	4 (3.8%)	5 (3.4%)	7 (2.5%)	4 (1.6%)	16 (2.4%)	10003988		
筋肉痛	1 (2.4%)	1 (0.9%)	2 (1.4%)	3 (1.1%)	1 (0.4%)	6 (0.9%)	10028411		
関節痛	0	2 (1.9%)	2 (1.4%)	2 (0.7%)	1 (0.4%)	5 (0.7%)	10003239		
骨痛	0	2 (1.9%)	2 (1.4%)	2 (0.7%)	1 (0.4%)	5 (0.7%)	10006002		
四肢痛	0	2 (1.9%)	2 (1.4%)	1 (0.4%)	2 (0.8%)	5 (0.7%)	10033425		
筋骨格系胸痛	0	1 (0.9%)	1 (0.7%)	3 (1.1%)	0	4 (0.6%)	10050819		
筋骨格痛	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10028391		

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	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
筋力低下	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10028372		
ミオパチー	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10028641		
デュプイトラン拘縮	0	0	0	1 (0.4%)	0	1 (0.1%)	10013872		
側腹部痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10016750		
四肢不快感	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10061224		
頚部痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10028836		
顎骨壊死	0	0	0	1 (0.4%)	0	1 (0.1%)	10064658		
血管障害	3 (7.1%)	5 (4.7%)	8 (5.4%)	24 (8.5%)	23 (9.5%)	55 (8.2%)	10047065		
高血圧	2 (4.8%)	2 (1.9%)	4 (2.7%)	10 (3.5%)	11 (4.5%)	25 (3.7%)	10020772		
低血圧	0	1 (0.9%)	1 (0.7%)	6 (2.1%)	5 (2.1%)	12 (1.8%)	10021097		
潮紅	1 (2.4%)	1 (0.9%)	2 (1.4%)	5 (1.8%)	2 (0.8%)	9 (1.3%)	10016825		
ほてり	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	2 (0.8%)	5 (0.7%)	10060800		
深部静脈血栓症	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	2 (0.8%)	4 (0.6%)	10051055		
起立性低血圧	0	0	0	2 (0.7%)	0	2 (0.3%)	10031127		
血腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10018852		
血栓性静脈炎	0	0	0	0	1 (0.4%)	1 (0.1%)	10043570		
血栓症	0	0	0	0	1 (0.4%)	1 (0.1%)	10043607		
血管拡張	0	0	0	0	1 (0.4%)	1 (0.1%)	10047141		
代謝および栄養障害	2 (4.8%)	14 (13.2%)	16 (10.8%)	17 (6.0%)	18 (7.4%)	51 (7.6%)	10027433		
食欲減退	2 (4.8%)	7 (6.6%)	9 (6.1%)	7 (2.5%)	6 (2.5%)	22 (3.3%)	10061428		
低カリウム血症	0	3 (2.8%)	3 (2.0%)	5 (1.8%)	3 (1.2%)	11 (1.6%)	10021015		
低ナトリウム血症	0	3 (2.8%)	3 (2.0%)	2 (0.7%)	1 (0.4%)	6 (0.9%)	10021036		
低カルシウム血症	0	0	0	5 (1.8%)	0	5 (0.7%)	10020947		
低リン酸血症	0	0	0	1 (0.4%)	4 (1.6%)	5 (0.7%)	10021058		
低マグネシウム血症	0	2 (1.9%)	2 (1.4%)	1 (0.4%)	0	3 (0.4%)	10021027		
水分過負荷	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10016803		
高血糖	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10020635		
低アルブミン血症	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10020942		
脱水	0	0	0	1 (0.4%)	0	1 (0.1%)	10012174		
酵素異常	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10014935		
体液貯留	0	0	0	0	1 (0.4%)	1 (0.1%)	10016807		
葉酸欠乏	0	0	0	1 (0.4%)	0	1 (0.1%)	10016880		

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	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
高カルシウム血症	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10020583		
高ナトリウム血症	0	0	0	0	1 (0.4%)	1 (0.1%)	10020679		
高尿酸血症	0	0	0	0	1 (0.4%)	1 (0.1%)	10020903		
低血糖症	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10020993		
腫瘍崩壊症候群	0	0	0	0	1 (0.4%)	1 (0.1%)	10045170		
ビタミンＢ１２欠乏	0	0	0	0	1 (0.4%)	1 (0.1%)	10047609		
臨床検査	3 (7.1%)	3 (2.8%)	6 (4.1%)	17 (6.0%)	13 (5.3%)	36 (5.3%)	10022891		
アラニンアミノトランスフェラーゼ増加	0	0	0	5 (1.8%)	4 (1.6%)	9 (1.3%)	10001551		
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	3 (1.1%)	5 (2.1%)	8 (1.2%)	10003481		
γ－グルタミルトランスフェラーゼ増加	0	0	0	3 (1.1%)	4 (1.6%)	7 (1.0%)	10017693		
体重減少	0	1 (0.9%)	1 (0.7%)	3 (1.1%)	3 (1.2%)	7 (1.0%)	10047895		
血中アルカリホスファターゼ増加	0	0	0	3 (1.1%)	1 (0.4%)	4 (0.6%)	10059570		
交差適合試験不適合	3 (7.1%)	0	3 (2.0%)	0	0	3 (0.4%)	10011414		
心電図ＱＴ延長	0	0	0	2 (0.7%)	0	2 (0.3%)	10014387		
体重増加	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10047899		
血中クレアチニン増加	0	0	0	0	1 (0.4%)	1 (0.1%)	10005483		
血中乳酸脱水素酵素減少	0	0	0	1 (0.4%)	0	1 (0.1%)	10005629		
血中乳酸脱水素酵素増加	0	0	0	0	1 (0.4%)	1 (0.1%)	10005630		
免疫グロブリン減少	0	0	0	1 (0.4%)	0	1 (0.1%)	10021499		
酸素飽和度異常	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10033317		
酸素飽和度低下	0	0	0	1 (0.4%)	0	1 (0.1%)	10033318		
トロポニン増加	0	0	0	1 (0.4%)	0	1 (0.1%)	10058267		
眼障害	1 (2.4%)	2 (1.9%)	3 (2.0%)	15 (5.3%)	15 (6.2%)	33 (4.9%)	10015919		
流涙増加	0	0	0	6 (2.1%)	6 (2.5%)	12 (1.8%)	10023644		
霧視	1 (2.4%)	0	1 (0.7%)	4 (1.4%)	0	5 (0.7%)	10047513		
結膜浮腫	0	0	0	0	3 (1.2%)	3 (0.4%)	10010726		
眼の障害	0	0	0	0	2 (0.8%)	2 (0.3%)	10015916		
眼刺激	0	0	0	2 (0.7%)	0	2 (0.3%)	10015946		

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	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
眼そう痒症	0	2 (1.9%)	2 (1.4%)	0	0	2 (0.3%)	10052140		
眼部腫脹	0	0	0	2 (0.7%)	0	2 (0.3%)	10015967		
眼充血	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10030041		
白内障	0	0	0	1 (0.4%)	0	1 (0.1%)	10007739		
結膜出血	0	0	0	0	1 (0.4%)	1 (0.1%)	10010719		
眼乾燥	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10013774		
眼のアレルギー	0	0	0	1 (0.4%)	0	1 (0.1%)	10015907		
眼脂	0	0	0	0	1 (0.4%)	1 (0.1%)	10015915		
眼瞼浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10015993		
心臓障害	1 (2.4%)	2 (1.9%)	3 (2.0%)	11 (3.9%)	8 (3.3%)	22 (3.3%)	10007541		
洞性頻脈	1 (2.4%)	0	1 (0.7%)	2 (0.7%)	3 (1.2%)	6 (0.9%)	10040752		
頻脈	0	1 (0.9%)	1 (0.7%)	5 (1.8%)	0	6 (0.9%)	10043071		
狭心症	0	0	0	2 (0.7%)	0	2 (0.3%)	10002383		
心房細動	0	0	0	0	2 (0.8%)	2 (0.3%)	10003658		
動悸	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10033557		
上室性頻脈	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10042604		
急性冠動脈症候群	0	0	0	0	1 (0.4%)	1 (0.1%)	10051592		
徐脈	0	0	0	0	1 (0.4%)	1 (0.1%)	10006093		
伝導障害	0	0	0	1 (0.4%)	0	1 (0.1%)	10010276		
精神障害	2 (4.8%)	2 (1.9%)	4 (2.7%)	6 (2.1%)	10 (4.1%)	20 (3.0%)	10037175		
不眠症	0	0	0	2 (0.7%)	7 (2.9%)	9 (1.3%)	10022437		
不安	1 (2.4%)	1 (0.9%)	2 (1.4%)	1 (0.4%)	0	3 (0.4%)	10002855		
錯乱状態	0	1 (0.9%)	1 (0.7%)	0	1 (0.4%)	2 (0.3%)	10010305		
うつ病	0	0	0	2 (0.7%)	0	2 (0.3%)	10012378		
落ち着きのなさ	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10038743		
激越	0	0	0	0	1 (0.4%)	1 (0.1%)	10001497		
譫妄	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10012218		
耳および迷路障害	1 (2.4%)	1 (0.9%)	2 (1.4%)	4 (1.4%)	4 (1.6%)	10 (1.5%)	10013993		
回転性めまい	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	2 (0.8%)	5 (0.7%)	10047340		
耳鳴	1 (2.4%)	0	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10043882		
耳痛	0	0	0	0	1 (0.4%)	1 (0.1%)	10014020		
耳そう痒症	0	0	0	0	1 (0.4%)	1 (0.1%)	10052138		

TSFAE01A_J: Number of Subjects With 1 or More Treatment-emergent Adverse Events Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
聴力低下	0	0	0	1 (0.4%)	0	1 (0.1%)	10048865		
肝胆道系障害	1 (2.4%)	2 (1.9%)	3 (2.0%)	3 (1.1%)	3 (1.2%)	9 (1.3%)	10019805		
肝機能異常	1 (2.4%)	1 (0.9%)	2 (1.4%)	2 (0.7%)	0	4 (0.6%)	10019670		
高ビリルビン血症	0	1 (0.9%)	1 (0.7%)	0	3 (1.2%)	4 (0.6%)	10020578		
肝細胞損傷	0	0	0	1 (0.4%)	0	1 (0.1%)	10019837		
腎および尿路障害	0	2 (1.9%)	2 (1.4%)	3 (1.1%)	4 (1.6%)	9 (1.3%)	10038359		
腎機能障害	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	0	3 (0.4%)	10062237		
尿閉	0	1 (0.9%)	1 (0.7%)	0	1 (0.4%)	2 (0.3%)	10046555		
急性腎不全	0	0	0	0	1 (0.4%)	1 (0.1%)	10069339		
高窒素血症	0	0	0	1 (0.4%)	0	1 (0.1%)	10003885		
慢性腎臓病	0	0	0	0	1 (0.4%)	1 (0.1%)	10064848		
失禁	0	0	0	0	1 (0.4%)	1 (0.1%)	10021639		
免疫系障害	0	1 (0.9%)	1 (0.7%)	3 (1.1%)	1 (0.4%)	5 (0.7%)	10021428		
低γグロブリン血症	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10020983		
薬物過敏症	0	0	0	1 (0.4%)	0	1 (0.1%)	10013700		
免疫抑制	0	0	0	1 (0.4%)	0	1 (0.1%)	10062016		
季節性アレルギー	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10048908		
傷害、中毒および処置合併症	0	0	0	0	2 (0.8%)	2 (0.3%)	10022117		
アレルギー性輸血反応	0	0	0	0	1 (0.4%)	1 (0.1%)	10066173		
皮下血腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10042345		
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1 (0.4%)	0	1 (0.1%)	10029104		
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.4%)	0	1 (0.1%)	10068349		

Key: TEAE=Treatment-emergent Adverse Events, D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone.
Note: Adverse events were coded using MedDRA Version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

表 2.7.4-付録-173 Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

TSFAE02A_J: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
Analysis set: all treated	42	106	148	283	243	674			
Total number of subjects with infusion related reactions related to study treatment	31 (73.8%)	39 (36.8%)	70 (47.3%)	132 (46.6%)	110 (45.3%)	312 (46.3%)			
MedDRA system organ class / Preferred term									
呼吸器、胸郭および縦隔障害	26 (61.9%)	28 (26.4%)	54 (36.5%)	86 (30.4%)	83 (34.2%)	223 (33.1%)	10038738		
呼吸困難	2 (4.8%)	6 (5.7%)	8 (5.4%)	24 (8.5%)	26 (10.7%)	58 (8.6%)	10013968		
咳嗽	6 (14.3%)	6 (5.7%)	12 (8.1%)	23 (8.1%)	17 (7.0%)	52 (7.7%)	10011224		
気管支痙攣	0	4 (3.8%)	4 (2.7%)	13 (4.6%)	22 (9.1%)	39 (5.8%)	10006482		
鼻閉	4 (9.5%)	13 (12.3%)	17 (11.5%)	7 (2.5%)	10 (4.1%)	34 (5.0%)	10028735		
咽喉刺激感	2 (4.8%)	7 (6.6%)	9 (6.1%)	8 (2.8%)	12 (4.9%)	29 (4.3%)	10043521		
アレルギー性鼻炎	10 (23.8%)	0	10 (6.8%)	5 (1.8%)	3 (1.2%)	18 (2.7%)	10039085		
喘鳴	0	2 (1.9%)	2 (1.4%)	6 (2.1%)	4 (1.6%)	12 (1.8%)	10047924		
鼻漏	0	0	0	6 (2.1%)	4 (1.6%)	10 (1.5%)	10039101		
喉頭浮腫	0	1 (0.9%)	1 (0.7%)	6 (2.1%)	2 (0.8%)	9 (1.3%)	10023845		
咽喉絞扼感	3 (7.1%)	0	3 (2.0%)	1 (0.4%)	4 (1.6%)	8 (1.2%)	10043528		
低酸素症	1 (2.4%)	0	1 (0.7%)	4 (1.4%)	0	5 (0.7%)	10021143		
くしゃみ	1 (2.4%)	2 (1.9%)	3 (2.0%)	2 (0.7%)	0	5 (0.7%)	10041232		
アレルギー性咳嗽	1 (2.4%)	0	1 (0.7%)	0	2 (0.8%)	3 (0.4%)	10053779		
発声障害	0	0	0	3 (1.1%)	0	3 (0.4%)	10013952		
鼻閉塞	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10028748		
口腔咽頭痛	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	3 (0.4%)	10068319		
湿性咳嗽	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10036790		
アレルギー性呼吸器症状	0	0	0	2 (0.7%)	0	2 (0.3%)	10063527		
窒息	0	0	0	1 (0.4%)	0	1 (0.1%)	10003497		
喘息	0	0	0	0	1 (0.4%)	1 (0.1%)	10003553		
喉頭不快感	0	0	0	1 (0.4%)	0	1 (0.1%)	10054115		
喉頭狭窄	0	0	0	1 (0.4%)	0	1 (0.1%)	10023862		

TSFAE02A_J: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
アレルギー性喉頭炎	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10064866		
喉頭刺激感	0	0	0	1 (0.4%)	0	1 (0.1%)	10058670		
鼻部不快感	0	0	0	1 (0.4%)	0	1 (0.1%)	10052437		
鼻部障害	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10062209		
口腔咽頭不快感	0	0	0	0	1 (0.4%)	1 (0.1%)	10068318		
口腔咽頭腫脹	0	0	0	0	1 (0.4%)	1 (0.1%)	10031118		
咽頭浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10034829		
呼気延長	0	0	0	1 (0.4%)	0	1 (0.1%)	10059411		
肺水腫	0	0	0	1 (0.4%)	0	1 (0.1%)	10037423		
気道うっ血	0	0	0	0	1 (0.4%)	1 (0.1%)	10052251		
低音性連続性ラ音	0	0	0	0	1 (0.4%)	1 (0.1%)	10039109		
副鼻腔障害	0	0	0	1 (0.4%)	0	1 (0.1%)	10062244		
上気道性喘鳴	0	0	0	1 (0.4%)	0	1 (0.1%)	10042241		
窒息感	0	0	0	1 (0.4%)	0	1 (0.1%)	10042444		
一般・全身障害および投与部位の状態	5 (11.9%)	11 (10.4%)	16 (10.8%)	34 (12.0%)	21 (8.6%)	71 (10.5%)	10018065		
悪寒	4 (9.5%)	6 (5.7%)	10 (6.8%)	13 (4.6%)	10 (4.1%)	33 (4.9%)	10008531		
発熱	1 (2.4%)	0	1 (0.7%)	6 (2.1%)	4 (1.6%)	11 (1.6%)	10037660		
胸部不快感	0	1 (0.9%)	1 (0.7%)	5 (1.8%)	2 (0.8%)	8 (1.2%)	10008469		
冷感	0	0	0	5 (1.8%)	0	5 (0.7%)	10016326		
疲労	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	1 (0.4%)	4 (0.6%)	10016256		
インフルエンザ様疾患	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10022004		
疼痛	0	1 (0.9%)	1 (0.7%)	0	1 (0.4%)	2 (0.3%)	10033371		
胸痛	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10008479		
溢出	0	0	0	1 (0.4%)	0	1 (0.1%)	10015866		
高熱	0	0	0	1 (0.4%)	0	1 (0.1%)	10020843		
注入部位内出血	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10059203		
注入部位そう痒感	0	0	0	0	1 (0.4%)	1 (0.1%)	10053664		
注入部位発疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10059830		
倦怠感	0	0	0	0	1 (0.4%)	1 (0.1%)	10025482		
非心臓性胸痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10062501		
粘膜浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10030111		

TSFAE02A_J: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
分泌物分泌	0	0	0	1 (0.4%)	0	1 (0.1%)	10053459		
苦悶感	0	0	0	1 (0.4%)	0	1 (0.1%)	10040007		
胃腸障害	3 (7.1%)	8 (7.5%)	11 (7.4%)	30 (10.6%)	21 (8.6%)	62 (9.2%)	10017947		
嘔吐	1 (2.4%)	6 (5.7%)	7 (4.7%)	16 (5.7%)	9 (3.7%)	32 (4.7%)	10047700		
悪心	3 (7.1%)	5 (4.7%)	8 (5.4%)	14 (4.9%)	6 (2.5%)	28 (4.2%)	10028813		
下痢	0	1 (0.9%)	1 (0.7%)	0	4 (1.6%)	5 (0.7%)	10012735		
腹痛	0	0	0	3 (1.1%)	0	3 (0.4%)	10000081		
口の錯感覚	0	1 (0.9%)	1 (0.7%)	2 (0.7%)	0	3 (0.4%)	10057372		
上腹部痛	1 (2.4%)	0	1 (0.7%)	0	1 (0.4%)	2 (0.3%)	10000087		
嚥下障害	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10013950		
口唇腫脹	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10024570		
消化不良	0	0	0	1 (0.4%)	0	1 (0.1%)	10013946		
口唇そう痒症	0	0	0	1 (0.4%)	0	1 (0.1%)	10070721		
嚥下痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10030094		
口蓋浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10056998		
舌そう痒症	0	0	0	0	1 (0.4%)	1 (0.1%)	10070072		
皮膚および皮下組織障害	0	3 (2.8%)	3 (2.0%)	26 (9.2%)	9 (3.7%)	38 (5.6%)	10040785		
そう痒症	0	1 (0.9%)	1 (0.7%)	8 (2.8%)	3 (1.2%)	12 (1.8%)	10037087		
多汗症	0	0	0	5 (1.8%)	1 (0.4%)	6 (0.9%)	10020642		
蕁麻疹	0	1 (0.9%)	1 (0.7%)	4 (1.4%)	1 (0.4%)	6 (0.9%)	10046735		
発疹	0	0	0	3 (1.1%)	1 (0.4%)	4 (0.6%)	10037844		
紅斑	0	0	0	3 (1.1%)	0	3 (0.4%)	10015150		
アレルギー性皮膚炎	0	0	0	0	2 (0.8%)	2 (0.3%)	10012434		
冷汗	0	0	0	1 (0.4%)	0	1 (0.1%)	10009866		
アレルギー性そう痒症	0	0	0	1 (0.4%)	0	1 (0.1%)	10063438		
紅斑性皮疹	0	0	0	0	1 (0.4%)	1 (0.1%)	10037855		
斑状皮疹	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10037867		
斑状丘疹状皮疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10037868		
そう痒性皮疹	0	0	0	1 (0.4%)	0	1 (0.1%)	10037884		
顔面腫脹	0	0	0	0	1 (0.4%)	1 (0.1%)	10042682		
血管障害	3 (7.1%)	0	3 (2.0%)	16 (5.7%)	13 (5.3%)	32 (4.7%)	10047065		
高血圧	2 (4.8%)	0	2 (1.4%)	5 (1.8%)	8 (3.3%)	15 (2.2%)	10020772		

TSFAE02A_J: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
潮紅	1 (2.4%)	0	1 (0.7%)	4 (1.4%)	2 (0.8%)	7 (1.0%)	10016825		
低血圧	0	0	0	5 (1.8%)	2 (0.8%)	7 (1.0%)	10021097		
ほてり	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10060800		
血管拡張	0	0	0	0	1 (0.4%)	1 (0.1%)	10047141		
眼障害	1 (2.4%)	2 (1.9%)	3 (2.0%)	10 (3.5%)	11 (4.5%)	24 (3.6%)	10015919		
流涙増加	0	0	0	5 (1.8%)	5 (2.1%)	10 (1.5%)	10023644		
結膜浮腫	0	0	0	0	3 (1.2%)	3 (0.4%)	10010726		
眼刺激	0	0	0	2 (0.7%)	0	2 (0.3%)	10015946		
眼そう痒症	0	2 (1.9%)	2 (1.4%)	0	0	2 (0.3%)	10052140		
眼部腫脹	0	0	0	2 (0.7%)	0	2 (0.3%)	10015967		
眼のアレルギー	0	0	0	1 (0.4%)	0	1 (0.1%)	10015907		
眼脂	0	0	0	0	1 (0.4%)	1 (0.1%)	10015915		
眼の障害	0	0	0	0	1 (0.4%)	1 (0.1%)	10015916		
眼瞼浮腫	0	0	0	0	1 (0.4%)	1 (0.1%)	10015993		
眼充血	0	0	0	1 (0.4%)	0	1 (0.1%)	10030041		
霧視	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10047513		
神経系障害	0	2 (1.9%)	2 (1.4%)	12 (4.2%)	5 (2.1%)	19 (2.8%)	10029205		
頭痛	0	2 (1.9%)	2 (1.4%)	7 (2.5%)	2 (0.8%)	11 (1.6%)	10019211		
浮動性めまい	0	0	0	1 (0.4%)	2 (0.8%)	3 (0.4%)	10013573		
錯感覚	0	0	0	2 (0.7%)	1 (0.4%)	3 (0.4%)	10033775		
味覚異常	0	0	0	1 (0.4%)	0	1 (0.1%)	10013911		
失神	0	0	0	1 (0.4%)	0	1 (0.1%)	10042772		
心臓障害	1 (2.4%)	2 (1.9%)	3 (2.0%)	9 (3.2%)	5 (2.1%)	17 (2.5%)	10007541		
洞性頻脈	1 (2.4%)	0	1 (0.7%)	2 (0.7%)	3 (1.2%)	6 (0.9%)	10040752		
頻脈	0	1 (0.9%)	1 (0.7%)	5 (1.8%)	0	6 (0.9%)	10043071		
動悸	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10033557		
上室性頻脈	0	0	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	10042604		
狭心症	0	0	0	1 (0.4%)	0	1 (0.1%)	10002383		
徐脈	0	0	0	0	1 (0.4%)	1 (0.1%)	10006093		
筋骨格系および結合組織障害	2 (4.8%)	1 (0.9%)	3 (2.0%)	5 (1.8%)	5 (2.1%)	13 (1.9%)	10028395		
背部痛	1 (2.4%)	1 (0.9%)	2 (1.4%)	1 (0.4%)	4 (1.6%)	7 (1.0%)	10003988		
筋骨格系胸痛	0	0	0	3 (1.1%)	0	3 (0.4%)	10050819		

TSFAE02A_J: Number of Subjects With 1 or More Treatment-emergent Infusion Related Reactions Related to Study Treatment by MedDRA System-Organ Class and Preferred Term; Safety Analysis Set (Studies GEN501 Part1, MMY2002, MMY3003 and MMY3004)

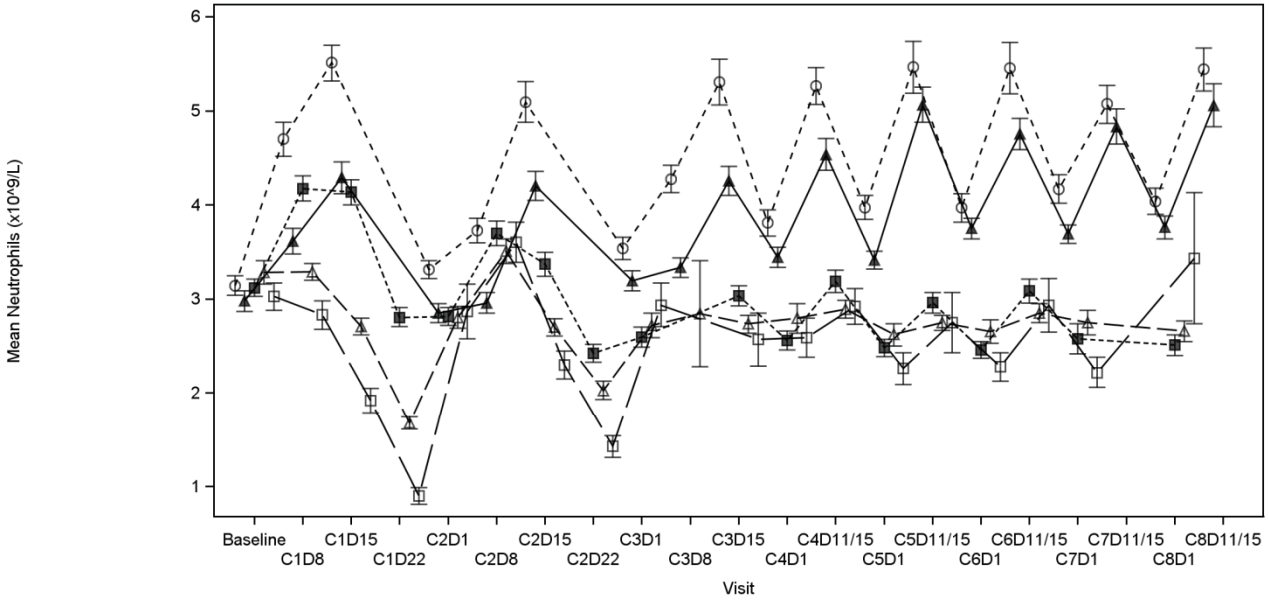
	GEN501 Part2 16 mg/kg	MMY2002 16 mg/kg	GEN501 Part2 16 mg/kg+MMY2002 16 mg/kg	MMY3003 DRd	MMY3004 DVd	Total	SOC/PT Code	Recoded SOC/PT Term	Recoded SOC/PT Code
骨痛	0	0	0	0	1 (0.4%)	1 (0.1%)	10006002		
筋骨格痛	0	0	0	1 (0.4%)	0	1 (0.1%)	10028391		
筋肉痛	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10028411		
血液およびリンパ系障害	0	2 (1.9%)	2 (1.4%)	1 (0.4%)	0	3 (0.4%)	10005329		
貧血	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10002034		
赤血球凝集	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10049190		
血小板減少症	0	0	0	1 (0.4%)	0	1 (0.1%)	10043554		
耳および迷路障害	0	0	0	0	2 (0.8%)	2 (0.3%)	10013993		
耳そう痒症	0	0	0	0	1 (0.4%)	1 (0.1%)	10052138		
回転性めまい	0	0	0	0	1 (0.4%)	1 (0.1%)	10047340		
免疫系障害	0	1 (0.9%)	1 (0.7%)	1 (0.4%)	0	2 (0.3%)	10021428		
薬物過敏症	0	0	0	1 (0.4%)	0	1 (0.1%)	10013700		
季節性アレルギー	0	1 (0.9%)	1 (0.7%)	0	0	1 (0.1%)	10048908		
感染症および寄生虫症	0	0	0	2 (0.7%)	0	2 (0.3%)	10021881		
結膜炎	0	0	0	1 (0.4%)	0	1 (0.1%)	10010741		
上気道感染	0	0	0	1 (0.4%)	0	1 (0.1%)	10046306		
臨床検査	0	0	0	2 (0.7%)	0	2 (0.3%)	10022891		
心電図ＱＴ延長	0	0	0	1 (0.4%)	0	1 (0.1%)	10014387		
酸素飽和度低下	0	0	0	1 (0.4%)	0	1 (0.1%)	10033318		
精神障害	2 (4.8%)	0	2 (1.4%)	0	0	2 (0.3%)	10037175		
不安	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10002855		
譫妄	1 (2.4%)	0	1 (0.7%)	0	0	1 (0.1%)	10012218		

Key: TEAE=Treatment-emergent Adverse Events, D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone.
Note: Adverse events were coded using MedDRA Version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02A_J.rtf] [JNJ-54767414\Z_SCS\DBR_SCS_2016\RE_SCS_2016\tsfae02a_j.sas] 16SEP2016, 14:33

図 2.7.4-付録-1 Mean Neutrophils (x10^9/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

GSFLAB02: Mean Neutrophils (x10^9/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

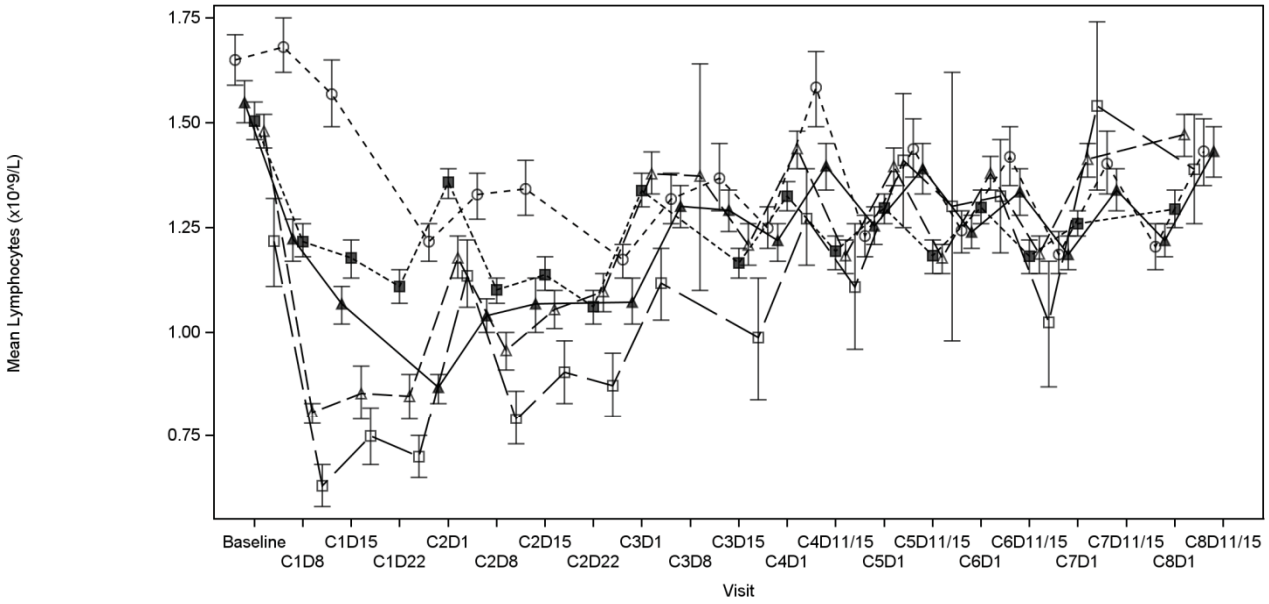


Number of Subjects																					
Vd	237	226	144		224	211	131		213	190	99	196	164	179	149	166	141	151	127	135	118
DVd	243	236	229		232	225	222		222	218	215	221	195	210	179	208	175	198	169	193	155
Rd	281	275	275	265	268	261	264	255	264		253	257	242	238	224	228	209	216		206	
DRd	318	308	310	305	309	304	307	306	305	14	300	298	291	290	284	287	275	285		279	
DPd	103	87	89	82	82	74	78	66	71		23	61	55	53	18	51	16	41		38	

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: If less than or equal to 10 subjects were measured at certain time point for the treatment, then the assessment would not be plotted due to high variability.

図 2.7.4-付録-2 Mean Lymphocytes (x10^9/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

GSFLAB03: Mean Lymphocytes (x10^9/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)



Number of Subjects

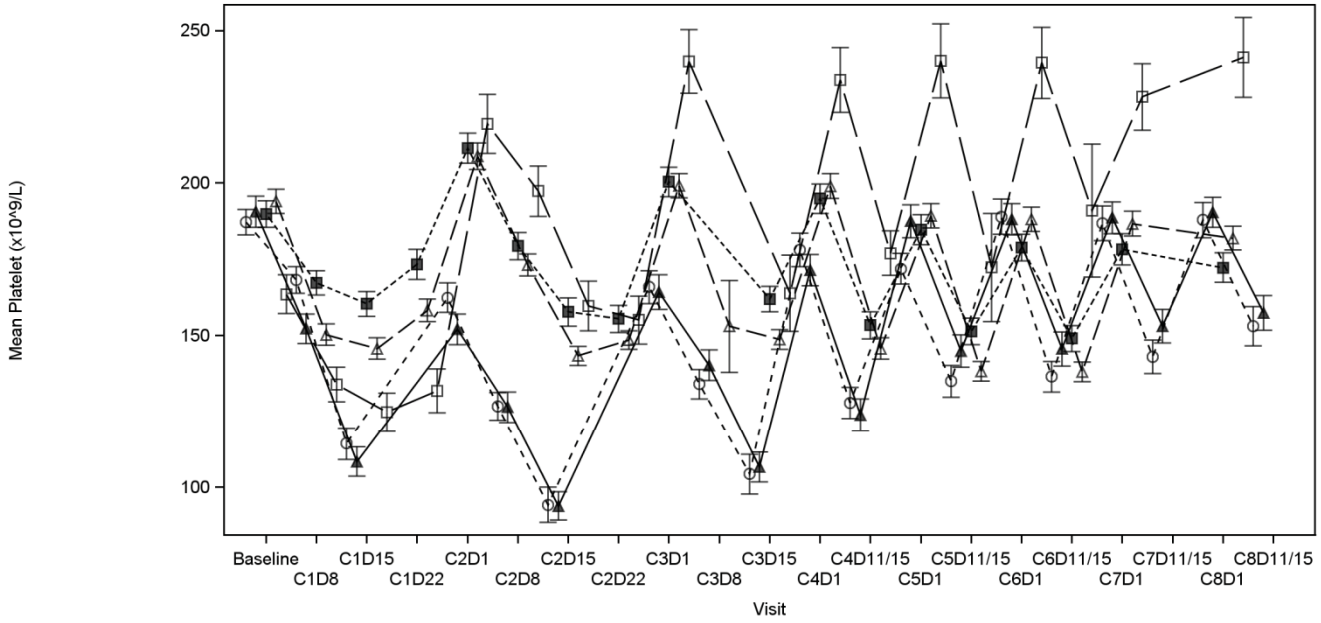
Vd	235	223	141		222	208	129		210	185	96	193	157	177	144	165	139	150	125	134	116
DVd	240	234	227		230	221	219		220	214	212	219	192	208	177	206	174	197	167	193	154
Rd	280	275	275	265	268	261	265	256	264		251	257	242	238	224	228	208	216		206	
DRd	318	308	310	302	307	303	307	303	305	14	299	298	291	290	284	287	275	285		279	
DPd	103	87	89	82	82	74	78	66	71		23	61	55	53	18	51	16	41		38	

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: If less than or equal to 10 subjects were measured at certain time point for the treatment, then the assessment would not be plotted due to high variability.

[GSFLAB03.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\GSFLAB03.SAS] 01JUN2016, 10:31

図 2.7.4-付録-3 Mean Platelets (x10^9/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

GSFLAB04: Mean Platelets (x10^9/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)



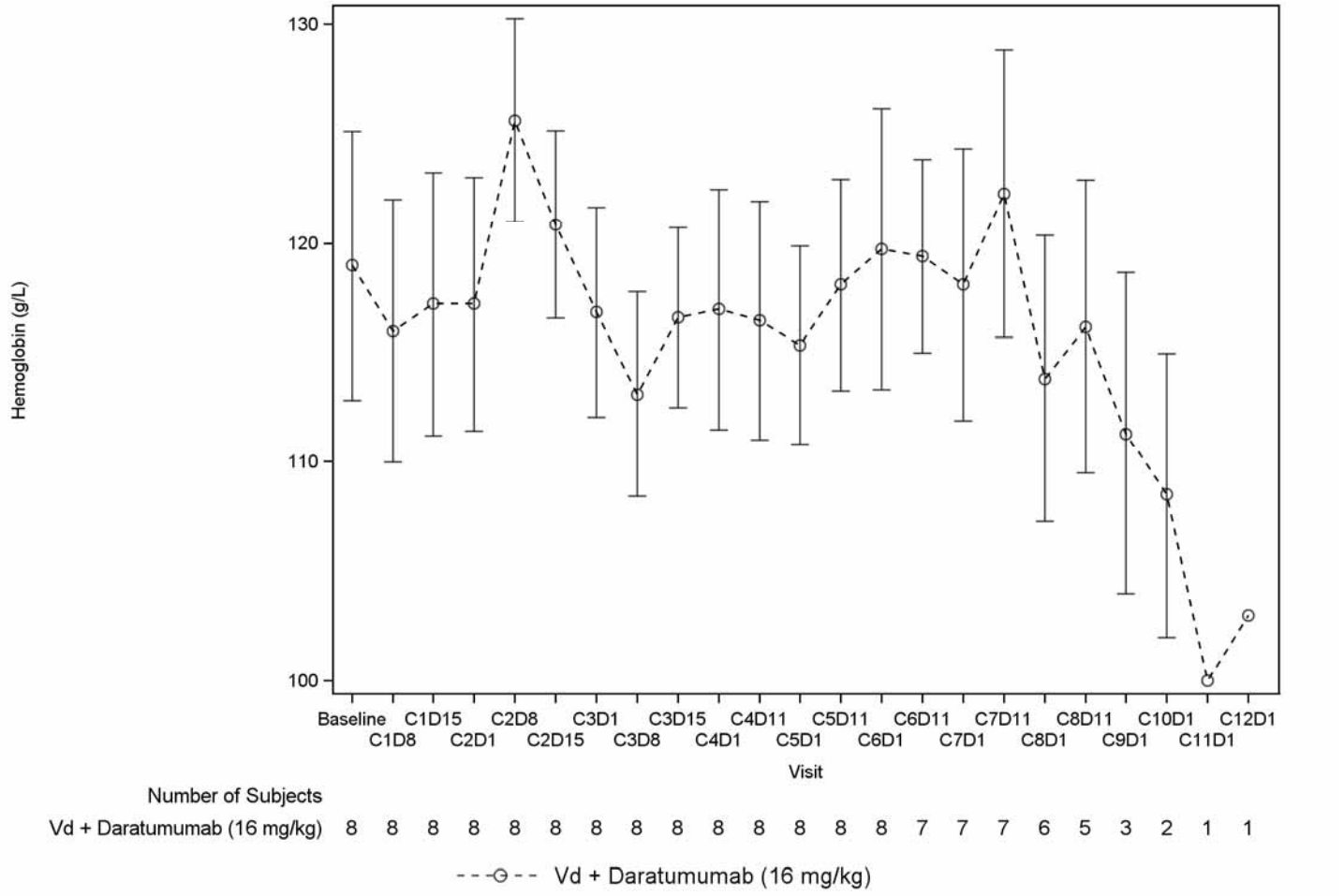
Number of Subjects

Vd	237	230	145		226	213	134		213	191	101	196	164	179	149	166	142	151	128	135	118
DVd	242	236	231		233	225	223		225	218	215	222	195	211	180	208	176	199	171	194	156
Rd	281	274	274	266	269	262	265	257	265		254	257	242	238	224	227	210	216		207	
DRd	318	310	311	306	309	304	307	307	305	14	300	298	289	290	284	286	274	285		279	
DPd	103	87	91	82	82	74	78	66	71		23	62	56	54	18	51	16	41		38	

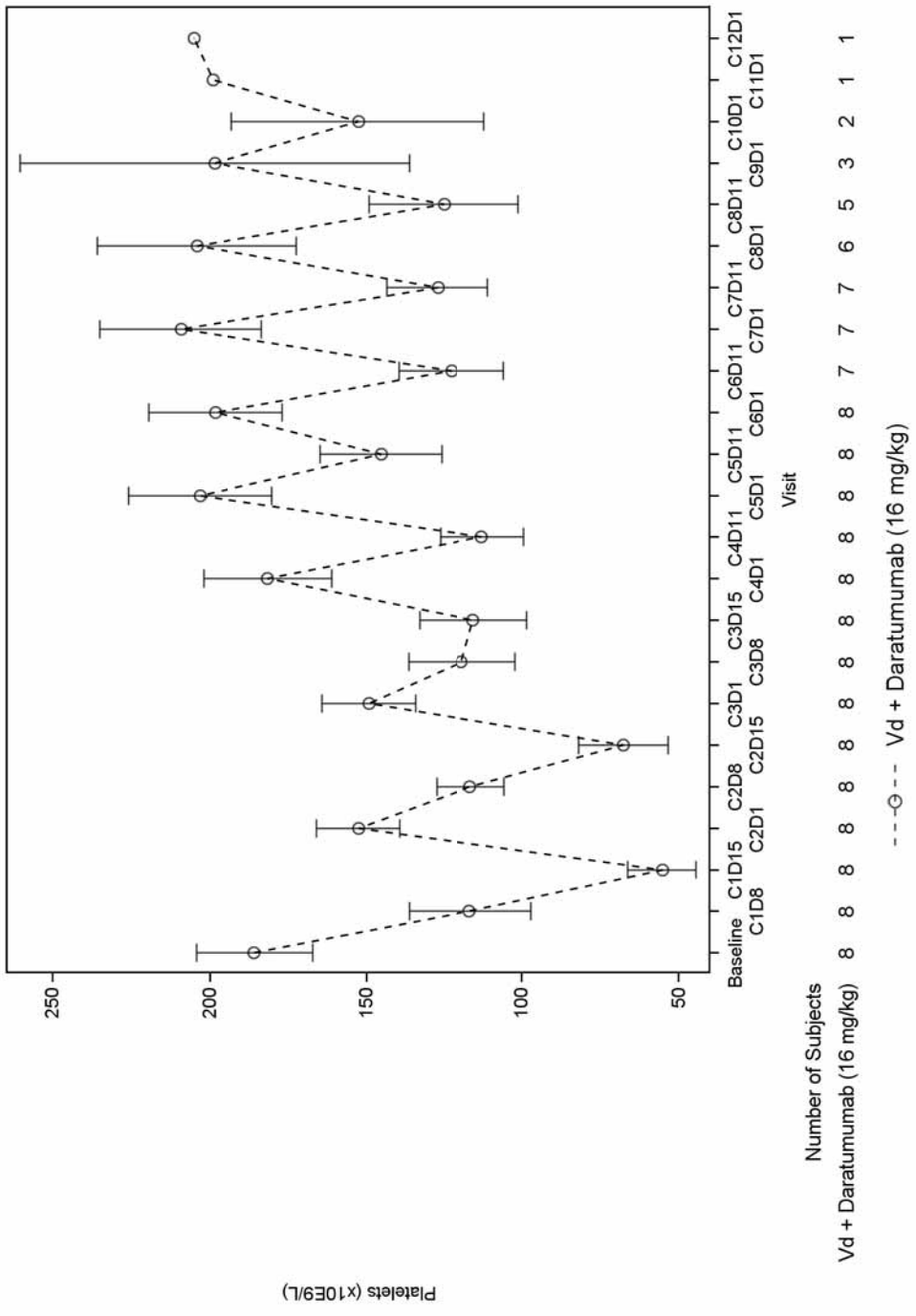
Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: If less than or equal to 10 subjects were measured at certain time point for the treatment, then the assessment would not be plotted due to high variability.

図 2.7.4-付録-4 Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)

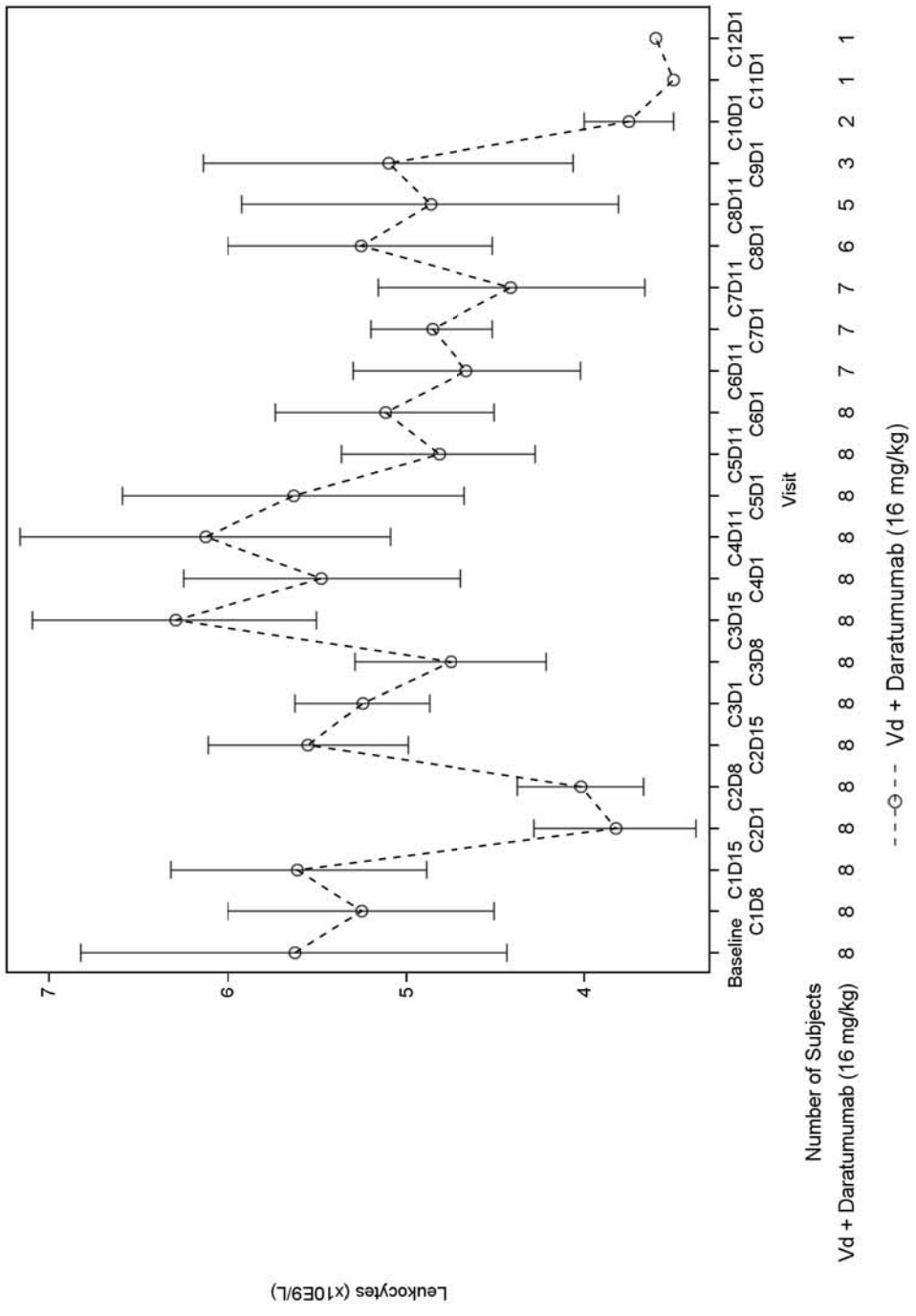
GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)



GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)

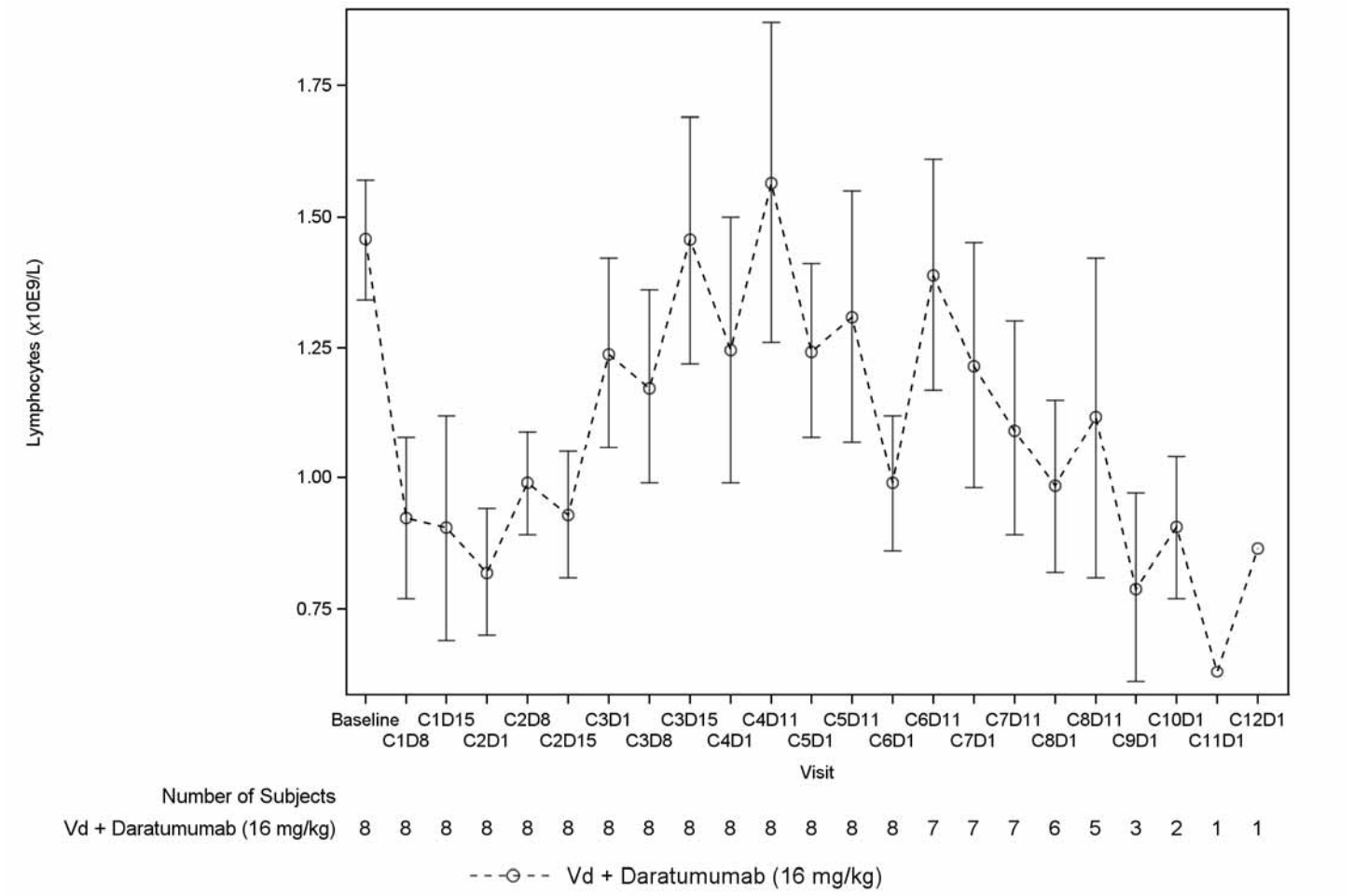


GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)

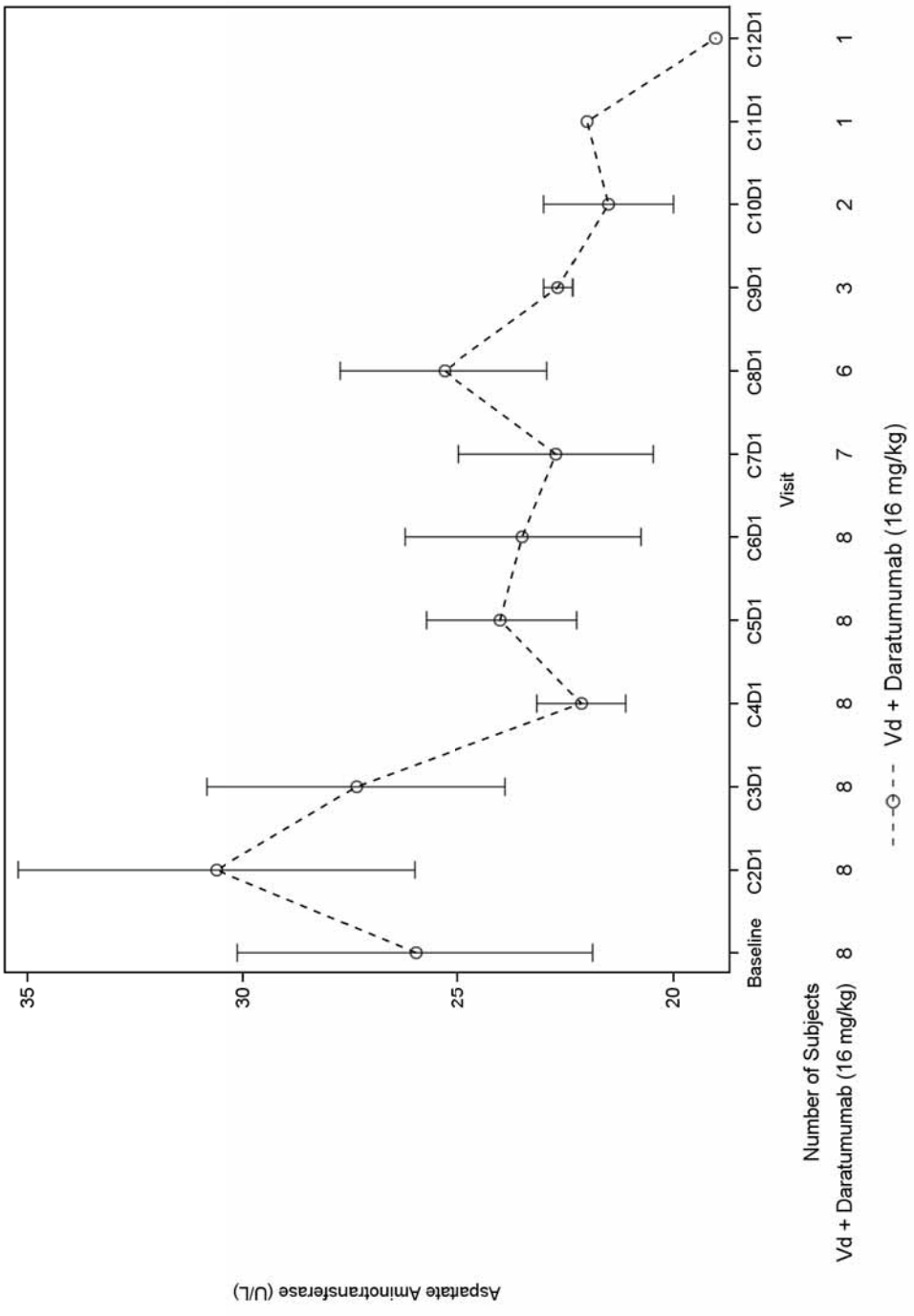


GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)

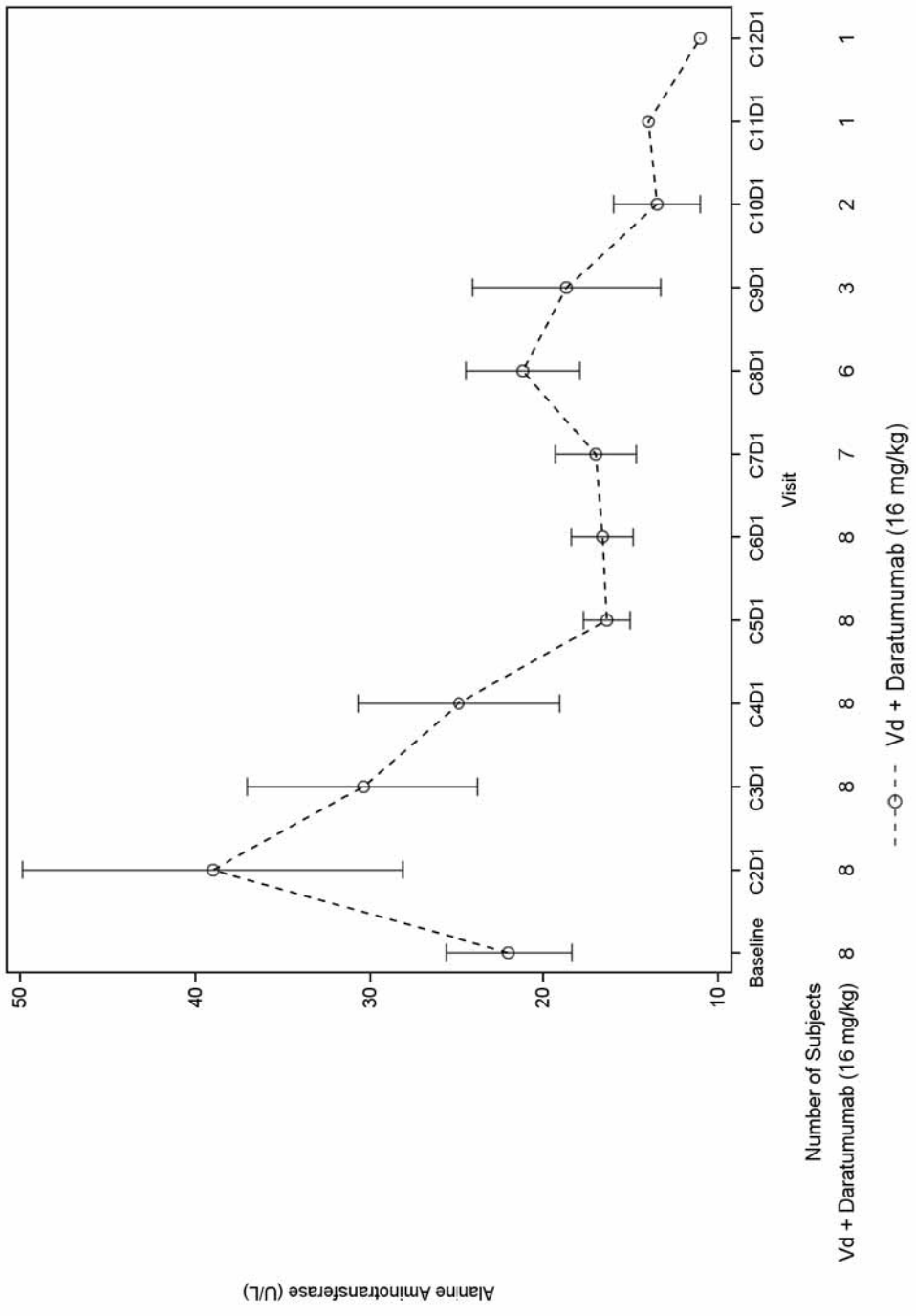
GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)



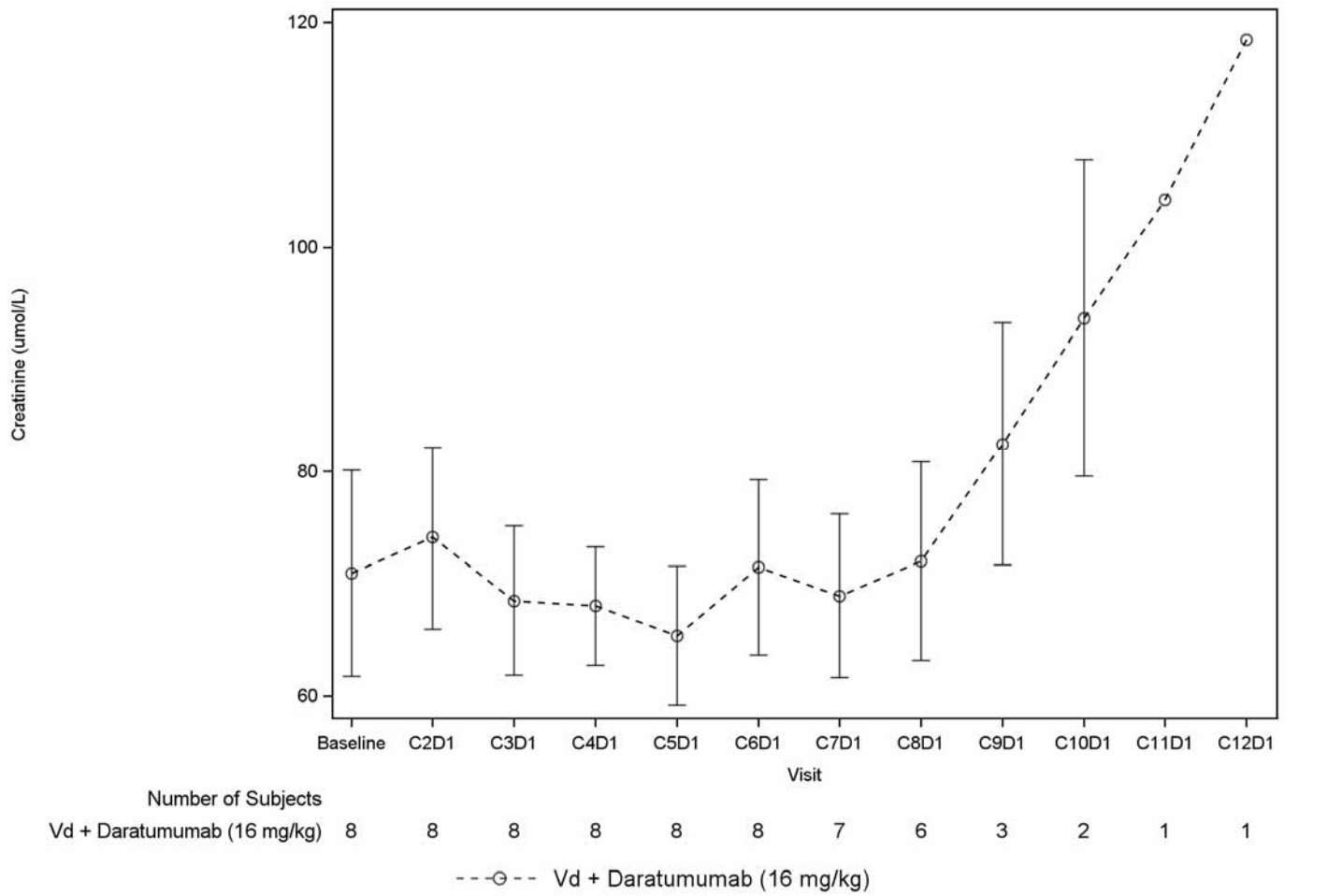
GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)



GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)



GSFLAB01: Mean (+/- SE) Values for Special Interest Laboratory Values (Hemoglobin, Platelet, WBC, Neutrophils, Lymphocyte, AST, ALT and Creatinine) Over Time; Safety Analysis Set (Study 54767414MMY1005)

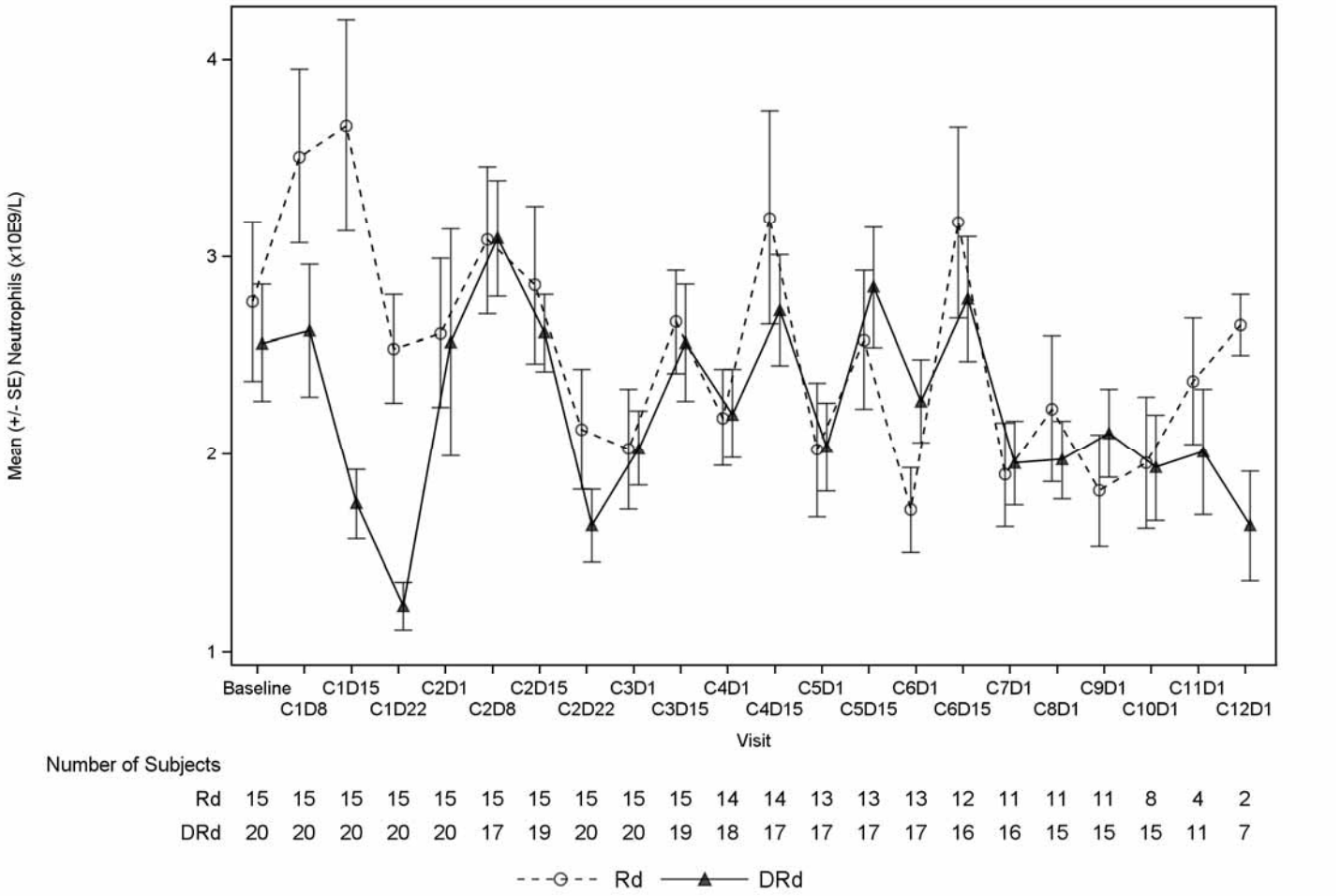


Key: Vd = bortezomib-dexamethasone.

[GSFLAB01.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\GSFLAB01.SAS] 28SEP2016, 03:59

図 2.7.4-付録-5 Mean (+/- SE) Neutrophils (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

GSFLAB02_3003_J: Mean (+/- SE) Neutrophils (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)



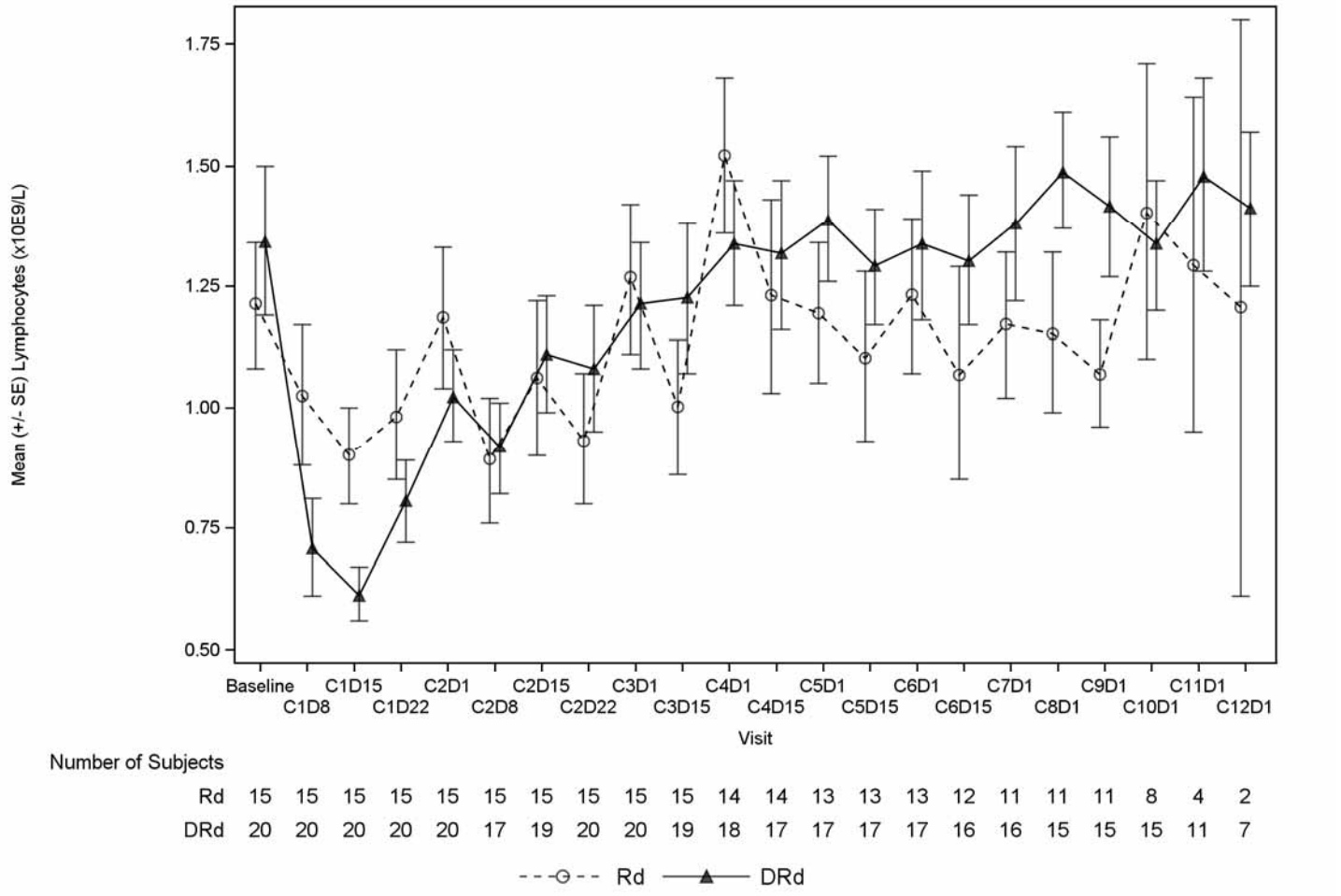
GSFLAB02_3003_J: Mean (+/- SE) Neutrophils (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

[GSFLAB02_3003_J.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\GSFLAB02_3003_J.SAS] 01JUL2016, 09:18

図 2.7.4-付録-6 Mean (+/- SE) Lymphocytes (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

GSFLAB03_3003_J: Mean (+/- SE) Lymphocytes (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

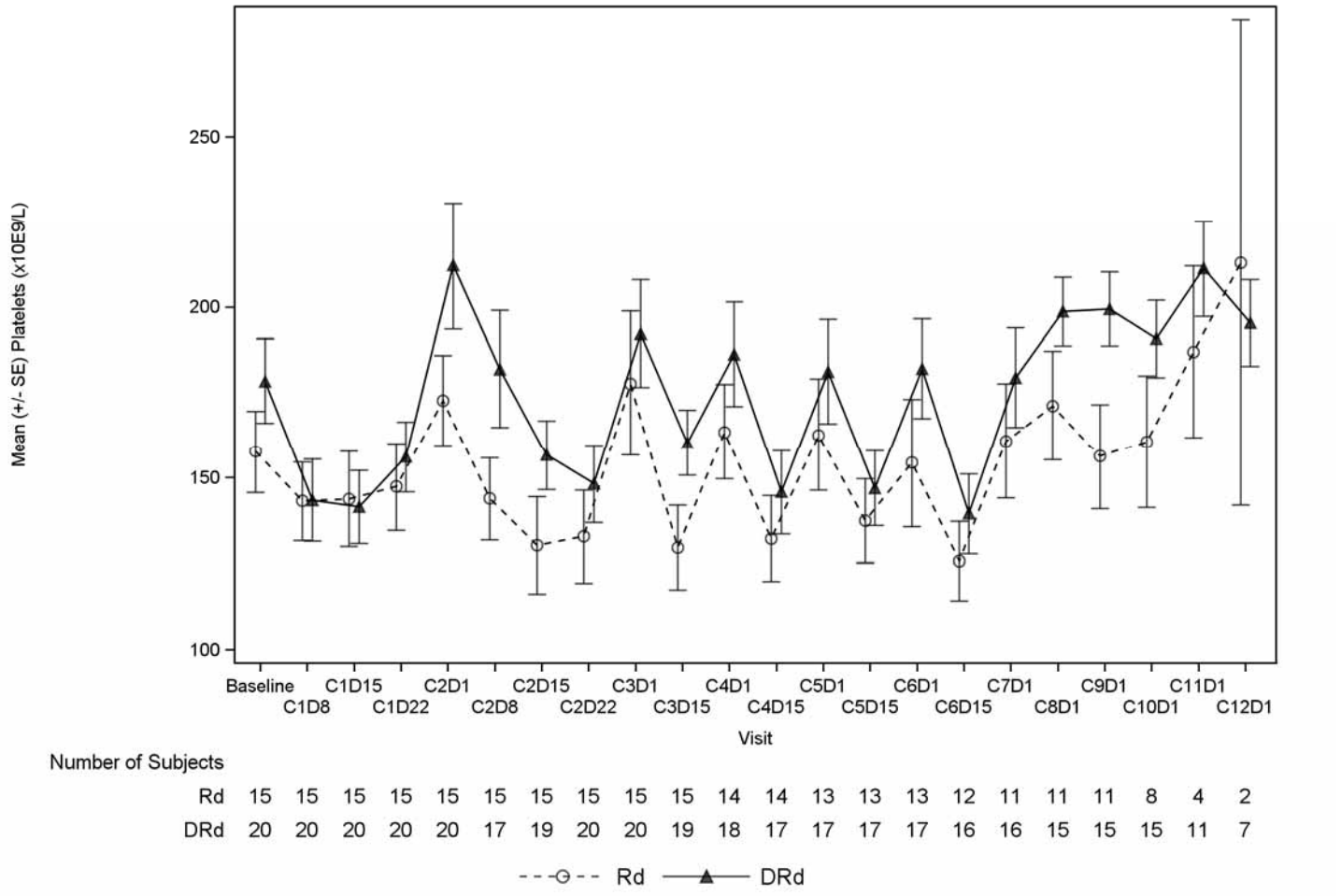


GSFLAB03_3003_J: Mean (+/- SE) Lymphocytes (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

図 2.7.4-付録-7 Mean (+/- SE) Platelets (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

GSFLAB04_3003_J: Mean (+/- SE) Platelets (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)



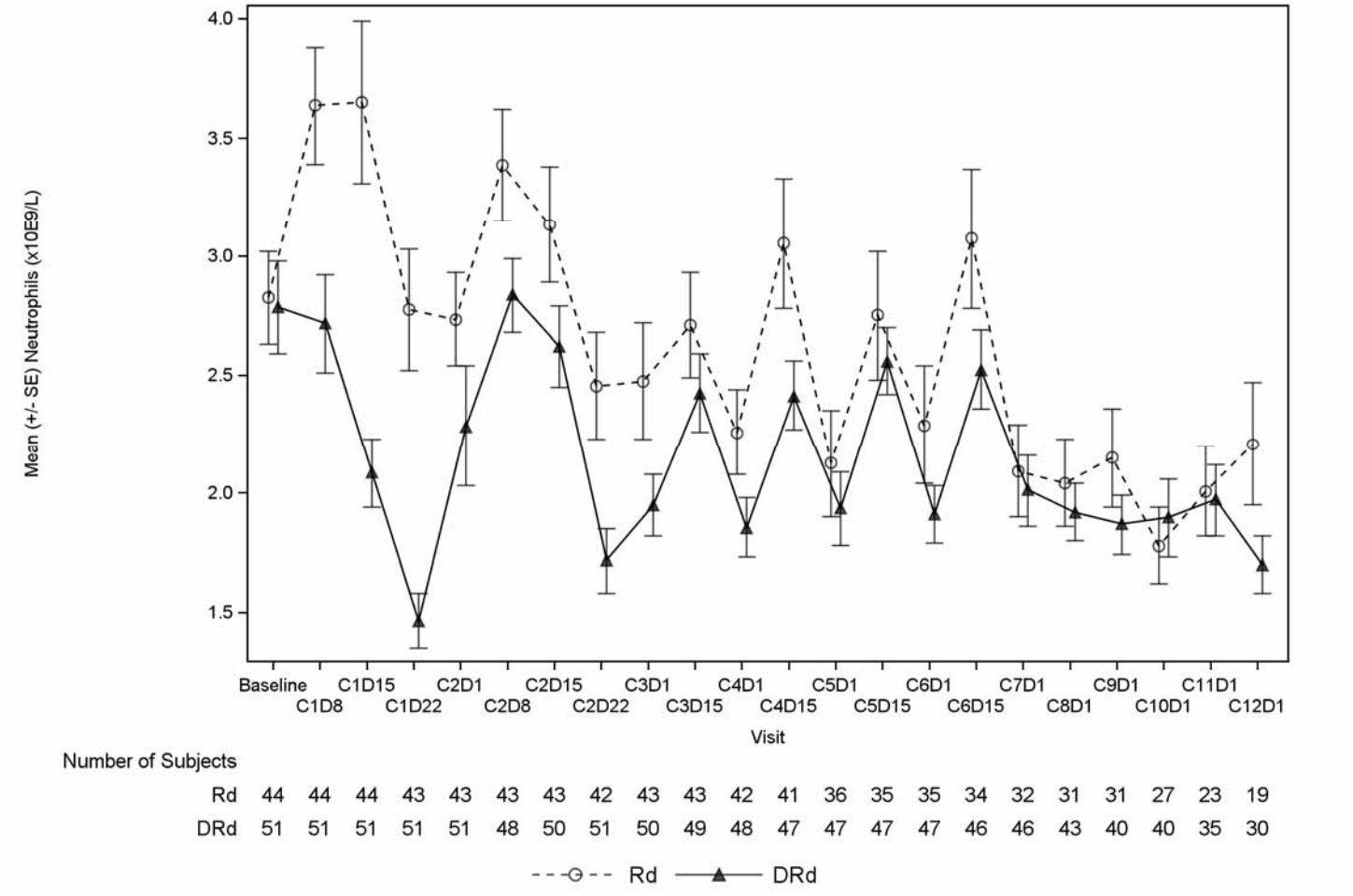
GSFLAB04_3003_J: Mean (+/- SE) Platelets (x10^9/L) Over Time (Cycles 1-12) (Japan Subgroup); Safety Analysis Set (Study 54767414MMY3003)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

[GSFLAB04_3003_J.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\GSFLAB04_3003_J.SAS] 01JUL2016, 09:17

図 2.7.4-付録-8 Mean (+/- SE) Neutrophils (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)

GSFLAB02_3003_A: Mean (+/- SE) Neutrophils (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)



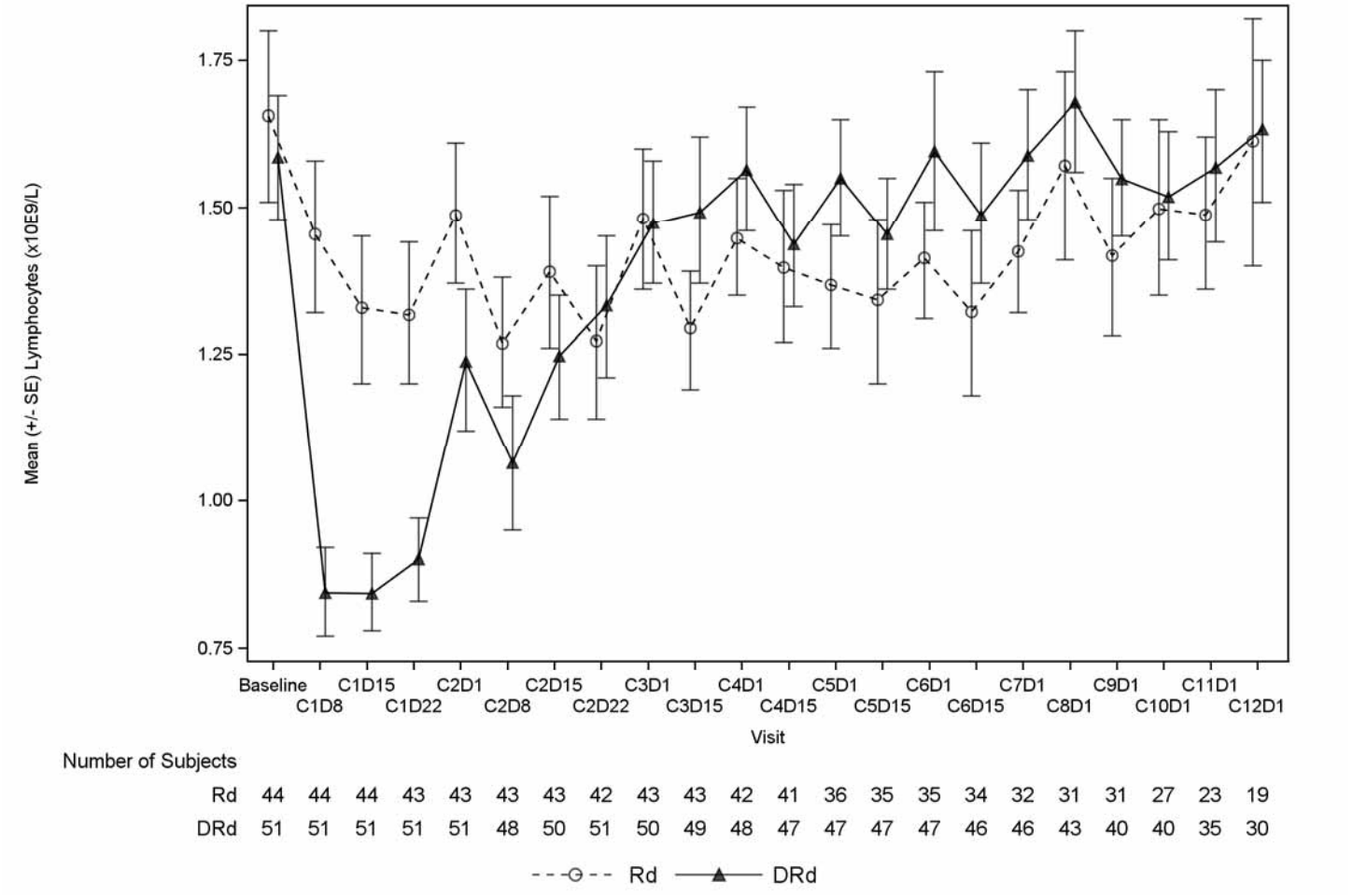
GSFLAB02_3003_A: Mean (+/- SE) Neutrophils (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

[GSFLAB02_3003_A.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\GSFLAB02_3003_A.SAS] 01JUL2016, 09:17

図 2.7.4-付録-9 Mean (+/- SE) Lymphocytes (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)

GSFLAB03_3003_A: Mean (+/- SE) Lymphocytes (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)



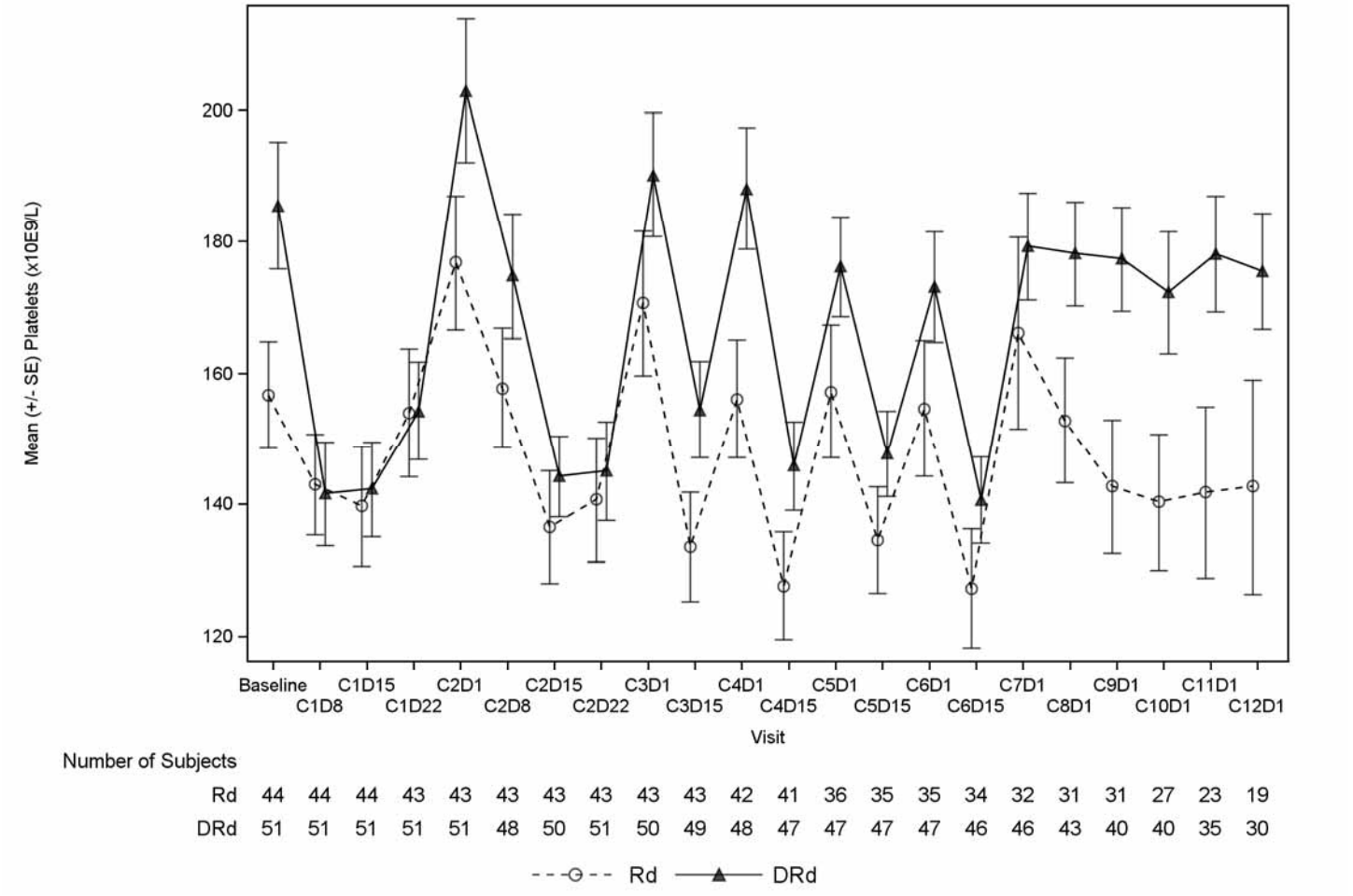
GSFLAB03_3003_A: Mean (+/- SE) Lymphocytes (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

[GSFLAB03_3003_A.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\GSFLAB03_3003_A.SAS] 01JUL2016, 09:17

図 2.7.4-付録-10 Mean (+/- SE) Platelets (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)

GSFLAB04_3003_A: Mean (+/- SE) Platelets (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)



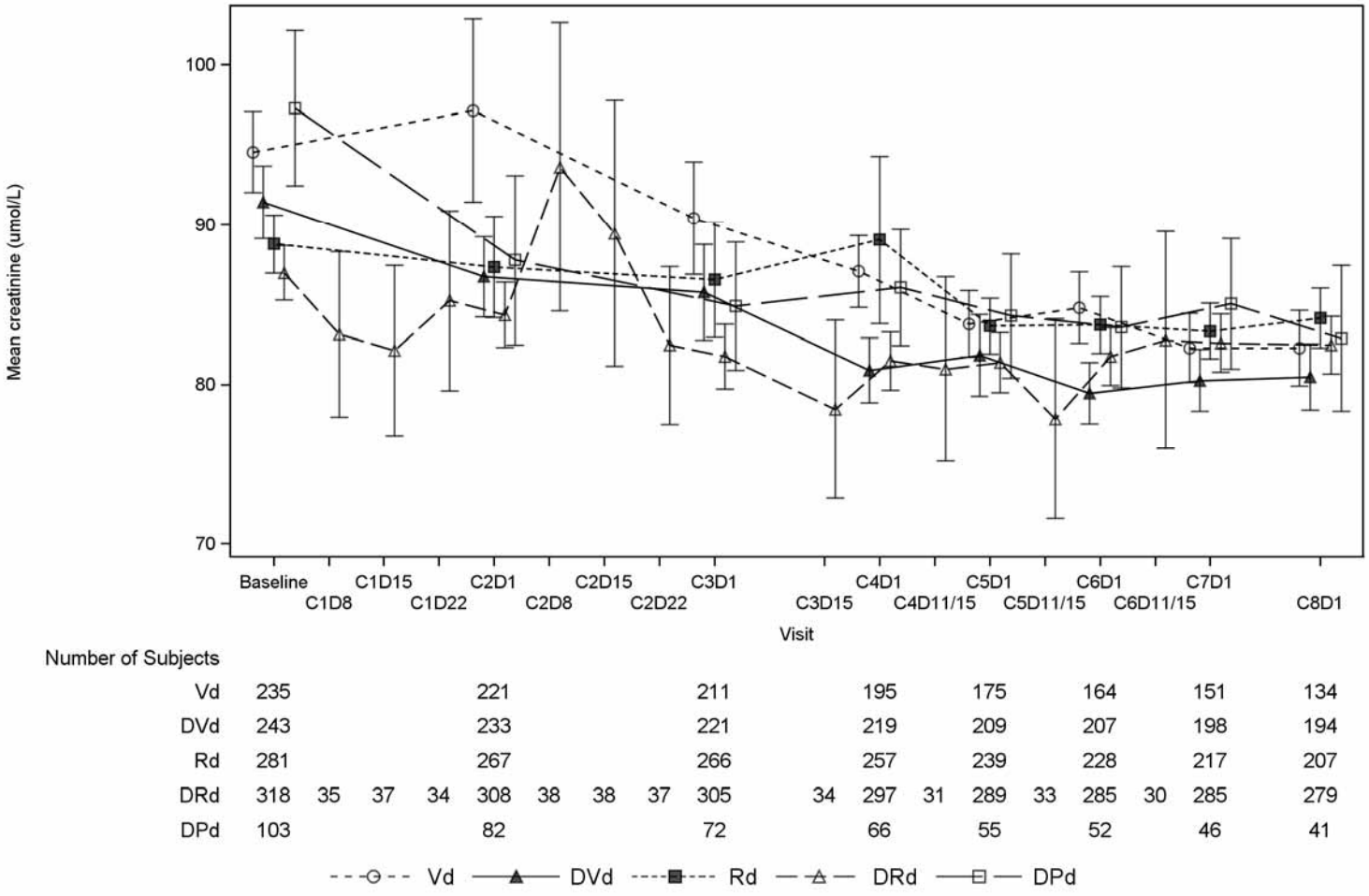
GSFLAB04_3003_A: Mean (+/- SE) Platelets (x10^9/L) Over Time (Cycles 1-12) (East Asian Subgroup); Safety Analysis Set (Study 54767414MMY3003)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.

[GSFLAB04_3003_A.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_JAPAN_SAR_2016\PROD\GSFLAB04_3003_A.SAS] 01JUL2016, 09:16

図 2.7.4-付録-11 Mean Creatinine (umol/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

GSFLAB08: Mean Creatinine (umol/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)



Number of Subjects																			
Vd	235				221				211			195		175		164		151	134
DVd	243				233				221			219		209		207		198	194
Rd	281				267				266			257		239		228		217	207
DRd	318	35	37	34	308	38	38	37	305		34	297	31	289	33	285	30	285	279
DPd	103				82				72			66		55		52		46	41

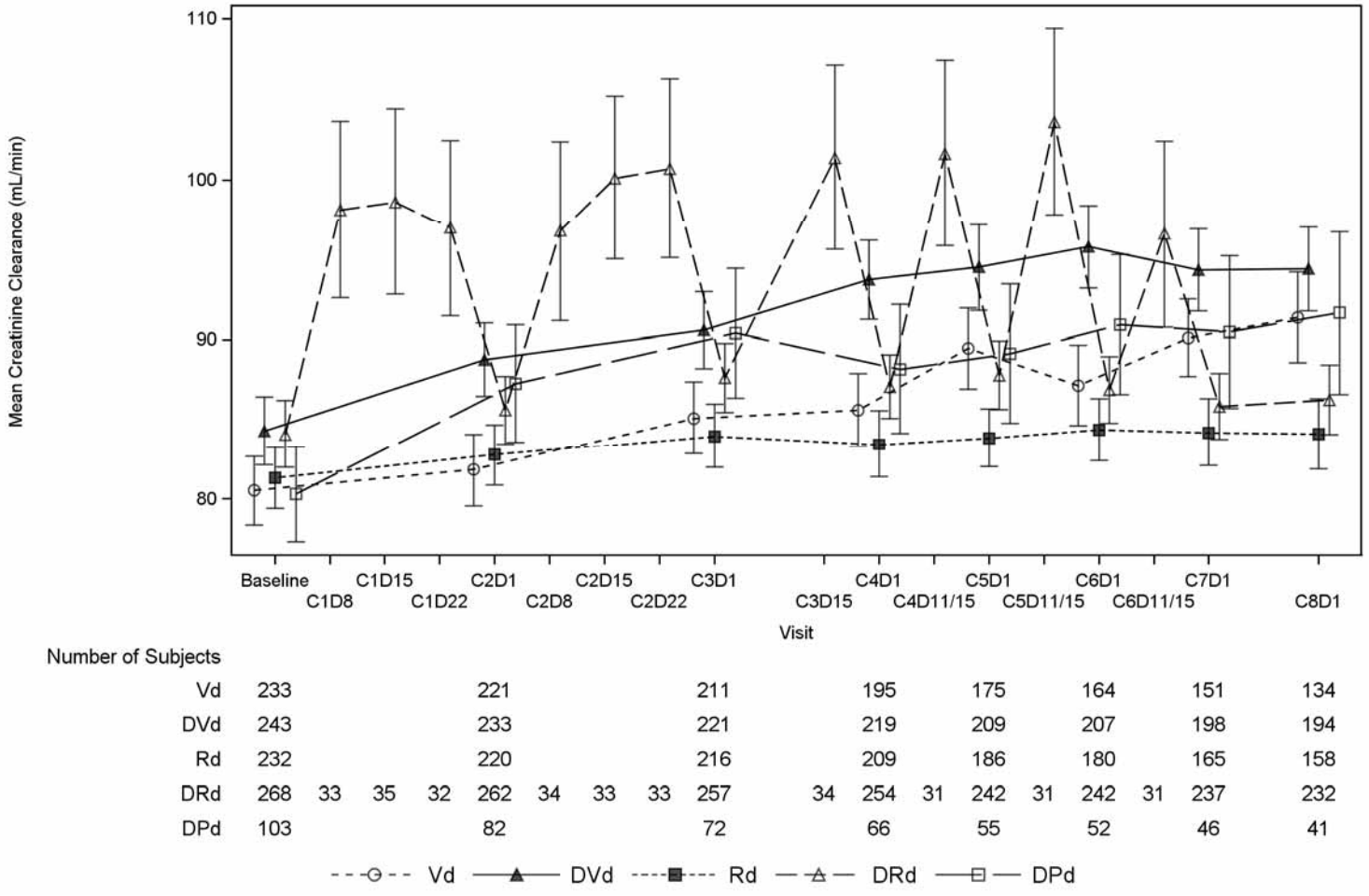
GSFLAB08: Mean Creatinine (umol/L) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: If less than or equal to 10 subjects were measured at certain time point for the treatment, then the assessment would not be plotted due to high variability.

[GSFLAB08.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\GSFLAB08.SAS] 01JUN2016, 10:32

図 2.7.4-付録-12 Mean Creatinine Clearance (mL/min) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

GSFLAB09: Mean Creatinine Clearance (mL/min) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)



GSFLAB09: Mean Creatinine Clearance (mL/min) Over Time (Cycles 1-8); Safety Analysis Set (Studies: MMY3003, MMY3004, MMY1001 and GEN503)

Key: D=Daratumumab, Vd=bortezomib-dexamethasone, Rd=lenalidomide-dexamethasone, Pd=pomalidomide-dexamethasone.
Note: If less than or equal to 10 subjects were measured at certain time point for the treatment, then the assessment would not be plotted due to high variability.

[GSFLAB09.RTF] [JNJ-54767414\Z_SCS\DBR_MMY_RR_2016\RE_MMY_RR_2016\PROD\GSFLAB09.SAS] 01JUN2016, 10:32

2.7.5 参考文献

2.7 臨床概要の参考文献の掲載先を以下に示す。

2.7.1 生物薬剤学試験及び関連する分析法：「参考文献」の項

2.7.2 臨床薬理試験：「参考文献」の項

2.7.3 臨床的有効性：「参考文献」の項

2.7.4 臨床的安全性：「参考文献」の項

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2.7.6.2 海外臨床第 III 相試験（MMY3004 試験，評価資料：5.3.5.1.2-1） 202
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2.7.6.6 国内臨床第 Ib 相試験（MMY1005 試験，評価資料：5.3.5.2.4-1） 405
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略号一覧表

略号又は略称	名称及び内容
ASCT	autologous stem cell transplantation（自家造血幹細胞移植）
AST	aspartate aminotransferase（アスパラギン酸アミノトランスフェラーゼ）
AUC	area under the serum concentration-time curve（血清中濃度-時間曲線下面積）
AUC_{last}	area under the serum concentration-time curve from time zero to the last quantifiable time（初回投与後の 0 時間から最終定量可能時間までの血清中濃度-時間曲線下面積）
BMI	body mass index（体格指数）
bpm	beats per minute（拍/分）
CI	confidence interval（信頼区間）
CL	clearance（クリアランス）
CR	complete response
CrCL	creatinine clearance（クレアチニン・クリアランス）
CRP	C-reactive protein（C-反応性たん白）
CT	computed tomography（コンピュータ断層撮影法）
CTD	common technical document
C_{max}	maximum serum concentration（最高血清中濃度）
C_{min}	minimum serum concentration（最低血清中濃度）
C_{trough}	serum trough concentration（血清中トラフ濃度）
DKd	daratumumab-carfilzomib-dexamethasone（本剤-カルフィルゾミブ-デキサメタゾン）
DKRd	daratumumab-carfilzomib-lenalidomide-dexamethasone（本剤-カルフィルゾミブ-レナリドミド-デキサメタゾン）
DLT	dose-limiting toxicity（用量制限毒性）
DPd	daratumumab-pomalidomide-dexamethasone（本剤-ポマリドミド-デキサメタゾン）
DRd	daratumumab-lenalidomide-dexamethasone（本剤-レナリドミド-デキサメタゾン）
DVd	daratumumab-bortezomib-dexamethasone（本剤-ボルテゾミブ-デキサメタゾン）
DVMP	daratumumab-bortezomib-melphalan-prednisone（本剤-ボルテゾミブ-メルファラン-prednisone）
DVTd	daratumumab-bortezomib-thalidomide-dexamethasone（本剤-ボルテゾミブ-サリドマイド-デキサメタゾン）
ECG	electrocardiogram（心電図）
ECOG	Eastern Cooperative Oncology Group
EORTC	European Organisation for Research and Treatment of Cancer（欧州がん研究治療機関）
EQ-5D-5L	European quality of life 5 dimension 5 level scale
FLC	free light chain（遊離軽鎖）
GFR	glomerular filtration rate（糸球体濾過率）
HR	hazard ratio（ハザード比）
IDSMB	independent data safety monitoring board（独立データ安全性モニタリング委員会）
Ig	immunoglobulin
IMiD	immunomodulatory drug（免疫調節薬）
IMWG	International Myeloma Working Group（国際骨髄腫作業部会）
IRC	independent review committee（独立評価委員会）
IRR	infusion related reaction
ITT	intent-to-treat

略号又は略称	名称及び内容
LLN	lower limit of normal（基準値下限）
MedDRA	Medical Dictionary for Regulatory Activities（医薬品規制用語集）
MM	multiple myeloma（多発性骨髄腫）
MR	minimal response
MRD	minimal residual disease（微小残存病変）
MRI	magnetic resonance imaging（核磁気共鳴画像法）
MTD	maximum tolerated dose（最大耐量）
NE	not estimable
NK	natural killer（ナチュラルキラー）
ORR	overall response rate（全奏効率）
OS	overall survival（全生存期間）
PD	progressive disease
Pd	pomalidomide-dexamethasone（ポマリドミド-デキサメタゾン）
PFS	progression-free survival（無増悪生存期間）
PI	proteasome inhibitor（プロテアソーム阻害剤）
PR	partial response
PT	preferred term（基本語）
QLQ-C30	quality of life questionnaire-core 30
QOL	quality of life（生活の質）
QT	QT interval（心電図 QT 間隔）
QTc	corrected QT interval（補正 QT 間隔）
QTcB	QT interval corrected by Bazett formula（Bazett 法で補正した QT 間隔）
QTcF	QT interval corrected by Fridericia formula（Fridericia 法で補正した QT 間隔）
Rd	lenalidomide-dexamethasone（レナリドミド-デキサメタゾン）
RP2D	recommended Phase 2 dose（第 II 相部分の推奨用量）
sCR	stringent complete response
TTP	time to progression（無増悪期間）
$t_{1/2}$	elimination half-life（消失半減期）
t_{max}	time to reach the maximum serum concentration（最高血清中濃度到達時間）
ULN	upper limit of normal（基準値上限）
V	volume of distribution（分布容積）
Vd	bortezomib-dexamethasone（ボルテゾミブ-デキサメタゾン）
VGPR	very good partial response

2.7.6　個々の試験のまとめ

全臨床試験一覧表

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
有効性 安全性 （第 III 相）	54767414 MMY3003	5.3.5.1.1	主要目的：再発又は難治性の MM 患者を対象に，DRd 療法と Rd 療法の有効性を PFS によって比較する。	ランダム化，非盲検，実薬対照，多施設共同，並行群間比較	DRd 群： 28 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で持続静脈内投与。レナリドミド及びデキサメタゾンを Rd 群と同じ用法・用量で投与。 Rd 群： 28 日間を 1 サイクルとし，レナリドミドは CrCL >60 mL/分の被験者には 25 mg を，CrCL 30～60 mL/分の被験者には 10 mg を Day 1～21 に経口投与。デキサメタゾンは総投与量 40 mg/週を静脈内又は経口投与。75 歳を超える又は過少体重（BMI：18.5 未満）の被験者にはデキサメタゾンを 20 mg/週で投与することを可とした。	569 例（DRd 群 286 例，Rd 群 283 例）	再発又は難治性の MM 患者	疾患進行若しくは許容できない毒性が認められる又はその他の中止基準に該当するまで	実施中 中間報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
有効性 安全性 （第 III 相）	54767414 MMY3004	5.3.5.1.2	主要目的：再発又は難治性の MM 患者を対象に，DVd 療法と Vd 療法の有効性を PFS によって比較する。	ランダム化，非盲検，実薬対照，多施設共同	DVd 群： サイクル 1～8（DVd 療法）： 21 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～3 は 1 週間隔（Day 1，8 及び 15），サイクル 4～8 は 3 週間隔（Day 1）で持続静脈内投与。ボルテゾミブ及びデキサメタゾンを Vd 群と同じ用法・用量で投与。 サイクル 9 以降（本剤のみ投与）： 28 日間を 1 サイクルとし，本剤 16 mg/kg を 4 週間隔（Day 1）で持続静脈内投与。 Vd 群： 21 日間を 1 サイクルとし，ボルテゾミブ 1.3 mg/m^2 を Day 1，4，8 及び 11 に皮下投与。デキサメタゾンは総投与量 80 mg/週を各サイクルの最初の 2 週間に静脈内又は経口投与。75 歳を超える又は過少体重（BMI：18.5 未満），コントロール不良の糖尿病又はステロイド療法に対する不耐性若しくは有害事象の既往を有する被験者には，デキサメタゾンを 20 mg/週で投与することを可とした。	498 例 （DVd 群 251 例，Vd 群 247 例）	再発又は難治性の MM 患者	DVd 群：DVd 療法を最大 8 サイクル実施後，本剤のみ疾患進行若しくは許容できない毒性が認められる又はその他の投与中止基準に該当するまで Vd 群：最大 8 サイクル	実施中 中間報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
有効性 安全性 薬物動態 薬力学 （第 II 相）	54767414 MMY2002	5.3.5.2.1	主要目的：PI 及び IMiD を含む 3 レジメン以上の前治療歴を有する，又は PI 及び IMiD の両剤に対して治療抵抗性を示す MM 患者を対象に，本剤の単剤療法の有効性を ORR（PR 以上）により検討する。	非盲検，多施設共同 Part 1：ランダム化 2 段階 Part 2：非ランダム化	Part 1（第 I/II 相試験用製剤）： 28 日間を 1 サイクルとする。 ・本剤 8 mg/kg を 4 週間隔（Day 1）で投与。 ・本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で投与。 Part 2（第 III 相試験用製剤）： 28 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で投与。	全体：124 例 本剤 8 mg/kg：18 例 本剤 16 mg/kg：106 例（Part 1：41 例，Part 2：65 例）	PI 及び IMiD を含む 3 レジメン以上の前治療歴を有する，又は PI 及び IMiD の両剤に対して治療抵抗性を示す MM 患者	疾患進行，許容できない毒性，本剤投与の中止又は同意撤回まで	実施中 中間報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
安全性 有効性 薬物動態 （第 I/II 相）	GEN501	5.3.5.2.2	主要目的：2 レジメン以上の前治療歴を有する再発又は難治性の MM 患者を対象に，本剤の単剤療法の安全性プロファイルを検討する。	非盲検，非ランダム化，多施設共同 Part 1：用量漸増 Part 2：維持用量	Part 1（第 I/II 相試験用製剤）： 本剤 0.005～24 mg/kg を初回投与後 3 週間ウォッシュアウトした後，1 週間隔で 6 回，計 7 回投与。初回投与前日及びウォッシュアウト後の投与前日に本剤の前投薬を実施した（計 2 回）。 Part 2（本剤 8 mg/kg は第 I/II 相試験用製剤，本剤 16 mg/kg は第 I/II 相試験用製剤又は第 III 相試験用製剤）： 本剤 8 mg/kg を 1 週間隔で 8 週間投与後，2 週間隔で 16 週間投与し，それ以降は 4 週間隔で投与。又は本剤 16 mg/kg を初回投与後 3 週間ウォッシュアウトした後，1 週間隔で 7 週間投与後，2 週間隔で 14 週間投与し，それ以降は 4 週間隔で投与。8 mg/kg 群の一部のコホート及び 16 mg/kg 群では初回投与前日に本剤の前投薬を実施した。	全体：104 例 Part 1 本剤 4 mg/kg 未満：20 例 本剤 4，8，16 及び 24 mg/kg：各 3 例 Part 2 本剤 8 mg/kg：30 例 本剤 16 mg/kg：42 例	2 レジメン以上の治療に対して抵抗性を示した，又は治療後に再発が認められた MM 患者	Part 1：8 週間 Part 2：96 週間又は疾患進行若しくは許容できない毒性が認められるまで	実施中 中間報告書
安全性 薬物動態 （第 I 相）	54767414 MMY1002	5.3.5.2.3	主要目的：再発又は難治性の MM を有する日本人患者を対象に，本剤の単剤療法の安全性及び忍容性を検討する。	非盲検，非ランダム化，多施設共同，用量漸増	第 1 期（Week 0～9，投与頻度の高いレジメン）： 本剤 8 mg/kg 又は 16 mg/kg を初回投与後 3 週間ウォッシュアウトした後，1 週間隔で Week 8 まで 6 回投与（計 7 回投与）。 第 2 期（Week 10 以降，第 1 期に比べ投与頻度の低いレジメン）： 28 日間を 1 サイクルとし，本剤 8 mg/kg 又は 16 mg/kg をサイクル 1～4 は 2 週間隔（Day 1 及び 15），サイクル 5 以降は 4 週間隔（Day 1）で投与。	全体：9 例 本剤 8 mg/kg：4 例 本剤 16 mg/kg：5 例	再発又は難治性の MM を有する日本人患者	疾患進行若しくは管理不能な有害事象が認められる又はその他の中止基準に合致するまで	完了 完全な報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
安全性 有効性 薬物動態 （第 Ib 相）	54767414 MMY1005	5.3.5.2.4	主要目的：再発又は難治性の MM を有する日本人患者を対象に，DVd 療法の安全性及び忍容性を検討する。	非盲検，非ランダム化，多施設共同	サイクル 1～8（DVd 療法）： 21 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～3 は 1 週間隔（Day 1，8 及び 15），サイクル 4～8 は 3 週間隔（Day 1）で持続静脈内投与。ボルテゾミブ 1.3 mg/ m^2 を Day 1，4，8 及び 11 に皮下投与。デキサメタゾン 20 mg を Day 1，2，4，5，8，9，11 及び 12（サイクル 1～3 は Day 15 も含む）に経口投与。75 歳を超える，過少体重（BMI：18.5 未満），コントロール不良の糖尿病又はステロイド療法に対する不耐性若しくは有害事象の既往を有する被験者には，デキサメタゾンを 20 mg/週で投与することを可とした。デキサメタゾンは本剤投与が行われる週には前投薬として静脈内投与（できない場合は経口投与）。 サイクル 9 以降（本剤のみ投与）： 28 日間を 1 サイクルとし，本剤 16 mg/kg を 4 週間隔（Day 1）で持続静脈内投与。	8 例	再発又は難治性の MM を有する日本人患者	疾患進行若しくは許容できない毒性が認められる又はその他の中止基準に該当するまで	実施中 中間報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
安全性 有効性 薬物動態 （第 I/II 相）	GEN503	5.3.5.4.1	主要目的：再発又は難治性の MM 患者を対象に，DRd 療法の安全性プロファイルを確立する。	非盲検，多施設共同 第 I 相部分：用量漸増 第 II 相部分：維持用量	第 I 相部分： 28 日間を 1 サイクルとし，本剤 2，4，8 又は 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で持続静脈内投与。第 I 相部分でのみ，初回投与前日に本剤の前投薬を実施した。レナリドミド 25 mg を各サイクルの Day 1～21 に経口投与し，デキサメタゾンは総投与量 40 mg/週を静脈内又は経口投与（サイクル 1 の最初の週は 20 mg/週を静脈内投与）。治験実施計画書改訂 5 版以降，75 歳を超える又は過少体重（BMI：18.5 未満）の被験者にはデキサメタゾンを 20 mg/週で投与することを可とした。 第 II 相部分： 28 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で，標準的な投与時間（1000 mL で約 6 時間）又は標準より短い投与時間（500 mL で約 3 時間）のいずれかで持続静脈内投与。レナリドミド 25 mg を各サイクルの Day 1～21 に経口投与し，デキサメタゾンは総投与量 40 mg/週を静脈内又は経口投与。治験実施計画書改訂 5 版以降，75 歳を超える又は過少体重（BMI：18.5 未満）の被験者にはデキサメタゾンを 20 mg/週で投与することを可とした。	全体：45 例 第 I 相部分：計 13 例（本剤 2，4 及び 16 mg/kg：各 3 例，8 mg/kg：4 例） 第 II 相部分：計 32 例（標準的な投与時間：21 例，標準より短い投与時間：11 例）	再発又は難治性の MM 患者	許容できない毒性又は疾患進行のいずれかが発現するまで	実施中 中間報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
安全性 有効性 薬物動態 （第 Ib 相）	54767414 MMY1001	5.3.5.4.2	主要目的： MM 患者に本剤を様々な治療レジメンと併用投与したときの安全性，忍容性（DLT 評価を含む）及び本剤の投与レジメンを評価する。 ＜併用レジメン＞ Pd：ポマリドミド，デキサメタゾン Vd：ボルテゾミブ，デキサメタゾン VTd：ボルテゾミブ，サリドマイド，デキサメタゾン VMP：ボルテゾミブ，メルファラン，prednisone	非盲検，非ランダム化，多施設共同	DPd 群： 28 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で持続静脈内投与。ポマリドミド 4 mg/日を Day 1～21 に経口投与。デキサメタゾンは，≤75 歳には総投与量 40 mg/週を，>75 歳には総投与量 20 mg/週を静脈内又は経口投与。 DVd 及び DVTd 群： 21 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8 及び 15），サイクル 3 以降は 3 週間隔（Day 1）で持続静脈内投与。ボルテゾミブ 1.3 mg/m^2 をサイクル 1～4 は Day 1，4，8 及び 11 に，サイクル 5 以降は Day 1 及び 8 に皮下投与。デキサメタゾン 20 mg をサイクル 1～2 は Day 1，2，4，5，8，9，15 及び 16 に，サイクル 3～4 は Day 1，2，4，5，8，9，11 及び 12 に，サイクル 5 以降は Day 1，2，8 及び 9 に静脈内又は経口投与。 DVTd 群では上記に加えサリドマイド 100 mg/日を連日投与。	全体：133 例 DPd 群：103 例 DVd 群：6 例 DVTd 群：12 例	DPd 群：レナリドミド及びボルテゾミブを含む 2 レジメン以上の前治療歴を有する再発又は難治性の MM 患者 DVd 及び DVTd 群：MM と初めて診断された患者（移植の適否は不問）	DPd 群：疾患進行まで DVd 及び DVTd 群：最大 18 サイクル又は移植の適応となるまで	実施中 中間報告書

試験の種類	試験番号	試験報告書添付場所	試験の目的	試験デザイン及び対照の種類	被験薬及び対照薬 投与方法　投与経路	被験者数	対象患者	投与期間	試験の進行状況，報告書の種類
					DVMP 群： 42 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1 は 1 週間隔（Day 1，8，15，22，29 及び 36），サイクル 2 以降は 3 週間隔（Day 1 及び 22）で持続静脈内投与。ボルテゾミブ 1.3 mg/m^2 をサイクル 1 は Day 1，4，8，11，22，25，29 及び 32 に，サイクル 2 以降は Day 1，8，22 及び 29 に皮下投与。メルファラン 9 mg/m^2 を Day 1～4 に経口投与。Prednisone 60 mg/m^2 を Day 1～4 に静脈内又は経口投与。	DVMP 群： 12 例	DVMP 群： MM と初めて診断され，高用量化学療法による造血幹細胞移植の対象でない患者	DVMP 群： 最大 9 サイクル	

2.7.6.1　国際共同臨床第 III 相試験（MMY3003 試験，評価資料：5.3.5.1.1-1）

2.7.6.1.1　概要

2.7.6.1.1.1　計画

(1) 治験の標題

再発又は難治性の多発性骨髄腫（MM）患者を対象とした，ダラツムマブ（以下本剤），レナリドミド及びデキサメタゾンの 3 剤併用療法（DRd 療法）とレナリドミド及びデキサメタゾンの 2 剤併用療法（Rd 療法）を比較する第 III 相試験

(2) 治験調整医師

[redacted] - [redacted], Athens, Greece

(3) 公表文献（引用文献）

- Dimopoulos MA, et al. Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2016 Oct;375(14):1319-31.
- Rajkumar SV, et al. Progress in Myeloma - A Monoclonal Breakthrough. N Engl J Med. 2016 Oct;375(14):1390-2.

(4) 治験実施期間

2014 年 6 月 [redacted] 日（最初の被験者がランダム化された日）～2016 年 3 月 7 日（クリニカルカットオフ日）

(5) 開発の相

第 III 相

(6) 目的

本治験の主要目的は，再発又は難治性の MM 患者を対象として，DRd 療法と Rd 療法の有効性を無増悪生存期間（PFS）によって比較することであった。

主な副次目的は以下のとおりであった：

- 無増悪期間（TTP），全奏効率（ORR）及び全生存期間（OS）を両群で比較する。
- Very good partial response（VGPR）以上の奏効率を両群で比較する。
- 奏効持続期間及び奏効到達期間を両群で比較する。
- 次の抗がん剤療法を実施するまでの期間を両群で比較する。
- 微小残存病変（MRD）陰性率を両群で比較する。

・ DRd 療法の安全性及び忍容性を評価する。

その他の副次目的は以下のとおりであった：

・ DRd 療法での本剤の薬物動態を評価する。

・ 本剤の免疫原性を評価する。

・ CD138 陽性の MM 細胞における，染色体転座，変異及び遺伝子シグネチャーに基づく部分集団での ORR を検討する。

・ European quality of life 5 dimension 5 level scale（EQ-5D-5L）及び欧州がん研究治療機関（EORTC）の quality of life questionnaire-core 30（QLQ-C30）の患者報告アウトカムを用いて，各療法の有効性を評価する。

探索的目的は，本剤の効果を予測するバイオマーカーを探索することであった。

(7) 治験方法

本治験は，再発又は難治性の MM 患者を対象に，DRd 療法と Rd 療法の有効性を PFS によって比較する第 III 相，ランダム化，非盲検，実薬対照，多施設共同，並行群間比較試験であった。約 560 例の被験者を DRd 群又は Rd 群に 1：1 の比でランダムに割り付けた。ランダム化にあたっては，中央検査機関によって判定されたスクリーニング時の国際病期分類の病期（I，II 又は III 期），前治療数（1 レジメン，2 又は 3 レジメン，4 レジメン以上）及びレナリドミドの前治療歴の有無を層別因子とし，層別因子の各層の割付け比が 1：1 となるように被験者をランダムに割り付けた。

本治験は，スクリーニング期（サイクル 1 Day 1 前 21 日以内），治療期（サイクル 1 Day 1 から治験薬投与中止まで）及び後観察期から構成された。後観察期は，投与中止時来院の直後から，被験者の死亡，追跡不能，同意撤回又は治験終了のいずれか早い時点までとした。

独立データモニタリング委員会は，主要評価項目の最終解析に先立ち，事前に規定した 2 回の中間解析時にデータをレビューした。また，2 回の中間解析のデータレビューに加えて，本治験期間中は定期的（1 サイクル以上の治験薬の投与を受けた又は中止した被験者が 50 例に達した時点，以降は 6 カ月ごと）に重篤な有害事象に関する評価も行うこととした。主要評価項目である PFS の解析は，295 件の PFS イベント発生後に実施することとした。PFS の主要解析後，本治験終了（330 件の死亡が発生した時点と定義）まで，治験実施計画書の規定に従い，本治験継続中の被験者を引き続き観察することとした。

(8) 被験者数（計画時及び解析時）

計画時：約 560 例を本治験に組み入れることとした（各群約 280 例）。

解析時：569 例（DRd 群 286 例，Rd 群 283 例）を intent-to-treat（ITT）解析対象集団とした。

(9) 診断及び主な組入れ基準

18 歳以上の男性又は女性で，MM の確定診断を受けており，1 レジメン以上の前治療で奏効［国際骨髄腫作業部会（IMWG）の治療効果判定規準に基づき治験担当医師が partial response（PR）以上と判定］を達成し，かつ直近のレジメン中又はレジメン以降に IMWG の治療効果判定規準に基づいた progressive disease（PD）が確認され，Eastern Cooperative Oncology Group（ECOG）の performance status スコアが 0，1 又は 2 である患者を本治験の対象とした。本剤若しくは他の抗 CD38 療法の前治療歴を有する患者，レナリドミドに対して治療抵抗性を示す又は忍容性が不良の患者，ランダム化前 2 週間以内若しくは治療薬剤の半減期の 5 倍のいずれか長い期間に MM に対する治療を受けた患者，ランダム化前 12 週間以内に自家造血幹細胞移植（ASCT）を受けた患者，過去に同種幹細胞移植を受けた患者（時期は問わない），ランダム化前 5 年以内に悪性腫瘍（MM 以外）の既往のある患者，又は MM による髄膜障害を有する患者は本治験から除外した。

(10) 被験薬，用量及び投与方法，ロット番号

治療期は 28 日間サイクルで構成された。本剤は持続静脈内投与した。DRd 群に割り付けられた被験者に本剤 16 mg/kg を以下のスケジュールで投与した。レナリドミド及びデキサメタゾンを Rd 群と同じ用法・用量で投与した。

- サイクル 1 及び 2：Day 1，8，15 及び 22（1 週間隔）
- サイクル 3～6：Day 1 及び 15（2 週間隔）
- サイクル 7 以降：Day 1（4 週間隔）

本剤のロット番号は以下のとおりであった。

[redacted]

(11) 対照薬，用量及び投与方法，ロット番号

レナリドミドは，クレアチニン・クリアランス（CrCL）が 60 mL/分を超える被験者には 25 mg を各サイクル（28 日間）の Day 1 から Day 21 まで毎日経口投与し，CrCL が 30～60 mL/分の被験者には 10 mg を Day 1 から Day 21 まで毎日経口投与した。レナリドミドは疾患進行又は許容できない毒性が認められるまで投与した。

デキサメタゾンは 40 mg/週を総投与量として投与した。75 歳を超える又は過少体重（体格指数：18.5 未満）の被験者にはデキサメタゾンを 20 mg/週で投与することを可とした。

レナリドミドのロット番号は以下のとおりであった。

[redacted]

デキサメタゾンのロット番号は以下のとおりであった。

[redacted]

(12) 投与期間

治験薬投与期間は，疾患進行又は許容できない毒性が認められるまでとした。

(13) 評価基準

有効性の評価：

治療効果及び PD の判定は，IMWG の治療効果判定規準に従い実施した。疾患評価には，血清及び尿中 M 蛋白の測定，血清遊離軽鎖，骨髄中の形質細胞浸潤，X 線撮影，核磁気共鳴画像法（MRI）又は低線量コンピュータ断層撮影法（CT）による骨格検査，身体所見又は MRI による髄外形質細胞腫の評価，アルブミン補正血清カルシウムの測定を用いた。また，生存状況及び次の抗がん剤治療に関する情報を収集した。

薬物動態の評価：

DRd 群の被験者から血液試料を採取し，本剤の薬物動態パラメータとして，本剤投与直前の最低血清中濃度（C_{min}）及び投与終了後の最高血清中濃度（C_{max}）を算出した。

免疫原性の評価：

DRd 群の被験者から検体を採取し，本剤に対する抗体産生について評価した。

バイオマーカーの評価：

全被験者から血液試料及び骨髄穿刺検体を採取し，高リスク染色体異常の部分集団における治療効果を検討し，MRD を評価した。両群を対象としたのは，本剤の有無による被験者間の結果を比較するためであった。

安全性の評価：

有害事象，臨床検査値（血液学的検査及び血液生化学検査），心電図（ECG），血圧及び体温，身体所見，並びに ECOG の performance status スコアに基づき安全性を評価した。サイクル 1 では，DRd 群の少なくとも 3 例の日本人被験者がサイクル 1 を完了するまで，事前に規定した安全性事象が DRd 群の日本人（日本の治験実施医療機関で組み入れられた）被験者に発現した場合，より迅速で詳細な安全性事象に関する報告，モニタリング及び評価を実施した。

機能状態及び満足できる生活状態：

機能状態及び満足できる生活状態を EORTC-QLQ-C30 及び EQ-5D-5L を用いて評価した。

医療資源の利用状況：

本治験期間中，治験実施計画書に基づく医療現場及び安全性モニタリングに関連した医療資源の利用状況に関する被験者のデータを，治験担当医師及び治験コーディネーターが電子症例報告書に収集した。

(14) 統計手法

主要な解析対象集団は ITT 解析対象集団とし，ランダム化された全被験者を対象とした。主な副次評価項目である ORR，VGPR 以上の奏効率，奏効持続期間及び奏効到達期間の解析は，奏効

評価対象集団を対象に実施した。奏効評価対象集団は MM の確定診断を受け，ベースライン又はスクリーニング来院時に測定可能病変を有し，かつ治験薬の投与を 1 回以上受け，ベースライン後の疾患評価を 1 回以上実施している被験者と定義した。Per-protocol 解析対象集団は，ランダム化され，適格性基準に抵触する重大な治験実施計画書違反が認められない被験者とした。薬物動態評価対象集団は，本剤の投与を 1 回以上受け，かつ初回投与後に薬物動態用検体の濃度が測定された被験者と定義した。安全性は，治験薬の投与（一部投与又は全量投与）を 1 回以上受けた被験者を対象に評価した。免疫反応評価対象集団は，本剤の初回投与後の免疫原性用検体を採取された被験者と定義した。

公表されているデータに基づいて Rd 群の PFS の中央値を 18 カ月と想定した。Rd 群に対して DRd 群が疾患進行又は死亡のリスクを 30%低減する［PFS のハザード比（HR）=0.70］と仮定した場合，DRd 群における PFS の中央値が 25.7 カ月となり，log-rank 検定（有意水準両側 0.05）により，検出力 85%で群間差を検出するには計 295 件の PFS イベントが必要とされた。累積期間 16 カ月に後観察期間 18 カ月間を加えた場合，本治験に必要な総被験者数は約 560 例（各群 280 例）であった。被験者数の算出では，年間脱落率 5%を考慮した。

長期生存観察は，330 件の死亡が認められるまで継続することとした。したがって，本治験では，log-rank 検定（有意水準両側 0.05）により，約 80%の検出力で死亡リスクの 27%の低減（HR=0.73）を検出することとした。

有効性の解析：

治療効果及び PD は，バリデートされたコンピュータ・アルゴリズム判定を用いて IMWG の治療効果判定規準に基づき評価した。主要評価項目である PFS の主要解析には，両群の PFS の分布を比較するため，層別 log-rank 検定を実施した。また，Kaplan-Meier 法を用いて両群の PFS の分布を推定した。治療効果（HR）及びその両側 95%信頼区間（CI）は，治療群のみを説明変数とする層別 Cox 回帰モデルを用いて推定した。

TTP，OS 及び次の抗がん剤療法までの時間を含む，time-to-event 型の有効性評価項目も log-rank 検定及び Cox 回帰モデルを用いて同様に解析した。OS の最終解析は，本治験終了時である 330 件の死亡が認められた後に実施することとした。OS は中間解析においても解析され，α 消費関数を用いて中止境界を決定することとした。2 回目の中間解析（177 件の PFS イベント発生時点）で 0.0001 の α が消費された。以降の解析［295 件の PFS イベント発生時点（174 件の死亡が予想される）における PFS の主要解析及び OS の最終解析時点］で消費される α は，その時点で観察された死亡数に基づき α 消費関数によって決定することとした。すなわち，消費される累積 α は，全体の α（0.05）に計画総死亡数（330 件）に対する認められた死亡数の割合を掛けた値に基づくこととした。PFS の有意性が既に確立されたとしても，OS についての決定的な結論が得られるまで OS の検討を計画どおり継続することに留意が必要である。ORR，VGPR 以上の奏効率及びその他の 2 値の評価項目の両群間の比較には，層別 Cochran-Mantel-Haenszel 検定を用いた。Mantel-Haenszel オッズ比及びその両側 95%CI を示し，治療効果の尺度とした。奏効持続期間は記述的に示し，統計学的な比較は実施しなかった。

1 回目の中間解析は，安全性を評価する目的で，治験薬投与を 8 週間以上受けた又は中止した被験者が 80 例に到達した時点で実施した。2 回目の中間解析は，安全性及び有効性の中間累積データを評価する目的で，計画された総イベント数の 60%に当たる 177 件の PFS イベントが累積し

た時点で実施した。PFS に関し Rd 群に対する DRd 群の優越性を立証するための有意水準は，Lan-DeMets の α 消費法による O'Brien-Fleming 境界を用い，中間解析時点で認められた PFS イベント数に基づき決定した。177 件の PFS イベントが認められたと仮定する場合，この中間解析で消費される α は 0.00762（両側）であった。認められた両側 p 値がこの有意水準を下回る場合，PFS に関し Rd 群に対する DRd 群の優越性が立証されることとした。

薬物動態解析：

血清中 daratumumab 濃度は記述統計量を用いて来院ごとに集計し，図示した。薬物動態の評価は，薬物動態評価対象集団を対象に実施した。欠測データは補完しなかった。要約統計量について，定量下限未満の濃度は 0 として取り扱った。投与前に採取した検体の値を C_{min}，投与終了時に採取した検体の値を C_{max} とした。Daratumumab の血清中濃度-時間データの母集団薬物動態解析は別途，母集団薬物動態解析計画書に示し，解析結果も別途報告することとした。

免疫原性解析：

免疫反応評価対象集団を対象に，本剤に対する抗体の発現割合（免疫原性）を要約した。

バイオマーカー解析：

バイオマーカーの検討は，complete response（CR）又は stringent complete response（sCR）を達成した被験者において，本剤を Rd 療法と併用した際に MRD が減少するか検討するため計画された。ITT 解析対象集団及び奏効評価対象集団を対象に，各群の MRD 陰性率を算出した。その他のバイオマーカー評価として，del17p，t(14;16)，t(4;14)などの高リスクの染色体異常を有する部分集団で，本剤を Rd 療法と併用した場合に臨床的有効性（ORR，PFS，OS）が改善するかを検討した。

安全性の解析：

有害事象は医薬品規制用語集（MedDRA）version 18.0 に従いコード化した。治療期に発現した全有害事象（治験薬の投与開始後に発現した有害事象，ベースライン以降に悪化した有害事象）を解析に含めた。発現した有害事象について被験者の割合を群別に要約した。有害事象，臨床検査値，ECG，バイタルサイン，身体所見及び ECOG の performance status スコアを要約した。死亡例，有害事象による投与中止例，高度の有害事象又は重篤な有害事象の発現例については適宜，要約，一覧表，データセット又は被験者の叙述を示した。臨床検査値，ECG，バイタルサイン及び身体所見は，各来院時の記述統計量及びベースラインからの変化量を要約した。臨床検査値，バイタルサイン及び ECG の顕著な異常（事前に規定した基準に該当）を要約した。ECG 異常及び身体所見異常の頻度集計を実施した。バイタルサインが臨床的に重要な基準範囲外を示した被験者の割合を要約した。臨床検査値のベースラインからの変化を投与前後のクロス集計表（低値，基準範囲内，高値）で示した。投与期間中の臨床検査値の Grade 分類を National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 に基づき示した。臨床検査値が基準値範囲外であった被験者の一覧表を作成した。臨床検査の顕著な異常値が認められた被験者の一覧表も作成した。

機能状態及び満足できる生活状態：

EORTC-QLQ-C30 ドメイン・スコアを実施時点ごとに要約した。治療効果とドメイン・スコアの変化の関係を探索した。EQ-5D-5L スコアを実施時点ごとに要約した。

医療資源利用状況：

医療資源利用状況を群別に記述的に要約した。

2.7.6.1.1.2 結果

(1) 対象集団

ランダム化された被験者は 569 例であった。人口統計学的特性及び疾患特性は両群間で類似していた。年齢の中央値は 65 歳，65 歳以上が 52%，男性が 59%であった。白人が 69%であり，アジア人が 18%，黒人又はアフリカ系アメリカ人が 34%であった。被験者のほとんど（95%）は ECOG の performance status スコアが 0 又は 1 であった。血清中の測定可能病変では，IgG 型が最も多く（54%），次いで IgA 型であった（18%）。測定可能病変が尿中のみの被験者は 14%，血清中遊離軽鎖のみの被験者は 13%で少数であった。MM の初回診断から本治験のランダム化までの期間の中央値は 3.6 年であった。すべての被験者に全身療法による前治療歴があり，63%の被験者に ASCT の前治療歴があった。全身療法の前治療数の中央値は 1 レジメン（範囲：1～11 レジメン）であり，19%の被験者に 3 レジメン以上の前治療歴があった。86%の被験者にプロテアソーム阻害剤の前治療歴があり，84%の被験者はボルテゾミブの前治療歴を有していた。55%の被験者に免疫調節薬の前治療歴があり，17%の被験者はレナリドミドの前治療歴を有していた。44%の被験者にプロテアソーム阻害剤及び免疫調節薬の両剤による前治療歴があった。27%の被験者は直近の前治療に対し治療抵抗性を示した。治験実施計画書に従い，レナリドミドに治療抵抗性を示した被験者は本治験から除外した。

(2) 有効性

有効性の結果：

再発又は難治性の MM 患者において，Rd 療法に本剤を上乗せすることによって，臨床アウトカム（PFS）は極めて有意に改善し，DRd 群では Rd 群と比べて疾患進行又は死亡のリスクが 63%低減した（HR=0.37，95%CI：0.27～0.52，p<0.0001）。クリニカルカットオフ日（2016 年 3 月 7 日）時点での観察期間の中央値は DRd 群 13.6 カ月，Rd 群 13.5 カ月であり，PFS の中央値は DRd 群で未到達であったが，Rd 群では 18.4 カ月であった。18 カ月無増悪生存率は DRd 群 77.9%，Rd 群 52.2%であった。PFS の改善は，事前に規定した感度分析及びすべての部分集団解析で一貫していた。TTP は Rd 群に比べて DRd 群で統計学的に有意に延長した（HR=0.34，95%CI：0.23～0.48，p<0.0001）。本剤を上乗せすることにより，ORR（DRd 群 93%，Rd 群 76%，p<0.0001），VGPR 以上の奏効率（DRd 群 76%，Rd 群 44%，p<0.0001），CR 以上の奏効率（DRd 群 43%，Rd 群 19%，p<0.0001）及び 10^{-4} 閾値での MRD 陰性率（DRd 群 29%，Rd 群 8%，p<0.0001）は有意に改善した。ORR 及び VGPR 以上の奏効率はいずれも事前に規定したすべての部分集団で一貫していた。本剤による奏効の継続も認められ，奏効持続期間の中央値は，DRd 群では未到達であったが，Rd 群では 17.4 カ月であった。死亡例は計 75 例（DRd 群 30 例，Rd 群 45 例）であり，OS は両群とも中央値に未到達であったが，HR は 0.64（95%CI：0.40～1.01，p=0.0534）であり，DRd 群で OS 延長の強い傾向が認められた。

患者報告アウトカム，医療資源利用状況及び医療経済：

EORTC-QLQ-C30 の一部のドメイン（Global Health Status，身体的機能）において，経時的なわずかな改善が両群で認められた。同様に，EQ-5D-5L では visual analog scale 及び効用値が経時的に改善する傾向が両群で認められた。患者報告アウトカムの結果から，全般的に，両群の被験者で治療期間中に健康関連の生活の質が維持されることが示された。

DRd 群の 67%，Rd 群の 56%の被験者が，治験の規定来院以外で入院又は外来を受診した。被験者が最も頻回に外来受診した医療機関は，DRd 群では治験実施医療機関，Rd 群では治験実施医療機関又はその他の医師の医療機関であった。最も多かった入院又は外来受診の理由は有害事象（DRd 群 48%，Rd 群 61%）であった。

(3) 安全性

本治験の安全性の結果から，再発又は難治性の MM 患者に対して，DRd 療法の安全性プロファイルは許容可能であることが示された。DRd 群で報告された有害事象は Rd 群と同様であり，また，レナリドミド及び本剤の単剤療法での既知の毒性と類似していた。

両群のほぼすべての被験者（DRd 群 98%，Rd 群 98%）で有害事象が発現した。発現割合が高かった有害事象（いずれかの群で発現割合が 20%以上）は，好中球減少症（DRd 群 59%，Rd 群 43%），下痢（DRd 群 43%，Rd 群 25%），疲労（DRd 群 35%，Rd 群 28%），上気道感染（DRd 群 32%，Rd 群 21%），貧血（DRd 群 31%，Rd 群 35%），便秘（DRd 群 29%，Rd 群 25%），咳嗽（DRd 群 29%，Rd 群 12%），血小板減少症（各群 27%），筋痙縮（DRd 群 26%，Rd 群 19%），鼻咽頭炎（DRd 群 24%，Rd 群 15%），悪心（DRd 群 24%，Rd 群 14%），発熱（DRd 群 20%，Rd 群 11%）であった。発熱性好中球減少症は DRd 群の 6%，Rd 群の 2%の被験者で認められた。Grade 3 又は 4 の有害事象の発現割合は DRd 群 81%，Rd 群 73%であった。発現割合が高かった Grade 3 又は 4 の有害事象（いずれかの群で発現割合が 10%以上）は，好中球減少症（DRd 群 52%，Rd 群 37%），血小板減少症（DRd 群 13%，Rd 群 14%），貧血（DRd 群 12%，Rd 群 20%）であった。Grade 3 又は 4 の感染症及び寄生虫症の発現割合は DRd 群 28%，Rd 群 23%であった。最も発現割合が高かった Grade 3 又は 4 の感染症及び寄生虫症（いずれかの群で発現割合が 5%以上）は，肺炎（各群 8%）であった。重篤な有害事象の発現割合は DRd 群 49%，Rd 群 42%であった。最も発現割合が高かった重篤な有害事象（いずれかの群で発現割合が 5%以上）は，肺炎（DRd 群 8%，Rd 群 9%）であった。

DRd 療法の忍容性は，有害事象による治験薬の投与中止割合が低いことから明らかになった（DRd 群 7%，Rd 群 8%）。最終投与後 30 日以内に死亡した被験者数は両群で同様であった（DRd 群 4%，Rd 群 6%）。最終投与後 30 日以内の主な死因として最も多く認められたものは，有害事象［DRd 群 11 例（4%），Rd 群 12 例（4%）］であった。転帰が死亡で発現割合が高かった有害事象は，急性腎不全（DRd 群 1 例，Rd 群 3 例），肺炎（各群 2 例），敗血症性ショック（DRd 群 3 例，Rd 群 1 例）であった。

好中球減少症の発現割合は Rd 群に比べて DRd 群で高く（全 Grade：DRd 群 59%，Rd 群 43%，Grade 3 又は 4：DRd 群 52%，Rd 群 37%），この傾向は最初の 2 サイクルで最も顕著であり（全 Grade：DRd 群 48.4%，Rd 群 25.6%，Grade 3 又は 4：DRd 群 41%，Rd 群 20%），以降のサイクルでは両群で同様であった。好中球減少症の発現割合がサイクル 1 及び 2 で Rd 群に比べて DRd

群で高かった理由は，このサイクルで本剤を頻繁に投与したためと考えられた。サイクル 1 及び 2 で好中球減少症の発現割合が高かったが，臨床的に重要な続発症へは至らず，感染症及び寄生虫症の発現割合は DRd 群と Rd 群で同様であった（全 Grade：DRd 群 39%，Rd 群 40%，Grade 3 又は 4：各群 8%）。好中球減少症のために治験薬の投与中止に至った被験者は少なかった（各群 0.4%）。

感染症の発現割合は DRd 群 84%，Rd 群 73%であった。Grade 3 又は 4 の感染症の発現割合は両群で同様であった（DRd 群 28%，Rd 群 23%）。感染症による治験薬の投与中止割合は低く（各群 2%），両群で同様であり，感染症によって死亡した被験者の割合も同様であった（各群 1%）。

本剤投与に関連した infusion related reaction（IRR）は 48%（135 例）の被験者で認められ，IRR のために治験薬の投与を中止した被験者は 1 例（消化不良，呼吸困難，発声障害，喉頭浮腫及び喘鳴）のみであった。IRR のほとんどは Grade 1 又は 2 であり，5%（15 例）の被験者が Grade 3 の IRR を発現したが，Grade 4 又は 5 の IRR を発現した被験者はいなかった。IRR のほとんど（96%，129/135 例）が本剤初回投与の Day 1 での発現であった。

二次性悪性腫瘍の発現割合は低く，両群で同様であった［DRd 群 3%（8 例），Rd 群 4%（10 例）］。

Daratumumab が間接クームス試験に影響を及ぼすことに関連した有害事象は認められなかった。

血液学的検査，血液生化学検査及び免疫グロブリンを含む臨床検査値からは，新たな知見は特定されなかった。

DRd 療法の安全性プロファイルは，年齢，性別，人種又は肝機能障害による部分集団解析で同様であった。腎機能障害を有する被験者は概して有害事象の発現割合が高かった。

(4) 薬物動態，免疫原性及びバイオマーカー

本剤 1 週間隔の投与期間の少なくとも 9 回目投与まで，daratumumab のピーク血清中濃度は継続して増加し，サイクル 3 の Day 1 投与後の最高血清中 daratumumab 濃度の平均値は，初回投与後の 2.9 倍であった。本剤を 1 週間隔で 8 回投与した後のサイクル 3 Day 1 の投与前の血清中 daratumumab トラフ濃度の平均値（標準偏差）は 607.73（231.98） μg/mL であった。その後，本剤 4 週間隔の投与期間中にトラフ及びピーク濃度はやや低下し，サイクル 12 Day 1 の投与前のトラフ濃度の平均値（標準偏差）は 255.35（123.58） μg/mL であった。これらの結果は，本剤の単剤療法又は他の併用療法試験で得られた結果と一貫していた。

本治験期間中に本剤に対する抗体が陽性となった被験者は 1 例であり，免疫原性のリスクが低いことが示された。当該被験者の抗体は中和抗体であったが，当該抗体の出現は一過性であった。

2.7.6.1.1.3　結論

DRd 療法は，1 レジメン以上の前治療歴を有する再発又は難治性の MM 患者において， Rd 療法と比べ有意に高い有効性を示した。DRd 療法は Rd 療法と比べて，PFS，TTP，ORR 及び MRD 陰性率を統計学的に有意に改善した。DRd 療法の安全性プロファイルはレジメンに含まれる個々の薬剤と同様であり，臨床的に管理可能であった。本治験での治験薬の投与中止及び死亡の割合

は低かった。以上より，1 レジメン以上の前治療歴を有する再発又は難治性の MM 患者の治療において，DRd 療法の良好なリスクベネフィットプロファイルが示された。

2.7.6.1.2 有害事象

2016 年 3 月 7 日のクリニカルカットオフ日時点での，因果関係を問わない有害事象及び治験薬と関連性がある有害事象をそれぞれ表 2.7.6.1-1 及び表 2.7.6.1-2 に示す。

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］

	Rd n (%)	DRd n (%)
Analysis set: safety	281	283
Total number of subjects with TEAE	274 (97.5%)	278 (98.2%)
MedDRA system organ class/Preferred term		
感染症および寄生虫症	204 (72.6%)	238 (84.1%)
上気道感染	58 (20.6%)	90 (31.8%)
鼻咽頭炎	43 (15.3%)	68 (24.0%)
肺炎	37 (13.2%)	40 (14.1%)
気管支炎	34 (12.1%)	38 (13.4%)
気道感染	22 (7.8%)	31 (11.0%)
インフルエンザ	13 (4.6%)	21 (7.4%)
副鼻腔炎	10 (3.6%)	18 (6.4%)
下気道感染	9 (3.2%)	17 (6.0%)
尿路感染	11 (3.9%)	15 (5.3%)
鼻炎	3 (1.1%)	15 (5.3%)
結膜炎	3 (1.1%)	11 (3.9%)
胃腸炎	4 (1.4%)	10 (3.5%)
ウイルス感染	7 (2.5%)	5 (1.8%)
膀胱炎	7 (2.5%)	4 (1.4%)
帯状疱疹	5 (1.8%)	6 (2.1%)
咽頭炎	7 (2.5%)	4 (1.4%)
口腔カンジダ症	4 (1.4%)	6 (2.1%)
口腔真菌感染	5 (1.8%)	5 (1.8%)
皮膚感染	5 (1.8%)	5 (1.8%)
感染	5 (1.8%)	4 (1.4%)
蜂巣炎	3 (1.1%)	5 (1.8%)
口腔ヘルペス	2 (0.7%)	6 (2.1%)
敗血症	6 (2.1%)	2 (0.7%)
歯膿瘍	6 (2.1%)	2 (0.7%)
耳感染	3 (1.1%)	4 (1.4%)
歯肉炎	4 (1.4%)	2 (0.7%)
限局性感染	5 (1.8%)	1 (0.4%)
真菌感染	1 (0.4%)	4 (1.4%)
肺感染	2 (0.7%)	3 (1.1%)
敗血症性ショック	2 (0.7%)	3 (1.1%)
足部白癬	3 (1.1%)	2 (0.7%)
気管支肺炎	1 (0.4%)	3 (1.1%)
丹毒	2 (0.7%)	2 (0.7%)
眼感染	2 (0.7%)	2 (0.7%)
ヘルペスウイルス感染	0	4 (1.4%)
粘膜感染	3 (1.1%)	1 (0.4%)
歯周炎	1 (0.4%)	3 (1.1%)
インフルエンザ性肺炎	0	4 (1.4%)
歯感染	2 (0.7%)	2 (0.7%)
創傷感染	3 (1.1%)	1 (0.4%)
虫垂炎	1 (0.4%)	2 (0.7%)
細気管支炎	1 (0.4%)	2 (0.7%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
カンジダ感染	2 (0.7%)	1 (0.4%)
毛包炎	1 (0.4%)	2 (0.7%)
皮膚真菌感染	1 (0.4%)	2 (0.7%)
ウイルス性胃腸炎	1 (0.4%)	2 (0.7%)
消化管感染	1 (0.4%)	2 (0.7%)
Ｈ１Ｎ１インフルエンザ	1 (0.4%)	2 (0.7%)
大葉性肺炎	1 (0.4%)	2 (0.7%)
細菌性肺炎	1 (0.4%)	2 (0.7%)
ＲＳウイルス感染	0	3 (1.1%)
皮膚カンジダ	3 (1.1%)	0
ウイルス性上気道感染	2 (0.7%)	1 (0.4%)
外陰部腟カンジダ症	0	3 (1.1%)
急性副鼻腔炎	0	2 (0.7%)
ウイルス性気管支炎	2 (0.7%)	0
カンピロバクター胃腸炎	0	2 (0.7%)
クロストリジウム・ディフィシレ感染	2 (0.7%)	0
ウイルス性結膜炎	1 (0.4%)	1 (0.4%)
感染性小腸結腸炎	2 (0.7%)	0
大腸菌性尿路感染	0	2 (0.7%)
せつ	0	2 (0.7%)
麦粒腫	2 (0.7%)	0
ウイルス性下気道感染	1 (0.4%)	1 (0.4%)
好中球減少性敗血症	0	2 (0.7%)
骨髄炎	2 (0.7%)	0
外耳炎	1 (0.4%)	1 (0.4%)
中耳炎	1 (0.4%)	1 (0.4%)
急性中耳炎	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)
耳下腺炎	0	2 (0.7%)
レンサ球菌性咽頭炎	1 (0.4%)	1 (0.4%)
レジオネラ菌性肺炎	1 (0.4%)	1 (0.4%)
ウイルス性気道感染	0	2 (0.7%)
皮下組織膿瘍	0	2 (0.7%)
扁桃炎	1 (0.4%)	1 (0.4%)
気管炎	1 (0.4%)	1 (0.4%)
細菌性上気道感染	0	2 (0.7%)
腟感染	1 (0.4%)	1 (0.4%)
四肢膿瘍	1 (0.4%)	0
急性扁桃炎	0	1 (0.4%)
アデノウイルス感染	1 (0.4%)	0
肛門膿瘍	1 (0.4%)	0
無症候性細菌尿	0	1 (0.4%)
細菌感染	0	1 (0.4%)
カンジダ性亀頭炎	0	1 (0.4%)
細菌性気管支炎	0	1 (0.4%)
カンピロバクター感染	0	1 (0.4%)
カテーテル留置部位膿瘍	0	1 (0.4%)
カテーテル留置部位感染	0	1 (0.4%)
慢性副鼻腔炎	0	1 (0.4%)
細菌性結膜炎	1 (0.4%)	0
コロナウイルス感染	0	1 (0.4%)
サイトメガロウイルス感染	0	1 (0.4%)
蓄膿	1 (0.4%)	0
ウイルス性腸炎	0	1 (0.4%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
喉頭蓋炎	0	1 (0.4%)
大腸菌性菌血症	0	1 (0.4%)
硬膜外膿瘍	0	1 (0.4%)
真菌性眼感染	1 (0.4%)	0
熱性感染症	1 (0.4%)	0
陰部単純ヘルペス	1 (0.4%)	0
真菌性性器感染	1 (0.4%)	0
ヘモフィルス感染	1 (0.4%)	0
単純ヘルペス	1 (0.4%)	0
咬傷感染	1 (0.4%)	0
感染性舌炎	0	1 (0.4%)
感染性筋炎	1 (0.4%)	0
感染性脊椎炎	0	1 (0.4%)
注入部位蜂巣炎	0	1 (0.4%)
真菌性角膜炎	1 (0.4%)	0
喉頭炎	1 (0.4%)	0
ウイルス性喉頭炎	0	1 (0.4%)
リステリア性敗血症	0	1 (0.4%)
鼻膿瘍	0	1 (0.4%)
鼻ヘルペス	1 (0.4%)	0
壊死性筋膜炎	1 (0.4%)	0
口腔感染	0	1 (0.4%)
口腔ウイルス感染	1 (0.4%)	0
中咽頭カンジダ症	0	1 (0.4%)
耳管炎	0	1 (0.4%)
爪囲炎	1 (0.4%)	0
眼窩周囲蜂巣炎	0	1 (0.4%)
百日咳	1 (0.4%)	0
ヘモフィルス性肺炎	0	1 (0.4%)
クレブシエラ菌性肺炎	0	1 (0.4%)
レンサ球菌性肺炎	0	1 (0.4%)
前立腺感染	0	1 (0.4%)
シュードモナス感染	0	1 (0.4%)
肺結核	1 (0.4%)	0
歯髄炎	1 (0.4%)	0
腎盂腎炎	0	1 (0.4%)
急性腎盂腎炎	1 (0.4%)	0
呼吸器モニリア症	0	1 (0.4%)
サルモネラ性菌血症	0	1 (0.4%)
軟部組織感染	0	1 (0.4%)
ブドウ球菌感染	1 (0.4%)	0
ブドウ球菌皮膚感染	1 (0.4%)	0
尿道炎	0	1 (0.4%)
尿路性敗血症	1 (0.4%)	0
子宮膿瘍	0	1 (0.4%)
水痘	1 (0.4%)	0
水痘帯状疱疹ウイルス感染	1 (0.4%)	0
ウイルス性鼻炎	0	1 (0.4%)
内臓リーシュマニア症	0	1 (0.4%)
外陰腟真菌感染	1 (0.4%)	0
外陰部腟炎	1 (0.4%)	0
血液およびリンパ系障害	184 (65.5%)	200 (70.7%)
好中球減少症	121 (43.1%)	168 (59.4%)
貧血	98 (34.9%)	88 (31.1%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
血小板減少症	77 (27.4%)	76 (26.9%)
白血球減少症	17 (6.0%)	21 (7.4%)
リンパ球減少症	15 (5.3%)	17 (6.0%)
発熱性好中球減少症	7 (2.5%)	16 (5.7%)
リンパ節症	2 (0.7%)	2 (0.7%)
白血球増加症	2 (0.7%)	0
骨髄機能不全	1 (0.4%)	0
骨髄浮腫	1 (0.4%)	0
凝血異常	0	1 (0.4%)
播種性血管内凝固	1 (0.4%)	0
好酸球増加症	0	1 (0.4%)
出血性素因	1 (0.4%)	0
出血性障害	1 (0.4%)	0
過粘稠度症候群	1 (0.4%)	0
内出血発生の増加傾向	0	1 (0.4%)
無胆汁色素尿性黄疸	1 (0.4%)	0
小球性貧血	1 (0.4%)	0
鉄芽球性貧血	1 (0.4%)	0
脾臓障害	1 (0.4%)	0
血栓性血小板減少性紫斑病	1 (0.4%)	0
胃腸障害	164 (58.4%)	216 (76.3%)
下痢	69 (24.6%)	121 (42.8%)
便秘	71 (25.3%)	83 (29.3%)
悪心	40 (14.2%)	68 (24.0%)
嘔吐	15 (5.3%)	47 (16.6%)
腹痛	11 (3.9%)	20 (7.1%)
上腹部痛	10 (3.6%)	21 (7.4%)
消化不良	6 (2.1%)	18 (6.4%)
口内炎	6 (2.1%)	17 (6.0%)
歯痛	5 (1.8%)	9 (3.2%)
口内乾燥	6 (2.1%)	7 (2.5%)
腹部膨満	5 (1.8%)	7 (2.5%)
胃食道逆流性疾患	6 (2.1%)	5 (1.8%)
口腔内潰瘍形成	4 (1.4%)	7 (2.5%)
腹部不快感	3 (1.1%)	6 (2.1%)
痔核	3 (1.1%)	6 (2.1%)
舌痛	4 (1.4%)	4 (1.4%)
嚥下障害	1 (0.4%)	6 (2.1%)
口腔内痛	4 (1.4%)	2 (0.7%)
齲歯	5 (1.8%)	0
放屁	0	5 (1.8%)
口の錯感覚	2 (0.7%)	3 (1.1%)
直腸出血	1 (0.4%)	4 (1.4%)
胃腸障害	0	4 (1.4%)
鼠径ヘルニア	3 (1.1%)	1 (0.4%)
嚥下痛	1 (0.4%)	3 (1.1%)
アフタ性口内炎	2 (0.7%)	1 (0.4%)
大腸炎	1 (0.4%)	2 (0.7%)
胃炎	1 (0.4%)	2 (0.7%)
裂孔ヘルニア	1 (0.4%)	2 (0.7%)
下腹部痛	1 (0.4%)	1 (0.4%)
肛門出血	1 (0.4%)	1 (0.4%)
便通不規則	0	2 (0.7%)
憩室穿孔	0	2 (0.7%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
おくび	1 (0.4%)	1 (0.4%)
胃障害	2 (0.7%)	0
吐血	1 (0.4%)	1 (0.4%)
口の感覚鈍麻	0	2 (0.7%)
過敏性腸症候群	2 (0.7%)	0
口唇腫脹	1 (0.4%)	1 (0.4%)
メレナ	2 (0.7%)	0
口腔粘膜水疱形成	1 (0.4%)	1 (0.4%)
地図状舌	1 (0.4%)	1 (0.4%)
腹部腫瘤	0	1 (0.4%)
腹壁血腫	0	1 (0.4%)
裂肛	0	1 (0.4%)
痔瘻	1 (0.4%)	0
バレット食道	1 (0.4%)	0
胆汁酸吸収不良	0	1 (0.4%)
呼気臭	1 (0.4%)	0
口唇のひび割れ	1 (0.4%)	0
口唇炎	0	1 (0.4%)
潰瘍性大腸炎	1 (0.4%)	0
歯不快感	0	1 (0.4%)
腸憩室	0	1 (0.4%)
心窩部不快感	0	1 (0.4%)
便失禁	1 (0.4%)	0
糞塊	1 (0.4%)	0
胃拡張	0	1 (0.4%)
胃出血	0	1 (0.4%)
出血性胃腸管血管異形成	0	1 (0.4%)
消化管運動障害	1 (0.4%)	0
消化器痛	1 (0.4%)	0
歯肉出血	1 (0.4%)	0
歯肉潰瘍	1 (0.4%)	0
血便排泄	0	1 (0.4%)
腸閉塞	1 (0.4%)	0
腸管穿孔	1 (0.4%)	0
大腸ポリープ	1 (0.4%)	0
口唇びらん	0	1 (0.4%)
口唇そう痒症	0	1 (0.4%)
弛緩歯	0	1 (0.4%)
下部消化管出血	1 (0.4%)	0
口腔内出血	1 (0.4%)	0
非感染性歯肉炎	0	1 (0.4%)
食道痛	1 (0.4%)	0
食道炎	1 (0.4%)	0
膵炎	1 (0.4%)	0
歯周の炎症	1 (0.4%)	0
肛門周囲痛	0	1 (0.4%)
直腸ポリープ	0	1 (0.4%)
直腸しぶり	0	1 (0.4%)
唾液腺結石	0	1 (0.4%)
歯の知覚過敏	0	1 (0.4%)
ストレス潰瘍	1 (0.4%)	0
顎下腺腫大	0	1 (0.4%)
舌潰瘍	1 (0.4%)	0
歯の脱落	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
一般・全身障害および投与部位の状態	156 (55.5%)	197 (69.6%)
疲労	78 (27.8%)	100 (35.3%)
発熱	31 (11.0%)	57 (20.1%)
無力症	36 (12.8%)	45 (15.9%)
末梢性浮腫	37 (13.2%)	43 (15.2%)
インフルエンザ様疾患	12 (4.3%)	17 (6.0%)
悪寒	9 (3.2%)	17 (6.0%)
非心臓性胸痛	5 (1.8%)	11 (3.9%)
倦怠感	4 (1.4%)	10 (3.5%)
末梢腫脹	6 (2.1%)	8 (2.8%)
胸痛	8 (2.8%)	5 (1.8%)
胸部不快感	1 (0.4%)	7 (2.5%)
全身健康状態低下	3 (1.1%)	5 (1.8%)
疼痛	4 (1.4%)	3 (1.1%)
顔面浮腫	3 (1.1%)	3 (1.1%)
冷感	1 (0.4%)	5 (1.8%)
歩行障害	3 (1.1%)	3 (1.1%)
浮腫	3 (1.1%)	2 (0.7%)
腋窩痛	2 (0.7%)	1 (0.4%)
嚢胞	1 (0.4%)	2 (0.7%)
医薬品副作用	0	2 (0.7%)
薬物不耐性	0	2 (0.7%)
異常感	2 (0.7%)	0
熱感	0	2 (0.7%)
びくびく感	0	2 (0.7%)
局所腫脹	2 (0.7%)	0
小結節	1 (0.4%)	1 (0.4%)
苦悶感	1 (0.4%)	1 (0.4%)
カテーテル留置部位関連反応	0	1 (0.4%)
捻髪音	1 (0.4%)	0
不快感	1 (0.4%)	0
運動耐性低下	0	1 (0.4%)
溢出	0	1 (0.4%)
脂肪組織増加	0	1 (0.4%)
全身性浮腫	1 (0.4%)	0
高熱	0	1 (0.4%)
治癒不良	0	1 (0.4%)
注入部位血管外漏出	0	1 (0.4%)
注入部位静脈炎	0	1 (0.4%)
注入部位発疹	0	1 (0.4%)
注射部位内出血	0	1 (0.4%)
注射部位紅斑	0	1 (0.4%)
注射部位知覚異常	0	1 (0.4%)
限局性浮腫	0	1 (0.4%)
粘膜乾燥	1 (0.4%)	0
粘膜の炎症	0	1 (0.4%)
多臓器不全	0	1 (0.4%)
分泌物分泌	0	1 (0.4%)
全身性炎症反応症候群	0	1 (0.4%)
圧痛	1 (0.4%)	0
口渇	1 (0.4%)	0
筋骨格系および結合組織障害	154 (54.8%)	162 (57.2%)
筋痙縮	52 (18.5%)	73 (25.8%)
背部痛	48 (17.1%)	50 (17.7%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
四肢痛	30 (10.7%)	21 (7.4%)
関節痛	21 (7.5%)	24 (8.5%)
筋力低下	22 (7.8%)	23 (8.1%)
筋骨格痛	16 (5.7%)	18 (6.4%)
筋骨格系胸痛	17 (6.0%)	15 (5.3%)
骨痛	12 (4.3%)	18 (6.4%)
筋肉痛	9 (3.2%)	16 (5.7%)
頚部痛	11 (3.9%)	6 (2.1%)
脊椎痛	6 (2.1%)	6 (2.1%)
顎痛	4 (1.4%)	6 (2.1%)
顎骨壊死	4 (1.4%)	5 (1.8%)
関節腫脹	6 (2.1%)	1 (0.4%)
側腹部痛	1 (0.4%)	4 (1.4%)
筋骨格硬直	3 (1.1%)	2 (0.7%)
ミオパチー	3 (1.1%)	2 (0.7%)
単径部痛	1 (0.4%)	3 (1.1%)
関節炎	1 (0.4%)	2 (0.7%)
脊柱管狭窄症	3 (1.1%)	0
滑液包炎	1 (0.4%)	1 (0.4%)
出血性関節症	0	2 (0.7%)
椎間板突出	0	2 (0.7%)
筋肉疲労	0	2 (0.7%)
筋骨格不快感	1 (0.4%)	1 (0.4%)
変形性関節症	1 (0.4%)	1 (0.4%)
病的骨折	2 (0.7%)	0
変形性脊椎症	1 (0.4%)	1 (0.4%)
顎関節症候群	1 (0.4%)	1 (0.4%)
腱炎	2 (0.7%)	0
筋萎縮症	0	1 (0.4%)
骨脱灰	1 (0.4%)	0
軟骨石灰化症	1 (0.4%)	0
尾骨痛	1 (0.4%)	0
結晶性関節障害	1 (0.4%)	0
デュプイトラン拘縮	0	1 (0.4%)
足変形	1 (0.4%)	0
痛風性関節炎	0	1 (0.4%)
椎間板圧迫	0	1 (0.4%)
顎障害	1 (0.4%)	0
関節滲出液	1 (0.4%)	0
関節硬直	0	1 (0.4%)
四肢不快感	0	1 (0.4%)
中足骨痛	0	1 (0.4%)
運動性低下	0	1 (0.4%)
筋緊張	1 (0.4%)	0
骨炎	0	1 (0.4%)
骨壊死	0	1 (0.4%)
骨粗鬆症	1 (0.4%)	0
足底筋膜炎	1 (0.4%)	0
脊椎障害	0	1 (0.4%)
滑液嚢腫	1 (0.4%)	0
腱石灰化	0	1 (0.4%)
腱痛	0	1 (0.4%)
開口障害	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
呼吸器、胸郭および縦隔障害	114 (40.6%)	170 (60.1%)
咳嗽	35 (12.5%)	82 (29.0%)
呼吸困難	32 (11.4%)	52 (18.4%)
発声障害	7 (2.5%)	14 (4.9%)
鼻出血	12 (4.3%)	9 (3.2%)
口腔咽頭痛	10 (3.6%)	11 (3.9%)
湿性咳嗽	8 (2.8%)	13 (4.6%)
労作性呼吸困難	5 (1.8%)	13 (4.6%)
鼻閉	4 (1.4%)	14 (4.9%)
肺塞栓症	11 (3.9%)	7 (2.5%)
しゃっくり	9 (3.2%)	8 (2.8%)
鼻漏	6 (2.1%)	11 (3.9%)
アレルギー性鼻炎	3 (1.1%)	13 (4.6%)
気管支痙攣	1 (0.4%)	13 (4.6%)
咽喉刺激感	0	9 (3.2%)
喘鳴	0	9 (3.2%)
低酸素症	1 (0.4%)	6 (2.1%)
肺水腫	2 (0.7%)	5 (1.8%)
喉頭浮腫	0	6 (2.1%)
胸水	2 (0.7%)	4 (1.4%)
副鼻腔うっ血	3 (1.1%)	3 (1.1%)
カタル	5 (1.8%)	0
慢性閉塞性肺疾患	3 (1.1%)	2 (0.7%)
肺障害	2 (0.7%)	2 (0.7%)
喀血	2 (0.7%)	1 (0.4%)
鼻乾燥	2 (0.7%)	1 (0.4%)
呼吸不全	1 (0.4%)	2 (0.7%)
くしゃみ	0	3 (1.1%)
急性肺水腫	1 (0.4%)	1 (0.4%)
アレルギー性呼吸器症状	0	2 (0.7%)
鼻閉塞	0	2 (0.7%)
咽頭紅斑	1 (0.4%)	1 (0.4%)
胸膜痛	1 (0.4%)	1 (0.4%)
誤嚥性肺炎	0	2 (0.7%)
肺臓炎	0	2 (0.7%)
上気道の炎症	2 (0.7%)	0
急性呼吸不全	1 (0.4%)	0
アレルギー性咽頭炎	0	1 (0.4%)
窒息	0	1 (0.4%)
無気肺	1 (0.4%)	0
気管支反応性亢進	1 (0.4%)	0
気管支拡張症	0	1 (0.4%)
胸水症	0	1 (0.4%)
間質性肺疾患	1 (0.4%)	0
喉頭不快感	0	1 (0.4%)
喉頭の炎症	1 (0.4%)	0
喉頭痛	0	1 (0.4%)
喉頭狭窄	0	1 (0.4%)
喉頭刺激感	0	1 (0.4%)
鼻部不快感	0	1 (0.4%)
器質化肺炎	0	1 (0.4%)
口腔咽頭不快感	1 (0.4%)	0
胸膜炎	1 (0.4%)	0
気胸	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
呼気延長	0	1 (0.4%)
肺石灰化	0	1 (0.4%)
肺高血圧症	0	1 (0.4%)
肺腫瘤	0	1 (0.4%)
気道うっ血	0	1 (0.4%)
鼻痛	1 (0.4%)	0
副鼻腔障害	0	1 (0.4%)
上気道性喘鳴	0	1 (0.4%)
窒息感	0	1 (0.4%)
頻呼吸	0	1 (0.4%)
咽喉絞扼感	0	1 (0.4%)
神経系障害	124 (44.1%)	140 (49.5%)
頭痛	19 (6.8%)	37 (13.1%)
振戦	24 (8.5%)	26 (9.2%)
浮動性めまい	24 (8.5%)	22 (7.8%)
末梢性感覚ニューロパチー	19 (6.8%)	23 (8.1%)
味覚異常	15 (5.3%)	21 (7.4%)
末梢性ニューロパチー	15 (5.3%)	12 (4.2%)
錯感覚	10 (3.6%)	14 (4.9%)
感覚鈍麻	5 (1.8%)	13 (4.6%)
失神	2 (0.7%)	10 (3.5%)
嗜眠	4 (1.4%)	6 (2.1%)
記憶障害	8 (2.8%)	2 (0.7%)
神経痛	3 (1.1%)	4 (1.4%)
認知障害	2 (0.7%)	4 (1.4%)
味覚消失	1 (0.4%)	4 (1.4%)
平衡障害	2 (0.7%)	3 (1.1%)
失神寸前の状態	0	5 (1.8%)
傾眠	4 (1.4%)	1 (0.4%)
注意力障害	1 (0.4%)	3 (1.1%)
下肢静止不能症候群	2 (0.7%)	1 (0.4%)
坐骨神経痛	3 (1.1%)	0
一過性脳虚血発作	2 (0.7%)	1 (0.4%)
アカシジア	2 (0.7%)	0
健忘	1 (0.4%)	1 (0.4%)
脳梗塞	1 (0.4%)	1 (0.4%)
体位性めまい	1 (0.4%)	1 (0.4%)
異常感覚	1 (0.4%)	1 (0.4%)
知覚過敏	0	2 (0.7%)
過眠症	1 (0.4%)	1 (0.4%)
味覚減退	2 (0.7%)	0
片頭痛	2 (0.7%)	0
神経系障害	1 (0.4%)	1 (0.4%)
ヘルペス後神経痛	2 (0.7%)	0
痙攣発作	0	2 (0.7%)
脊髄圧迫	2 (0.7%)	0
第７脳神経麻痺	2 (0.7%)	0
視野欠損	0	2 (0.7%)
無嗅覚	0	1 (0.4%)
失語症	1 (0.4%)	0
失声症	0	1 (0.4%)
アテトーゼ	1 (0.4%)	0
灼熱感	0	1 (0.4%)
頚動脈硬化症	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
小脳性運動失調	0	1 (0.4%)
脳出血	1 (0.4%)	0
脳血管発作	0	1 (0.4%)
認知症	1 (0.4%)	0
労作性めまい	1 (0.4%)	0
構語障害	0	1 (0.4%)
統合運動障害	1 (0.4%)	0
てんかん	0	1 (0.4%)
蟻走感	1 (0.4%)	0
不全片麻痺	1 (0.4%)	0
運動低下	0	1 (0.4%)
肋間神経痛	1 (0.4%)	0
虚血性脳卒中	1 (0.4%)	0
レルミット徴候	0	1 (0.4%)
意識消失	1 (0.4%)	0
不随意性筋収縮	1 (0.4%)	0
筋痙直	0	1 (0.4%)
眼振	0	1 (0.4%)
嗅覚錯誤	0	1 (0.4%)
末梢性感覚運動ニューロパチー	1 (0.4%)	0
腓骨神経麻痺	0	1 (0.4%)
精神運動亢進	1 (0.4%)	0
感覚運動障害	1 (0.4%)	0
感覚障害	0	1 (0.4%)
副鼻腔炎に伴う頭痛	0	1 (0.4%)
脊髄浮腫	0	1 (0.4%)
三叉神経障害	0	1 (0.4%)
上位運動ニューロンの病変	1 (0.4%)	0
血管性脳症	1 (0.4%)	0
代謝および栄養障害	95 (33.8%)	116 (41.0%)
食欲減退	29 (10.3%)	32 (11.3%)
低カリウム血症	22 (7.8%)	30 (10.6%)
高血糖	19 (6.8%)	25 (8.8%)
低カルシウム血症	11 (3.9%)	18 (6.4%)
低リン酸血症	11 (3.9%)	16 (5.7%)
低マグネシウム血症	12 (4.3%)	8 (2.8%)
高尿酸血症	8 (2.8%)	7 (2.5%)
脱水	2 (0.7%)	10 (3.5%)
高カルシウム血症	5 (1.8%)	5 (1.8%)
低ナトリウム血症	2 (0.7%)	8 (2.8%)
痛風	8 (2.8%)	1 (0.4%)
低アルブミン血症	5 (1.8%)	2 (0.7%)
高カリウム血症	2 (0.7%)	3 (1.1%)
ビタミンＢ１２欠乏	3 (1.1%)	2 (0.7%)
高脂血症	2 (0.7%)	2 (0.7%)
高コレステロール血症	1 (0.4%)	2 (0.7%)
低血糖症	2 (0.7%)	1 (0.4%)
ビタミンD欠乏	2 (0.7%)	1 (0.4%)
糖尿病	0	2 (0.7%)
体液平衡失調	1 (0.4%)	1 (0.4%)
高ナトリウム血症	1 (0.4%)	1 (0.4%)
鉄欠乏	1 (0.4%)	1 (0.4%)
栄養障害	2 (0.7%)	0
アシドーシス	0	1 (0.4%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
悪液質	0	1 (0.4%)
電解質失調	0	1 (0.4%)
酵素異常	0	1 (0.4%)
水分過負荷	0	1 (0.4%)
体液貯留	0	1 (0.4%)
葉酸欠乏	0	1 (0.4%)
食物不耐性	0	1 (0.4%)
高リン酸塩血症	1 (0.4%)	0
高トリグリセリド血症	0	1 (0.4%)
食欲亢進	1 (0.4%)	0
多飲症	1 (0.4%)	0
テタニー	1 (0.4%)	0
１型糖尿病	0	1 (0.4%)
２型糖尿病	1 (0.4%)	0
皮膚および皮下組織障害	83 (29.5%)	113 (39.9%)
発疹	29 (10.3%)	35 (12.4%)
そう痒症	29 (10.3%)	28 (9.9%)
多汗症	8 (2.8%)	20 (7.1%)
皮膚乾燥	7 (2.5%)	10 (3.5%)
蕁麻疹	6 (2.1%)	8 (2.8%)
紅斑	7 (2.5%)	6 (2.1%)
寝汗	5 (1.8%)	4 (1.4%)
全身性皮疹	5 (1.8%)	4 (1.4%)
斑状丘疹状皮疹	3 (1.1%)	5 (1.8%)
皮膚病変	3 (1.1%)	3 (1.1%)
顔面腫脹	3 (1.1%)	3 (1.1%)
褥瘡性潰瘍	1 (0.4%)	3 (1.1%)
皮膚炎	2 (0.7%)	2 (0.7%)
斑状出血	1 (0.4%)	3 (1.1%)
斑状皮疹	1 (0.4%)	3 (1.1%)
皮膚潰瘍	1 (0.4%)	3 (1.1%)
日光角化症	2 (0.7%)	1 (0.4%)
湿疹	1 (0.4%)	2 (0.7%)
脱毛症	0	2 (0.7%)
水疱	0	2 (0.7%)
冷汗	1 (0.4%)	1 (0.4%)
ざ瘡様皮膚炎	0	2 (0.7%)
アレルギー性皮膚炎	1 (0.4%)	1 (0.4%)
多形紅斑	1 (0.4%)	1 (0.4%)
男性型多毛症	1 (0.4%)	1 (0.4%)
過角化	1 (0.4%)	1 (0.4%)
点状出血	0	2 (0.7%)
そう痒性皮疹	1 (0.4%)	1 (0.4%)
皮膚障害	2 (0.7%)	0
皮膚色素過剰	0	2 (0.7%)
皮膚腫脹	0	2 (0.7%)
接触性皮膚炎	1 (0.4%)	0
薬疹	0	1 (0.4%)
紅色症	0	1 (0.4%)
全身紅斑	0	1 (0.4%)
毛髪成長異常	0	1 (0.4%)
手皮膚炎	0	1 (0.4%)
多毛症	1 (0.4%)	0
乏汗症	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
嵌入爪	0	1 (0.4%)
爪甲脱落症	0	1 (0.4%)
皮膚疼痛	0	1 (0.4%)
アレルギー性そう痒症	0	1 (0.4%)
全身性そう痒症	0	1 (0.4%)
壊疽性膿皮症	1 (0.4%)	0
丘疹性皮疹	0	1 (0.4%)
小水疱性皮疹	1 (0.4%)	0
酒さ	0	1 (0.4%)
皮膚灼熱感	1 (0.4%)	0
皮膚亀裂	1 (0.4%)	0
うっ滞性皮膚炎	1 (0.4%)	0
毛細血管拡張症	1 (0.4%)	0
血管炎性皮疹	0	1 (0.4%)
黄色腫	0	1 (0.4%)
乾皮症	1 (0.4%)	0
精神障害	93 (33.1%)	96 (33.9%)
不眠症	55 (19.6%)	55 (19.4%)
不安	12 (4.3%)	18 (6.4%)
うつ病	5 (1.8%)	18 (6.4%)
激越	9 (3.2%)	7 (2.5%)
落ち着きのなさ	5 (1.8%)	8 (2.8%)
易刺激性	5 (1.8%)	6 (2.1%)
気分変化	5 (1.8%)	6 (2.1%)
錯乱状態	7 (2.5%)	2 (0.7%)
睡眠障害	4 (1.4%)	3 (1.1%)
譫妄	5 (1.8%)	1 (0.4%)
抑うつ気分	2 (0.7%)	3 (1.1%)
神経過敏	5 (1.8%)	0
抑うつ症状	2 (0.7%)	1 (0.4%)
精神障害	1 (0.4%)	2 (0.7%)
気分動揺	1 (0.4%)	2 (0.7%)
感情障害	1 (0.4%)	1 (0.4%)
幻覚	1 (0.4%)	1 (0.4%)
適応障害	0	1 (0.4%)
精神緩慢	0	1 (0.4%)
まとまりのない会話	1 (0.4%)	0
失見当識	1 (0.4%)	0
気分変調性障害	1 (0.4%)	0
言葉もれ	1 (0.4%)	0
リビドー消失	1 (0.4%)	0
精神症状	0	1 (0.4%)
精神病性障害	1 (0.4%)	0
睡眠時驚愕	1 (0.4%)	0
ストレス	1 (0.4%)	0
涙ぐむ	0	1 (0.4%)
思考異常	1 (0.4%)	0
血管障害	46 (16.4%)	80 (28.3%)
高血圧	7 (2.5%)	21 (7.4%)
低血圧	6 (2.1%)	19 (6.7%)
深部静脈血栓症	11 (3.9%)	5 (1.8%)
潮紅	5 (1.8%)	8 (2.8%)
血腫	5 (1.8%)	4 (1.4%)
表在性血栓性静脈炎	6 (2.1%)	3 (1.1%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
起立性低血圧	2 (0.7%)	4 (1.4%)
静脈炎	1 (0.4%)	5 (1.8%)
ほてり	2 (0.7%)	3 (1.1%)
血栓症	2 (0.7%)	2 (0.7%)
塞栓症	0	3 (1.1%)
血栓性静脈炎	0	3 (1.1%)
動脈硬化症	2 (0.7%)	0
末梢冷感	0	2 (0.7%)
静脈血栓症	0	2 (0.7%)
大動脈瘤	1 (0.4%)	0
大動脈拡張	0	1 (0.4%)
出血性梗塞	0	1 (0.4%)
虚血	1 (0.4%)	0
リンパ浮腫	0	1 (0.4%)
蒼白	1 (0.4%)	0
末梢動脈狭窄	0	1 (0.4%)
表在性静脈炎	0	1 (0.4%)
血栓後症候群	1 (0.4%)	0
レイノー現象	1 (0.4%)	0
静脈閉塞	1 (0.4%)	0
四肢静脈血栓症	1 (0.4%)	0
臨床検査	48 (17.1%)	63 (22.3%)
アラニンアミノトランスフェラーゼ増加	10 (3.6%)	15 (5.3%)
体重減少	9 (3.2%)	16 (5.7%)
血中クレアチニン増加	11 (3.9%)	9 (3.2%)
アスパラギン酸アミノトランスフェラーゼ増加	9 (3.2%)	9 (3.2%)
γ－グルタミルトランスフェラーゼ増加	7 (2.5%)	7 (2.5%)
血中アルカリホスファターゼ増加	5 (1.8%)	6 (2.1%)
心電図ＱＴ延長	1 (0.4%)	5 (1.8%)
体重増加	4 (1.4%)	2 (0.7%)
Ｃ－反応性蛋白増加	2 (0.7%)	2 (0.7%)
腎クレアチニン・クリアランス減少	2 (0.7%)	1 (0.4%)
免疫グロブリン減少	0	3 (1.1%)
血中乳酸脱水素酵素増加	1 (0.4%)	1 (0.4%)
血圧上昇	0	2 (0.7%)
糸球体濾過率減少	2 (0.7%)	0
国際標準比増加	0	2 (0.7%)
アラニンアミノトランスフェラーゼ異常	0	1 (0.4%)
抗凝固薬濃度治療量以下	1 (0.4%)	0
アスパラギン酸アミノトランスフェラーゼ異常	0	1 (0.4%)
血中クレアチンホスホキナーゼ増加	0	1 (0.4%)
血中葉酸減少	1 (0.4%)	0
血中鉄減少	0	1 (0.4%)
血中乳酸脱水素酵素減少	0	1 (0.4%)
血圧低下	0	1 (0.4%)
体温上昇	1 (0.4%)	0
心雑音	0	1 (0.4%)
診断法	1 (0.4%)	0
フィブリンＤダイマー増加	1 (0.4%)	0
ヘリコバクター検査陽性	1 (0.4%)	0
好中球中毒性顆粒存在	0	1 (0.4%)
酸素飽和度低下	0	1 (0.4%)
前立腺特異性抗原増加	0	1 (0.4%)
肺動脈圧上昇	0	1 (0.4%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
網状赤血球数増加	0	1 (0.4%)
血清フェリチン減少	0	1 (0.4%)
トロポニン増加	0	1 (0.4%)
静脈雑音	1 (0.4%)	0
腎および尿路障害	45 (16.0%)	50 (17.7%)
腎機能障害	13 (4.6%)	20 (7.1%)
急性腎不全	15 (5.3%)	4 (1.4%)
頻尿	3 (1.1%)	6 (2.1%)
慢性腎臓病	4 (1.4%)	3 (1.1%)
排尿困難	4 (1.4%)	2 (0.7%)
腎不全	5 (1.8%)	1 (0.4%)
尿閉	5 (1.8%)	0
高窒素血症	1 (0.4%)	3 (1.1%)
血尿	1 (0.4%)	3 (1.1%)
夜間頻尿	1 (0.4%)	2 (0.7%)
尿失禁	2 (0.7%)	1 (0.4%)
腎結石症	0	2 (0.7%)
ベンスジョーンズ蛋白尿	1 (0.4%)	0
膀胱結石	0	1 (0.4%)
失禁	0	1 (0.4%)
ケトン尿	1 (0.4%)	0
下部尿路症状	1 (0.4%)	0
排尿異常	1 (0.4%)	0
尿意切迫	0	1 (0.4%)
多尿	1 (0.4%)	0
腎仙痛	0	1 (0.4%)
腎嚢胞	0	1 (0.4%)
腎障害	0	1 (0.4%)
腎腫瘤	1 (0.4%)	0
尿道出血	0	1 (0.4%)
尿路閉塞	0	1 (0.4%)
眼障害	35 (12.5%)	57 (20.1%)
霧視	14 (5.0%)	19 (6.7%)
白内障	8 (2.8%)	18 (6.4%)
眼乾燥	3 (1.1%)	5 (1.8%)
眼刺激	1 (0.4%)	7 (2.5%)
流涙増加	1 (0.4%)	7 (2.5%)
眼脂	2 (0.7%)	1 (0.4%)
視力低下	1 (0.4%)	2 (0.7%)
結膜出血	1 (0.4%)	1 (0.4%)
眼出血	0	2 (0.7%)
眼痛	1 (0.4%)	1 (0.4%)
眼部腫脹	0	2 (0.7%)
眼充血	0	2 (0.7%)
眼窩周囲浮腫	1 (0.4%)	1 (0.4%)
視力障害	0	2 (0.7%)
眼瞼炎	0	1 (0.4%)
失明	1 (0.4%)	0
結膜刺激	1 (0.4%)	0
眼のアレルギー	0	1 (0.4%)
眼の障害	0	1 (0.4%)
眼の炎症	0	1 (0.4%)
眼球浮腫	0	1 (0.4%)
眼瞼浮腫	0	1 (0.4%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
眼瞼下垂	1 (0.4%)	0
眼瞼発疹	1 (0.4%)	0
緑内障	0	1 (0.4%)
水晶体混濁	1 (0.4%)	0
黄斑変性	1 (0.4%)	0
後嚢破裂	0	1 (0.4%)
屈折障害	0	1 (0.4%)
網膜静脈血栓症	1 (0.4%)	0
網膜症	1 (0.4%)	0
硝子体剥離	1 (0.4%)	0
硝子体浮遊物	0	1 (0.4%)
硝子体出血	1 (0.4%)	0
傷害、中毒および処置合併症	45 (16.0%)	45 (15.9%)
転倒	8 (2.8%)	11 (3.9%)
挫傷	6 (2.1%)	10 (3.5%)
肋骨骨折	4 (1.4%)	2 (0.7%)
脊椎圧迫骨折	2 (0.7%)	4 (1.4%)
裂傷	2 (0.7%)	3 (1.1%)
靭帯捻挫	0	4 (1.4%)
創傷	4 (1.4%)	0
鎖骨骨折	2 (0.7%)	1 (0.4%)
節足動物咬傷	2 (0.7%)	0
背部損傷	1 (0.4%)	1 (0.4%)
圧迫骨折	1 (0.4%)	1 (0.4%)
眼挫傷	1 (0.4%)	1 (0.4%)
足骨折	0	2 (0.7%)
股関節部骨折	1 (0.4%)	1 (0.4%)
注入に伴う反応	2 (0.7%)	0
関節脱臼	2 (0.7%)	0
関節損傷	0	2 (0.7%)
処置による疼痛	2 (0.7%)	0
橈骨骨折	1 (0.4%)	1 (0.4%)
皮膚擦過傷	1 (0.4%)	1 (0.4%)
熱傷	0	2 (0.7%)
各種物質毒性	1 (0.4%)	1 (0.4%)
創合併症	1 (0.4%)	1 (0.4%)
脳ヘルニア	0	1 (0.4%)
顔面損傷	1 (0.4%)	0
顔面骨骨折	1 (0.4%)	0
大腿骨頚部骨折	1 (0.4%)	0
手骨折	0	1 (0.4%)
上腕骨骨折	1 (0.4%)	0
四肢損傷	1 (0.4%)	0
肉離れ	0	1 (0.4%)
頚部損傷	0	1 (0.4%)
過量投与	1 (0.4%)	0
骨盤骨折	1 (0.4%)	0
眼窩周囲挫傷	0	1 (0.4%)
腓骨神経損傷	0	1 (0.4%)
処置後合併症	1 (0.4%)	0
外傷後疼痛	1 (0.4%)	0
瘢痕	1 (0.4%)	0
引っかき傷	1 (0.4%)	0
皮膚創傷	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
胸骨損傷	0	1 (0.4%)
硬膜下血腫	1 (0.4%)	0
腱断裂	1 (0.4%)	0
脛骨骨折	1 (0.4%)	0
歯牙破折	1 (0.4%)	0
輸血関連呼吸困難	1 (0.4%)	0
外傷性血腫	1 (0.4%)	0
上肢骨折	0	1 (0.4%)
創傷出血	0	1 (0.4%)
手首関節骨折	0	1 (0.4%)
心臓障害	25 (8.9%)	41 (14.5%)
心房細動	7 (2.5%)	9 (3.2%)
頻脈	2 (0.7%)	9 (3.2%)
狭心症	1 (0.4%)	7 (2.5%)
動悸	3 (1.1%)	4 (1.4%)
洞性頻脈	0	4 (1.4%)
急性心筋梗塞	3 (1.1%)	0
心房粗動	1 (0.4%)	2 (0.7%)
徐脈	2 (0.7%)	1 (0.4%)
左室機能不全	0	2 (0.7%)
心筋梗塞	1 (0.4%)	1 (0.4%)
心筋虚血	1 (0.4%)	1 (0.4%)
心嚢液貯留	2 (0.7%)	0
上室性頻脈	1 (0.4%)	1 (0.4%)
心室性期外収縮	1 (0.4%)	1 (0.4%)
急性冠動脈症候群	0	1 (0.4%)
不整脈	0	1 (0.4%)
第一度房室ブロック	0	1 (0.4%)
心アミロイドーシス	0	1 (0.4%)
心停止	1 (0.4%)	0
うっ血性心不全	0	1 (0.4%)
心肥大	0	1 (0.4%)
心肺不全	0	1 (0.4%)
伝導障害	0	1 (0.4%)
冠動脈疾患	1 (0.4%)	0
拡張機能障害	0	1 (0.4%)
期外収縮	0	1 (0.4%)
僧帽弁閉鎖不全症	0	1 (0.4%)
心膜炎	1 (0.4%)	0
洞性不整脈	0	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	18 (6.4%)	16 (5.7%)
扁平上皮癌	3 (1.1%)	2 (0.7%)
基底細胞癌	2 (0.7%)	2 (0.7%)
形質細胞性白血病	2 (0.7%)	1 (0.4%)
脂肪腫	0	2 (0.7%)
アクロコルドン	0	1 (0.4%)
急性単球性白血病	0	1 (0.4%)
腺癌	0	1 (0.4%)
肛門直腸の良性新生物	1 (0.4%)	0
乳房の良性新生物	0	1 (0.4%)
肺の良性新生物	1 (0.4%)	0
良性新生物	1 (0.4%)	0
膀胱の良性新生物	1 (0.4%)	0

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
甲状腺の良性新生物	0	1 (0.4%)
膀胱移行上皮癌	1 (0.4%)	0
ボーエン病	0	1 (0.4%)
エプスタイン・バーウイルス関連リンパ増殖性障害	0	1 (0.4%)
皮膚血管腫	1 (0.4%)	0
ケラトアカントーマ	0	1 (0.4%)
肺腺癌	1 (0.4%)	0
形質細胞腫	1 (0.4%)	0
前立腺癌	1 (0.4%)	0
直腸腺癌	1 (0.4%)	0
シュワン細胞腫	1 (0.4%)	0
脂漏性角化症	0	1 (0.4%)
耳および迷路障害	12 (4.3%)	18 (6.4%)
回転性めまい	6 (2.1%)	4 (1.4%)
耳鳴	1 (0.4%)	8 (2.8%)
難聴	1 (0.4%)	2 (0.7%)
耳痛	2 (0.7%)	1 (0.4%)
耳不快感	1 (0.4%)	1 (0.4%)
聴力低下	0	2 (0.7%)
片耳難聴	0	1 (0.4%)
耳出血	0	1 (0.4%)
中耳の炎症	1 (0.4%)	0
頭位性回転性めまい	1 (0.4%)	0
生殖系および乳房障害	17 (6.0%)	10 (3.5%)
骨盤痛	6 (2.1%)	2 (0.7%)
勃起不全	2 (0.7%)	3 (1.1%)
前立腺炎	2 (0.7%)	1 (0.4%)
腟出血	2 (0.7%)	1 (0.4%)
良性前立腺肥大症	2 (0.7%)	0
萎縮性外陰腟炎	1 (0.4%)	0
乳房嚢胞	0	1 (0.4%)
性器水疱	1 (0.4%)	0
骨盤血腫	0	1 (0.4%)
前立腺腫大	0	1 (0.4%)
精巣腫瘤	1 (0.4%)	0
精巣痛	0	1 (0.4%)
腟逆流	0	1 (0.4%)
外陰腟痛	1 (0.4%)	0
肝胆道系障害	7 (2.5%)	11 (3.9%)
高ビリルビン血症	2 (0.7%)	4 (1.4%)
肝障害	3 (1.1%)	1 (0.4%)
肝機能異常	0	2 (0.7%)
脂肪肝	1 (0.4%)	1 (0.4%)
肝細胞損傷	0	2 (0.7%)
胆管結石	1 (0.4%)	0
胆石症	0	1 (0.4%)
肝腫瘤	1 (0.4%)	0
内分泌障害	10 (3.6%)	4 (1.4%)
クッシング様症状	4 (1.4%)	1 (0.4%)
副甲状腺機能亢進症	1 (0.4%)	1 (0.4%)
ステロイド離脱症候群	2 (0.7%)	0
クッシング症候群	1 (0.4%)	0
高コルチコイド症	0	1 (0.4%)

表 2.7.6.1-1 有害事象［MMY3003 試験，安全性解析対象集団］（続き）

	Rd n (%)	DRd n (%)
甲状腺機能亢進症	0	1 (0.4%)
甲状腺機能低下症	1 (0.4%)	0
下垂体依存性クッシング症候群	1 (0.4%)	0
免疫系障害	3 (1.1%)	10 (3.5%)
季節性アレルギー	1 (0.4%)	4 (1.4%)
低γグロブリン血症	0	4 (1.4%)
薬物過敏症	1 (0.4%)	1 (0.4%)
食物アレルギー	1 (0.4%)	0
免疫抑制	0	1 (0.4%)
先天性、家族性および遺伝性障害	0	2 (0.7%)
角膜ジストロフィー	0	1 (0.4%)
包茎	0	1 (0.4%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02A.RTF] [JNJ-54767414\MMY3003\DBR_CSR\RE_CSR\PROD\TSFAE02A.SAS] 13MAY2016, 14:48

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
Analysis set: safety	281			283			
Total number of subjects with TEAE related to study treatment	233 (82.9%)	218 (77.6%)	202 (71.9%)	269 (95.1%)	215 (76.0%)	257 (90.8%)	223 (78.8%)
MedDRA system organ class/Preferred term							
血液およびリンパ系障害	146 (52.0%)	141 (50.2%)	41 (14.6%)	184 (65.0%)	61 (21.6%)	181 (64.0%)	32 (11.3%)
好中球減少症	107 (38.1%)	107 (38.1%)	16 (5.7%)	156 (55.1%)	43 (15.2%)	153 (54.1%)	15 (5.3%)
血小板減少症	67 (23.8%)	65 (23.1%)	10 (3.6%)	63 (22.3%)	23 (8.1%)	61 (21.6%)	5 (1.8%)
貧血	55 (19.6%)	54 (19.2%)	8 (2.8%)	53 (18.7%)	13 (4.6%)	52 (18.4%)	3 (1.1%)
白血球減少症	12 (4.3%)	12 (4.3%)	2 (0.7%)	21 (7.4%)	11 (3.9%)	20 (7.1%)	3 (1.1%)
リンパ球減少症	12 (4.3%)	8 (2.8%)	11 (3.9%)	15 (5.3%)	7 (2.5%)	12 (4.2%)	8 (2.8%)
発熱性好中球減少症	6 (2.1%)	6 (2.1%)	2 (0.7%)	14 (4.9%)	4 (1.4%)	14 (4.9%)	5 (1.8%)
白血球増加症	2 (0.7%)	0	2 (0.7%)	0	0	0	0
好酸球増加症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
出血性障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0
リンパ節症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
鉄芽球性貧血	1 (0.4%)	1 (0.4%)	0	0	0	0	0
一般・全身障害および投与部位の状態	90 (32.0%)	76 (27.0%)	64 (22.8%)	156 (55.1%)	81 (28.6%)	116 (41.0%)	93 (32.9%)
疲労	56 (19.9%)	49 (17.4%)	33 (11.7%)	83 (29.3%)	35 (12.4%)	74 (26.1%)	41 (14.5%)
無力症	21 (7.5%)	18 (6.4%)	13 (4.6%)	31 (11.0%)	8 (2.8%)	26 (9.2%)	15 (5.3%)
末梢性浮腫	20 (7.1%)	9 (3.2%)	16 (5.7%)	27 (9.5%)	1 (0.4%)	6 (2.1%)	25 (8.8%)
発熱	7 (2.5%)	6 (2.1%)	6 (2.1%)	26 (9.2%)	23 (8.1%)	15 (5.3%)	9 (3.2%)
悪寒	3 (1.1%)	2 (0.7%)	2 (0.7%)	15 (5.3%)	14 (4.9%)	1 (0.4%)	1 (0.4%)
倦怠感	2 (0.7%)	2 (0.7%)	1 (0.4%)	8 (2.8%)	2 (0.7%)	5 (1.8%)	5 (1.8%)
末梢腫脹	3 (1.1%)	2 (0.7%)	2 (0.7%)	6 (2.1%)	2 (0.7%)	1 (0.4%)	6 (2.1%)
インフルエンザ様疾患	2 (0.7%)	2 (0.7%)	1 (0.4%)	6 (2.1%)	4 (1.4%)	3 (1.1%)	3 (1.1%)
胸部不快感	0	0	0	5 (1.8%)	5 (1.8%)	0	0
冷感	0	0	0	5 (1.8%)	5 (1.8%)	0	0
顔面浮腫	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
全身健康状態低下	1 (0.4%)	1 (0.4%)	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
薬物不耐性	0	0	0	2 (0.7%)	0	0	2 (0.7%)
びくびく感	0	0	0	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
非心臓性胸痛	0	0	0	2 (0.7%)	2 (0.7%)	0	0
浮腫	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
疼痛	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
苦悶感	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
医薬品副作用	0	0	0	1 (0.4%)	0	0	1 (0.4%)
胸痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
運動耐性低下	0	0	0	1 (0.4%)	0	0	1 (0.4%)
溢出	0	0	0	1 (0.4%)	1 (0.4%)	0	0
脂肪組織増加	0	0	0	1 (0.4%)	0	0	1 (0.4%)
異常感	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
熱感	0	0	0	1 (0.4%)	0	0	1 (0.4%)
歩行障害	0	0	0	1 (0.4%)	0	1 (0.4%)	0
全身性浮腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
高熱	0	0	0	1 (0.4%)	1 (0.4%)	0	0
注入部位発疹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
多臓器不全	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
分泌物分泌	0	0	0	1 (0.4%)	1 (0.4%)	0	0
全身性炎症反応症候群	0	0	0	1 (0.4%)	0	1 (0.4%)	0
胃腸障害	90 (32.0%)	80 (28.5%)	44 (15.7%)	152 (53.7%)	74 (26.1%)	108 (38.2%)	62 (21.9%)
下痢	30 (10.7%)	30 (10.7%)	7 (2.5%)	83 (29.3%)	28 (9.9%)	72 (25.4%)	18 (6.4%)
便秘	42 (14.9%)	41 (14.6%)	8 (2.8%)	42 (14.8%)	12 (4.2%)	36 (12.7%)	16 (5.7%)
悪心	15 (5.3%)	14 (5.0%)	6 (2.1%)	37 (13.1%)	25 (8.8%)	22 (7.8%)	9 (3.2%)
嘔吐	2 (0.7%)	2 (0.7%)	0	23 (8.1%)	22 (7.8%)	6 (2.1%)	2 (0.7%)

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
上腹部痛	5 (1.8%)	2 (0.7%)	4 (1.4%)	15 (5.3%)	3 (1.1%)	4 (1.4%)	14 (4.9%)
消化不良	4 (1.4%)	1 (0.4%)	4 (1.4%)	10 (3.5%)	1 (0.4%)	4 (1.4%)	8 (2.8%)
口内炎	4 (1.4%)	2 (0.7%)	3 (1.1%)	9 (3.2%)	6 (2.1%)	7 (2.5%)	5 (1.8%)
腹痛	4 (1.4%)	3 (1.1%)	2 (0.7%)	8 (2.8%)	5 (1.8%)	6 (2.1%)	2 (0.7%)
口内乾燥	3 (1.1%)	2 (0.7%)	1 (0.4%)	5 (1.8%)	2 (0.7%)	3 (1.1%)	5 (1.8%)
腹部膨満	3 (1.1%)	3 (1.1%)	2 (0.7%)	4 (1.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
腹部不快感	2 (0.7%)	0	2 (0.7%)	3 (1.1%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
胃食道逆流性疾患	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	1 (0.4%)
口腔内潰瘍形成	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	0
口腔内痛	2 (0.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0
憩室穿孔	0	0	0	2 (0.7%)	0	0	2 (0.7%)
放屁	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	0
胃炎	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
胃腸障害	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	0
口腔粘膜水疱形成	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
口の錯感覚	0	0	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	0
腹壁血腫	0	0	0	1 (0.4%)	0	1 (0.4%)	0
裂肛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
アフタ性口内炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
胆汁酸吸収不良	0	0	0	1 (0.4%)	0	1 (0.4%)	0
便通不規則	0	0	0	1 (0.4%)	0	1 (0.4%)	0
大腸炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
齲歯	1 (0.4%)	0	1 (0.4%)	0	0	0	0
嚥下障害	0	0	0	1 (0.4%)	1 (0.4%)	0	0
心窩部不快感	0	0	0	1 (0.4%)	0	0	1 (0.4%)
おくび	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
糞塊	1 (0.4%)	1 (0.4%)	0	0	0	0	0
胃拡張	0	0	0	1 (0.4%)	0	0	1 (0.4%)
胃障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0
胃出血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
消化管運動障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
消化器痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
舌痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
痔核	0	0	0	1 (0.4%)	0	1 (0.4%)	0
口の感覚鈍麻	0	0	0	1 (0.4%)	0	1 (0.4%)	0
腸管穿孔	1 (0.4%)	1 (0.4%)	0	0	0	0	0
口唇そう痒症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
口唇腫脹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
メレナ	1 (0.4%)	1 (0.4%)	0	0	0	0	0
非感染性歯肉炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
嚥下痛	0	0	0	1 (0.4%)	1 (0.4%)	0	0
膵炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
地図状舌	1 (0.4%)	0	1 (0.4%)	0	0	0	0
舌潰瘍	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
感染症および寄生虫症	88 (31.3%)	66 (23.5%)	83 (29.5%)	118 (41.7%)	72 (25.4%)	95 (33.6%)	97 (34.3%)
上気道感染	15 (5.3%)	11 (3.9%)	14 (5.0%)	33 (11.7%)	25 (8.8%)	27 (9.5%)	27 (9.5%)
肺炎	14 (5.0%)	12 (4.3%)	13 (4.6%)	23 (8.1%)	12 (4.2%)	20 (7.1%)	16 (5.7%)
気管支炎	13 (4.6%)	7 (2.5%)	12 (4.3%)	14 (4.9%)	8 (2.8%)	8 (2.8%)	13 (4.6%)
気道感染	8 (2.8%)	7 (2.5%)	8 (2.8%)	11 (3.9%)	7 (2.5%)	10 (3.5%)	9 (3.2%)
鼻咽頭炎	7 (2.5%)	5 (1.8%)	6 (2.1%)	10 (3.5%)	5 (1.8%)	8 (2.8%)	9 (3.2%)
下気道感染	5 (1.8%)	5 (1.8%)	5 (1.8%)	7 (2.5%)	3 (1.1%)	6 (2.1%)	5 (1.8%)
帯状疱疹	3 (1.1%)	3 (1.1%)	2 (0.7%)	4 (1.4%)	4 (1.4%)	4 (1.4%)	3 (1.1%)
口腔カンジダ症	2 (0.7%)	1 (0.4%)	1 (0.4%)	5 (1.8%)	0	2 (0.7%)	4 (1.4%)
口腔真菌感染	3 (1.1%)	2 (0.7%)	3 (1.1%)	4 (1.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)
インフルエンザ	2 (0.7%)	2 (0.7%)	2 (0.7%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	4 (1.4%)
副鼻腔炎	2 (0.7%)	2 (0.7%)	2 (0.7%)	4 (1.4%)	2 (0.7%)	3 (1.1%)	3 (1.1%)
ウイルス感染	4 (1.4%)	4 (1.4%)	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
感染	2 (0.7%)	2 (0.7%)	1 (0.4%)	3 (1.1%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
皮膚感染	3 (1.1%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
尿路感染	1 (0.4%)	1 (0.4%)	0	4 (1.4%)	2 (0.7%)	2 (0.7%)	4 (1.4%)
歯肉炎	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	0	2 (0.7%)	2 (0.7%)
咽頭炎	4 (1.4%)	4 (1.4%)	4 (1.4%)	0	0	0	0
歯膿瘍	4 (1.4%)	3 (1.1%)	4 (1.4%)	0	0	0	0
気管支肺炎	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
結膜炎	0	0	0	3 (1.1%)	3 (1.1%)	1 (0.4%)	1 (0.4%)
膀胱炎	3 (1.1%)	2 (0.7%)	3 (1.1%)	0	0	0	0
胃腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	2 (0.7%)	1 (0.4%)
ヘルペスウイルス感染	0	0	0	3 (1.1%)	2 (0.7%)	2 (0.7%)	3 (1.1%)
肺感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	0	2 (0.7%)
粘膜感染	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)	0	1 (0.4%)	0
インフルエンザ性肺炎	0	0	0	3 (1.1%)	1 (0.4%)	1 (0.4%)	3 (1.1%)
鼻炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	2 (0.7%)	2 (0.7%)
足部白癬	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
細気管支炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
蜂巣炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
丹毒	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
真菌感染	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
限局性感染	2 (0.7%)	2 (0.7%)	2 (0.7%)	0	0	0	0
口腔ヘルペス	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
細菌性肺炎	0	0	0	2 (0.7%)	2 (0.7%)	0	1 (0.4%)
ＲＳウイルス感染	0	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
敗血症	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚カンジダ	2 (0.7%)	0	2 (0.7%)	0	0	0	0
歯感染	2 (0.7%)	1 (0.4%)	1 (0.4%)	0	0	0	0
四肢膿瘍	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
急性扁桃炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
肛門膿瘍	1 (0.4%)	1 (0.4%)	0	0	0	0	0
細菌感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
細菌性気管支炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
ウイルス性気管支炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
カンピロバクター胃腸炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
カンジダ感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
コロナウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
サイトメガロウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
蓄膿	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
感染性小腸結腸炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
大腸菌性菌血症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
眼感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
真菌性眼感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
熱性感染症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
毛包炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
皮膚真菌感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
真菌性性器感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
Ｈ１Ｎ１インフルエンザ	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ヘモフィルス感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
感染性筋炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
注入部位蜂巣炎	0	0	0	1 (0.4%)	1 (0.4%)	0	0
真菌性角膜炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
喉頭炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
リステリア性敗血症	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
大葉性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
ウイルス性下気道感染	0	0	0	1 (0.4%)	0	1 (0.4%)	0

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
鼻ヘルペス	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
壊死性筋膜炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
中咽頭カンジダ症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
中耳炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
急性中耳炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
パラインフルエンザウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
耳下腺炎	0	0	0	1 (0.4%)	0	1 (0.4%)	0
眼窩周囲蜂巣炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
レンサ球菌性咽頭炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
ヘモフィルス性肺炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
クレブシエラ菌性肺炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
レジオネラ菌性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
腎盂腎炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
呼吸器モニリア症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
敗血症性ショック	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ブドウ球菌皮膚感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮下組織膿瘍	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
扁桃炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
細菌性上気道感染	0	0	0	1 (0.4%)	0	0	1 (0.4%)
尿道炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
腟感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
水痘	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
外陰部腟カンジダ症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
外陰部腟炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
創傷感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
神経系障害	84 (29.9%)	62 (22.1%)	56 (19.9%)	98 (34.6%)	33 (11.7%)	73 (25.8%)	51 (18.0%)
振戦	21 (7.5%)	8 (2.8%)	18 (6.4%)	23 (8.1%)	4 (1.4%)	14 (4.9%)	19 (6.7%)
味覚異常	13 (4.6%)	12 (4.3%)	6 (2.1%)	16 (5.7%)	4 (1.4%)	14 (4.9%)	8 (2.8%)
浮動性めまい	14 (5.0%)	13 (4.6%)	6 (2.1%)	13 (4.6%)	6 (2.1%)	5 (1.8%)	8 (2.8%)
頭痛	10 (3.6%)	7 (2.5%)	9 (3.2%)	17 (6.0%)	13 (4.6%)	4 (1.4%)	5 (1.8%)
末梢性感覚ニューロパチー	11 (3.9%)	11 (3.9%)	1 (0.4%)	16 (5.7%)	2 (0.7%)	16 (5.7%)	0
末梢性ニューロパチー	7 (2.5%)	7 (2.5%)	1 (0.4%)	10 (3.5%)	1 (0.4%)	9 (3.2%)	0
錯感覚	4 (1.4%)	4 (1.4%)	1 (0.4%)	5 (1.8%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
嗜眠	3 (1.1%)	2 (0.7%)	3 (1.1%)	5 (1.8%)	2 (0.7%)	5 (1.8%)	3 (1.1%)
感覚鈍麻	2 (0.7%)	1 (0.4%)	2 (0.7%)	5 (1.8%)	0	3 (1.1%)	2 (0.7%)
記憶障害	5 (1.8%)	1 (0.4%)	5 (1.8%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
味覚消失	1 (0.4%)	0	1 (0.4%)	4 (1.4%)	1 (0.4%)	2 (0.7%)	3 (1.1%)
平衡障害	2 (0.7%)	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
注意力障害	1 (0.4%)	1 (0.4%)	0	3 (1.1%)	2 (0.7%)	2 (0.7%)	3 (1.1%)
神経痛	2 (0.7%)	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
失神寸前の状態	0	0	0	4 (1.4%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
失神	0	0	0	4 (1.4%)	2 (0.7%)	2 (0.7%)	3 (1.1%)
傾眠	3 (1.1%)	3 (1.1%)	1 (0.4%)	0	0	0	0
アカシジア	2 (0.7%)	0	2 (0.7%)	0	0	0	0
体位性めまい	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
異常感覚	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
味覚減退	2 (0.7%)	1 (0.4%)	2 (0.7%)	0	0	0	0
下肢静止不能症候群	2 (0.7%)	1 (0.4%)	1 (0.4%)	0	0	0	0
健忘	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
失語症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
脳梗塞	1 (0.4%)	1 (0.4%)	0	0	0	0	0
構語障害	0	0	0	1 (0.4%)	0	1 (0.4%)	0
蟻走感	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
知覚過敏	0	0	0	1 (0.4%)	0	1 (0.4%)	0
過眠症	1 (0.4%)	0	1 (0.4%)	0	0	0	0

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
肋間神経痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0
意識消失	1 (0.4%)	1 (0.4%)	0	0	0	0	0
片頭痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
不随意性筋収縮	1 (0.4%)	1 (0.4%)	0	0	0	0	0
筋痙直	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
神経系障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
嗅覚錯誤	0	0	0	1 (0.4%)	0	1 (0.4%)	0
ヘルペス後神経痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0
精神運動亢進	1 (0.4%)	0	1 (0.4%)	0	0	0	0
副鼻腔炎に伴う頭痛	0	0	0	1 (0.4%)	0	0	1 (0.4%)
脊髄圧迫	1 (0.4%)	0	1 (0.4%)	0	0	0	0
一過性脳虚血発作	0	0	0	1 (0.4%)	0	0	1 (0.4%)
上位運動ニューロンの病変	1 (0.4%)	1 (0.4%)	0	0	0	0	0
第７脳神経麻痺	1 (0.4%)	1 (0.4%)	0	0	0	0	0
視野欠損	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
筋骨格系および結合組織障害	68 (24.2%)	50 (17.8%)	41 (14.6%)	98 (34.6%)	27 (9.5%)	64 (22.6%)	61 (21.6%)
筋痙縮	40 (14.2%)	33 (11.7%)	21 (7.5%)	62 (21.9%)	11 (3.9%)	52 (18.4%)	33 (11.7%)
筋力低下	15 (5.3%)	3 (1.1%)	14 (5.0%)	19 (6.7%)	1 (0.4%)	2 (0.7%)	18 (6.4%)
筋肉痛	5 (1.8%)	5 (1.8%)	3 (1.1%)	8 (2.8%)	3 (1.1%)	5 (1.8%)	4 (1.4%)
四肢痛	6 (2.1%)	5 (1.8%)	1 (0.4%)	4 (1.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)
背部痛	1 (0.4%)	1 (0.4%)	0	8 (2.8%)	7 (2.5%)	4 (1.4%)	1 (0.4%)
関節痛	3 (1.1%)	3 (1.1%)	0	4 (1.4%)	2 (0.7%)	3 (1.1%)	4 (1.4%)
筋骨格系胸痛	2 (0.7%)	0	2 (0.7%)	4 (1.4%)	3 (1.1%)	0	1 (0.4%)
ミオパチー	3 (1.1%)	2 (0.7%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	0	2 (0.7%)
骨痛	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	2 (0.7%)
関節腫脹	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
筋肉疲労	0	0	0	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
筋骨格痛	0	0	0	2 (0.7%)	2 (0.7%)	0	0
頚部痛	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
筋萎縮症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
デュプイトラン拘縮	0	0	0	1 (0.4%)	1 (0.4%)	0	0
側腹部痛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
出血性関節症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
関節滲出液	1 (0.4%)	1 (0.4%)	0	0	0	0	0
運動性低下	0	0	0	1 (0.4%)	0	0	1 (0.4%)
筋緊張	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
筋骨格硬直	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
骨壊死	0	0	0	1 (0.4%)	0	0	1 (0.4%)
顎骨壊死	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
骨粗鬆症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
脊柱管狭窄症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
脊椎障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
脊椎痛	1 (0.4%)	0	1 (0.4%)	0	0	0	0
腱痛	0	0	0	1 (0.4%)	0	0	1 (0.4%)
呼吸器、胸郭および縦隔障害	43 (15.3%)	30 (10.7%)	28 (10.0%)	121 (42.8%)	103 (36.4%)	33 (11.7%)	35 (12.4%)
呼吸困難	12 (4.3%)	8 (2.8%)	5 (1.8%)	35 (12.4%)	32 (11.3%)	8 (2.8%)	7 (2.5%)
咳嗽	4 (1.4%)	4 (1.4%)	2 (0.7%)	35 (12.4%)	32 (11.3%)	11 (3.9%)	8 (2.8%)
肺塞栓症	11 (3.9%)	11 (3.9%)	4 (1.4%)	7 (2.5%)	1 (0.4%)	7 (2.5%)	2 (0.7%)
気管支痙攣	0	0	0	13 (4.6%)	13 (4.6%)	0	0
発声障害	5 (1.8%)	1 (0.4%)	4 (1.4%)	8 (2.8%)	3 (1.1%)	0	5 (1.8%)
しゃっくり	6 (2.1%)	2 (0.7%)	5 (1.8%)	7 (2.5%)	1 (0.4%)	0	6 (2.1%)
アレルギー性鼻炎	0	0	0	10 (3.5%)	8 (2.8%)	4 (1.4%)	3 (1.1%)
鼻閉	0	0	0	8 (2.8%)	8 (2.8%)	0	0
湿性咳嗽	2 (0.7%)	2 (0.7%)	2 (0.7%)	6 (2.1%)	5 (1.8%)	4 (1.4%)	4 (1.4%)
鼻漏	0	0	0	8 (2.8%)	8 (2.8%)	0	0
咽喉刺激感	0	0	0	8 (2.8%)	8 (2.8%)	1 (0.4%)	0

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
喘鳴	0	0	0	7 (2.5%)	7 (2.5%)	1 (0.4%)	0
低酸素症	0	0	0	6 (2.1%)	6 (2.1%)	1 (0.4%)	1 (0.4%)
喉頭浮腫	0	0	0	6 (2.1%)	6 (2.1%)	0	0
口腔咽頭痛	5 (1.8%)	2 (0.7%)	5 (1.8%)	1 (0.4%)	1 (0.4%)	0	0
労作性呼吸困難	0	0	0	5 (1.8%)	4 (1.4%)	1 (0.4%)	2 (0.7%)
鼻出血	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	0
肺水腫	0	0	0	3 (1.1%)	1 (0.4%)	0	2 (0.7%)
アレルギー性呼吸器症状	0	0	0	2 (0.7%)	2 (0.7%)	0	0
肺障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
鼻閉塞	0	0	0	2 (0.7%)	2 (0.7%)	0	0
肺臓炎	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
くしゃみ	0	0	0	2 (0.7%)	2 (0.7%)	0	0
窒息	0	0	0	1 (0.4%)	1 (0.4%)	0	0
気管支拡張症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
カタル	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
慢性閉塞性肺疾患	0	0	0	1 (0.4%)	0	1 (0.4%)	0
胸水症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
喉頭不快感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
喉頭の炎症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
喉頭狭窄	0	0	0	1 (0.4%)	1 (0.4%)	0	0
喉頭刺激感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
鼻部不快感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
咽頭紅斑	0	0	0	1 (0.4%)	0	0	1 (0.4%)
誤嚥性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
呼気延長	0	0	0	1 (0.4%)	1 (0.4%)	0	0
副鼻腔うっ血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
副鼻腔障害	0	0	0	1 (0.4%)	1 (0.4%)	0	0
上気道性喘鳴	0	0	0	1 (0.4%)	1 (0.4%)	0	0
窒息感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
咽喉絞扼感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
精神障害	76 (27.0%)	9 (3.2%)	73 (26.0%)	74 (26.1%)	6 (2.1%)	13 (4.6%)	72 (25.4%)
不眠症	47 (16.7%)	3 (1.1%)	46 (16.4%)	46 (16.3%)	2 (0.7%)	4 (1.4%)	45 (15.9%)
不安	8 (2.8%)	1 (0.4%)	7 (2.5%)	10 (3.5%)	1 (0.4%)	1 (0.4%)	9 (3.2%)
激越	8 (2.8%)	0	8 (2.8%)	6 (2.1%)	0	0	6 (2.1%)
うつ病	2 (0.7%)	0	2 (0.7%)	11 (3.9%)	2 (0.7%)	5 (1.8%)	9 (3.2%)
易刺激性	5 (1.8%)	1 (0.4%)	4 (1.4%)	6 (2.1%)	0	0	6 (2.1%)
気分変化	5 (1.8%)	0	5 (1.8%)	6 (2.1%)	0	0	6 (2.1%)
落ち着きのなさ	4 (1.4%)	1 (0.4%)	4 (1.4%)	4 (1.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)
神経過敏	5 (1.8%)	0	5 (1.8%)	0	0	0	0
睡眠障害	3 (1.1%)	2 (0.7%)	3 (1.1%)	2 (0.7%)	0	0	2 (0.7%)
抑うつ気分	1 (0.4%)	0	1 (0.4%)	3 (1.1%)	0	1 (0.4%)	3 (1.1%)
錯乱状態	2 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
精神障害	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	0	0	2 (0.7%)
気分動揺	1 (0.4%)	0	1 (0.4%)	2 (0.7%)	0	1 (0.4%)	2 (0.7%)
感情障害	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
譫妄	1 (0.4%)	0	1 (0.4%)	0	0	0	0
まとまりのない会話	1 (0.4%)	1 (0.4%)	0	0	0	0	0
気分変調性障害	1 (0.4%)	0	1 (0.4%)	0	0	0	0
幻覚	1 (0.4%)	0	1 (0.4%)	0	0	0	0
言葉もれ	1 (0.4%)	0	1 (0.4%)	0	0	0	0
リビドー消失	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
精神病性障害	1 (0.4%)	0	1 (0.4%)	0	0	0	0
ストレス	1 (0.4%)	0	1 (0.4%)	0	0	0	0
皮膚および皮下組織障害	48 (17.1%)	39 (13.9%)	26 (9.3%)	80 (28.3%)	49 (17.3%)	46 (16.3%)	26 (9.2%)
そう痒症	18 (6.4%)	18 (6.4%)	0	22 (7.8%)	18 (6.4%)	13 (4.6%)	1 (0.4%)
発疹	15 (5.3%)	10 (3.6%)	6 (2.1%)	20 (7.1%)	7 (2.5%)	16 (5.7%)	2 (0.7%)
多汗症	4 (1.4%)	1 (0.4%)	4 (1.4%)	14 (4.9%)	11 (3.9%)	2 (0.7%)	4 (1.4%)

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
紅斑	4 (1.4%)	2 (0.7%)	2 (0.7%)	5 (1.8%)	3 (1.1%)	0	2 (0.7%)
斑状丘疹状皮疹	2 (0.7%)	2 (0.7%)	0	5 (1.8%)	4 (1.4%)	2 (0.7%)	3 (1.1%)
全身性皮疹	3 (1.1%)	3 (1.1%)	1 (0.4%)	3 (1.1%)	1 (0.4%)	3 (1.1%)	0
蕁麻疹	1 (0.4%)	1 (0.4%)	0	5 (1.8%)	5 (1.8%)	1 (0.4%)	0
皮膚乾燥	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.7%)
顔面腫脹	3 (1.1%)	0	3 (1.1%)	1 (0.4%)	0	0	1 (0.4%)
斑状出血	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.7%)	0	1 (0.4%)	1 (0.4%)
寝汗	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	0	1 (0.4%)
斑状皮疹	1 (0.4%)	1 (0.4%)	0	2 (0.7%)	0	2 (0.7%)	0
日光角化症	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ざ瘡様皮膚炎	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	2 (0.7%)
アレルギー性皮膚炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
湿疹	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
多形紅斑	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
男性型多毛症	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
点状出血	0	0	0	2 (0.7%)	0	0	2 (0.7%)
そう痒性皮疹	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
皮膚潰瘍	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
脱毛症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
冷汗	0	0	0	1 (0.4%)	1 (0.4%)	0	0
褥瘡性潰瘍	0	0	0	1 (0.4%)	0	0	1 (0.4%)
接触性皮膚炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
薬疹	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
紅色症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
全身紅斑	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
毛髪成長異常	0	0	0	1 (0.4%)	0	0	1 (0.4%)
手皮膚炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
多毛症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
爪甲脱落症	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
皮膚疼痛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
アレルギー性そう痒症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
壊疽性膿皮症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
丘疹性皮疹	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
皮膚亀裂	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚色素過剰	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
皮膚病変	0	0	0	1 (0.4%)	0	1 (0.4%)	0
うっ滞性皮膚炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
毛細血管拡張症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
血管炎性皮疹	0	0	0	1 (0.4%)	0	1 (0.4%)	0
代謝および栄養障害	43 (15.3%)	22 (7.8%)	38 (13.5%)	61 (21.6%)	17 (6.0%)	32 (11.3%)	46 (16.3%)
高血糖	17 (6.0%)	2 (0.7%)	17 (6.0%)	20 (7.1%)	1 (0.4%)	2 (0.7%)	20 (7.1%)
食欲減退	9 (3.2%)	9 (3.2%)	6 (2.1%)	19 (6.7%)	7 (2.5%)	17 (6.0%)	6 (2.1%)
低カリウム血症	12 (4.3%)	7 (2.5%)	9 (3.2%)	14 (4.9%)	5 (1.8%)	7 (2.5%)	10 (3.5%)
低リン酸血症	6 (2.1%)	3 (1.1%)	4 (1.4%)	7 (2.5%)	1 (0.4%)	5 (1.8%)	3 (1.1%)
低カルシウム血症	2 (0.7%)	0	2 (0.7%)	8 (2.8%)	5 (1.8%)	6 (2.1%)	6 (2.1%)
低マグネシウム血症	2 (0.7%)	2 (0.7%)	2 (0.7%)	3 (1.1%)	1 (0.4%)	1 (0.4%)	3 (1.1%)
低アルブミン血症	3 (1.1%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	1 (0.4%)	0	0
脱水	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
糖尿病	0	0	0	2 (0.7%)	0	0	2 (0.7%)
痛風	2 (0.7%)	2 (0.7%)	1 (0.4%)	0	0	0	0
低ナトリウム血症	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	0
水分過負荷	0	0	0	1 (0.4%)	1 (0.4%)	0	0
体液貯留	0	0	0	1 (0.4%)	0	0	1 (0.4%)
葉酸欠乏	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
高コレステロール血症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
高脂血症	1 (0.4%)	0	1 (0.4%)	0	0	0	0

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
高尿酸血症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
食欲亢進	1 (0.4%)	0	1 (0.4%)	0	0	0	0
多飲症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
１型糖尿病	0	0	0	1 (0.4%)	0	0	1 (0.4%)
２型糖尿病	1 (0.4%)	0	1 (0.4%)	0	0	0	0
血管障害	27 (9.6%)	20 (7.1%)	11 (3.9%)	55 (19.4%)	24 (8.5%)	30 (10.6%)	15 (5.3%)
深部静脈血栓症	9 (3.2%)	9 (3.2%)	3 (1.1%)	5 (1.8%)	1 (0.4%)	5 (1.8%)	2 (0.7%)
高血圧	1 (0.4%)	0	1 (0.4%)	13 (4.6%)	10 (3.5%)	1 (0.4%)	5 (1.8%)
潮紅	5 (1.8%)	0	5 (1.8%)	8 (2.8%)	5 (1.8%)	1 (0.4%)	3 (1.1%)
低血圧	2 (0.7%)	2 (0.7%)	0	7 (2.5%)	6 (2.1%)	1 (0.4%)	0
表在性血栓性静脈炎	6 (2.1%)	5 (1.8%)	1 (0.4%)	3 (1.1%)	0	3 (1.1%)	1 (0.4%)
ほてり	2 (0.7%)	0	2 (0.7%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
静脈炎	1 (0.4%)	1 (0.4%)	0	4 (1.4%)	0	4 (1.4%)	1 (0.4%)
塞栓症	0	0	0	3 (1.1%)	0	3 (1.1%)	1 (0.4%)
起立性低血圧	0	0	0	3 (1.1%)	2 (0.7%)	3 (1.1%)	1 (0.4%)
血栓性静脈炎	0	0	0	3 (1.1%)	0	3 (1.1%)	1 (0.4%)
血栓症	2 (0.7%)	2 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
血腫	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
静脈血栓症	0	0	0	2 (0.7%)	0	2 (0.7%)	0
出血性梗塞	0	0	0	1 (0.4%)	0	1 (0.4%)	0
蒼白	1 (0.4%)	1 (0.4%)	0	0	0	0	0
末梢冷感	0	0	0	1 (0.4%)	0	1 (0.4%)	0
表在性静脈炎	0	0	0	1 (0.4%)	0	1 (0.4%)	0
四肢静脈血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
臨床検査	24 (8.5%)	20 (7.1%)	11 (3.9%)	31 (11.0%)	17 (6.0%)	27 (9.5%)	14 (4.9%)
アラニンアミノトランスフェラーゼ増加	5 (1.8%)	5 (1.8%)	2 (0.7%)	9 (3.2%)	5 (1.8%)	9 (3.2%)	3 (1.1%)
体重減少	4 (1.4%)	4 (1.4%)	1 (0.4%)	8 (2.8%)	3 (1.1%)	6 (2.1%)	5 (1.8%)
アスパラギン酸アミノトランスフェラーゼ増加	3 (1.1%)	3 (1.1%)	2 (0.7%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
血中クレアチニン増加	4 (1.4%)	4 (1.4%)	1 (0.4%)	2 (0.7%)	0	2 (0.7%)	0
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
体重増加	4 (1.4%)	0	4 (1.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
心電図ＱＴ延長	1 (0.4%)	1 (0.4%)	0	3 (1.1%)	2 (0.7%)	3 (1.1%)	0
血中アルカリホスファターゼ増加	0	0	0	3 (1.1%)	3 (1.1%)	3 (1.1%)	3 (1.1%)
腎クレアチニン・クリアランス減少	2 (0.7%)	2 (0.7%)	0	0	0	0	0
血中乳酸脱水素酵素減少	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
血圧上昇	0	0	0	1 (0.4%)	0	0	1 (0.4%)
体温上昇	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
フィブリンＤダイマー増加	1 (0.4%)	1 (0.4%)	0	0	0	0	0
ヘリコバクター検査陽性	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
免疫グロブリン減少	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
好中球中毒性顆粒存在	0	0	0	1 (0.4%)	0	1 (0.4%)	0
酸素飽和度低下	0	0	0	1 (0.4%)	1 (0.4%)	0	0
トロポニン増加	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
静脈雑音	1 (0.4%)	1 (0.4%)	0	0	0	0	0
眼障害	14 (5.0%)	6 (2.1%)	12 (4.3%)	40 (14.1%)	15 (5.3%)	9 (3.2%)	29 (10.2%)
白内障	6 (2.1%)	0	6 (2.1%)	14 (4.9%)	1 (0.4%)	2 (0.7%)	14 (4.9%)
霧視	4 (1.4%)	1 (0.4%)	4 (1.4%)	10 (3.5%)	4 (1.4%)	5 (1.8%)	8 (2.8%)
流涙増加	1 (0.4%)	1 (0.4%)	1 (0.4%)	6 (2.1%)	6 (2.1%)	0	0

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
眼刺激	0	0	0	4 (1.4%)	2 (0.7%)	1 (0.4%)	2 (0.7%)
眼乾燥	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
眼部腫脹	0	0	0	2 (0.7%)	2 (0.7%)	0	0
視力低下	0	0	0	2 (0.7%)	0	0	2 (0.7%)
視力障害	0	0	0	2 (0.7%)	0	0	2 (0.7%)
結膜刺激	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
眼のアレルギー	0	0	0	1 (0.4%)	1 (0.4%)	0	0
眼の障害	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
眼出血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
眼球浮腫	0	0	0	1 (0.4%)	0	0	1 (0.4%)
眼瞼発疹	1 (0.4%)	1 (0.4%)	0	0	0	0	0
水晶体混濁	1 (0.4%)	0	1 (0.4%)	0	0	0	0
眼充血	0	0	0	1 (0.4%)	1 (0.4%)	0	0
眼窩周囲浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0
網膜静脈血栓症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
硝子体浮遊物	0	0	0	1 (0.4%)	0	0	1 (0.4%)
腎および尿路障害	10 (3.6%)	7 (2.5%)	5 (1.8%)	15 (5.3%)	3 (1.1%)	14 (4.9%)	3 (1.1%)
腎機能障害	5 (1.8%)	5 (1.8%)	1 (0.4%)	10 (3.5%)	2 (0.7%)	10 (3.5%)	0
急性腎不全	2 (0.7%)	2 (0.7%)	0	0	0	0	0
腎不全	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
高窒素血症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
慢性腎臓病	0	0	0	1 (0.4%)	0	1 (0.4%)	0
排尿困難	0	0	0	1 (0.4%)	0	0	1 (0.4%)
頻尿	1 (0.4%)	0	1 (0.4%)	0	0	0	0
多尿	1 (0.4%)	0	1 (0.4%)	0	0	0	0
腎嚢胞	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
尿失禁	1 (0.4%)	0	1 (0.4%)	0	0	0	0
尿閉	1 (0.4%)	0	1 (0.4%)	0	0	0	0
心臓障害	6 (2.1%)	5 (1.8%)	3 (1.1%)	18 (6.4%)	11 (3.9%)	4 (1.4%)	8 (2.8%)
心房細動	2 (0.7%)	1 (0.4%)	1 (0.4%)	3 (1.1%)	0	1 (0.4%)	2 (0.7%)
頻脈	0	0	0	5 (1.8%)	5 (1.8%)	0	0
狭心症	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.1%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
徐脈	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	1 (0.4%)
動悸	0	0	0	2 (0.7%)	1 (0.4%)	0	1 (0.4%)
洞性頻脈	0	0	0	2 (0.7%)	2 (0.7%)	0	1 (0.4%)
上室性頻脈	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
急性心筋梗塞	1 (0.4%)	1 (0.4%)	0	0	0	0	0
伝導障害	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
拡張機能障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
心筋虚血	0	0	0	1 (0.4%)	0	1 (0.4%)	0
心膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0
心室性期外収縮	1 (0.4%)	1 (0.4%)	0	0	0	0	0
傷害、中毒および処置合併症	4 (1.4%)	1 (0.4%)	4 (1.4%)	7 (2.5%)	0	2 (0.7%)	6 (2.1%)
挫傷	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	0	1 (0.4%)	4 (1.4%)
各種物質毒性	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
転倒	1 (0.4%)	0	1 (0.4%)	0	0	0	0
引っかき傷	1 (0.4%)	0	1 (0.4%)	0	0	0	0
脊椎圧迫骨折	0	0	0	1 (0.4%)	0	0	1 (0.4%)
創合併症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
内分泌障害	8 (2.8%)	0	8 (2.8%)	2 (0.7%)	0	0	2 (0.7%)
クッシング様症状	4 (1.4%)	0	4 (1.4%)	1 (0.4%)	0	0	1 (0.4%)
ステロイド離脱症候群	2 (0.7%)	0	2 (0.7%)	0	0	0	0
クッシング症候群	1 (0.4%)	0	1 (0.4%)	0	0	0	0
高コルチコイド症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
下垂体依存性クッシング症候群	1 (0.4%)	0	1 (0.4%)	0	0	0	0

表 2.7.6.1-2 治験薬と関連性がある有害事象［MMY3003 試験，安全性解析対象集団］
（続き）

	Rd			DRd			
	Related to Treatment	Related to LEN	Related to DEX	Related to Treatment	Related to DARA	Related to LEN	Related to DEX
耳および迷路障害	3 (1.1%)	2 (0.7%)	3 (1.1%)	6 (2.1%)	4 (1.4%)	4 (1.4%)	2 (0.7%)
回転性めまい	3 (1.1%)	2 (0.7%)	3 (1.1%)	3 (1.1%)	2 (0.7%)	1 (0.4%)	0
耳鳴	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
聴力低下	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5 (1.8%)	4 (1.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
扁平上皮癌	2 (0.7%)	2 (0.7%)	0	0	0	0	0
急性単球性白血病	0	0	0	1 (0.4%)	0	1 (0.4%)	0
基底細胞癌	1 (0.4%)	1 (0.4%)	0	0	0	0	0
エプスタイン・バーウイルス関連リンパ増殖性障害	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚血管腫	1 (0.4%)	0	1 (0.4%)	0	0	0	0
前立腺癌	1 (0.4%)	1 (0.4%)	0	0	0	0	0
肝胆道系障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.4%)	3 (1.1%)	4 (1.4%)	3 (1.1%)
肝機能異常	0	0	0	2 (0.7%)	2 (0.7%)	2 (0.7%)	2 (0.7%)
肝細胞損傷	0	0	0	2 (0.7%)	1 (0.4%)	2 (0.7%)	1 (0.4%)
高ビリルビン血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
生殖系および乳房障害	3 (1.1%)	3 (1.1%)	1 (0.4%)	2 (0.7%)	0	2 (0.7%)	0
勃起不全	2 (0.7%)	2 (0.7%)	0	2 (0.7%)	0	2 (0.7%)	0
骨盤痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
免疫系障害	0	0	0	3 (1.1%)	3 (1.1%)	1 (0.4%)	1 (0.4%)
薬物過敏症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
低γグロブリン血症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
免疫抑制	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
先天性、家族性および遺伝性障害	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
角膜ジストロフィー	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)

Keys: Rd = lenalidomide-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone; LEN = lenalidomide; DEX = dexamethasone; DARA = daratumumab.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

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2.7.6.1.3　個別症例の詳細

最終投与後 30 日以内の疾患進行以外の理由による死亡例，及び日本人被験者で認められた治験薬と関連性がある重篤な有害事象の詳細経過を以下に示す。日本人以外の被験者で認められた治験薬と関連性がある重篤な有害事象の詳細経過は，治験総括報告書【CTD 5.3.5.1.1-1】に示した。

2.7.6.1.3.1　最終投与後 30 日以内の死亡（疾患進行以外の理由による死亡）

(1) DRd 群

1) 被験者識別番号 101002

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

Second primary malignancies

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-08-15	2014-11-21	99	2014-12-04	112	ADVERSE EVENT (Acute monocytic leukaemia)	-

■ **Discontinuation of study treatment due to AE and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
急性単球性白血病 Acute monoblastic leukemia	2014-11-28 2014-12-03	106 6	Y 4	Not related Not related PROBABLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
発熱性好中球減少症 Febrile neutropenia	2014-11-10 2014-11-13	88 4	Y 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-
発熱性好中球減少症 Febrile neutropenia	2014-11-26 -	104 -	Y 3	Not related Possible VERY LIKELY	Not applicable NOT APPLICABLE Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	-
急性単球性白血病 Acute monoblastic leukemia	2014-12-04 2014-12-04	112 1	Y 5	Not related Not related PROBABLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	-

■ Second primary malignancies

Dictionary-Derived Term Reported Term for the Clinical Event	Diagnosis of 2nd Primary Malignancy Diagnosis Date/Time of 2nd Primary Malig	Recurrence of a prior existing malig.? Initial Diagnosis Date	Confirm by pathology diagnosis obtained? Confirmation Method Specimen source or sample	Stage of the disease Staging sytem	Concomitant or Additional Trtmnt Given	Surgery	Radiotherapy	Systemic therapy Specific Regimen	Palliative supportive care provided	Outcome of Event
急性単球性白血病 ACUTE MONOBLASTIC LEUKEMIA	ACUTE MONOBLASTIC LEUKEMIA 2014-11-28	N -	Y ASPIRATE BONE MARROW ASPIRATE AND BIOPSY	U -	U	N	N	N -	Y	NOT RECOVERED/NOT RESOLVED

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
激越 Agitation	2014-08-16 -	2 -	N 2	Not related Very likely NOT RELATED	Dose not changed DRUG INTERRUPTED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
貧血 Anemia	2014-11-11 2014-11-13	89 3	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
浮動性めまい Dizzyness	2014-11-10 2014-11-11	88 2	N 1	Not related Possible DOUBTFUL	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
労作性呼吸困難 Intermittent shortness of breath on exertion	2014-10-15 -	62 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
転倒 Ground level fall	2014-11-03 -	81 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
頭痛 Headache	2014-11-06 2014-11-07	84 2	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
不眠症 Insomnia	2014-08-16 -	2 -	N 2	Not related Very likely DOUBTFUL	Dose not changed DRUG INTERRUPTED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
悪心 Intermittent nausea	2014-10-08 -	55 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
頚部損傷 Sore neck (from fall)	2014-11-03 -	81 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
好中球減少症 Neutropenia	2014-10-01 2014-11-09	48 40	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
顎痛 Lower jaw pain	2014-10-15 -	62 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
発疹 Skin rash scalp	2014-09-10 -	27 -	N 1	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
歯の知覚過敏 Lower teeth sensitive	2014-10-15 -	62 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
口内炎 Mucositis (oral)	2014-11-26 -	104 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N

■ Hematology/Chemistry Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	2.2	2014-08-13/ -2	Cycle 1 day 1	2.2	x10E9/L	2.5-7.5	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	2.2	2014-08-19/ 5	Cycle 1 day 8	2.3	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.2	2014-08-27/ 13	Cycle 1 day 15	2.2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.2	2014-09-03/ 20	Cycle 1 day 22	0.7	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.2	2014-09-10/ 27	Cycle 2 day 1	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.2	2014-09-18/ 35	Cycle 2 day 8	1.3	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.2	2014-09-24/ 41	Cycle 2 day 15	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.2	2014-10-01/ 48	Cycle 2 day 22	0.6	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.2	2014-10-08/ 55	Cycle 3 day 1	0.6	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.2	2014-10-22/ 69	Cycle 3 day 15	0.6	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.2	2014-11-05/ 83	Cycle 4 day 1	0.4	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	2.2	2014-11-10/ 88	Cycle 4 day 2 unscheduled 1	0.8	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.2	2014-11-11/ 89	Cycle 4 day 2 unscheduled 2	0.3	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	2.2	2014-11-12/ 90	Cycle 4 day 2 unscheduled 3	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.2	2014-11-13/ 91	Cycle 4 day 2 unscheduled 4	1.3	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.2	2014-11-21/ 99	Cycle 4 day 15	0.9	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.2	2014-11-26/ 104	Cycle 4 day 15 unscheduled 1	0.1	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	2.2	2014-11-28/ 106	Cycle 4 day 15 unscheduled 2	0.3	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	2.2	2014-11-29/ 107	Cycle 4 day 15 unscheduled 3	0.6	x10E9/L	2.5-7.5	3

■ **Demographics and Baseline Characteristics**

□ Country: Canada
□ Study site identifier: CA00098
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 73.1
□ Baseline height(cm): 163
□ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2014-12-03 Adverse Event

□ Study discontinuation: 2014-12-04 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
192.03	280.00	1925.00	2014-08-15	2014-11-21	3.25

■ **NARRATIVE TEXT**

被験者 101002 は，6[redacted] 歳の白人男性で，2004 年 11 月 16 日に初めて病期 II（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，疲労，胃食道逆流性疾患及び背部痛であった。ベースラインの ECOG スコアは 1 であった。裂肛，胆嚢切除，結腸切除，回腸瘻造設，出血性腸憩室，骨髄異形成，痔核，喫煙及び帯状疱疹の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はシクロホスファミド，デキサメタゾン，ドキソルビシン，治験薬，メルファラン，prednisone，ビンクリスチン及び ASCT，レジメン 2 はボルテゾミブ，デキサメタゾン及び veliparib であった。

治験組入れ時の併用薬は，メサドン，バラシクロビル，paracetamol／コデイン，ジメンヒドリナート，オンダンセトロン，フィルグラスチム，アスピリン及びパントプラゾールナトリウムセスキ水和物であった。

サイクル 1 の期間中，被験者はデキサメタゾンの投与量を自身で減量し，Day 15 及び Day 22 に 12 mg，Day 16 及び Day 23 に 8 mg を服用した。

Day 48（2014 年 10 月 1 日）に，**非重篤な有害事象の Grade 3 の好中球減少症**が報告された（臨床検査値は上記の表を参照）。治験担当医師は，本事象とレナリドミドとの因果関係を「ほぼ確実」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治療は実施せず，治験薬の処置も実施しなかった。Day 88 に，被験者は発熱（38.4°C）のために救急救命室を受診し，**重篤な有害事象の Grade 3 の発熱性好中球減少症**のために入院した。治験担当医師は，本事象とレナリドミドとの因果関係を「ほぼ確実」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。フィルグラスチム及びレボフロキサシンによる治療を実施した。本事象は Day 91 に回復し，同日，被験者は退院した。

Day 104 に，被験者は**重篤な有害事象の Grade 3 の発熱性好中球減少症**を再発し，入院に至った。悪心，腹痛及び粘膜炎が認められた。治験担当医師は，本事象とレナリドミドとの因果関係を「ほぼ確実」，デキサメタゾンとの因果関係を「可能性小」，本剤との因果関係を「関連なし」と判断した。フィルグラスチム及びピペラシリン／タゾバクタムによる治療を実施した。発熱性好中球減少症のために，Day 99～Day 105 のレナリドミドを休薬した。

Day 106 に，**重篤な有害事象の Grade 4 の急性単球性白血病**が報告され，骨髄生検及びフローサイトメトリー分析で確認された。治験担当医師は，本事象とレナリドミドとの因果関係を「可能性大」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。Day 111 に，本事象のために治験薬の投与を中止した。レナリドミドの最終投与日は Day 98，本剤及びデキサメタゾンの最終投与日は Day 99 であった。Day 112 に，被験者は急性単球性白血病のために死亡した。剖検は実施されなかった。治験担当医師は，おそらくアルキル化剤への曝露が急性単芽球性白血病の原因であると判断した。死亡時に，発熱性好中球減少症は未回復であった。

2) 被験者識別番号 340005

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-07-07	2014-08-26	51	2014-08-28	53	ADVERSE EVENT (SEPTIC SHOCK)	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2014-08-28 2014-08-28	53 1	Y 5	Doubtful Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	Unknown

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2014-08-25 -	50 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
貧血 Anemia	2014-07-14 2014-08-24	8 42	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
無力症 Asthenia	2014-08-25 -	50 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
咳嗽 Caugh	2014-08-23 -	48 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
好中球減少症 Neutropenia	2014-08-25 -	50 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
好中球減少症 Neutropenia	2014-08-18 2014-08-24	43 7	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2014-07-21 2014-08-03	15 14	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Hematology Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (white blood cell decreased)	5.2	2014-07-14/ 8	Cycle 1 day 8	4.3	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	5.2	2014-07-21/ 15	Cycle 1 day 15	1.4	x10E9/L	4.5-11	3
Leukocytes low (white blood cell decreased)	5.2	2014-07-28/ 22	Cycle 1 day 22	1.5	x10E9/L	4.5-11	3
Leukocytes low (white blood cell decreased)	5.2	2014-08-11/ 36	Cycle 2 day 8	4.2	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	5.2	2014-08-18/ 43	Cycle 2 day 15	2.2	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	5.2	2014-08-25/ 50	Cycle 2 day 22	2.8	x10E9/L	4.5-11	2
Neutrophils low (neutrophil count decreased)	2	2014-07-07/ 1	Cycle 1 day 1	2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2014-07-14/ 8	Cycle 1 day 8	2.1	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2014-07-21/ 15	Cycle 1 day 15	0.5	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2014-07-28/ 22	Cycle 1 day 22	0.5	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2014-08-11/ 36	Cycle 2 day 8	2.4	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2014-08-18/ 43	Cycle 2 day 15	0.7	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2014-08-25/ 50	Cycle 2 day 22	1.4	x10E9/L	2.5-7.5	2

■ Demographics and Baseline Characteristics

- □ Country: Spain
- □ Study site identifier: ES00349
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Male
- □ Baseline weight(kg): 82
- □ Baseline height(cm): 172
- □ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2014-08-28 Adverse Event

□ Study discontinuation: 2014-08-28 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
128.00	320.00	1050.00	2014-07-07	2014-08-26	1.68

■ **NARRATIVE TEXT**

被験者 340005 は，7[redacted]歳の白人男性で，2004 年に初めて病期 II（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，無力症，背部痛，末梢性ニューロパチー及び灰白髄炎であった。ベースラインの ECOG スコアは 1 であった。痔瘻切除，虫垂切除，A 型肝炎感染及び扁桃摘出の既往歴を有した。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はカルムスチン，シクロホスファミド，デキサメタゾン，ドキソルビシン，インターフェロン，メルファラン，prednisone，ビンクリスチン及び ASCT，レジメン 2 はボルテゾミブ及びデキサメタゾン，レジメン 3 はデキサメタゾン及びレナリドミドであった。

治験組入れ時の併用薬はなかった。

Day 15（2014 年 7 月 21 日）に，**非重篤な有害事象の Grade 3 の好中球減少症**が報告された（臨床検査値は上記の表を参照）。治験担当医師は，本事象とレナリドミドとの因果関係を「ほぼ確実」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。フィルグラスチムの投与後，Day 28 に本事象は回復した。

Day 43 に，**非重篤な有害事象の Grade 3 の好中球減少症**の再発が報告されたが，フィルグラスチム投与後，Day 50 に Grade 1 に改善した。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。治験薬の処置は実施しなかった。

Day 53 に，被験者は自宅で転倒し，意識不明の状態で発見された。チアノーゼを伴う発熱及び無呼吸が認められ，病院到着時に死亡が確認された。疾患進行の徴候は認められなかった。死因はおそらく呼吸器に起因する**重篤な有害事象の敗血症性ショック**と考えられた。本事象の病原体は不明であった。剖検は実施されなかった。治験担当医師は，本事象と本剤との因果関係を「多分なし」，レナリドミド又はデキサメタゾンとの因果関係を「関連

なし」と判断した。レナリドミド，本剤及びデキサメタゾンの最終投与日は，それぞれ Day 49，Day 50 及び Day 51 であった。死亡時に，好中球減少症は未回復であった。

3) 被験者識別番号 340017

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-09-10	2015-07-01	295	2015-07-30	324	ADVERSE EVENT	-

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
腹痛 Abdominal pain	2015-02-24 2015-02-24	168 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
アラニンアミノトランスフェラーゼ増加 Alanine aminotransferase increased	2015-06-29 2015-07-03	293 5	N 2	Not related Not related NOT RELATED	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
アラニンアミノトランスフェラーゼ増加 Alanine aminotransferase increased	2015-07-03 2015-07-15	297 13	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2015-07-17 2015-07-23	311 7	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-07-07 2015-07-15	301 9	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2015-06-29 2015-07-03	293 5	N 2	Not related Not related NOT RELATED	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2015-07-15 2015-07-17	309 3	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	U RECOVERED/RESOLVED	N
貧血 Anemia	2015-07-23 -	317 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	U NOT RECOVERED/NOT RESOLVED	N
貧血 Anemia	2015-07-03 2015-07-07	297 5	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	U RECOVERED/RESOLVED	N
アスパラギン酸アミノトランスフェラーゼ増加 Aspartate aminotransferase increased	2015-06-29 -	293 -	N 1	Not related Not related NOT RELATED	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
眼瞼炎 Blepharitis	2014-08-26 2014-10-01	-15 37	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
咳嗽 Cough	2015-01-28 2015-02-11	141 15	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
下痢 Diarrhea	2015-02-24 2015-02-24	168 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
発熱性好中球減少症 Febril neutropenia	2015-07-28 2015-07-30	322 3	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	N
高ビリルビン血症 Blood bilirubin increased	2015-06-17 2015-06-29	281 13	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
高ビリルビン血症 Blood bilirubin increased	2015-07-15 2015-07-17	309 3	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
高ビリルビン血症 Blood bilirubin increased	2015-06-29 2015-07-03	293 5	N 3	Not related Not related NOT RELATED	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
高ビリルビン血症 Blood bilirubin increased	2015-07-07 2015-07-15	301 9	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
高ビリルビン血症 Blood bilirubin increased	2015-07-03 2015-07-07	297 5	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
高ビリルビン血症 Blood bilirubin increased	2015-01-28 2015-06-17	141 141	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2014-09-24 2014-09-30	15 7	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2014-11-19 2014-12-17	71 29	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2014-10-29 2014-11-05	50 8	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2014-10-01 2014-10-07	22 7	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2014-10-08 2014-10-15	29 8	N 3	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-01-14 2015-01-28	127 15	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-07-03 2015-07-07	297 5	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-02-11 2015-06-17	155 127	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
寝汗 Night sweats	2014-08-26 2014-10-01	-15 37	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
発熱 Discontinuate low fever	2014-08-26 2014-10-01	-15 37	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombopenia	2015-07-23 -	317 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
上肢骨折 Right shoulder fracture	2015-06-17 2015-07-16	281 30	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
上気道感染 Upper respiratory infection	2015-01-14 2015-01-28	127 15	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
嘔吐 Vomit	2015-02-24 2015-02-24	168 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

■ Hematology/Chemistry Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	2.6	2014-09-24/ 15	Cycle 1 day 15	0.9	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.6	2014-10-01/ 22	Cycle 1 day 22	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2014-10-08/ 29	Cycle 2 day 1	0.5	x10E9/L	2.5-7.5	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	2.6	2014-10-15/ 36	Cycle 2 day 8	2.2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.6	2014-10-22/ 43	Cycle 2 day 15	2.1	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.6	2014-10-29/ 50	Cycle 2 day 22	0.9	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.6	2014-11-19/ 71	Cycle 3 day 15	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2014-12-02/ 84	Cycle 4 day 1	1.4	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2014-12-17/ 99	Cycle 4 day 15	1.7	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.6	2014-12-30/ 112	Cycle 5 day 1	2.1	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.6	2015-01-14/ 127	Cycle 5 day 15	1.4	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-02-11/ 155	Cycle 6 day 15	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-02-25/ 169	Cycle 7 day 1	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-03-24/ 196	Cycle 8 day 1	1.4	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-04-22/ 225	Cycle 9 day 1	1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-05-20/ 253	Cycle 10 day 1	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-06-29/ 293	Cycle 11 day 8 unscheduled 1	1.56	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.6	2015-07-03/ 297	Cycle 11 day 15 unscheduled 1	0.9	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.6	2015-07-07/ 301	Cycle 11 day 15 unscheduled 2	1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.6	2015-07-15/ 309	End of treatment	1.62	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.6	2015-07-23/ 317	End of treatment unscheduled 2	1.63	x10E9/L	2.5-7.5	1

■ **Demographics and Baseline Characteristics**

□ Country: Spain
□ Study site identifier: ES00349
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Female
□ Baseline weight(kg): 55
□ Baseline height(cm): 155
□ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-07-15 Progressive Disease

□ Study discontinuation: 2015-07-30 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
316.56	1680.00	5375.00	2014-09-10	2015-07-01	9.69

■ **NARRATIVE TEXT**

被験者 340017 は，6[redacted] 歳の白人女性で，2013 年 11 月に初めて病期 II（スクリーニング時）の MM と診断され，本剤，デキサメタゾン及びレナリドミドを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血及び無力症であった。ベースラインの ECOG スコアは 1 であった。胆嚢切除の既往歴を有した。

被験者は 1 レジメンの前治療（カルフィルゾミブ，メルファラン及び prednisone）を受けていた。

治験組入れ時の併用薬は，オメプラゾールであった。

ベースラインの好中球数は 2.6×10^9/L（正常範囲：$2.5\text{-}7.5\times10^9$/L）であった。

Day 15～Day 155 に，**非重篤な有害事象の Grade 2～3 の好中球減少症**が複数回認められた（臨床検査値は上記の表を参照）。治験担当医師は，これらの事象と治験薬との因果関係を「関連なし」と判断したが，Day 127 及び Day 155 に発現した事象のみレナリドミドとの因果関係を「可能性小」と判断した。フィルグラスチムによる治療を実施した。Day 29 の好中球減少症のために，Day 29～Day 35 にレナリドミド，Day 29 に本剤，Day 29 及び Day 30 にデキサメタゾンを休薬した。Day 281 に，好中球減少症は回復した。

ECOG スコアは Day 57 に 0 まで改善したが，Day 281 に 1，Day 309 に 2 に悪化した。同日（Day 309）に，疾患進行のために治験薬の投与を中止した。本剤，レナリドミド及びデキサメタゾンの最終投与日は，それぞれ Day 281，Day 292 及び Day 295 であった。Day 317 に，MM に対する次の治療を開始した（ボルテゾミブ及びデキサメタゾン）。Day 322 に，被験者は発熱のために入院した（体温不明）。胸部 X 線写真では右肺門周囲の浸潤影が認めら

れ，好中球数は 0.68×10^9/L であった。**重篤な有害事象の発熱性好中球減少症**が報告された。治験担当医師は，本事象と治験薬との因果関係は「関連なし」，疾患進行が原因と判断した。血液培養検査で菌増殖は認められなかった。腎不全及び低血圧が認められた（発現日不明）。セフェピム及びアミカシンによる治療を開始したが奏効せず，Day 324 に，疾患進行のために死亡した。剖検は実施されなかった。

4) 被験者識別番号 340058

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-02-26	2015-03-17	20	2015-03-27	30	ADVERSE EVENT (SEPTIC SHOCK)	-

■ **Discontinuation of study treatment due to AE; Infections and infestations, Grade 3 or 4; Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2015-03-17 2015-03-26	20 10	Y 4	Doubtful Doubtful DOUBTFUL	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	VIRAL (FLU A)

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2015-03-27 2015-03-27	30 1	Y 5	Doubtful Doubtful DOUBTFUL	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	VIRAL (FLU A)

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-03-17 2015-03-22	20 6	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2015-03-27 2015-03-27	30 1	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2015-03-23 2015-03-24	26 2	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
インフルエンザ Flu a	2015-03-15 2015-03-17	18 3	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
鼻閉 Nasal congestion	2015-02-26T14:30 2015-02-26T16:15	1 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-03-12 2015-03-16	15 5	N 1	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-03-17 -	20 -	N 4	Not related Not related POSSIBLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
血小板減少症 Thrombocitopenia	2015-03-19 -	22 -	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
血小板減少症 Thrombocytopenia	2015-03-17 2015-03-18	20 2	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombopenia	2015-03-12 2015-03-16	15 5	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

■ Hematology Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	-	2015-02-18/ -8	Screening	122	g/L	135-175	1
Hemoglobin low (anemia)	119	2015-02-26/ 1	Cycle 1 day 1	119	g/L	135-175	1
Hemoglobin low (anemia)	119	2015-03-05/ 8	Cycle 1 day 8	125	g/L	135-175	1
Hemoglobin low (anemia)	119	2015-03-12/ 15	Cycle 1 day 15	126	g/L	135-175	1
Hemoglobin low (anemia)	119	2015-03-17/ 20	Cycle 1 day 16 unscheduled 1	92	g/L	135-175	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	119	2015-03-19/ 22	Cycle 1 day 22	100	g/L	135-175	1
Hemoglobin low (anemia)	119	2015-03-23/ 26	Cycle 1 day 22 unscheduled 1	73	g/L	135-175	3
Hemoglobin low (anemia)	119	2015-03-24/ 27	Cycle 1 day 22 unscheduled 2	71	g/L	135-175	3
Hemoglobin low (anemia)	119	2015-03-26/ 29	End of treatment	96	g/L	135-175	2
Hemoglobin low (anemia)	119	2015-03-27/ 30	End of treatment	79	g/L	135-175	3
Leukocytes low (white blood cell decreased)	9.1	2015-03-12/ 15	Cycle 1 day 15	4.3	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	9.1	2015-03-17/ 20	Cycle 1 day 16 unscheduled 1	0.7	x10E9/L	4.5-11	4
Leukocytes low (white blood cell decreased)	9.1	2015-03-19/ 22	Cycle 1 day 22	0.1	x10E9/L	4.5-11	4
Leukocytes low (white blood cell decreased)	9.1	2015-03-26/ 29	End of treatment	0.1	x10E9/L	4.5-11	4
Lymphocytes low (lymphocyte count decreased)	3.3	2015-03-17/ 20	Cycle 1 day 16 unscheduled 1	0.59	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	3.3	2015-03-19/ 22	Cycle 1 day 22	0	x10E9/L	1.5-3.5	4
Lymphocytes low (lymphocyte count decreased)	3.3	2015-03-26/ 29	End of treatment	0.08	x10E9/L	1.5-3.5	4
Neutrophils low (neutrophil count decreased)	4.5	2015-03-12/ 15	Cycle 1 day 15	1.6	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	4.5	2015-03-17/ 20	Cycle 1 day 16 unscheduled 1	0.02	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	4.5	2015-03-19/ 22	Cycle 1 day 22	0	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	4.5	2015-03-26/ 29	End of treatment	0.02	x10E9/L	2.5-7.5	4
Platelets low (platelet count decreased)	208	2015-03-12/ 15	Cycle 1 day 15	65	x10E9/L	150-350	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	208	2015-03-17/ 20	Cycle 1 day 16 unscheduled 1	47	x10E9/L	150-350	3
Platelets low (platelet count decreased)	208	2015-03-19/ 22	Cycle 1 day 22	19	x10E9/L	150-350	4
Platelets low (platelet count decreased)	208	2015-03-26/ 29	End of treatment	6	x10E9/L	150-350	4

■ **Demographics and Baseline Characteristics**

□ Country: Spain
□ Study site identifier: ES00444
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Male
□ Baseline weight(kg): 74
□ Baseline height(cm): 178
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-03-27 Adverse Event

□ Study discontinuation: 2015-03-27 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
48.00	120.00	500.00	2015-02-26	2015-03-17	0.66

■ NARRATIVE TEXT

被験者 340058 は，5[redacted]歳の白人男性で，2010 年 11 月 23 日に初めて病期 I（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，不安及び血中コレステロール増加であった。ベースラインの ECOG スコアは 0 であった。白内障手術，脳血管発作，心筋虚血（冠動脈虚血性心疾患），下痢，下肢切断（左下肢の顆下切断），Grade 4 の粘膜の炎症，腎結石症，末梢動脈閉塞性疾患及び左冠動脈中間枝と両腸骨動脈のステント装着の既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，カルボシステイン，シクロホスファミド，デキサメタゾン，ドキソルビシン，インターフェロン α，メルファラン，prednisone，ビンクリスチン及び ASCT）を受けていたが，すべての薬剤に対して治療抵抗性を示した。

治験組入れ時の併用薬は，アスピリン，アトルバスタチン，クロピドグレル，ランソプラゾール，ロラゼパム，エゼチミブ及びシロスタゾールであった。

(60)

ベースラインのヘモグロビン値は 119 g/L（正常範囲：135-175 g/L），好中球数 4.5×10^9/L（正常範囲：2.5-7.5$\times10^9$/L）及び血小板数 208×10^9/L（正常範囲：150-350$\times10^9$/L）であった。

Day 18（2015 年 3 月 15 日）に，**非重篤な有害事象の Grade 2 のインフルエンザ**（記載語：A 型インフルエンザ）が報告され，治験薬との因果関係は「関連なし」と判断された。治験薬の処置は実施しなかった。Day 20 に，本事象は無処置で回復した。同日（Day 20）に，被験者は感染再発のために集中治療室に入院し，咽頭培養のポリメラーゼ連鎖反応はインフルエンザ A 型+B 型陽性であり，**重篤な有害事象の Grade 4 の敗血症性ショック**に至った（臨床検査値は上記の表を参照）。徴候・症状として咳嗽，発熱及び下痢が認められた。非重篤な有害事象の貧血，好中球減少症及び血小板減少症も認められた（臨床検査値は上記の表を参照）。Day 20 より胸部 X 線検査を実施した（結果不明）。Day 21 の尿の血清学的検査では，*Streptococcus pneumonia* 抗原陽性であった。その他の培養（末梢血，鼻咽頭滲出液，気管支肺胞洗浄液，尿及び直腸）検査では，その他の菌について陰性であった。敗血症性ショックとすべての治験薬との因果関係は「多分なし」と判断されたが，治験薬の投与を中止した。本剤，デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 15，Day 16 及び Day 20 であった。Day 28 に，気管支肺胞洗浄液にガラクトマンナンが検出された。敗血症性ショックに対する治療は，アミオダロン，ドブタミン，アミカシン，シプロフロキサシン，ダプトマイシン，ピペラシリン／タゾバクタム，カスポファンギン，フィルグラスチム，イミペネム，オセルタミビル，フロセミド，ノルエピネフリン，levosimendan，リネゾリド，アセチルシステイン，ブデソニド，ヒドロコルチゾン，イプラトロピウム臭化物，アムロジピン，デキサメタゾン及びヒト免疫グロブリンであった。血小板及び濃厚赤血球を輸血した。治療は奏効せず，被験者は多臓器不全を併発した。Day 30 に，ECOG スコアは 5 に悪化し，同日，被験者は敗血症性ショックのために死亡した。剖検は実施しなかった。

5) 被験者識別番号 450006

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-23	2015-02-12	52	2015-03-12	80	ADVERSE EVENT (PNEUMONIA)	-

■ Discontinuation of study treatment due to AE and Infections and infestations, Grade 3 or 4 and Serious AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-02-14T10:42 2015-02-21	54 8	Y 3	Not related Possible NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	No

■ Infections and infestations, Grade 3 or 4 and Serious AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-02-21 2015-03-12	61 20	Y 4	Not related Possible NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	VIRAL (INFLUENZA A)

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-03-12 2015-03-12	80 1	Y 5	Not related Possible NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	VIRAL (INFLUENZA A)

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
心房細動 Atrial fibrillation	2015-02-24 2015-02-27	64 4	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
便秘 Constipation	2015-02-24 -	64 -	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
下痢 Loose stool	2015-02-16 -	56 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
心電図ＱＴ延長 QTC prolongatin nos	2015-03-03 -	71 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
幻覚 Hallucinations	2015-03-03 -	71 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
低γグロブリン血症 Hypogammaglobulinemia	2015-02-22 2015-03-12	62 19	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
不眠症 Insomnia	2015-01-06T14:56 -	15 -	N 1	Not related Possible NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
筋痙縮 Leg crapms	2015-01-06T14:56 -	15 -	N 1	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
肺動脈圧上昇 Increased pulmonary pressure	2015-02-25 -	65 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
発熱 Fever	2015-02-02 2015-02-02	42 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-02-27 2015-02-28	67 2	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
表在性血栓性静脈炎 Superficial thrombophlebitis	2015-02-11T13:37 -	51 -	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
振戦 Tremor	2015-01-06T14:56 -	15 -	N 1	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N

■ Demographics and Baseline Characteristics

- □ Country: Denmark
- □ Study site identifier: DK00050
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Male
- □ Baseline weight(kg): 100
- □ Baseline height(cm): 178
- □ Baseline ECOG score: 0

■ Disposition Information

- □ Treatment discontinuation: 2015-02-21 Adverse Event
- □ Study discontinuation: 2015-03-12 Death
- □ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
128.00	320.00	1050.00	2014-12-23	2015-02-12	1.71

■ **NARRATIVE TEXT**

被験者 450006 は，7[redacted]歳の白人男性で，2010 年 4 月 22 日に初めて病期 I（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，聴覚障害及び末梢性感覚ニューロパチーであった。ベースラインの ECOG スコアは 0 であった。帯状疱疹感染の既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，ドキソルビシン，レナリドミド及び ASCT）を受けていた。

治験組入れ時の併用薬は，paracetamol，カルシウム，オキシコドン及びゾレドロン酸であった。

Day 54（2015 年 2 月 14 日）に，被験者は**重篤な有害事象の Grade 3 の肺炎**のために入院し，胸部 X 線写真で肺炎が確認された。発熱（38.8°C），呼吸困難及び粘液を伴う咳嗽が認められた。本事象のために治験薬の投与を中止した。レナリドミド，本剤及びデキサメタゾンの最終投与日は，それぞれ Day 49，Day 51 及び Day 52 であった。本事象に対し，シプロフロキサシン，ピペラシリン／タゾバクタム（Tazocin），フルコナゾール，カスポファンギン及び paracetamol による治療を実施した。Day 61 に，**肺炎は Grade 4 に悪化し**，被験者は集中治療室に移送された。気管分泌物のポリメラーゼ連鎖反応分析で A 型インフルエンザウイルス陽性が確認され（日付不明），本事象の病原体であると判断された。オセルタミビル及びアシクロビルを含む抗ウイルス薬治療を開始した。また，スルファメトキサゾール／トリメトプリム（Bactrim），メロペネム，メチルプレドニゾロンコハク酸エステルナトリウム，イプラトロピウム／フェノテロール（Duovent），ピペラシリン／タゾバクタム，カスポファンギン及びシプロフロキサシン，予防としてフロセミド，レミフェンタニル，ミダゾラム及びモルヒネによる治療を実施した。Day 65 に，**非重篤な有害事象の Grade 2 の肺動脈圧上昇**が報告された。治験担当医師は，肺動脈圧上昇と治験薬との因果関係を「関連なし」，肺炎とデキサメタゾンとの因果関係を「可能性小」，肺炎と本剤又はレナリドミドとの因果関係を「関連なし」と判断した。Day 67 に，被験者の状態が悪化し，補助換気を必要としたため気管切開を施行した。両肺に不可逆性の線維性変化が認められたため，治療を終了した。Day 71 に，**非重篤な有害事象の Grade 2 の心電図 QT 延長**が報告された。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。葉酸，アミオダロン，melatonin 及び予防としてクロニジンによる治療も実施した。Day 80 に，被験者の ECOG スコアは 5 に悪化し，同日，被験者は肺炎のために死亡した。剖検は実施されなかった。

死亡時に，肺動脈圧上昇及び心電図 QT 延長は未回復であった。

6) 被験者識別番号 490011

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-16	2015-03-24	99	2015-03-31	106	ADVERSE EVENT (SEPTIC SHOCK)	-

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2015-03-31T12:45 2015-03-31	106 1	Y 5	Possible Possible POSSIBLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	N	No

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
下痢 Diarrhea	2014-12-31 2015-01-01	16 2	N 1	Probable Probable PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
発声障害 Hoarseness	2014-12-18 2015-01-28	3 42	N 1	Not related Probable NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
低リン酸血症 Hypophosphatamie	2015-02-10 2015-03-10	57 29	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
白血球減少症 Leukopenia	2015-03-31T12:33 2015-03-31	106 1	N 4	Possible Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	U RECOVERED/RESOLVED	N
鼻咽頭炎 Common cold	2015-03-16 -	91 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
鼻咽頭炎 Common cold	2015-01-07 2015-01-14	23 8	N 1	Probable Probable PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-01-05T08:45 2015-01-20	21 16	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-03-10T08:42 2015-03-24	85 15	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

■ Hematology Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low (lymphocyte count decreased)	3.4	2014-12-30/ 15	Cycle 1 day 15	1.1	x10E9/L	1.5-3.5	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low (lymphocyte count decreased)	3.4	2015-01-05/ 21	Cycle 1 day 22	1.2	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	3.4	2015-01-13/ 29	Cycle 2 day 1	0.7	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	3.4	2015-01-20/ 36	Cycle 2 day 8	1.1	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	3.4	2015-01-27/ 43	Cycle 2 day 15	0.9	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	3.4	2015-02-03/ 50	Cycle 2 day 22	0.8	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	3.4	2015-02-10/ 57	Cycle 3 day 1	0.6	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	3.4	2015-03-10/ 85	Cycle 4 day 1	1.1	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	3.4	2015-03-24/ 99	Cycle 4 day 15	1.4	x10E9/L	1.5-3.5	1
Neutrophils low (neutrophil count decreased)	-	2014-12-04/ -12	Screening	2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.7	2014-12-30/ 15	Cycle 1 day 15	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.7	2015-01-05/ 21	Cycle 1 day 22	0.8	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.7	2015-01-13/ 29	Cycle 2 day 1	0.7	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2.7	2015-02-03/ 50	Cycle 2 day 22	1.3	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.7	2015-02-10/ 57	Cycle 3 day 1	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.7	2015-03-10/ 85	Cycle 4 day 1	0.8	x10E9/L	2.5-7.5	3

■ Demographics and Baseline Characteristics

□ Country: Germany
□ Study site identifier: DE00422
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 94.9
□ Baseline height(cm): 177
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-03-31 Death

□ Study discontinuation: 2015-03-31 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
197.53	480.00	1575.00	2014-12-16	2015-03-24	3.25

■ **NARRATIVE TEXT**

被験者 490011 は，6[redacted]歳の白人男性で，2012 年 9 月に初めて病期 I（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，動脈性高血圧症，胆石症，腎結石症，多発ニューロパチー及び冠動脈疾患であった。ベースラインの ECOG スコアは 0 であった。急性心筋梗塞（非 ST 上昇型心筋梗塞）及び脳虚血の既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，ドキソルビシン，メルファラン及び ASCT）を受けていた。

治験組入れ時の併用薬は，アスピリン，アロプリノール，アトルバスタチン，カルシウム／ビタミン D，ガバペンチン，nebivolol，パントプラゾール，ラミプリル，スピロノラクトン，シプロフロキサシン及びエノキサパリンナトリウムであった。

Day 21（2015 年 1 月 5 日）に，**非重篤な有害事象の Grade 3 の好中球減少症**が報告され（臨床検査値は上記の表を参照），本事象とレナリドミドとの因果関係は「ほぼ確実」，本剤又はデキサメタゾンとの因果関係は「関連なし」と判断された。本事象のためにレナリドミドを休薬し，次サイクル（サイクル 2）の開始を延期した。フィルグラスチムによる治療を実施した。好中球減少症は Day 36 に回復したため，同日，サイクル 2 を開始した。

Day 85 に，別の**非重篤な有害事象の Grade 3 の好中球減少症**が報告され（臨床検査値は上記の表を参照），本事象とレナリドミドとの因果関係は「ほぼ確実」，本剤又はデキサメタゾンとの因果関係は「関連なし」と判断された。本事象に対する治験薬の処置及び治療は実施しなかった。好中球減少症は Day 99 に回復した。

Day 105 に，被験者は状態が不良で，腹部と胸部に疼痛を訴えた。Day 106 に，被験者は息切れ，呼吸不全及び敗血症性ショックのために救急救命室を受診した。臨床検査では，白血球 0.7×10^9/L（正常範囲：4.5-11$\times10^9$/L），血小板 46/nL（正常範囲：163-337/nL），プロ脳性ナトリウム利尿ペプチド 53694 pg/mL（正常範囲：<125 pg/mL），クレアチンキナーゼ 8186 U/L（正常範囲：30-200 U/L），クレアチンキナーゼ-MB 86.8 U/L（正常範囲：<24 U/L），C-反応性たん白（CRP）49.43 mg/dL（正常範囲：<0.5 ng/mL），クレアチニン値 3.87 mg/dL（正常範囲：0.7-1.3 mg/dL），トロポニン I

322 pg/mL（正常範囲：0-14 pg/mL）であり，血液ガス分析では，代謝性アシドーシス（pH 7.18，塩基過剰−13.9 mmol/L，乳酸 7 mm/L，pO_2 69.8 mm Hg，pCO_2 35.2 mm Hg）が認められた。その結果，**重篤な有害事象の敗血症性ショック**及び**非重篤な有害事象の Grade 4 の白血球減少症**が報告され，被験者は入院した。治験担当医師は，白血球減少症と本剤及びレナリドミドとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「関連なし」，敗血症性ショックとすべての治験薬との因果関係を「可能性小」と判断した。敗血症性ショックのために治験薬の投与を中止した。レナリドミドの最終投与日は Day 84，本剤及びデキサメタゾンの最終投与日は Day 99 であった。電解質液及びノルエピネフリンによる治療を実施した。被験者は治療中に意識を消失し，冷汗及び呼吸困難が認められた。収縮期血圧 75 mm Hg，人工呼吸下の酸素飽和度 80%であった。蘇生にもかかわらず，同日（Day 106），被験者は敗血症性ショックのために死亡した。剖検は実施されなかった。治験担当医師は，敗血症性ショックにより急性心不全が発現したと判断した。

7) 被験者識別番号 700020

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-11	2015-02-25	77	2015-03-02	82	ADVERSE EVENT (Pneumonia bacterial)	-

■ **Discontinuation of study treatment due to AE; Infections and infestations, Grade 3 or 4; and Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
細菌性肺炎 Bilateral bacterial pneumonia	2015-02-25 2015-03-01	77 5	Y 4	Possible Possible NOT RELATED	Dose not changed DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/ RESOLVED	N	BACTERIAL (COCCI)

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
細菌性肺炎 Bilateral bacterial pneumonia	2015-03-01T00:00 2015-03-02	81 2	Y 5	Not related Possible NOT RELATED	Drug withdrawn NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	N	BACTERIAL (COCCI)

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
胃出血 Stomach bleeding	2015-02-28T16:00 2015-03-01	80 2	N 3	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
胸水症 Left-sided hydrothorax	2015-02-20T10:00 -	72 -	N 2	Not related Possible NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
好中球減少症 Neutropenia	2014-12-24T12:51 2014-12-28T11:26	14 5	N 3	Not related Not related DOUBTFUL	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
肺水腫 Pulmonary edema	2015-02-25T21:00 2015-03-02	77 6	N 3	Not related Possible NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N

■ Demographics and Baseline Characteristics

- □ Country: Russia
- □ Study site identifier: RU00192
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Female
- □ Baseline weight(kg): 50
- □ Baseline height(cm): 150
- □ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-03-02 Adverse Event

□ Study discontinuation: 2015-03-02 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
159.66	440.00	680.00	2014-12-11	2015-02-25	2.53

■ **NARRATIVE TEXT**

被験者 700020 は，7[redacted]歳の白人女性で，2013 年 11 月 7 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，高血圧，冠動脈疾患，第 12 胸椎骨折，腎 CrCL 低下であった。ベースラインの ECOG スコアは 1 であった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，メルファラン及びプレドニゾロン，レジメン 2 はベンダムスチン及びプレドニゾロンであった。

治験組入れ時の併用薬は，バルサルタン及びメトプロロールであった。

CrCL 低値（36.9 mL/分）のために，レナリドミドをサイクル 1 及び 2 では 10 mg，サイクル 3 では 15 mg に減量した。

Day 14（2014 年 12 月 24 日）に，**非重篤な有害事象の Grade 3 の好中球減少症**が報告され（好中球数：0.69×10^9/L，正常範囲：$2.5\text{-}7.5\times10^9$/L），本事象とレナリドミドとの因果関係は「多分なし」，本剤又はデキサメタゾンとの因果関係は「関連なし」と判断された。本事象のために Day 15 から Day 18 までレナリドミドを休薬した。フィルグラスチム投与後，Day 18 に本事象は回復した。Day 20 の好中球数は 1.45×10^9/L であった。

Day 70 に，被験者は予定された治験薬投与のために入院したが，歩行時の息切れ及び肋骨の疼痛を訴えた。Day 72 に，胸部 X 線写真で左側に胸水症（第 9 肋骨レベルまで）が認められ，**非重篤な有害事象の Grade 2 の胸水症**が報告された。本事象に対する治験薬の処置は実施しなかった。胸水症に対してフロセミド及びヒトアルブミンによる治療を実施した。Day 77 に，被験者の状態が悪化し，**重篤な有害事象の細菌性肺炎**（記載語：両側性細菌性肺炎）及び**非重篤な有害事象の Grade 3 の肺水腫**が認められた。細菌性肺炎の病原体は細菌性球菌であった。高血圧クリーゼも認められた。治験担当医師は，胸水症及び肺水腫とデキサメタゾンとの因果関係を「可能性小」，レナリドミド又は本剤との因果関係を「関連なし」，細菌性肺炎と本剤又はデキサメタゾンとの因果関係を「可能性小」，レナリドミドとの因果関係を「関連なし」と判断した。Day 79 の胸部 X 線写真では，左胸腔の胸水量がわずかに増加していた。また Day 80 に，**非重篤な有害事象の Grade 3 の胃出血**が発現し，デキサメタゾンとの因果関係は「ほぼ確実」，レナリドミド又

は本剤との因果関係は「関連なし」と判断された。glyceryl trinitrate，アミノフィリン，セフォペラゾン，ドパミン，トラネキサム酸，エタンシラート，ファモチジン及びアミノカプロン酸による治療を実施し，新鮮凍結血漿及び濃厚赤血球を輸血した。肺炎のために治験薬の投与を中止した。本剤，デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 71，Day 72 及び Day 77 であった。Day 81 に，胃出血は回復した。被験者の状態は悪化し，集中治療にもかかわらず Day 82 に肺炎のために死亡した。Day 119 の剖検の結果，疾患進行及び肺炎が死因として報告された。

死亡時に，肺水腫及び胸水症は未回復であった。

8) 被験者識別番号 700026

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-25	2015-01-09	16	2015-01-15	22	ADVERSE EVENT (Cardiopulmonary failure)	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
心肺不全 Acute cardiopulmonary failure	2015-01-15T06:30 2015-01-15T07:00	22 1	Y 5	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	NA	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
全身性炎症反応症候群 Systemic inflammatory response syndrome	2015-01-11T16:00 -	18 -	Y 4	Doubtful Doubtful POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	No

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-01-08T11:00 -	15 -	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
発熱 Fever	2015-01-06T10:00 -	13 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N

■ Demographics and Baseline Characteristics

- □ Country: Russia
- □ Study site identifier: RU00204
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Female
- □ Baseline weight(kg): 80
- □ Baseline height(cm): 158
- □ Baseline ECOG score: 0

■ Disposition Information

- □ Treatment discontinuation: 2015-01-15 Adverse Event
- □ Study discontinuation: 2015-01-15 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
32.00	120.00	375.00	2014-12-25	2015-01-09	0.53

■ **NARRATIVE TEXT**

被験者 700026 は，7[redacted]歳の白人女性で，2010 年 2 月 9 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，高血圧であった。ベースライン（Day 1）の ECOG スコアは 0，好中球数は 2.1×10^9/L（正常範囲：$2.5\text{-}7.5\times10^9$/L）であった。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，メルファラン及びプレドニゾロン，レジメン 2 はメルファラン及びプレドニゾロン，レジメン 3 はボルテゾミブ及びデキサメタゾンであった。

治験組入れ時の併用薬はなかった。

サイクル 1 の Day 1 に，レナリドミド 25 mg とデキサメタゾン 20 mg（40 mg/週）を投与した。Day 13（2015 年 1 月 6 日）に，**非重篤な有害事象の Grade 2 の発熱**（体温：38°C）が報告された。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。治験薬の処置は実施しなかった。paracetamol 及びアジスロマイシンによる治療を実施した。Day 15 に，**非重篤な有害事象の Grade 3 の好中球減少症**（好中球数：0.98×10^9/L）が発現した。治験担当医師は，本事象とレナリドミドとの因果関係を「可能性小」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。フィルグラスチムによる治療を実施した。Day 18 に，被験者の状態が悪化し，呼吸困難，発熱の再発を伴う頻脈及び低血圧の症状が認められ，**全身性炎症反応症候群（Grade 4 の重篤な有害事象）**が示唆され，被験者は入院した。治験担当医師は，これらの事象と本剤及びデキサメタゾンとの因果関係を「多分なし」，レナリドミドとの因果関係を「可能性小」と判断した。好中球減少症及び全身性炎症反応症候群のために Day 16 から Day 21 までレナリドミドを休薬した。本剤及びデキサメタゾンに対する処置は実施しなかった。Day 19 の胸部 X 線写真で心臓陰影の拡大が認められた。Day 21 の再検査では右上葉の肺炎及び左側の胸水が認められた。プレドニゾロン，グリチルリチン酸，セフトリアキソン，オメプラゾール，フルコナゾール，プロポフォール，ジゴキシン，リネゾリド及びフロセミドによる治療を実施した。Day 22 に，被験者の状態が悪化し，心肺蘇生を施行したにもかかわらず被験者は死亡した。剖検では**急性心肺不全**が死因として確認された。剖検の結果，MM（Grade IIIA 又は B のびまん性結節型），原因不明の小-大結節性肝硬変及び動脈性高血圧が認められた。原疾患の後遺症として肺動脈の大，中及び小分枝の血栓塞栓症（下位脛部静脈から）が認められた。治験担当医師は，死因と治験薬との因果関係を「関連なし」と判断した。本剤及びレナリドミドの最終投与日は Day 15，デキサメタゾンの最終投与日は Day 16 であった。

死亡時に，発熱，好中球減少症及び全身性炎症反応症候群は未回復であった。

9) 被験者識別番号 820002

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infusion-related Reactions, Grade 3 or 4

Infections and infestations, Grade 3 or 4

Serious AEs

Second primary malignancies

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-09-23	2015-03-18	177	2015-03-27	186	ADVERSE EVENT (Pneumonia)	-

■ **Discontinuation of study treatment due to AE; Infections and infestations, Grade 3 or 4; and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Infectious pneumonitis	2015-03-19 2015-03-27	178 9	Y 4	Not related Not related POSSIBLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	BACTERIAL (SPUTUM)

■ Infusion-related Reactions, Grade 3 or 4 and Serious AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Pathogen
低血圧 Hypotension	2014-11-18T14:48 2014-11-18T23:50	57 1	Y 3	Possible Not related NOT RELATED	Dose not changed Dose not changed Dose not changed	DARATUMUMAB DEXAMETHASONE LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
好中球減少症 Neutrophil count decreased	2014-10-07 2014-10-08	15 2	Y 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-
好中球減少症 Neutrophil count decreased	2014-10-09 2014-10-10	17 2	Y 4	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-
好中球減少症 Neutrophil count decreased	2014-10-11 2014-10-12	19 2	Y 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-
圧迫骨折 Aggravated of multiple compression fracture	2015-02-23 -	154 -	Y 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Infectious pneumonitis	2015-03-27 2015-03-27	186 1	Y 5	Not related Not related POSSIBLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	N	BACTERIAL (SPUTUM)

■ Second primary malignancies

Dictionary-Derived Term Reported Term for the Clinical Event	Diagnosis of 2nd Primary Malignancy Diagnosis Date/Time of 2nd Primary Malig	Recurrence of a prior existing malig.? Initial Diagnosis Date	Confirm by pathology diagnosis obtained? Confirmation Method Specimen source or sample	Stage of the disease Staging sytem	Concomitant or Additional Trtmnt Given	Surgery	Radiotherapy	Systemic therapy Specific Regimen	Palliative supportive care provided	Outcome of Event
皮膚転移 RIGHT FLANK SKIN SITE METASTATIC ADENOCARCINOMA	RIGHT FLANK SKIN SITE METASTATIC ADENOCARCINOMA 2015-03-23	N -	Y BIOPSY RT. FLANK SKIN SITE PUNCH BIOPSY	U -	N	-	-	- -	-	NOT RECOVERED/ NOT RESOLVED

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
腺癌 Right flank skin site metastatic adenocarcinoma(carcinoma of unknown origin)	2015-03-23 -	182 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
悪寒 Chills	2014-09-23T11:40 2014-09-23T11:45	1 1	N 1	Possible Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	Y
食欲減退 Anorexia	2014-10-06 2014-11-30	14 56	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
食欲減退 Anorexia	2015-02-23 -	154 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
下痢 Diarrhea	2015-03-25 -	184 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
下痢 Diarrhea	2015-02-10 2015-02-13	141 4	N 1	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
下痢 Diarrhea	2014-10-06 2014-10-13	14 8	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
下痢 Diarrhea	2014-10-23 2014-10-26	31 4	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
低カルシウム血症 Hypocalcemia	2015-03-23 2015-03-23	182 1	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
低カルシウム血症 Hypocalcemia	2015-02-09 2015-03-22	140 42	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
低血圧 Hypotension	2015-03-26 -	185 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
低酸素症 Hypoxia	2014-09-23T12:00 2014-09-23T12:10	1 1	N 1	Possible Doubtful NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	Y
好中球減少症 Neutrophil count decreased	2014-10-28 2014-10-29	36 2	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutrophil count decreased	2014-11-17 2014-11-18	56 2	N 4	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose reduced	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutophil count decreased	2014-11-03 2014-11-04	42 2	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutrophil count decreased	2014-11-10 2014-11-11	49 2	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutrophil count decreased	2015-03-25 2015-03-26	184 2	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
胸水 Lt pleural effusion	2015-03-19 -	178 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
全身性そう痒症 Whole body itching	2015-03-22 2015-03-22	181 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
皮膚潰瘍 Coccyx site sikn ulceration	2015-03-25 -	184 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N

■ Hematology Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (white blood cell decreased)	-	2014-09-03/ -20	Screening	4.1	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2014-09-23/ 1	Cycle 1 day 1	3.88	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2014-09-29/ 7	Cycle 1 day 8	2.2	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2014-10-07/ 15	Cycle 1 day 15	2.11	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2014-10-08/ 16	Cycle 1 day 16	1.54	x10E9/L	4.5-11	3
Leukocytes low (white blood cell decreased)	3.88	2014-10-09/ 17	Cycle 1 day 16 unscheduled 1	2.16	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2014-10-10/ 18	Cycle 1 day 16 unscheduled 2	1.86	x10E9/L	4.5-11	3
Leukocytes low (white blood cell decreased)	3.88	2014-10-11/ 19	Cycle 1 day 16 unscheduled 3	2.34	x10E9/L	4.5-11	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (white blood cell decreased)	3.88	2014-10-12/ 20	Cycle 1 day 16 unscheduled 4	3.41	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2014-10-14/ 22	Cycle 1 day 22	4.1	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2014-10-21/ 29	Cycle 2 day 1	2.54	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2014-10-28/ 36	Cycle 2 day 8	2.34	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2014-11-03/ 42	Cycle 2 day 9 unscheduled 1	3.75	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2014-11-10/ 49	Cycle 2 day 16 unscheduled 1	2.92	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2014-11-17/ 56	Cycle 2 day 23 unscheduled 1	3.47	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2015-01-02/ 102	Cycle 4 day 15	2.81	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2015-01-12/ 112	Cycle 5 day 1	3.16	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2015-02-23/ 154	Cycle 6 day 15	4.43	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2015-03-09/ 168	Cycle 7 day 1	4.49	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.88	2015-03-25/ 184	Cycle 7 day 15 unscheduled 1	1.32	x10E9/L	4.5-11	3
Leukocytes low (white blood cell decreased)	3.88	2015-03-26/ 185	Cycle 7 day 15 unscheduled 2	2.07	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	3.88	2015-03-27/ 186	End of treatment	4.35	x10E9/L	4.5-11	1
Lymphocytes low (lymphocyte count decreased)	1.78	2014-09-29/ 7	Cycle 1 day 8	0.71	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-07/ 15	Cycle 1 day 15	0.83	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-08/ 16	Cycle 1 day 16	0.34	x10E9/L	1.5-3.5	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-09/ 17	Cycle 1 day 16 unscheduled 1	0.96	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-10/ 18	Cycle 1 day 16 unscheduled 2	0.76	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-11/ 19	Cycle 1 day 16 unscheduled 3	0.79	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-12/ 20	Cycle 1 day 16 unscheduled 4	0.81	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-14/ 22	Cycle 1 day 22	0.65	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-21/ 29	Cycle 2 day 1	0.77	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.78	2014-10-28/ 36	Cycle 2 day 8	1.06	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2015-01-02/ 102	Cycle 4 day 15	1.24	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2015-01-12/ 112	Cycle 5 day 1	1.47	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2015-02-23/ 154	Cycle 6 day 15	1.39	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2015-03-09/ 168	Cycle 7 day 1	1.49	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.78	2015-03-25/ 184	Cycle 7 day 15 unscheduled 1	0.38	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	1.78	2015-03-26/ 185	Cycle 7 day 15 unscheduled 2	0.44	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	1.78	2015-03-27/ 186	End of treatment	0.26	x10E9/L	1.5-3.5	3
Neutrophils low (neutrophil count decreased)	-	2014-09-03/ -20	Screening	1.7466	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2014-09-23/ 1	Cycle 1 day 1	1.7	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2014-09-29/ 7	Cycle 1 day 8	1.31	x10E9/L	2.5-7.5	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	1.7	2014-10-07/ 15	Cycle 1 day 15	0.83	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2014-10-08/ 16	Cycle 1 day 16	0.72	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2014-10-09/ 17	Cycle 1 day 16 unscheduled 1	0.4	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.7	2014-10-10/ 18	Cycle 1 day 16 unscheduled 2	0.33	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.7	2014-10-11/ 19	Cycle 1 day 16 unscheduled 3	0.65	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2014-10-12/ 20	Cycle 1 day 16 unscheduled 4	1.84	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2014-10-21/ 29	Cycle 2 day 1	1.44	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.7	2014-10-28/ 36	Cycle 2 day 8	0.68	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2014-11-03/ 42	Cycle 2 day 9 unscheduled 1	0.9	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2014-11-10/ 49	Cycle 2 day 16 unscheduled 1	0.89	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2014-11-17/ 56	Cycle 2 day 23 unscheduled 1	0.38	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.7	2014-11-18/ 57	Cycle 3 day 1	2.46	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2014-12-02/ 71	Cycle 3 day 15	2.3	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2014-12-16/ 85	Cycle 4 day 1	1.3	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.7	2015-01-02/ 102	Cycle 4 day 15	1.24	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.7	2015-01-12/ 112	Cycle 5 day 1	1.15	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.7	2015-01-26/ 126	Cycle 5 day 15	1.46	x10E9/L	2.5-7.5	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	1.7	2015-02-09/ 140	Cycle 6 day 1	1.26	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.7	2015-02-23/ 154	Cycle 6 day 15	2.34	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2015-03-09/ 168	Cycle 7 day 1	2.37	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.7	2015-03-25/ 184	Cycle 7 day 15 unscheduled 1	0.88	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.7	2015-03-26/ 185	Cycle 7 day 15 unscheduled 2	1.6	x10E9/L	2.5-7.5	1

■ Demographics and Baseline Characteristics

□ Country: Korea
□ Study site identifier: KR00124
□ Race: Asian
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): 47.2
□ Baseline height(cm): 156
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2015-03-27 Adverse Event

□ Study discontinuation: 2015-03-27 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
280.15	520.00	1395.00	2014-09-23	2015-03-18	5.82

■ NARRATIVE TEXT

被験者 820002 は，7[redacted] 歳のアジア人男性で，2012 年 12 月 26 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，良性前立腺肥大症，心拡大，骨溶解，骨減少症，骨粗鬆症，末梢性ニューロパチー，脊髄圧迫（T1-L5）及び多汗症であった。ベースラインの ECOG スコアは 1 であった。スクリーニング時のバイタルサインは，体温 36.6°C，脈拍数 78 拍/分（bpm）及び血圧 140/90 mm Hg であった。白内障手術，帯状疱疹，肺炎，バンコマイシン耐性腸球菌感染の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，メルファラン及び prednisone，レジメン 2 はボルテゾミブ及びデキサメタゾンであった。被験者はレジメン 2 に対して治療抵抗性を示した。

治験組入れ時の併用薬はゾレドロン酸であった。

Day 1（2014 年 9 月 23 日）の本剤投与開始から 130 分後に，**非重篤な有害事象の Grade 1 の悪寒**，本事象発現の 20 分後に**非重篤な有害事象の Grade 1 の低酸素症**が発現した。治験担当医師は，両事象は IRR であり，悪寒と本剤との因果関係を「可能性小」，レナリドミド又はデキサメタゾンとの因果関係を「関連なし」，低酸素症と本剤との因果関係を「可能性小」，デキサメタゾンとの因果関係を「多分なし」，レナリドミドとの因果関係を「関連なし」と判断した。投与前の血圧は 150/80 mm Hg であった。治験実施計画書に従い前投薬を実施した。これらの事象に対する治験薬の処置は実施しなかった。酸素，ペチジン及び piprinhydrinate による治療を実施した。投与終了 30 分後の血圧は 105/69 mm Hg であった。両事象は発現日に回復した。その後本剤を 16 回投与したが，これらの事象は再発しなかった。

Day 14 に，被験者は予定された本剤投与のために入院した。Day 15 に，**重篤な有害事象の Grade 3 の好中球減少症**が報告され，Day 17 に **Grade 4** に悪化したが，Day 19 に **Grade 3** に改善した（臨床検査値は上記の表を参照）。本事象のために入院期間を延長した。治験担当医師は，本事象とレナリドミドとの因果関係を「可能性小」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。Day 15～Day 20 に，本事象のためにレナリドミドの投与を休薬したが，本剤又はデキサメタゾンに対する処置は実施しなかった。フィルグラスチム及び smofkabiven perifer による治療を実施した。本事象は Day 20 に回復した。Day 22 に，被験者は退院した。

Day 36～Day 184 に，**非重篤な有害事象の好中球減少症**の再発が報告され，**Grade 3～4** であったが，発現後 2 日以内に回復した（臨床検査値は上記の表を参照）。治験担当医師は，本事象とレナリドミドとの因果関係を「可能性小」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。フィルグラスチム及び smofkabiven perifer による治療を実施した。好中球減少症のために，Day 32～Day 42 のレナリドミドの投与を休薬し，Day 43～Day 49 は 15 mg，サイクル 3 以降は 10 mg に減量した。本剤又はデキサメタゾンに対する処置は実施しなかった。

Day 56 に，被験者はサイクル 3 の投与開始のために入院した。Day 57 の投与前の血圧は 99/68 mm Hg であった。治験実施計画書に従い前投薬を実施した。投与終了後の血圧は 80/50 mm Hg であった。**重篤な有害事象の Grade 3 の低血圧**が報告され，入院期間を延長した。治験担当医師は，本事象は IRR であり，本剤との因果関係を「可能性小」，レナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。本事象に対し塩化ナトリウムによる治療を実施した。本事象は発現日に回復し，被験者は Day 58 に退院した。

Day 154 に，被験者は**重篤な有害事象の Grade 2 の圧迫骨折**（記載語：複数の圧迫骨折の悪化）のため入院し，脊椎の MRI スキャンで確認された。両下肢の疼痛及び歩行障害も訴えた。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。paracetamol／トラマドール（Ultracet）による治療を実施した。Day 156 に，被験者は退院した。

Day 178 に，被験者は呼吸困難を訴え救急救命室を受診した。**重篤な有害事象の Grade 4 の肺炎**（記載語：感染性肺臓炎）と**非重篤な有害事象の Grade 3 の胸水**（記載語：左胸水）が報告され（胸部 X 線写真で確認），被験者は入院した。肺炎の原因は細菌と報告された。Day 178 の CT による肺動脈造影図では，左胸水，右肺の多発性すりガラス様陰影及び左下肺の浸潤影が認められた。Day 179 に，胸水ドレナージのために左肺に経皮的カテーテルを挿入した。酸素，イプラトロピウム臭化物，propacetamol，ピペラシリンナトリウム，piprinhydrinate，アンブロキソール，levodropropizine，バンコマイシン，メロペネム，メトロニダゾール，スルファメトキサゾール／トリメトプリム（Bactim），ペラミビル及びメチルプレドニゾロンコハク酸エステルナトリウムによる治療を実施した。Day 182 に，**非重篤な有害事象の Grade 1 の腺癌**［記載語：右側腹皮膚の転移性腺癌（原因不明の癌），病期不明］が報告され，右体幹皮膚のパンチ生検による病理学的検査で確認された。Day 185 に，**非重篤な有害事象の Grade 3 の低血圧**が報告された。治験担当医師は，肺炎とレナリドミドとの因果関係を「可能性小」，本剤又はデキサメタゾンとの因果関係を「関連なし」，胸水，低血圧，腺癌と治験薬との因果関係を「関連なし」と判断した。肺炎及び医師の判断により，Day 186 の治験薬の投与を中止した。同日に，被験者は肺炎のために死亡した。剖検は実施されなかった。本剤，デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 168，Day 175 及び Day 177 であった。

10) 被験者識別番号 820013

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infusion-related Reactions, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-11-05	2016-02-04	457	2016-02-06	459	ADVERSE EVENT (Multi-organ failure)	-

■ Infusion-related Reactions, Grade 3 or 4

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Pathogen
肺水腫 Pulmonary edema	2014-11-05T10:50 2014-11-05T16:25	1 1	N 3	Very likely Not related NOT RELATED	Drug interrupted Dose not changed Dose not changed	DARATUMUMAB DEXAMETHASONE LENALIDOMIDE	Y RECOVERED/RESOLVED	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
多臓器不全 Multiple organ failure	2016-02-06 2016-02-06	459 1	Y 5	Possible Possible POSSIBLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	U FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
無力症 General weakness	2016-02-03 -	456 -	N 3	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
咳嗽 Cough	2016-02-03 -	456 -	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
食欲減退 Anorexia	2014-12-15 -	41 -	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
疲労 Fatigue	2015-12-10 -	401 -	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
喀血 Hemoptysis	2015-03-05 2015-03-07	121 3	N 1	Doubtful Doubtful DOUBTFUL	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
喀血 Hemoptysis	2014-11-20 2014-11-20	16 1	N 1	Doubtful Doubtful DOUBTFUL	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
低カリウム血症 Hypokalemia	2014-11-22T05:07 2014-12-03T09:10	18 12	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
低カリウム血症 Hypokalemia	2014-10-24T10:27 2014-11-18T05:24	-12 26	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
湿性咳嗽 Sputum	2015-11-03 2015-11-29	364 27	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
発熱 Fever	2014-11-15T23:00 2014-11-17	11 3	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
発熱 Fever	2014-11-05T11:30 2014-11-05T13:30	1 1	N 1	Very likely Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	Y
上気道感染 Upper respiratory infection	2015-04-21 2015-04-26	168 6	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
上気道感染 Upper respiratory infection	2015-10-06 2015-10-12	336 7	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Demographics and Baseline Characteristics

□ Country: Korea
□ Study site identifier: KR00121
□ Race: Asian
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): 65
□ Baseline height(cm): 160
□ Baseline ECOG score: 2

■ Disposition Information

□ Treatment discontinuation: 2016-02-06 Death

□ Study discontinuation: 2016-02-06 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
433.78	2640.00	8625.00	2014-11-05	2016-02-04	15.01

■ **NARRATIVE TEXT**

被験者 820013 は，7[redacted]歳のアジア人男性で，2007 年 2 月 9 日に初めて病期 I（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，背部痛，良性前立腺肥大症，慢性胃炎，排尿困難，高血圧及び末梢性ニューロパチーであった。ベースラインの ECOG スコアは 2 であった。気管支拡張症，形質細胞腫，脊髄圧迫及び結核の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はメルファラン，プレドニゾロン及びサリドマイド，レジメン 2 はボルテゾミブ，デキサメタゾン，メルファラン及びプレドニゾロンであった。

治験組入れ時の併用薬は，酸化マグネシウム，プレガバリン，シロドシン，炭酸カルシウム，アムロジピン，ラクツロース，ポリカルボフィルカルシウム，炭酸水素ナトリウム，ベタネコール塩化物及びベンジダミンであった。

Day 1（2014 年 11 月 5 日）の本剤投与開始から 100 分後及び 120 分後に，それぞれ**非重篤な有害事象の Grade 3 の肺水腫及び Grade 1 の発熱**が報告された。両事象は IRR と判断された。治験担当医師は，これらの事象と本剤との因果関係を「ほぼ確実」，レナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。投与前の血圧は 115/69 mm Hg であった。治験実施計画書に従い前投薬を実施した。肺水腫及び発熱のために本剤の投与を 335 分間中断した。これらの事象に対するレナリドミド又はデキサメタゾンの処置は実施しなかった。アスピリン，クロルフェニラミン，フロセミド，ヒドロコルチゾンコハク酸エステルナトリウム及び propacetamol による治療を実施した。発熱は投与中断 160 分後に回復した。肺水腫は投与中断 335 分後に回復した。投与を再開して終了した。その後本剤を 26 回投与したが，肺水腫及び発熱は再発しなかった。

Day 141 に，ECOG スコアは 1 に改善した。

Day 456 に，**非重篤な有害事象の Grade 3 の無力症及び Grade 1 の咳嗽**が報告され，本剤，レナリドミド及びデキサメタゾンとの因果関係は「可能性小」と判断された。これらの事象のためにレナリドミドの投与を中断し，Day 457 にこれまでと同じ投与量を投与した。本剤及びデキサメタゾンに対する処置は実施しなかった。これらの事象に対する治療も実施しなかった。Day 459 に，被験者の状態は急速に悪化し，運動不能となり病院に搬送された。病院到着時の心電図は平坦で，心肺蘇生を実施した。同日（Day 459），被験者は**多臓器不全**のために死亡し，**多臓器不全は重篤な有害事象と判断された**。治験担当医師は，本事象と本剤，レナリドミド及びデキサメタゾンとの因果関係を「可能性小」と判断した。本剤，デキサメタゾン及びレナリドミ

ドの最終投与日は，それぞれ Day 449，Day 456 及び Day 457 であった。治験担当医師は，当該被験者の死亡は疾患進行に関連するものではないと判断し，肺炎が敗血症及び多臓器不全に進行した可能性があると考えた。剖検は実施されなかった。死亡時に，無力症及び咳嗽は未回復であった。

11) 被験者識別番号 972018

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infusion-related Reactions, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-15	2015-03-01	77	2015-03-03	79	ADVERSE EVENT	-

■ **Infusion-related Reactions, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Pathogen
高血圧 Rise in blood pressure (nos)-hypertension(nos)	2014-12-15T12:00 2014-12-15T12:45	1 1	N 3	Very likely Not related NOT RELATED	Drug interrupted Dose not changed Dose not changed	DARATUMUMAB DEXAMETHASONE LENALIDOMIDE	N RECOVERED/RESOLVED	-NA

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
発熱 Fever	2014-12-16 2015-01-01	2 17	Y 2	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-NA
背部痛 Back pain	2015-02-18T18:00 -	66 -	Y 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	-NA
急性腎不全 Acute renal failure	2015-03-03 2015-03-03	79 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	U FATAL	N	-NA

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-02-21T18:50 2015-02-23T14:14	69 3	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
貧血 Anemia	2014-12-30T08:23 2014-12-31T08:52	16 2	N 3	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2014-12-20T16:20 2014-12-22T00:11	6 3	N 3	Not related Not related VERY LIKELY	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2014-12-25T15:34 2014-12-27T00:49	11 3	N 3	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
無力症 General weekness	2015-01-05 -	22 -	N 1	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
悪寒 Chills	2015-01-01T12:40 2015-01-01T13:00	18 1	N 2	Very likely Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	Y
悪寒 Chills	2014-12-15T12:00 2014-12-15T12:30	1 1	N 2	Very likely Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	Y
便秘 Constipation	2015-02-22 2015-02-23	70 2	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
吐血 Vometing (coffe ground)	2014-12-21 2014-12-21	7 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
高カルシウム血症 Hypercalcemia	2015-02-21T19:25 2015-02-22T10:24	69 2	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
高カルシウム血症 Hypercalcemia	2014-12-20T16:20 2014-12-22T08:31	6 3	N 4	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
高カルシウム血症 Hypercalcemia	2015-02-24T08:04 2015-03-02	72 7	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
低アルブミン血症 Hypoalbuminemia	2015-02-22 -	70 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
腎機能障害 Renal function impairment	2014-12-23T18:35 -	9 -	N 2	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose reduced	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
腎機能障害 Renal function impairment	2014-12-23T08:28 2014-12-23T18:35	9 1	N 3	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
腎機能障害 Renal function impairment	2014-12-20T16:20 2014-12-23T08:28	6 4	N 2	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-02-11T08:52 2015-02-18T20:11	59 8	N 2	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2014-12-21 2014-12-30	7 10	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-02-22T08:04 -	70 -	N 2	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N

■ **Hematology/Chemistry Abnormalities**

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Calcium corrected (hypercalcemia)	-	2014-12-14/ -1	Cycle 1 day 1	2.6145	-	2.11935-2.5948	1
Calcium corrected high (hypercalcemia)	2.65	2014-12-14/ -1	Cycle 1 day 1	2.65	mmol/L	2.07-2.64	1
Calcium corrected (hypercalcemia)	2.65	2015-01-12/ 29	Cycle 2 day 1	2.6883	-	2.11935-2.5948	1
Calcium corrected (hypercalcemia)	2.65	2015-02-11/ 59	Cycle 3 day 1	2.7382	-	2.11935-2.5948	1
Calcium corrected (hypercalcemia)	2.65	2015-02-22/ 70	Cycle 3 day 8 unscheduled 1	2.9368	-	2.11935-2.5948	2
Calcium corrected (hypercalcemia)	2.65	2015-03-01/ 77	End of treatment	3.4354	-	2.11935-2.5948	4
Calcium corrected high (hypercalcemia)	2.65	2015-01-12/ 29	Disease evaluation 1	2.81	mmol/L	2.07-2.64	1
Calcium corrected high (hypercalcemia)	2.65	2015-02-11/ 59	Disease evaluation 2	2.72	mmol/L	2.07-2.64	1
Creatinine high (creatinine increased)	124.644	2014-12-14/ -1	Cycle 1 day 1	124.644	umol/L	70.72-106.08	1
Creatinine high (creatinine increased)	124.644	2015-01-12/ 29	Cycle 2 day 1	275.808	umol/L	70.72-106.08	2
Creatinine high (creatinine increased)	124.644	2015-02-11/ 59	Cycle 3 day 1	220.116	umol/L	70.72-106.08	2
Creatinine high (creatinine increased)	124.644	2015-02-22/ 70	Cycle 3 day 8 unscheduled 1	153.816	umol/L	70.72-106.08	1
Creatinine high (creatinine increased)	124.644	2015-03-01/ 77	End of treatment	182.988	umol/L	70.72-106.08	2
Urate high (hyperuricemia)	493.684	2014-12-14/ -1	Cycle 1 day 1	493.684	umol/L	208.18-428.256	1
Urate high (hyperuricemia)	493.684	2015-01-12/ 29	Cycle 2 day 1	463.944	umol/L	208.18-428.256	1
Urate high (hyperuricemia)	493.684	2015-03-01/ 77	End of treatment	434.204	umol/L	208.18-428.256	1

■ **Demographics and Baseline Characteristics**

□ Country: Israel
□ Study site identifier: IL00067
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 76
□ Baseline height(cm): 189
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-03-03 Progressive Disease

□ Study discontinuation: 2015-03-03 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
145.68	400.00	335.00	2014-12-15	2015-03-01	2.53

■ **NARRATIVE TEXT**

被験者 972018 は，6[redacted] 歳の白人男性で，2010 年 7 月に初めて病期 III（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，良性前立腺肥大症，慢性腎臓病，変形性脊椎症，脂質異常症，肋骨骨折，裂孔ヘルニア，高血圧，低アルブミン血症，甲状腺機能低下症，錯感覚及び胃食道逆流性疾患であった。ベースラインの ECOG スコアは 0 であった。乳頭様甲状腺癌の既往歴を有した。スクリーニング時のバイタルサインは，体温 37.1°C，脈拍数 70 bpm，血圧 157/78 mm Hg であった。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド，デキサメタゾン，メルファラン，サリドマイド及び ASCT，レジメン 2 はボルテゾミブ，シクロホスファミド及びデキサメタゾン，レジメン 3 はボルテゾミブ，カルフィルゾミブ，シスプラチン，シクロホスファミド，デキサメタゾン，ドキソルビシン，エトポシド，レナリドミド，メルファラン，ポマリドミド及びサリドマイドであった。被験者はレジメン 2 及びレジメン 3 に対して治療抵抗性を示した。

治験組入れ時の併用薬は，アシクロビル，スルファメトキサゾール／トリメトプリム（Bactrim），アスピリン，ビソプロロール，レボチロキシンナトリウム，オメプラゾール，タムスロシン，ブロチゾラム及びラクツロースであった。

CrCL 低値（57.6 mL/分）のために，レナリドミドは 10 mg で投与を開始した。

Day 1（2014 年 12 月 15 日）の本剤投与開始から 95 分後に，**非重篤な有害事象の Grade 3 の高血圧**（投与開始から 90 分後の血圧は 186/103 mm Hg）及び **Grade 2 の悪寒**が報告され，IRR と判断された。治験担当医師は，これらの事象と本剤との因果関係を「ほぼ確実」，レナリドミド又はデキサメタ

ゾンとの因果関係を「関連なし」と判断した。投与前の血圧は 122/65 mm Hg であった。治験実施計画書に従い前投薬を実施した。これらの事象のために本剤の投与を 45 分間中断したが，レナリドミド又はデキサメタゾンの処置は実施しなかった。ヒドロコルチゾン，metamizole 及びプロメタジンによる治療を実施した。悪寒及び高血圧は，それぞれ本剤投与中断から 30 分後及び 45 分後に回復した。投与を再開して終了した。その後本剤を 8 回投与したが，高血圧は再発しなかった。

Day 2 に，**重篤な有害事象の Grade 2 の発熱**が報告され，治験薬との因果関係は「関連なし」と判断された。Day 6 に，被験者は錯乱を訴え入院した。体温は 37.8°C であった。同日，**非重篤な有害事象の Grade 2 の腎機能障害**が報告された。治験担当医師は，腎機能障害とレナリドミドとの因果関係を「可能性大」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。発熱のために治験薬を休薬した。本剤，デキサメタゾン及びレナリドミドの発熱発現前の投与日はそれぞれ Day 1，Day 2 及び Day 6 であった。metamizole，アジスロマイシン及び塩化ナトリウムによる治療を実施し，被験者は Day 7 に退院した。Day 9 に，**非重篤な有害事象の腎機能障害は Grade 3 に悪化したが**，同日，**Grade 2 に改善した**。Day 18 に，発熱は回復し，治験薬の投与を開始した。腎機能障害のためにレナリドミドをサイクル 2 から 5 mg に減量した。

Day 18 の本剤投与開始から 110 分後に，**非重篤な有害事象の Grade 2 の悪寒**が報告され，IRR と判断された。治験担当医師は，本事象と本剤との因果関係を「ほぼ確実」，レナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。投与前の血圧は 129/72 mm Hg であった。治験実施計画書に従い前投薬を実施した。本事象のために本剤の投与を 20 分間中断したが，レナリドミド又はデキサメタゾンの処置は実施しなかった。ヒドロコルチゾン及びプロメタジンによる治療を実施した。投与中断から 20 分後に，悪寒は回復した。投与を再開して終了した。その後本剤を 7 回投与したが，悪寒は再発しなかった。

Day 66 に，**重篤な有害事象の Grade 3 の背部痛**が報告され，被験者は入院した。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。Day 67 に MRI スキャン，Day 71 に CT スキャンを実施した（結果は未報告）。オキシコドン／ナロキソン（Targin），ブロチゾラム，デキサメタゾン及びオキシコドンによる治療を実施した。Day 77 に，被験者は錯乱状態を発現した。臨床検査値から腎機能の悪化が認められた（臨床検査値は上記の表を参照）。Day 79 に，**重篤な有害事象の急性腎不全**が報告され，入院期間を延長した。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。モルヒネ及び輸液による治療を実施した。Day 79 に，ECOG スコアは 5 に悪化し，同日，被験者は急性腎不全及び疾患進行（肋骨及び頭蓋の新たな溶解病変）のために死亡した。剖検は実施されなかった。本剤，デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 73，Day 74 及び Day 77 であった。

(2) Rd 群

1) 被験者識別番号 101009

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-11-05	2014-11-13	9	2014-11-19	15	ADVERSE EVENT (RENAL FAILURE)	-

■ **Discontinuation of study treatment due to AE and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
腎不全 Renal failure	2014-11-07 2014-11-18	3 12	Y 3	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
腎不全 Renal failure	2014-11-19 2014-11-19	15 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2014-11-07 2014-11-09	3 3	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
アスパラギン酸アミノトランスフェラーゼ増加 Elevated ast	2014-11-07 -	3 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
血中アルカリホスファターゼ増加 Increased alkaline phosphatase - renal	2014-11-07 -	3 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
血中クレアチニン増加 Elevated creatinine(single observation)	2014-11-04 2014-11-07	-1 4	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
錯乱状態 Increased confusion	2014-11-07 -	3 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
譫妄 Delirium	2014-11-07 -	3 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
低血圧 Hypotension	2014-11-07 -	3 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA

■ Hematology/Chemistry Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine high (creatinine increased)	-	2014-10-16/ -20	Screening	144	umol/L	64-104	1
Creatinine high (creatinine increased)	-	2014-11-04/ -1	Screening unscheduled 1	168	umol/L	64-104	2
Creatinine high (creatinine increased)	168	2014-11-04/ -1	Cycle 1 day 1	168	umol/L	35-97	2
Creatinine high (creatinine increased)	168	2014-11-07/ 3	Cycle 1 day 1 unscheduled 1	217	umol/L	35-97	2
Creatinine high (creatinine increased)	168	2014-11-09/ 5	Cycle 1 day 1 unscheduled 2	376	umol/L	35-97	3
Hemoglobin low (anemia)	-	2014-10-16/ -20	Screening	88	g/L	120-160	2
Hemoglobin low (anemia)	81	2014-11-04/ -1	Cycle 1 day 1	81	g/L	120-160	2
Hemoglobin low (anemia)	81	2014-11-07/ 3	Cycle 1 day 1 unscheduled 1	66	g/L	120-160	3
Lymphocytes low (lymphocyte count decreased)	-	2014-10-16/ -20	Screening	0.64	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.3	2014-11-04/ -1	Cycle 1 day 1	0.3	x10E9/L	1.5-3.5	3
Urate high (hyperuricemia)	-	2014-10-16/ -20	Screening	525	umol/L	210-450	1
Urate high (hyperuricemia)	584	2014-11-04/ -1	Cycle 1 day 1	584	umol/L	145-345	1

■ Demographics and Baseline Characteristics

□ Country: Canada
□ Study site identifier: CA00102
□ Race: White
□ Age(yrs): 7[redacted]
□ Sex: Female
□ Baseline weight(kg): -
□ Baseline height(cm): 153
□ Baseline ECOG score: 2

■ Disposition Information

□ Treatment discontinuation: 2014-11-19 Adverse Event

□ Study discontinuation: 2014-11-19 Death

(101)

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	40.00	90.00	2014-11-05	2014-11-13	0.30

■ **NARRATIVE TEXT**

被験者 101009 は，7[redacted]歳の白人女性で，2010 年 9 月 23 日に初めて病期 III（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，胃食道逆流性疾患，貧血，食欲減退，背部痛，認知障害，錯乱状態，譫妄，傾眠，疲労，疼痛，高カリウム血症，高血圧，甲状腺機能低下症，失禁，免疫性血小板減少性紫斑病，口内炎，神経痛，末梢性圧痕浮腫（両下肢及び両足），精神病性障害，帯状疱疹，構語障害，一過性脳虚血発作，女性不妊手術，ウイルス性発疹であった。ベースラインの ECOG スコアは 2 であった。両側卵管卵巣摘除，膀胱修復，子宮摘出，胸水，肺炎，反復性尿路感染，一過性脳虚血発作（左側）及び扁桃摘出の既往歴を有した。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，デキサメタゾン，メルファラン及び ASCT，レジメン 2 はボルテゾミブ，シクロホスファミド及びデキサメタゾン，レジメン 3 はシクロホスファミド及び prednisone であった。被験者はレジメン 3 に対して治療抵抗性を示した。

治験組入れ時の併用薬は，フロセミド，ヒドロモルフォン，メトプロロール，ハロペリドール，ガバペンチン，アスピリン，ナイスタチン及びバラシクロビルであった。

Day −1 に，クレアチニン値は 168 µmol/L（正常範囲：35-97 µmol/L）であり，**非重篤な有害事象の Grade 2 の血中クレアチニン増加**が報告された。ベースラインの腎機能の状態は，サイクル 1 の Day 1 に Grade 1 の腎機能障害であった（CrCL：24.8 mL/分）。症状として錯乱及び脱力が認められた。Day 3（2014 年 11 月 7 日）に，クレアチニン値は 217 µmol/L，尿素値は 12.2（単位及び正常範囲は未報告）であった。Day 3 に，**重篤な有害事象の Grade 3 の腎不全**が報告され，被験者は敗血症の疑いで入院したが，血液培養の結果は陰性であったため敗血症の可能性は除外された。Day 3 の胸部 X 線検査では，心不全，融合性肺浸潤影，胸水又は目視可能な破壊性骨病変は認められなかった。MM が本事象の原因として疑われた。同日（Day 3）に，**非重篤な有害事象の Grade 2 の錯乱状態，Grade 2 の低血圧，Grade 2 の貧血，Grade 1 の譫妄，Grade 1 のアスパラギン酸アミノトランスフェラーゼ増加及び Grade 1 の血中アルカリホスファターゼ増加**が報告された。治験担当医師は，すべての事象と治験薬との因果関係を「関連なし」と判断した。ピペラシリン／タゾバクタム（Zosyn）による治療を実施した。濃厚赤血球も輸血した（ベースラインのヘモグロビン値：81 g/L，正常範囲：120-160 g/L）。貧血は Day 5 に回復した。Day 1～Day 9 にレナリドミド 10 mg，サイクル 1 の Day 1 にデキサメタゾン 40 mg を投与した。腎不全のために治

験薬の投与を中止し，デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 1 及び Day 9 であった。Day 15 に，ECOG スコアは 5 に悪化し，同日，被験者は腎不全のために死亡した。剖検は実施されなかった。

2) 被験者識別番号 300002

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-29	2015-08-30	245	2015-09-02	248	ADVERSE EVENT (SEPTIC SHOCK)	-

■ **Infections and infestations, Grade 3 or 4 and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2015-08-31 2015-09-02	246 3	Y 4	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	U RECOVERED/RESOLVED	NA	No

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2015-09-02 2015-09-02	248 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	U FATAL	N	No

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
骨痛 Bone pain	2015-03-26 2015-04-24	88 30	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
蜂巣炎 Calfs cellulitis	2015-03-12 2015-04-20	74 40	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
蜂巣炎 Lower libs cellulitis	2015-08-11 -	226 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
高血糖 Hyperglucemia	2015-03-17 2015-03-26	79 10	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
高血糖 Hyperglucemia	2015-06-19 2015-08-10	173 53	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
低カルシウム血症 Hypocalcemia	2015-03-17 2015-03-26	79 10	N 2	Not related Very likely NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
筋力低下 Proximal muscle weakness	2015-05-22 -	145 -	N 1	Not related Very likely NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
２型糖尿病 Diabetes type ii worsening	2015-02-24 2015-03-26	58 31	N 3	Not related Possible NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

■ Demographics and Baseline Characteristics

□ Country: Greece
□ Study site identifier: GR90041
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): -
□ Baseline height(cm): 181
□ Baseline ECOG score: 0

■ Disposition Information

□ Treatment discontinuation: 2015-09-02 Death

□ Study discontinuation: 2015-09-02 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1400.00	4700.00	2014-12-29	2015-08-30	8.05

■ NARRATIVE TEXT

被験者 300002 は，6[redacted]歳の白人男性で，2012 年 3 月 7 日に初めて病期 II（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，動脈性高血圧，骨痛，2 型糖尿病，高尿酸血症及び骨溶解であった。ベースラインの

ECOG スコアは 0 であった。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，レナリドミド，メルファラン，メスナ及び ASCT）を受けていた。

治験組入れ時の併用薬は，ビルダグリプチン／メトホルミン（Eucreas），グリメピリド，アロプリノール，テルミサルタン，ゾレドロン酸及びトラマドールであった。

Day 74（2015 年 3 月 12 日）に，**非重篤な有害事象の Grade 2 の蜂巣炎**（記載語：腓腹の蜂巣炎）が報告された。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。本事象に対するレナリドミド又はデキサメタゾンの処置は実施しなかった。フロセミド及びアモキシシリン／クラブラン酸（Augmentin）による治療を実施した。蜂巣炎は Day 113 に回復した。

Day 226 に，**非重篤な有害事象の Grade 2 の蜂巣炎**（記載語：両下肢の蜂巣炎）が報告された。同日の好中球数は 2×10^9/L であった。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。本事象に対するレナリドミド又はデキサメタゾンの処置は実施しなかった。アモキシシリン及びアモキシシリン／クラブラン酸（Augmentin）による治療を実施した。

Day 246 に，被験者は昏睡状態で救急救命室に搬送された。直ちに挿管し，**重篤な有害事象の Grade 4 の敗血症性ショック**のために入院した。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。本事象のために治験薬を休薬した。敗血症性ショックの原因として誤嚥に伴う呼吸器感染が疑われた。剖検は実施されなかった。臨床検査又は血液培養検査の結果は入手できなかった。Day 248 に，被験者は敗血症性ショックのために死亡した。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 243 及び Day 245 であった。

死亡時に，蜂巣炎は未回復であった。

3) 被験者識別番号 320010

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-01-20	2015-05-25	126	2015-06-08	140	ADVERSE EVENT (General weakness due to neurological syndrome)	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
神経系障害 General weakness due to neurological syndrome	2015-06-08 2015-06-08	140 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
呼吸困難 Dyspnea	2015-03-06 -	46 -	N 1	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
神経系障害 General weakness due to neurological syndrome	2015-05-04 2015-06-08	105 36	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED WITH SEQUELAE	N
好中球減少症 Neutropenia	2015-02-20 2015-02-27	32 8	N 3	Not related Not related VERY LIKELY	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-03-27 2015-04-03	67 8	N 3	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
末梢性浮腫 Malleolar edema	2015-02-06 -	18 -	N 1	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
動悸 Palpitations	2015-03-13 2015-03-13	53 1	N 2	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Demographics and Baseline Characteristics

□ Country: Belgium
□ Study site identifier: BE00106
□ Race: White
□ Age(yrs): 7[redacted]
□ Sex: Female
□ Baseline weight(kg): -
□ Baseline height(cm): 154
□ Baseline ECOG score: 2

■ Disposition Information

□ Treatment discontinuation: 2015-05-27 Non-compliance with Study Drug

□ Study discontinuation: 2015-06-08 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	640.00	1485.00	2015-01-20	2015-05-25	4.14

■ NARRATIVE TEXT

被験者 320010 は，7[redacted] 歳の白人女性で，2001 年 9 月 6 日に初めて病期 II（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，不整脈，便秘，嚥下障害，労作性呼吸困難，疲労，不眠症，ランバート・イート

ン筋無力症候群，末梢性ニューロパチー及び不穏であった。ベースラインの ECOG スコアは 2 であった。脊椎圧迫骨折（D5，D9，D10，L1，L2 及び L5），子宮摘出，左肋骨骨折，圧迫骨折 D9 に対する外科手術及び大腿骨骨折の既往歴を有した。

前治療は，レジメン 1 がドキソルビシン，メルファラン，prednisone，ビンクリスチン及び ASCT，レジメン 2 がサリドマイド，レジメン 3 がシクロホスファミド及びレナリドミドで，続く 2 レジメンがボルテゾミブであった。

治験組入れ時の併用薬は，ビソプロロール，ロラゼパム，ロルメタゼパム，ミルタザピン，マクロゴール（Movicol），オメプラゾール，パミドロン酸二ナトリウム，paracetamol 及びピコスルファートナトリウムであった。

Day 46 に，非重篤な有害事象の Grade 3 の好中球減少症のためにレナリドミドを 15 mg に減量した。同日，ECOG スコアは 1 に改善したが，Day 74 に再度 2 に悪化した。

Day 105（2015 年 5 月 4 日）に，**非重篤な有害事象の Grade 3 の神経系障害**（記載語：神経症候群による全身脱力）が報告された。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。本事象に対する治験薬の処置及び治療は実施しなかった。レナリドミド及びデキサメタゾンの最終投与日は Day 126 であった。

Day 127 に，被験者は予定されていた緩和病棟に入院した。

Day 128 に，被験者は治験薬の服薬を遵守しておらず，以降の治験薬投与を拒否したため，レナリドミド及びデキサメタゾンの投与を中止した。

Day 140 に，感覚運動ニューロパチーの症状が増え，**神経系障害**が悪化し，**重篤な有害事象の神経系障害**のために死亡した。剖検は実施されなかった。リスク因子はランバート・イートン症候群であった。治験担当医師は，神経系障害と治験薬との因果関係を「関連なし」と判断した。本事象に対する治療は実施しなかった。

4) 被験者識別番号 340009

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

Second primary malignancies

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-07-17	2014-11-05	112	2014-11-21	128	ADVERSE EVENT (Pulmonary adenocarcinoma)	-

■ Discontinuation of study treatment due to AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺腺癌 Pulmonary adenocarcinoma	2014-11-21 2014-11-21	128 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	U FATAL	NA	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺腺癌 Pulmonary adenocarcinoma	2014-10 2014-11-21	77 52	Y 2	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	U RECOVERED/RESOLVED	NA	-
肺腺癌 Pulmonary adenocarcinoma	2014-11-21 2014-11-21	128 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	U FATAL	NA	-

■ Second primary malignancies

Dictionary-Derived Term Reported Term for the Clinical Event	Diagnosis of 2nd Primary Malignancy Diagnosis Date/Time of 2nd Primary Malig	Recurrence of a prior existing malig.? Initial Diagnosis Date	Confirm by pathology diagnosis obtained? Confirmation Method Specimen source or sample	Stage of the disease Staging sytem	Concomitant or Additional Trtmnt Given	Surgery	Radiotherapy	Systemic therapy Specific Regimen	Palliative supportive care provided	Outcome of Event
肺腺癌 PULMONARY ADENOCARCINOMA	PULMONARY ADENOCARCINOMA 2014-11-02	N -	Y BIOPSY PULMONAR TISSUE	IV TNM	Y	-	-	- -	Y	FATAL

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
腹部不快感 Gastric discomfort	2014-07-24 -	8 -	N 1	Not related Probable NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
貧血 Anemia	2014-10-08 2014-10-21	84 14	N 3	Not related Possible POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
貧血 Anemia	2014-09-10 2014-10-07	56 28	N 1	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
貧血 Anemia	2014-10-21 -	97 -	N 2	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
無力症 Asthenia	2014-11-05 -	112 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
無力症 Asthenia	2014-07-17 2014-08-14	1 29	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
無力症 Asthenia	2014-10-08 2014-10-15	84 8	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
平衡障害 Physical instability	2014-09-24 -	70 -	N 2	Not related Very likely NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
徐脈 Bradycardia	2014-08-28 2014-09-10	43 14	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
便秘 Constipation	2014-07-31 2014-08-07	15 8	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
咳嗽 Cough	2014-08-27 2014-09-10	42 15	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
食欲減退 Anorexia	2014-07-17 2014-08-14	1 29	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
全身健康状態低下 Worsering general status	2014-11-05 -	112 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
不眠症 Insomnia	2014-09-24 -	70 -	N 2	Not related Very likely NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
白血球減少症 Leucopenia	2014-09-24 2014-10-15	70 22	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2014-09-24 2014-10-07	70 14	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2014-10-08 2014-10-15	84 8	N 3	Not related Possible POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2014-10-29 -	105 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
発熱 Fever	2014-08-27 2014-08-28	42 2	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
血小板減少症 Thrombocytopenia	2014-09-24 2014-10-07	70 14	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
血小板減少症 Thrombocytopenia	2014-10-08 2014-10-29	84 22	N 1	Not related Possible POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
血小板減少症 Thrombocytopenia	2014-10-29 -	105 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA

■ Demographics and Baseline Characteristics

□ Country: Spain
□ Study site identifier: ES00349
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): -
□ Baseline height(cm): 168
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2014-11-21 Adverse Event

□ Study discontinuation: 2014-11-21 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	560.00	1680.00	2014-07-17	2014-11-05	3.68

■ NARRATIVE TEXT

被験者 340009 は，6[redacted]歳の白人男性で，2010 年 4 月に初めて病期 III（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，疼痛，2 型糖尿病，高コレステロール血症，高血圧及び慢性腎不全であった。ベースラインの ECOG スコアは 1 であった。良性前立腺肥大症，虚血性心筋症，血管グラフト（冠動脈バイパス），経尿道的前立腺摘除及び喫煙の既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，デキサメタゾン，メルファラン及び ASCT）を受けていた。

治験組入れ時の併用薬は，ビソプロロール，アトルバスタチン，glyceryl trinitrate，インスリングラルギン，ロラゼパム，ロサルタン及びオメプラゾールであった。

Day 77（2014 年 10 月，日付不明）に，**重篤な有害事象の Grade 2 の肺腺癌**が報告された。Day 109 に，失神の発現後，近医を受診し，肺組織生検により肺腺癌（第Ⅳ期）と診断された。X 線検査では肺結節，胸部 CT スキャンでは副腎，後腹膜，膵周囲及び骨の病変，肺 CT スキャンでは右肺門及び縦隔リンパ節病変，腹部 CT スキャンではリンパ節症及び腫瘍インプラントを示唆する複数の結節を伴う左副腎及び後腹膜への転移，膵周囲及び腹腔体幹周囲の転移性浸潤，並びに転移拡大を示唆する脊柱及び骨盤の溶骨性病変が認められた。肺腺癌とレナリドミド又はデキサメタゾンとの因果関係は「関連なし」と判断された。本事象のためにレナリドミド及びデキサメタゾンの投与を中断したが，Day 84 及び Day 91 にそれぞれレナリドミド及びデキサメタゾンを 15 mg 及び 20 mg に減量して投与を再開した。

Day 91 に，ECOG スコアは 2 に悪化した。肺腺癌のためにサイクル 5 の開始を延期した。

Day 119 に，発熱（38°C）が認められ，持続性疼痛を訴えたために穿刺検査を実施した。同日の CT スキャンでは，腺癌による浸潤及び合併症としての小さい気胸が確認された。Day 127 に，被験者は疼痛，呼吸困難，機能低下，無力症及び食欲不振のために入院し，緩和治療を実施した。身体所見では，血圧 123/60 mm Hg，心拍数 68 bpm，体温 33.6°C，酸素飽和度 97%で，全身状態は不良であったが意識はあった。CT スキャン及び生検では，二次性悪性腫瘍として肺腺癌が確認された。Day 128 に，被験者は肺腺癌のために死亡した。剖検は実施されなかった。レナリドミド及びデキサメタゾンの最終投与日は，それぞれ Day 90 及び Day 112 であった。

5) 被験者識別番号 340043

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-01-20	2015-10-14	268	2015-10-23	277	ADVERSE EVENT (Cerebral haemorrhage)	-

■ Discontinuation of study treatment due to AE and Serious AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
脳出血 Massive cerebral hemorrhage	2015-10-22 2015-10-23	276 2	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
発熱性好中球減少症 Neutropenic fever	2015-09-20 2015-09-22	244 3	Y 3	Not related Possible VERY LIKELY	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-
硬膜下血腫 Subdural hematoma	2015-10-17 -	271 -	Y 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	U NOT RECOVERED/NOT RESOLVED	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-03-03 -	43 -	N 1	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERING/RESOLVING	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
背部痛 Lumbar pain	2015-01-20 2015-01-27	1 8	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
失明 Progressive visual loss	2015-05-28 -	129 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
不全片麻痺 Hemiparesis	2015-10-04 2015-10-04	258 1	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
筋骨格系胸痛 Rib pain	2015-01-20 2015-01-27	1 8	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2015-10-15 -	269 -	N 4	Not related Not related POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
好中球減少症 Neutropenia	2015-03-17 2015-05-12	57 57	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2015-06-23 2015-07-06	155 14	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2015-05-12 2015-06-09	113 29	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2015-10-01 2015-10-15	255 15	N 2	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-06-09 2015-06-22	141 14	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
好中球減少症 Neutropenia	2015-09-20 2015-09-22	244 3	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
発疹 Skin rash	2015-02-11 -	23 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERING/RESOLVING	NA
ブドウ球菌感染 Aureus marsa infection	2015-03-06 2015-03-10	46 5	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
ブドウ球菌感染 Methicillin-resistant staphylococcus aureus infection	2015-01-26 2015-02-17	7 23	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
血小板減少症 Thrombocytopenia	2015-10-15 -	269 -	N 3	Not related Not related POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
血小板減少症 Thrombocytopenia	2015-03-03 2015-10-15	43 227	N 1	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
一過性脳虚血発作 Transient isquemic stroke	2015-10-04 2015-10-04	258 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	U RECOVERED/RESOLVED	N

■ **Hematology Abnormalities**

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	139	2015-03-03/ 43	Cycle 2 day 15	124	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-03-10/ 50	Cycle 2 day 22	118	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-03-17/ 57	Cycle 3 day 1	118	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-03-31/ 71	Cycle 3 day 15	116	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-04-14/ 85	Cycle 4 day 1	114	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-04-28/ 99	Cycle 4 day 15	118	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-05-12/ 113	Cycle 5 day 1	120	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-05-26/ 127	Cycle 5 day 15	119	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-06-09/ 141	Cycle 6 day 1	119	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-06-23/ 155	Cycle 6 day 15	122	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-07-07/ 169	Cycle 7 day 1	111	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-08-04/ 197	Cycle 8 day 1	114	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-09-04/ 228	Cycle 9 day 1	108	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-09-20/ 244	Cycle 9 day 15 unscheduled 1	88	g/L	135-175	2
Hemoglobin low (anemia)	139	2015-09-22/ 246	Cycle 9 day 15 unscheduled 2	97	g/L	135-175	2
Hemoglobin low (anemia)	139	2015-10-01/ 255	Cycle 10 day 1	104	g/L	135-175	1
Hemoglobin low (anemia)	139	2015-10-15/ 269	Cycle 10 day 15	96	g/L	135-175	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	-	2015-01-08/ -12	Screening	2.2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-01-20/ 1	Cycle 1 day 1	2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-02-10/ 22	Cycle 1 day 22	2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-02-17/ 29	Cycle 2 day 1	2.2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-02-23/ 35	Cycle 2 day 8	2.2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-03-03/ 43	Cycle 2 day 15	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-03-10/ 50	Cycle 2 day 22	1.7	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-03-17/ 57	Cycle 3 day 1	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-03-31/ 71	Cycle 3 day 15	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-04-14/ 85	Cycle 4 day 1	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-04-28/ 99	Cycle 4 day 15	1.2	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-05-12/ 113	Cycle 5 day 1	0.96	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2015-05-26/ 127	Cycle 5 day 15	0.6	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2015-06-09/ 141	Cycle 6 day 1	1.3	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-06-23/ 155	Cycle 6 day 15	0.7	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2015-07-07/ 169	Cycle 7 day 1	2	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2	2015-09-20/ 244	Cycle 9 day 15 unscheduled 1	0.56	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	2	2015-09-22/ 246	Cycle 9 day 15 unscheduled 2	1.1	x10E9/L	2.5-7.5	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	2	2015-10-01/ 255	Cycle 10 day 1	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2	2015-10-15/ 269	Cycle 10 day 15	0.4	x10E9/L	2.5-7.5	4
Platelets low (platelet count decreased)	182	2015-01-27/ 8	Cycle 1 day 8	105	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-03-03/ 43	Cycle 2 day 15	132	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-03-10/ 50	Cycle 2 day 22	75	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-03-17/ 57	Cycle 3 day 1	149	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-03-31/ 71	Cycle 3 day 15	132	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-04-14/ 85	Cycle 4 day 1	144	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-04-28/ 99	Cycle 4 day 15	102	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-05-12/ 113	Cycle 5 day 1	109	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-05-26/ 127	Cycle 5 day 15	97	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-06-09/ 141	Cycle 6 day 1	121	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-06-23/ 155	Cycle 6 day 15	86	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-07-07/ 169	Cycle 7 day 1	133	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-08-04/ 197	Cycle 8 day 1	119	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-09-04/ 228	Cycle 9 day 1	95	x10E9/L	150-350	1
Platelets low (platelet count decreased)	182	2015-09-20/ 244	Cycle 9 day 15 unscheduled 1	51	x10E9/L	150-350	2
Platelets low (platelet count decreased)	182	2015-09-22/ 246	Cycle 9 day 15 unscheduled 2	56	x10E9/L	150-350	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	182	2015-10-15/ 269	Cycle 10 day 15	30	x10E9/L	150-350	3

■ **Demographics and Baseline Characteristics**

□ Country: Spain
□ Study site identifier: ES00349
□ Race: White
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): -
□ Baseline height(cm): 166
□ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-10-23 Adverse Event

□ Study discontinuation: 2015-10-23 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1480.00	4800.00	2015-01-20	2015-10-14	8.80

■ **NARRATIVE TEXT**

被験者 340043 は，7[redacted]歳の白人男性で，2010 年 2 月に初めて病期 I（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，無力症，高血圧，レジオネラ感染，ヘルペス後神経痛，処置後甲状腺機能低下症及び足指切断であった。ベースラインの ECOG スコアは 1 であった。虫垂切除及び右鼡径部ヘルニア修復の既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，デキサメタゾン，レナリドミド，メルファラン及び prednisone）を受けていた。

治験組入れ時の併用薬は，ラミプリル，オメプラゾール，プレガバリン，レボチロキシンナトリウム及びレボフロキサシンであった。

Day 57（2015 年 3 月 17 日）に，**非重篤な有害事象の Grade 2 の好中球減少症**（好中球数：1.2×10^9/L）が報告され，Day 113 に Grade 3（好中球数：0.96×10^9/L）に悪化した。フィルグラスチムによる治療を実施した。本期間中の感染はなかった。好中球減少症は Day 141 に Grade 2（好中球数：1.3×10^9/L）に改善し，Day 155 に再度 Grade 3（好中球数：0.7×10^9/L）に悪化したが，フィルグラスチム投与後の Day 168 に回復した。Day 169 の好中球数は 2.0×10^9/L であった。治験担当医師は，本事象とデキサメタゾン又はレナリドミドとの因果関係を「関連なし」と判断し，本事象に対するレナリドミド又はデキサメタゾンの処置は実施しなかった。

Day 244 に，被験者は発熱のために救急救命室を受診した。好中球数は 0.56×10^9/L であった。胸部 X 線写真の所見は正常で，感染巣は認められなかった。**重篤な有害事象の Grade 3 の発熱性好中球減少症**が発現し，被験者は翌日（Day 245）入院した。血液培養検査で病原体は認められなかった。治験担当医師は，本事象とデキサメタゾンとの因果関係を「可能性小」，レナリドミドとの因果関係を「ほぼ確実」と判断した。本事象のためにレナリドミド及びデキサメタゾンを休薬した。休薬前の最終投与日はそれぞれ Day 244 及び Day 249 であった。ピペラシリン／タゾバクタム，アミカシン，フィルグラスチム及びセフロキシムによる治療を実施した。Day 246 に，発熱性好中球減少症は回復し，被験者は退院した。

Day 255 に，ECOG スコアは 1 に悪化し，**非重篤な有害事象の Grade 2 の好中球減少症**（好中球数：1.1×10^9/L）が報告された。治験担当医師は，本事象とレナリドミドとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「関連なし」と判断した。

Day 258 に，**非重篤な有害事象の Grade 2 の不全片麻痺**及び **Grade 1 の一過性脳虚血発作**が報告されたが，治験薬との因果関係は「関連なし」と判断された。両事象に対する治験薬の処置は実施しなかった。クロピドグレルによる治療を実施した。両事象は発現日に回復した。

Day 269 に，**好中球減少症は Grade 4 に悪化**した。本事象のために治験薬を休薬した。フィルグラスチムによる治療を実施した。Day 271 に，偶発的に頭部を打撲し，神経学的症状が認められ，**重篤な有害事象の Grade 4 の硬膜下血腫**のために入院した。同日の血小板数は 30×10^9/L（正常範囲：150-350×10^9/L）であった。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。アスピリンによる治療が血腫の原因と考えられた。Day 271 に，濃厚赤血球を輸血した。Day 275 に，凝固パラメータ及び血小板数が回復後，穿孔術により血腫を除去した。翌日（Day 276），**重篤な有害事象の脳出血**（記載語：大量の脳出血）が認められた。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。Day 277 に，被験者は大量の脳出血のため死亡した。剖検は実施されなかった。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 262 及び Day 268 であった。

6) 被験者識別番号 440017

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-11-03	2014-11-17	15	2014-11-29	27	ADVERSE EVENT (PNEUMONIA)	-

■ Discontinuation of study treatment due to AE; Infections and infestations, Grade 3 or 4; Serious AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2014-11-20T21:00 2014-11-28	18 9	Y 4	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	Unknown

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2014-11-29 2014-11-29	27 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	NA	Unknown

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anaemia	2014-11-17 -	15 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
心房細動 Fast atrial fibrillation	2014-11-23 2014-11-23	21 1	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA
咳嗽 Dry cough	2014-11-18 -	16 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERING/RESOLVING	NA
インフルエンザ様疾患 Flu like symptoms	2014-11-15 -	13 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
腎不全 Anuric renal failure	2014-11-25 2014-11-25	23 1	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA

■ Demographics and Baseline Characteristics

- □ Country: United Kingdom
- □ Study site identifier: GB00371
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Male
- □ Baseline weight(kg): -
- □ Baseline height(cm): 179.5
- □ Baseline ECOG score: 0

■ Disposition Information

- □ Treatment discontinuation: 2014-11-29 Adverse Event
- □ Study discontinuation: 2014-11-29 Death
- □ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	120.00	-	2014-11-03	2014-11-17	0.49

■ **NARRATIVE TEXT**

被験者 440017 は，7[redacted]歳の白人男性で，2012 年 3 月 21 日に初めて病期 III（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，便秘及びビタミン B12 欠乏であった。ベースラインの ECOG スコアは 0 であった。両側ヘルニア修復，前立腺腫大，感覚鈍麻（左顔面のしびれ感），心筋梗塞（1982 年）及び頭蓋骨骨折の既往歴を有した。

被験者は 1 レジメンの前治療（シクロホスファミド，デキサメタゾン，レナリドミド及びメルファラン）を受けていた。

治験組入れ時の併用薬は，ポリエチレングリコール，ゾレドロン酸及びヒドロキソコバラミンであった。

ベースラインのヘモグロビン値は 87 g/L（正常範囲：135-175 g/L），好中球数 2.6×10^9/L（正常範囲：$2.5\text{-}7.5\times10^9$/L）及び血小板数 157×10^9/L（正常範囲：$150\text{-}350\times10^9$/L）であった。

Day 13（2014 年 11 月 15 日）に，**非重篤な有害事象の Grade 1 のインフルエンザ様疾患**（記載語：インフルエンザ様症状），Day 16 に**非重篤な有害事象の Grade 1 の咳嗽**が報告された。治験担当医師は，両事象と治験薬との因果関係を「関連なし」と判断した。両事象に対する治療は実施されなかった。Day 18 に，被験者は発熱及び乾性咳嗽に関連する息切れの悪化を訴え，集中治療室に入院した。入院時は平熱で，室内気での酸素飽和度 85%の低酸素性が認められたが，酸素流量 8 L/分で 95%に改善した。身体所見では左下肺に捻髪音を伴う空気取込減少が認められた。胸部 X 線写真では右中肺野の限局性浸潤影及び左肺野全体のびまん性気腔陰影が認められた。臨床検査では，CRP 367，ヘモグロビン値 99，好中球数 1.5，血小板数 97，白血球数 2.0 であった（単位及び正常範囲は未報告）。Day 18 に，**重篤な有害事象の Grade 4 の肺炎**が報告され，治験薬との因果関係は「関連なし」，骨髄腫の合併症と判断された。本事象の病原体は不明であった。本事象のためにレナリドミドを休薬し，デキサメタゾンの投与を中止した。デキサメタゾンの最終投与日は Day 15 であった。被験者の状態は急速に悪化し，低酸素症，頻脈，低血圧及び呼吸不全が認められ，二相性陽圧換気，ノルアドレナリンの投与及び挿管を実施した。凝固障害も認められ，ビタミン K 及び新鮮凍結血漿を投与した。Day 19 に，気管支鏡検査を実施し，気管支肺胞洗浄検査及び胸水培養の結果は陰性であった。被験者の状態は悪化し続け，補助換気の使用が増し，変力薬／昇圧薬も投与した。肺炎に対し酸素，ピペラシリン／タゾバクタム（Tazocin），クラリスロマイシン，メロペネム，カスポファンギン，アシクロビル及びスルファメトキサゾール／トリメトプリム（Bactrim）による治療を実施した。CT スキャンでは，左肺底部及び左上葉に広範囲の浸潤影，肺のその他部位に多発性の小斑状浸潤影，結節及びすりガラス陰影，右側にごく少量の胸水が認められた。Day 21 に，**Grade 3 の頻脈性心房細動**の合併症が発現したため，直流通電除細動を実施し，アミオダロンを投与したところ，洞調律に戻り，本事象は回復した。Day 23 に，**非重篤な有害事象の Grade 4 の腎不全**（記載語：無尿性腎不全）が報告され，持続的静静脈血液濾過透析を開始したところ，本事象は発現日に回復した。治験担当医師は，心房細動及び腎不全と治験薬との因果関係を「関連なし」と判断した。Day 26 の頭部 CT スキャンで脳室拡大及び全脳腫脹を伴うびまん性の急性硬膜下出血が認められたため，保存療法を勧められた。Day 27 に，ECOG スコアが 5 に悪化し，被験者は肺炎のために死亡した。剖検は実施されなかった。

7) 被験者識別番号 480018

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-01-23	2015-08-30	220	2015-08-30	220	ADVERSE EVENT (CARDIAC ARREST)	-

■ **Discontinuation of study treatment due to AE; Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
心停止 Cardiac arrest	2015-08-30 2015-08-30	220 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	NA	-

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
肺炎 Pneumonia	2015-08-02 2015-08-10	192 9	N 2	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
腎機能障害 Renal function impairment	2015-05-22 2015-08-13	120 84	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose reduced	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
上気道感染 Upper respiratory tract infection	2015-05-13 2015-05-18	111 6	N 2	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

■ Demographics and Baseline Characteristics

- □ Country: Poland
- □ Study site identifier: PL00200
- □ Race: White
- □ Age(yrs): 6[redacted]
- □ Sex: Female
- □ Baseline weight(kg): -
- □ Baseline height(cm): 155
- □ Baseline ECOG score: 1

■ Disposition Information

- □ Treatment discontinuation: 2015-08-30 Adverse Event
- □ Study discontinuation: 2015-08-30 Death
- □ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1200.00	3455.00	2015-01-23	2015-08-30	7.23

■ NARRATIVE TEXT

被験者 480018 は，6[redacted] 歳の白人女性で，2010 年 6 月 28 日に初めて病期 III（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症はなかった。ベースラインの ECOG スコアは 1 であった。高血圧の既往歴を有した。スクリーニング時（Day −11）の心電図所見は正常であった。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾンリン酸エステルナトリウム，ドキソルビシン，サリドマイド，ビンクリスチン及び ASCT）を受けていた。

治験組入れ時の併用薬はなかった。

Day 120 に，非重篤な有害事象の Grade 2 の腎機能障害のためにレナリドミドを 25 mg から 10 mg に減量した。治験担当医師は，腎機能障害と治験薬との因果関係を「関連なし」と判断した。Day 148 に，レナリドミドを 25 mg に増量した。

Day 220 に，被験者は突然意識を失い，**重篤な有害事象の心停止**のために自宅で死亡した。剖検は実施されなかった。治験担当医師は，心停止と治験薬との因果関係を「関連なし」と判断した。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 217 及び Day 220 であった。

8) 被験者識別番号 480038

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-03-10	2015-09-15	190	2015-10-05	210	ADVERSE EVENT	-

■ **Discontinuation of study treatment due to AE; and Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺水腫 Pulmonary oedema	2015-10-05T09:00 2015-10-05T10:50	210 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	NA	BACTERIAL (ACINNETOBACTER LOEWFFLI;ENTEROCCOCUA FOECALIS)

■ **Infections and infestations, Grade 3 or 4; and Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
感染 Unspecified infection-	2015-09-07T14:00 -	182 -	Y 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	No

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
間質性肺疾患 Interstitial pneumonia	2015-09-22T14:00 -	197 -	Y 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	BACTERIAL (ACINETOBACTER LWOFFII;ENNEROCOCCUS FOECALIS)

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
骨髄機能不全 Bone marrow aplasia	2015-09-23 -	198 -	Y 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA	-
肝障害 Infiltration in the liver (unspecified)	2015-10-01T06:01 -	206 -	Y 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	NA NOT RECOVERED/NOT RESOLVED	NA	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Aneamia	2015-10-05 -	210 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
貧血 Anemia	2015-09-25 2015-09-25	200 1	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	NA RECOVERED/RESOLVED	NA
呼吸困難 Dyspnoe	2015-10-01 -	206 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
喀血 Hemoptysis	2015-09-22T14:00 2015-10-05	197 14	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	NA RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
高カルシウム血症 Hypercalcemia	2015-09-29 2015-09-29	204 1	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
高血圧 Hypertensio	2015-09-29 2015-10-04	204 6	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
低アルブミン血症 Hypoalbuminemia	2015-09-23 -	198 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
インフルエンザ Flu-lake infection	2015-02-23 2015-03-06	-15 12	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
易刺激性 Irritability	2015-03-10T10:00 -	1 -	N 1	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
無胆汁色素尿性黄疸 Icterus hemolitic	2015-10-04T06:01 -	209 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
筋骨格系胸痛 Pain in the ribs	2015-03-17T10:00 -	8 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
好中球減少症 Neutropenia	2015-09-20 2015-09-25	195 6	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-10-03 -	208 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
発熱 Febris	2015-09-07 -	182 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
傾眠 Somnolentia	2015-03-10T10:00 -	1 -	N 2	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
脊椎痛 Pain in the spine	2015-03-17 -	8 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
血小板減少症 Thrombocytopenia	2015-09-26 -	201 -	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	NA NOT RECOVERED/NOT RESOLVED	NA

■ Demographics and Baseline Characteristics

□ Country: Poland
□ Study site identifier: PL00206
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Female
□ Baseline weight(kg): 68
□ Baseline height(cm): 158
□ Baseline ECOG score: 2

■ Disposition Information

□ Treatment discontinuation: 2015-10-05 Adverse Event

□ Study discontinuation: 2015-10-05 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1120.00	3675.00	2015-03-10	2015-09-15	6.24

■ **NARRATIVE TEXT**

被験者 480038 は，5[redacted] 歳の白人女性で，2014 年 2 月 18 日に初めて病期 II（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，白内障，片側失明及び斜視であった。ベースラインの ECOG スコアは 2 であった。ベースライン（Day 1）の心電図所見は正常で，血圧は 120/70 mm Hg であった。

被験者は 1 レジメンの前治療（シクロホスファミド，デキサメタゾン及びサリドマイド）を受けていた。

治験組入れ時の併用薬は，オメプラゾール及びヘパリンであった。

Day 182（2015 年 9 月 7 日）に，被験者は発熱（39°C，5 日間持続），脱力及び背部痛のために来院した。**非重篤な有害事象の Grade 3 の発熱**及び**重篤な有害事象の Grade 3 の感染**（記載語：詳細不明の感染）が報告され，同日に被験者は入院した。これらの事象に対する治験薬の処置は実施しなかった。Day 180～Day 182 に，感染に対してアモキシシリンを投与した。胸部 X 線写真では炎症の徴候は認められなかった。Day 197 に，**重篤な有害事象の Grade 4 の間質性肺疾患**及び**非重篤な有害事象の Grade 2 の喀血**が報告された。*Acinnetobacter loewffli* 及び *Enterococcus faecalis* が本事象の病原体と報告された。翌日（Day 198），**重篤な有害事象の Grade 4 の骨髄機能不全**（記載語：骨髄無形成）が報告された。同日，疾患進行が認められた。Day 204 に，**非重篤な有害事象の Grade 4 の高カルシウム血症**（同日に回復），Day 206 に，**非重篤な有害事象の Grade 3 の呼吸困難**が報告された。胸部 X 線写真（撮影日不明）では肺炎の所見が認められた。これらの事象に対して paracetamol，セフタジジム，セフェピム，レボフロキサシン，アミカシン，カスポファンギン，アシクロビル，人血清アルブミン，ケトプロフェン，メロペネム，テイコプラニン，スルファメトキサゾール／トリメトプリム（Bactrim）及びヒト免疫グロブリンによる治療を実施した。Day 200 及び Day 201 にそれぞれ報告された貧血及び血小板減少症に対し，Day 200～Day 208 に血小板（計 21 単位）及び濃厚赤血球（計 7 単位）を輸血した。Day 204 に**非重篤な有害事象の Grade 4 の高血圧**，Day 206 に**重篤な有害事象の Grade 4 の肝障害**（記載語：肝臓の浸潤），Day 209 に**非重篤な有害事象の Grade 2 の無胆汁色素尿性黄疸**（記載語：溶血性黄疸）が報告された（ビリルビン値は不明）。高血圧は Day 209，喀血は Day 210 に回復した。同日（Day 210），**重篤な有害事象の肺水腫**と診断された。エナラプリル，ヒドロコルチゾン，ジゴキシン，フロセミド，glyceryl trinitrate，イプラトロピウム，モルヒネ及びテオフィリンによる治療を実施した。CRP 値は 300 mg/L であったが，治療後 100 mg/L に減少した（日付不明）。治療にもかかわらず，被験者の状態は悪化し続け，Day 210 の ECOG スコアは 5，ビリルビン値は

61.047 μmol/L（正常範囲：0.0-20.52 μmol/L）であった。同日，被験者は肺水腫のために死亡した。剖検が実施された（日付不明，データ不明）。レナリドミド及びデキサメタゾンの最終投与日は，それぞれ Day 189 及び Day 190 であった。

治験担当医師は，すべての事象と治験薬との因果関係を「関連なし」と判断した。

死亡時に，感染，間質性肺疾患，骨髄機能不全，呼吸困難，無胆汁色素尿性黄疸，肝障害及び発熱は未回復であった。

9) 被験者識別番号 700040

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-02-17	2015-02-26	10	2015-03-02	14	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
急性呼吸不全 Acute respiratory failure	2015-03-02 2015-03-02	14 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	NA	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気胸 Right-side pneumothorax	2015-02-25T13:00 2015-02-26	9 2	Y 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-
急性呼吸不全 Acute respiratory failure	2015-02-27T16:20 2015-03-02T05:59	11 4	Y 4	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-
急性呼吸不全 Acute respiratory failure	2015-03-02 2015-03-02	14 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	NA	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
播種性血管内凝固 Disseminated intravascular coagulation	2015-03-02 -	14 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA

■ Demographics and Baseline Characteristics

- □ Country: Russia
- □ Study site identifier: RU00183
- □ Race: White
- □ Age(yrs): 5
- □ Sex: Male
- □ Baseline weight(kg): -
- □ Baseline height(cm): 176
- □ Baseline ECOG score: 2

■ **Disposition Information**

□ Treatment discontinuation: 2015-03-02 Adverse Event

□ Study discontinuation: 2015-03-02 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	80.00	250.00	2015-02-17	2015-02-26	0.33

■ **NARRATIVE TEXT**

被験者 700040 は，5[redacted]歳の白人男性で，2013 年 1 月 28 日に初めて病期 II（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，高血圧，動脈硬化症，慢性閉塞性肺疾患及び脂肪性肝炎であった。ベースラインの ECOG スコアは 2 であった。

被験者は 1 レジメンの前治療（ボルテゾミブ，デキサメタゾン，ドキソルビシン及びビンクリスチン）を受けていた。

治験組入れ時の併用薬は，エナラプリル及びクロドロン酸ナトリウムであった。

Day 9（2015 年 2 月 25 日）に，被験者の状態は悪化し，息切れも認められた。同日の胸部 X 線写真で右側の気胸が認められた。**重篤な有害事象の Grade 3 の気胸**が発現し，被験者は集中治療室に入院した。治験担当医師は，本事象とレナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。気胸に対してデキサメタゾンによる治療を実施した。Day 10 に，被験者の状態は安定し，血液内科に移送された。Day 11 に，被験者の状態は再度悪化し，息切れが増加した。同日，**重篤な有害事象の Grade 4 の急性呼吸不全**が報告され，被験者は集中治療室に移送された。Day 14 に，**非重篤な有害事象の Grade 3 の播種性血管内凝固**が報告された。治験担当医師は，これらの事象とレナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。播種性血管内凝固に対する治験薬の処置は実施しなかったが，急性呼吸不全のために治験薬の投与を中止した。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 8 及び Day 10 であった。デキサメタゾン，フロセミド，ドパミン，エノキサパリンナトリウム及び硝酸イソソルビドによる治療を実施した。Day 14 に，被験者は急性呼吸不全のために死亡した。同日の剖検では，両側肺炎，肺水腫，急性呼吸不全，右気胸，急性心血管虚脱，播種性血管内凝固，肺塞栓症及び多臓器不全が報告され，主な死因は基礎疾患の進行であった。

10) 被験者識別番号 886017

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-18	2014-12-24	7	2015-01-04	18	ADVERSE EVENT (Sepsis)	-

■ **Discontinuation of study treatment due to AE and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症 Sepsis	2015-01-04T00:00 2015-01-04T00:00	18 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	NA	Unknown

■ Infections and infestations, Grade 3 or 4

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症 Sepsis	2014-12-24T00:00 2015-01-04T00:00	7 12	Y 4	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	No

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症 Sepsis	2014-12-24T00:00 2015-01-04T00:00	7 12	Y 4	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	No

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2014-12-25T00:00 2015-01-01T00:00	8 8	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
食欲減退 Poor appetite	2014-12-11T00:00 2014-12-16T00:00	-7 6	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
胃食道逆流性疾患 Acid regurgitation	2014-12-22T00:00 2014-12-24T00:00	5 3	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
しゃっくり Hiccup	2014-12-19T00:00 2014-12-24T00:00	2 6	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
不眠症 Insomnia	2014-12-22T00:00 2014-12-24T00:00	5 3	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
ストレス潰瘍 Strees ulcer	2015-01-01T00:00 -	15 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
上気道感染 Upper respiratory infection	2014-12-22T00:00 2014-12-24T00:00	5 3	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

■ Hematology Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	80	2014-12-16/ -2	Screening	80	g/L	135-175	2
Hemoglobin low (anemia)	80	2014-12-25/ 8	Cycle 1 day 8	71	g/L	135-175	3
Hemoglobin low (anemia)	80	2015-01-01/ 15	Cycle 1 day 15	95	g/L	135-175	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (white blood cell decreased)	3.5	2014-12-16/ -2	Screening	3.5	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.5	2014-12-25/ 8	Cycle 1 day 8	4.2	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	3.5	2015-01-01/ 15	Cycle 1 day 15	1	x10E9/L	4.5-11	3
Lymphocytes low (lymphocyte count decreased)	0.65	2014-12-16/ -2	Screening	0.65	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.65	2014-12-25/ 8	Cycle 1 day 8	0.17	x10E9/L	1.5-3.5	4
Lymphocytes low (lymphocyte count decreased)	0.65	2015-01-01/ 15	Cycle 1 day 15	0.14	x10E9/L	1.5-3.5	4
Neutrophils low (neutrophil count decreased)	2.23	2014-12-16/ -2	Screening	2.23	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.23	2015-01-01/ 15	Cycle 1 day 15	0.68	x10E9/L	2.5-7.5	3
Platelets low (platelet count decreased)	236	2015-01-01/ 15	Cycle 1 day 15	122	x10E9/L	150-350	1

■ Demographics and Baseline Characteristics

□ Country: Taiwan
□ Study site identifier: TW00056
□ Race: Asian
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): -
□ Baseline height(cm): 162.5
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2015-01-04 Adverse Event

□ Study discontinuation: 2015-01-04 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	20.00	70.00	2014-12-18	2014-12-24	0.23

■ **NARRATIVE TEXT**

被験者 886017 は，7[redacted]歳のアジア人男性で，2009 年 6 月 1 日に初めて病期 III（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，霧視，高血圧，高血圧性心疾患，聴覚障害，クッシング様症状及び骨粗鬆症であった。ベースラインの ECOG スコアは 1 であった。背部痛，骨痛，白内障，胸部不快感，おとがいしびれ症候群，顔面（おとがい）痛，左下顎の慢性骨髄炎，冷汗，便秘，咳嗽，下痢，浮動性めまい，上腹部痛，感覚鈍麻（両足のしびれ感），発熱，帯状疱疹，関節痛（膝痛），口腔の感覚鈍麻（左唇部分のしびれ感），四肢（左大腿部）痛，口腔内痛，大腿骨骨折（観血的整復を必要とした），口腔カンジダ症，顎骨壊死，大腿骨骨幹部の病的骨折，ヘルペス後神経痛，口腔咽頭痛，歯科手術，白内障手術，歯痛，耳鳴及び上気道感染の既往歴を有した。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，デキサメタゾン，メルファラン，プレドニゾロン及びサリドマイド，レジメン 2 はボルテゾミブ，メルファラン，プレドニゾロン及びサリドマイド，レジメン 3 はシクロホスファミド，プレドニゾロン及びサリドマイドであった。

治験組入れ時の併用薬は，アムロジピン，ペントキシフィリン及びトコフェロールであった。

Day 7（2014 年 12 月 24 日）に，**重篤な有害事象の Grade 4 の敗血症**が報告され，被験者は追加評価及び補助療法のため Day 8 に入院した。徴候及び症状は意識障害，脱力及び発熱（37.5°C）であった。敗血症の病原体は不明であった。治験担当医師は，本事象とレナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。治験薬をまず休薬し，その後，敗血症のために中止した。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 1 及び Day 7 であった。フルマゼニル，モキシフロキサシン，フロモキセフナトリウム，ピペラシリン／タゾバクタム，ラニチジン，トラネキサム酸，テイコプラニン，セフェピム，ドキシサイクリン，エソメプラゾール，炭酸水素ナトリウム，ドパミン並びに電解質及びブドウ糖による治療を実施した。新鮮凍結血漿，濃厚赤血球及び血小板を数単位輸血した。Day 15 に，ヘモグロビン値 95 g/L（正常範囲：135-175 g/L），好中球数 0.68×10^9/L（正常範囲：$2.5\text{-}7.5\times10^9$/L），白血球数 1.0×10^9/L（正常範囲：$4.5\text{-}11\times10^9$/L），リンパ球数 0.14×10^9/L（正常範囲：$1.5\text{-}3.5\times10^9$/L）及び血小板数 122×10^9/L（正常範囲：$150\text{-}350\times10^9$/L）であった。Day 16 から非侵襲性の陽圧換気を開始した。積極的な治療にもかかわらず，被験者の状態は悪化し，蘇生禁止が指示された。Day 18 に，被験者は敗血症のために死亡した。剖検は実施されなかった。

11) 被験者識別番号 972016

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-12-17	2015-01-03	18	2015-01-10	25	ADVERSE EVENT (Pneuminia)	-

■ **Discontinuation of study treatment due to AE and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-01-06 2015-01-09	21 4	Y 4	Not related Not related DOUBTFUL	Not applicable DRUG WITHDRAWN Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	Unknown

■ **Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-01-03T19:07 2015-01-06	18 4	Y 3	Not related Not related DOUBTFUL	Not applicable DRUG INTERRUPTED Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	Unknown
敗血症 Sepsis	2015-01-05 2015-01-06	20 2	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-01-06 2015-01-09	21 4	Y 4	Not related Not related DOUBTFUL	Not applicable DRUG WITHDRAWN Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	Unknown
敗血症性ショック Septic shock	2015-01-08 -	23 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-01-03T19:07 2015-01-06	18 4	Y 3	Not related Not related DOUBTFUL	Not applicable DRUG INTERRUPTED Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	Unknown
肺炎 Pneumonia	2015-01-10 2015-01-10	25 1	Y 5	Not related Not related DOUBTFUL	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y FATAL	NA	Unknown

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
腹痛 Abdominal pain	2014-12-09 2014-12-17	-8 9	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
進行性高血圧 Accelerated hypertension	2014-12-13 2014-12-13	-4 1	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
貧血 Anemia	2015-01-05 -	20 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
心房細動 Atrial fibrilation	2015-01-08 -	23 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
譫妄 Delirium	2015-01-03 -	18 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
うつ病 Depression	2014-12 -	1 -	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
呼吸困難 Dyspnea	2015-01-05 2015-01-06	20 2	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA
呼吸困難 Dyspnea	2015-01-03 2015-01-05	18 3	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
排尿困難 Dysuria	2014-12-09 2014-12-17	-8 9	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
発熱性好中球減少症 Febrile neutropenia	2015-01-03 2015-01-08	18 6	N 3	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
低カルシウム血症 Hypocalcemia	2015-01-04 -	19 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
低血糖症 Hypoglycemia	2015-01-05 2015-01-05	20 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
低カリウム血症 Hypokalemia	2015-01-05 -	20 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
好中球減少症 Neutropenia	2015-01-05 -	20 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
肺炎 Pneumonia	2014-12 2015-01-02	1 17	N 2	Not related Not related DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA
腎不全 Renal failure	2015-01-03 -	18 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
血小板減少症 Trombocytopenia	2015-01-05 -	20 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA

■ Hematology/Chemistry Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (white blood cell decreased)	-	2014-11-30/ -17	Screening	3.83	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	5.03	2015-01-03/ 18	Cycle 1 day 15 unscheduled 1	1.7	x10E9/L	4.5-11	3
Leukocytes low (white blood cell decreased)	5.03	2015-01-05/ 20	Cycle 1 day 15 unscheduled 2	0.97	x10E9/L	4.5-11	4
Leukocytes low (white blood cell decreased)	5.03	2015-01-08/ 23	Cycle 1 day 15 unscheduled 3	2.92	x10E9/L	4.5-11	2
Lymphocytes low (lymphocyte count decreased)	-	2014-11-30/ -17	Screening	1.19	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	1.64	2014-12-25/ 9	Cycle 1 day 8	0.64	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.64	2015-01-01/ 16	Cycle 1 day 15	0.54	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.64	2015-01-03/ 18	Cycle 1 day 15 unscheduled 1	0.5	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	1.64	2015-01-08/ 23	Cycle 1 day 15 unscheduled 3	0.26	x10E9/L	1.5-3.5	3
Neutrophils low (neutrophil count decreased)	-	2014-11-30/ -17	Screening	2.24	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.98	2015-01-03/ 18	Cycle 1 day 15 unscheduled 1	1.1	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	2.98	2015-01-05/ 20	Cycle 1 day 15 unscheduled 2	0.64	x10E9/L	2.5-7.5	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	2.98	2015-01-08/ 23	Cycle 1 day 15 unscheduled 3	2.27	x10E9/L	2.5-7.5	1
Platelets low (platelet count decreased)	-	2014-11-30/ -17	Screening	145	x10E9/L	150-350	1
Platelets low (platelet count decreased)	176	2014-12-25/ 9	Cycle 1 day 8	141	x10E9/L	150-350	1
Platelets low (platelet count decreased)	176	2015-01-01/ 16	Cycle 1 day 15	138	x10E9/L	150-350	1
Platelets low (platelet count decreased)	176	2015-01-03/ 18	Cycle 1 day 15 unscheduled 1	112	x10E9/L	150-350	1
Platelets low (platelet count decreased)	176	2015-01-05/ 20	Cycle 1 day 15 unscheduled 2	75	x10E9/L	150-350	1
Platelets low (platelet count decreased)	176	2015-01-08/ 23	Cycle 1 day 15 unscheduled 3	45	x10E9/L	150-350	3
Urate high (hyperuricemia)	-	2014-11-30/ -17	Screening	416.36	umol/L	136.804-344.984	1

■ Demographics and Baseline Characteristics

□ Country: Israel
□ Study site identifier: IL00066
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Female
□ Baseline weight(kg): -
□ Baseline height(cm): 155
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2015-01-10 Adverse Event

□ Study discontinuation: 2015-01-10 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	120.00	450.00	2014-12-17	2015-01-03	0.59

■ **NARRATIVE TEXT**

被験者 972016 は，6[redacted] 歳の白人女性で，2011 年 9 月 20 日に初めて病期 III（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，うつ病，2 型糖尿病，高脂血症，高血圧，尿失禁，心筋虚血，肥満，骨粗鬆症及び無力症であった。ベースラインの ECOG スコアは 1 であった。深部静脈血栓症，腎結石症及び骨粗鬆症性骨折の既往歴を有した。

治験組入れ時の併用薬は，アスピリン，アムロジピン，ベザフィブラート，エナラプリル，インスリンアスパルト，インスリングラルギン，メトホルミン，オメプラゾール，プラバスタチンナトリウム，ソリフェナシン及び paracetamol／オキシコドン（Tylox）であった。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，レナリドミド，メルファラン，サリドマイド及び ASCT）を受けていた。

ベースラインの CrCL は 79.2 mL/分であった。骨髄穿刺液中の形質細胞の割合は 40%であった。サイクル 1 の Day 1 のヘモグロビン値は 98 g/L（正常範囲：120-160 g/L），白血球数 5.03×10^9/L（正常範囲：4.5-11.0×10^9/L），リンパ球数 1.64×10^9/L（正常範囲：1.5-3.5×10^9/L），好中球数 2.98×10^9/L（正常範囲：2.5-7.5×10^9/L）及び血小板数 176×10^9/L（正常範囲：150-350×10^9/L）であった。サイクル 1 の Day 1 にレナリドミド 25 mg 及びデキサメタゾン 40 mg を投与した。

Day 1 に，**非重篤な有害事象の Grade 2 の肺炎**が報告された。治験担当医師は，本事象とレナリドミドとの因果関係を「多分なし」，デキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。セフロキシムナトリウムによる治療を実施した。Day 18 に，**肺炎は Grade 3 に悪化し，重篤な有害事象**と判断され，被験者は入院した。Day 18 の胸部 X 線写真では右肺に広範囲の浸潤が認められた。同日（Day 18），**非重篤な有害事象の Grade 2 の呼吸困難，Grade 2 の譫妄，Grade 3 の腎不全，Grade 3 の発熱性好中球減少症**が報告された（臨床検査値は上記の表を参照）。体温は 38.5°C であった。治験担当医師は，発熱性好中球減少症とレナリドミドとの因果関係を「ほぼ確実」と判断した以外は，これらの事象と治験薬との因果関係を「関連なし」と判断した。Day 20 に，再度胸部 X 線検査を実施した（結果は未入手）。同日（Day 20），**呼吸困難は Grade 3** に悪化し，**非重篤な有害事象の Grade 3 の敗血症**も報告された。治験担当医師は，敗血症と治験薬との因果関係を「関連なし」と判断した。Day 21 に，気管支鏡検査及び胸部 X 線検査を実施した。呼吸不全が認められた。Day 21 に，**肺炎が重篤な有害事象の Grade 4 に悪化**したため，被験者を集中治療室に移送し，挿管した。治験薬の投与を中止した。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 14 及び Day 18 であった。これらの事象に対し，デキサメタゾン，metamizole sodium，オセルタミビル，レボフロキサシン，paracetamol，フロセミド，フィルグラスチム，ヘパリン，レボフロキサシン，アセチルシステイン，ジアゼパム，ブドウ糖，塩化カリウム，リン酸ナトリウム／リン酸カリウム（Reducto），エスシタロプラム，ヒドロコルチゾン酢酸エステル，イプラトロピウム臭化物，スルファメトキサゾール／トリメトプリム（Bactrim），セフトリアキソンナトリウム，持続的気道陽圧による治療を実施した。呼吸困難は Day 21 に回復した。入院期間中，被験者の状態は更に悪化し，急性腎不全も発現し，Day 22 に

透析を実施した。Day 23 に，**非重篤な有害事象の Grade 3 の敗血症性ショック**が報告された。Day 23 の臨床検査では，ヘモグロビン値 95 g/L，白血球数 2.92×10^9/L，リンパ球数 0.26×10^9/L，好中球数 2.27×10^9/L 及び血小板数 45×10^9/L であった。治験担当医師は，本事象と治験薬との因果関係を「関連なし」と判断した。Day 23 から Day 25 まで胸部 X 線検査を繰り返し実施した。Day 25 に，心肺蘇生及び透析を実施した。被験者は補助療法に反応せず，多臓器不全が認められた。Day 25 に，被験者は肺炎のために死亡した。剖検は実施されなかった。

12) 被験者識別番号 972038

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death
2015-02-02	2015-02-24	23	2015-03-05	32	ADVERSE EVENT (Acute kidney injury)

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
背部痛 Back pain	2015-02-04 2015-02-09	3 6	Y 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-NA
錯乱状態 Severe confusion	2015-02-19 -	18 -	Y 4	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
急性腎不全 Acute renal failure	2015-02-24 2015-03-04	23 9	Y 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	NA
急性腎不全 Acute renal failure	2015-03-05 2015-03-05	32 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	N	NA

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-02-20 2015-02-23	19 4	N 3	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
背部痛 Back pain	2015-02-01 2015-02-02	-1 2	Y 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
悪寒 Chills	2015-02-18 2015-02-18	17 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
発熱性好中球減少症 Febrile neutropenia	2015-02-19 2015-02-19	18 1	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
高リン酸塩血症 Hyperphosphatemia	2015-02-26 -	25 -	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
低カルシウム血症 Hypocalcemia	2015-02-21 2015-02-23	20 3	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
筋骨格痛 Shoulder pain	2015-02-10 -	9 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
好中球減少症 Neutropenia	2015-02-17 2015-02-23	16 7	N 3	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
嚥下痛 Pain in swallowing	2015-02-17 2015-02-22	16 6	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
血小板減少症 Trombocytopenia	2015-02-17 -	16 -	N 4	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
血小板減少症 Trombocytopenia	2015-02-05 2015-02-07	4 3	N 2	Not related Not related VERY LIKELY	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA

■ **Hematology/Chemistry Abnormalities**

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Albumin low (hypoalbumine-mia)	40	2015-02-21/ 20	Cycle 1 day 15 unscheduled 3	25	g/L	36-55	2
Albumin low (hypoalbumine-mia)	40	2015-02-24/ 23	Cycle 1 day 22	23	g/L	36-55	2
Albumin low (hypoalbumine-mia)	40	2015-02-26/ 25	Cycle 1 day 22 unscheduled 1	24	g/L	36-55	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Albumin low (hypoalbumine-mia)	40	2015-03-02/ 29	End of treatment	26	g/L	36-55	2
Albumin low (hypoalbumine-mia)	40	2015-03-02/ 29	End of treatment	21	g/L	33-49	2
Creatinine high (creatinine increased)	57.46	2015-02-24/ 23	Cycle 1 day 22	233.376	umol/L	70.72- 106.08	2
Creatinine high (creatinine increased)	57.46	2015-02-26/ 25	Cycle 1 day 22 unscheduled 1	356.252	umol/L	70.72- 106.08	3
Creatinine high (creatinine increased)	57.46	2015-03-02/ 29	End of treatment	362.44	umol/L	70.72- 106.08	3
Neutrophils low (neutrophil count decreased)	12.7	2015-02-17/ 16	Cycle 1 day 15	0.85	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	12.7	2015-02-19/ 18	Cycle 1 day 15 unscheduled 1	0.45	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	12.7	2015-02-20/ 19	Cycle 1 day 15 unscheduled 2	0.53	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	12.7	2015-02-23/ 22	Cycle 1 day 22	2.03	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	12.7	2015-03-02/ 29	End of treatment	1.91	x10E9/L	2.5-7.5	1
Potassium low (hypokalemia)	4.2	2015-02-21/ 20	Cycle 1 day 15 unscheduled 3	2.8	mmol/L	3.5-5.2	3
Potassium high (hyperkalemia)	4.2	2015-02-26/ 25	Cycle 1 day 22 unscheduled 1	5.3	mmol/L	3.5-5.2	1
Sodium low (hyponatremia)	132	2015-02-01/ -1	Cycle 1 day 1	132	mmol/L	136-148	1
Sodium low (hyponatremia)	132	2015-03-02/ 29	End of treatment	133	mmol/L	136-148	1
Urate high (hyperuricemia)	303.348	2015-02-26/ 25	Cycle 1 day 22 unscheduled 1	529.372	umol/L	208.18- 428.256	1
Urate high (hyperuricemia)	303.348	2015-03-02/ 29	End of treatment	612.644	umol/L	208.18- 428.256	4

■ **Demographics and Baseline Characteristics**

□ Country: Israel
□ Study site identifier: IL00067
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Male
□ Baseline weight(kg): -
□ Baseline height(cm): 174
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-03-04 Progressive Disease

□ Study discontinuation: 2015-03-05 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	160.00	400.00	2015-02-02	2015-02-24	0.76

■ **NARRATIVE TEXT**

被験者 972038 は，5[redacted] 歳の白人男性で，2013 年 4 月 23 日に初めて病期 I（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，筋骨格系胸痛，血小板減少症及び無力症であった。ベースラインの ECOG スコアは 0 であった。

治験組入れ時の併用薬はフェンタニルであった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド及びデキサメタゾン，レジメン 2 はシスプラチン，シクロホスファミド，デキサメタゾン，ドキソルビシン，エトポシド及びサリドマイドであった。被験者はレジメン 1 及び 2 に対して治療抵抗性を示した。

Day −1（2015 年 2 月 1 月）に，被験者は**重篤な有害事象の Grade 2 の背部痛**のために入院した。全骨格検査では，本事象は古い溶骨性骨病変が原因であることが示された。フェンタニルによる治療を実施した。本事象は Day 1 に回復し，被験者は退院した。Day 3 に，被験者は**重篤な有害事象の Grade 3 の背部痛**の再発のために再入院した。Day 4〜Day 10 に，放射線療法を施行した。モルヒネ及びパミドロン酸二ナトリウムによる治療も実施した。背部痛は Day 8 に回復し，被験者は退院した。治験担当医師は，背部痛と治験薬との因果関係を「関連なし」と判断した。これらの事象に対する治験薬の処置は実施しなかった。

Day 18 に，体温が 38°C で，**非重篤な有害事象の Grade 3 の発熱性好中球減少症**（臨床検査値は上記の表を参照）及び**重篤な有害事象の Grade 4 の錯乱状態**が認められ，被験者は入院した。治験担当医師は，両事象と治験薬との因果関係を「関連なし」と判断した。両事象のためにレナリドミドを休薬した。レナリドミドの事象発現前の投与日は Day 16 であった。デキサメタゾンの処置は実施しなかった。両事象に対しフィルグラスチム，アシクロビル，ヒドロコルチゾンコハク酸エステルナトリウム，オセルタミビル，バンコマイシン，フルコナゾール，ピペラシリン／タゾバクタム（Tazocin）及び塩化ナトリウムによる治療を実施した。発熱性好中球減少症は発現日（Day 18）に回復した。Day 23 に，**重篤な有害事象の Grade 4 の急性腎不全**が報告された（臨床検査値は上記の表を参照）。同期間中に遊離軽鎖値増加による疾患進行が認められた（Day 16 に最初の所見，その後 Day 24 に確認）。治験担当医師は，**急性腎不全**と治験薬との因果関係を「関連なし」と判断した。Day 24 に，腎臓及び尿路の超音波検査を実施した（結果は未入手）。本事象に対しフロセミドによる治療を実施した。Day 29 に，腎機能パラメータは更に悪化し，ECOG スコアも 4 に悪化した。Day 31 に，疾患進行のために治験薬の投与を中止した。レナリドミド及びデキサメタゾンの最終投与日は，それぞれ Day 16 及び Day 23 であった。Day 31 に，被験者は退院した。Day 32 に，被験者は急性腎不全及び疾患進行のために死亡した。剖検は実施されなかった。

死亡時に，錯乱状態は未回復であった。

2.7.6.1.3.2　治験薬と関連性がある重篤な有害事象（日本人被験者）

(1) DRd 群

1) 被験者識別番号 810003

■ **REASON FOR NARRATIVE SELECTION**

Serious AEs

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
塞栓症 Thromboembolic event	2015-04-30 2015-05-19	44 20	Y 2	Not related Possible PROBABLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-
塞栓症 Thromboembolic event	2015-05-19 2015-05-24	63 6	Y 1	Not related Possible PROBABLE	Dose not changed DOSE NOT CHANGED Dose reduced	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
血中クレアチンホスホキナーゼ増加 CPK increased	2016-02-03T08:23 2016-03-02T09:21	323 29	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
疲労 Fatigue	2015-08-23 -	159 -	N 2	Not related Probable NOT RELATED	Dose not changed DOSE REDUCED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
鼻咽頭炎 Common cold	2015-10-24 2015-10-26	221 3	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	Y
鼻咽頭炎 Common cold	2016-01-23 2016-01-26	312 4	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	Y

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-03-23 2015-03-25	6 3	N 3	Possible Not related PROBABLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-05-07 2015-05-20	51 14	N 3	Possible Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-04-08 2015-04-15T08:49	22 8	N 3	Possible Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血栓性静脈炎 Thrombotic phlebitis	2015-05-19 2015-05-24	63 6	N 1	Not related Possible PROBABLE	Dose not changed DOSE NOT CHANGED Dose reduced	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血栓性静脈炎 Thrombotic phlebitis	2015-05-04 2015-05-19	48 16	N 2	Not related Possible PROBABLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Demographics and Baseline Characteristics

□ Country: Japan
□ Study site identifier: JP91223
□ Race: Asian
□ Age(yrs): 4[redacted]
□ Sex: Male
□ Baseline weight(kg): 71.9
□ Baseline height(cm): 166.5
□ Baseline ECOG score: 0

■ Disposition Information

□ Treatment discontinuation: Subject Ongoing on Treatment

□ Study discontinuation: Subject Ongoing on Study

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
362.07	1396.40	4190.00	2015-03-18	2016-03-10	11.79

■ **NARRATIVE TEXT**

被験者 810003 は，4[redacted]歳のアジア人男性で，2010 年 10 月に初めて病期 I（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は 1 レジメンの前治療（シクロホスファミド，デキサメタゾン，ドキソルビシン，メルファラン，ビンクリスチン及び ASCT）を受けていた。

Day 44（2015 年 4 月 30 日）に，左前腕及び上腕の腫脹並びに**重篤な有害事象の Grade 2 の塞栓症**（記載語：血栓塞栓症）が報告された。Day 48 に，**非重篤な有害事象の Grade 2 の血栓性静脈炎**が報告され，被験者は入院した。同日の CT スキャンでは左尺側皮静脈の異常が認められた。入院時の臨床検査では，フィブリン分解産物高値（44.7 mcg/mL）及び D ダイマー高値（23.8 mcg/mL，正常範囲：不明）が認められた。治験担当医師は，塞栓症及び血栓性静脈炎とデキサメタゾンとの因果関係を「可能性小」，レナリドミドとの因果関係を「可能性大」，本剤との因果関係を「関連なし」と判断した。これらの事象のために治験薬を休薬した。本剤，デキサメタゾン及びレナリドミドの事象発現前の投与日は，それぞれ Day 43，Day 44 及び Day 47 であり，次サイクル（サイクル 3）の開始を延期した。ダルテパリンナトリウム，ヘパリン，アセトアミノフェン，ドリペネム及びトラマドールによる治療を実施した。

Day 63 に，**塞栓症及び血栓性静脈炎は Grade 1 に改善した。**サイクル 3 は Day 64 に開始したが，塞栓症及び血栓性静脈炎のためにレナリドミドの投与量を 15 mg に減量した。塞栓症に対しエドキサバンによる治療を実施し，血栓性静脈炎に対する治療は実施しなかった。Day 64 に ECOG スコアは 1 に悪化した。塞栓症及び血栓性静脈炎は Day 68 に回復し，被験者は退院した。

Day 92 に，ECOG スコアは 0 に改善した。

非重篤な有害事象の Grade 2 の疲労のために，デキサメタゾンの投与量をサイクル 7 から 20 mg/週に減量した。

非重篤な有害事象の Grade 1 の鼻咽頭炎 2 件が Day 221 及び Day 312 に報告され，それぞれ Day 223 及び Day 315 に回復した。治験担当医師は，本事象は IRR と判断したが，本剤，レナリドミド又はデキサメタゾンとの因果関係を「関連なし」と判断した。両事象に対する治験薬の処置は実施しなかった。葛根湯による治療を実施した。

Day 323 に，ECOG スコアは再度 1 に悪化した。

本報告書（クリニカルカットオフ日の 2016 年 3 月 7 日時点）では，被験者は治験薬の投与継続中であった。

2) 被験者識別番号 810016

■ **REASON FOR NARRATIVE SELECTION**

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Infections and infestations, Grade 3 or 4; Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pheumonia	2015-11-08 2015-12-28	200 51	Y 3	Doubtful Probable NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	No

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-11-12 -	204 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
貧血 Anemia	2015-10-15 2015-11-12	176 29	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
貧血 Anemia	2015-06-29 2015-10-15	68 109	N 3	Not related Not related VERY LIKELY	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
便秘 Constipaion	2015-11-15 2015-11-15	207 1	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
褥瘡性潰瘍 Decubitus(back)	2015-11-12 2015-11-18	204 7	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
しゃっくり Hiccups	2015-04-23T10:30 -	1 -	N 1	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-07-06 2015-07-16	75 11	N 3	Not related Very likely VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-06-11 2015-06-15	50 5	N 3	Not related Very likely VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-05-07 2015-05-25	15 19	N 3	Not related Very likely VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-06-01 2015-06-08	40 8	N 3	Not related Very likely VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-06-08 2015-06-11	47 4	N 4	Not related Very likely VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-11-16 2015-11-19	208 4	N 3	Not related Very likely NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
鼻咽頭炎 Common cold	2015-08-12 2015-08-19	112 8	N 1	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-06-08 2015-06-15	47 8	N 4	Doubtful Not related VERY LIKELY	Drug interrupted DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-05-07 2015-05-14	15 8	N 3	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-11-24 2015-12-03	216 10	N 3	Doubtful Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-11-16 2015-11-19	208 4	N 3	Doubtful Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-10-01 2015-11-12	162 43	N 3	Doubtful Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-07-16 2015-07-17	85 2	N 3	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-06-15 2015-06-29	54 15	N 3	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
好中球減少症 Neutropenia	2015-07-30 2015-09-17	99 50	N 3	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好中球減少症 Neutropenia	2015-05-14 2015-05-25	22 12	N 4	Doubtful Not related VERY LIKELY	Drug interrupted DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
発熱 Fever	2015-11-12 2015-11-15	204 4	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-06-11 2015-07-30	50 50	N 3	Doubtful Not related VERY LIKELY	Drug interrupted DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-05-14 2015-06-08	22 26	N 3	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-07-30 2015-09-17	99 50	N 4	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-10-15 2015-11-12	176 29	N 4	Doubtful Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-11-12 2015-11-16	204 5	N 3	Doubtful Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
血小板減少症 Thrombocytopenia	2015-06-08 2015-06-11	47 4	N 4	Doubtful Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-11-19 -	211 -	N 3	Doubtful Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
血小板減少症 Thrombocytopenia	2015-09-17 2015-10-15	148 29	N 3	Doubtful Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
血小板減少症 Thrombocytopenia	2015-11-16 2015-11-19	208 4	N 4	Doubtful Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
上気道感染 Upper respiratory tract infection	2015-09-16 2015-09-25	147 10	N 2	Not related Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Hematology Abnormalities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	-	2015-04-02/ -21	Screening	119	g/L	135-175	1
Hemoglobin low (anemia)	118	2015-04-22/ -1	Cycle 1 day 1	118	g/L	135-175	1
Hemoglobin low (anemia)	118	2015-04-30/ 8	Cycle 1 day 8	117	g/L	135-175	1
Hemoglobin low (anemia)	118	2015-05-07/ 15	Cycle 1 day 15	117	g/L	135-175	1
Hemoglobin low (anemia)	118	2015-05-14/ 22	Cycle 1 day 22	108	g/L	135-175	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	118	2015-05-21/ 29	Cycle 2 day 1	110	g/L	135-175	1
Hemoglobin low (anemia)	118	2015-05-25/ 33	Cycle 2 day 1 unscheduled 1	103	g/L	135-175	1
Hemoglobin low (anemia)	118	2015-06-01/ 40	Cycle 2 day 9 unscheduled 1	97	g/L	135-175	2
Hemoglobin low (anemia)	118	2015-06-08/ 47	Cycle 2 day 16 unscheduled 1	93	g/L	135-175	2
Hemoglobin low (anemia)	118	2015-06-11/ 50	Cycle 2 day 22	83	g/L	135-175	2
Hemoglobin low (anemia)	118	2015-06-15/ 54	Cycle 2 day 22 unscheduled 1	85	g/L	135-175	2
Hemoglobin low (anemia)	118	2015-06-18/ 57	Cycle 3 day 1	86	g/L	135-175	2
Hemoglobin low (anemia)	118	2015-06-29/ 68	Cycle 3 day 8 unscheduled 1	71	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-07-06/ 75	Cycle 3 day 16 unscheduled 1	70	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-07-16/ 85	Cycle 4 day 1	64	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-07-17/ 86	Cycle 4 day 2	59	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-07-30/ 99	Cycle 4 day 15	77	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-08-13/ 113	Cycle 4 day 22 unscheduled 1	58	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-08-20/ 120	Cycle 5 day 1	74	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-09-03/ 134	Cycle 5 day 15	64	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-09-17/ 148	Cycle 6 day 1	63	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-10-01/ 162	Cycle 6 day 15	69	g/L	135-175	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	118	2015-10-15/ 176	Cycle 7 day 1	83	g/L	135-175	2
Hemoglobin low (anemia)	118	2015-11-12/ 204	Cycle 7 day 22 unscheduled 1	55	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-11-16/ 208	Cycle 7 day 22 unscheduled 2	71	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-11-19/ 211	Cycle 7 day 22 unscheduled 3	75	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-11-24/ 216	Cycle 7 day 22 unscheduled 4	76	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-11-26/ 218	End of treatment	71	g/L	135-175	3
Hemoglobin low (anemia)	118	2015-12-03/ 225	End of treatment unscheduled 1	67	g/L	135-175	3
Lymphocytes low (lymphocyte count decreased)	-	2015-04-02/ -21	Screening	0.67	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-04-22/ -1	Cycle 1 day 1	0.93	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-04-30/ 8	Cycle 1 day 8	0.56	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-05-07/ 15	Cycle 1 day 15	0.38	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.93	2015-05-14/ 22	Cycle 1 day 22	0.45	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.93	2015-05-21/ 29	Cycle 2 day 1	0.48	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.93	2015-05-25/ 33	Cycle 2 day 1 unscheduled 1	0.52	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-06-01/ 40	Cycle 2 day 9 unscheduled 1	0.28	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.93	2015-06-08/ 47	Cycle 2 day 16 unscheduled 1	0.18	x10E9/L	1.5-3.5	4
Lymphocytes low (lymphocyte count decreased)	0.93	2015-06-11/ 50	Cycle 2 day 22	0.29	x10E9/L	1.5-3.5	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low (lymphocyte count decreased)	0.93	2015-06-15/ 54	Cycle 2 day 22 unscheduled 1	0.54	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-06-18/ 57	Cycle 3 day 1	0.53	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-06-29/ 68	Cycle 3 day 8 unscheduled 1	0.531	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-07-06/ 75	Cycle 3 day 16 unscheduled 1	0.47	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.93	2015-07-16/ 85	Cycle 4 day 1	0.961	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-07-17/ 86	Cycle 4 day 2	0.576	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-07-30/ 99	Cycle 4 day 15	0.7	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-08-13/ 113	Cycle 4 day 22 unscheduled 1	0.51	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-08-20/ 120	Cycle 5 day 1	0.9	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-09-03/ 134	Cycle 5 day 15	1.42	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-09-17/ 148	Cycle 6 day 1	0.63	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-10-01/ 162	Cycle 6 day 15	0.97	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-10-15/ 176	Cycle 7 day 1	0.77	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.93	2015-11-12/ 204	Cycle 7 day 22 unscheduled 1	1.1	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-11-16/ 208	Cycle 7 day 22 unscheduled 2	0.31	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.93	2015-11-19/ 211	Cycle 7 day 22 unscheduled 3	0.87	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-11-24/ 216	Cycle 7 day 22 unscheduled 4	1.16	x10E9/L	1.5-3.5	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low (lymphocyte count decreased)	0.93	2015-11-26/ 218	End of treatment	1.25	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.93	2015-12-03/ 225	End of treatment unscheduled 1	0.87	x10E9/L	1.5-3.5	1
Neutrophils low (neutrophil count decreased)	-	2015-04-02/ -21	Screening	1.52	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.03	2015-04-22/ -1	Cycle 1 day 1	1.03	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-04-30/ 8	Cycle 1 day 8	1.45	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-05-07/ 15	Cycle 1 day 15	0.87	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-05-14/ 22	Cycle 1 day 22	0.16	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.03	2015-05-21/ 29	Cycle 2 day 1	0.45	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.03	2015-05-25/ 33	Cycle 2 day 1 unscheduled 1	1.17	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-06-01/ 40	Cycle 2 day 9 unscheduled 1	1.16	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-06-08/ 47	Cycle 2 day 16 unscheduled 1	0.24	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.03	2015-06-11/ 50	Cycle 2 day 22	0.45	x10E9/L	2.5-7.5	4
Neutrophils low (neutrophil count decreased)	1.03	2015-06-15/ 54	Cycle 2 day 22 unscheduled 1	0.77	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-06-18/ 57	Cycle 3 day 1	0.64	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-06-29/ 68	Cycle 3 day 8 unscheduled 1	1.012	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-07-06/ 75	Cycle 3 day 16 unscheduled 1	1.833	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.03	2015-07-16/ 85	Cycle 4 day 1	0.641	x10E9/L	2.5-7.5	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils low (neutrophil count decreased)	1.03	2015-07-17/ 86	Cycle 4 day 2	1.08	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-07-30/ 99	Cycle 4 day 15	0.53	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-08-13/ 113	Cycle 4 day 22 unscheduled 1	0.83	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-08-20/ 120	Cycle 5 day 1	0.63	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-09-03/ 134	Cycle 5 day 15	0.85	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-09-17/ 148	Cycle 6 day 1	1.82	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.03	2015-10-01/ 162	Cycle 6 day 15	0.75	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-10-15/ 176	Cycle 7 day 1	0.75	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-11-12/ 204	Cycle 7 day 22 unscheduled 1	1.34	x10E9/L	2.5-7.5	2
Neutrophils low (neutrophil count decreased)	1.03	2015-11-16/ 208	Cycle 7 day 22 unscheduled 2	0.75	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-11-19/ 211	Cycle 7 day 22 unscheduled 3	0.99	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-11-24/ 216	Cycle 7 day 22 unscheduled 4	0.94	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-11-26/ 218	End of treatment	0.7	x10E9/L	2.5-7.5	3
Neutrophils low (neutrophil count decreased)	1.03	2015-12-03/ 225	End of treatment unscheduled 1	2.23	x10E9/L	2.5-7.5	1
Platelets low (platelet count decreased)	-	2015-04-02/ -21	Screening	120	x10E9/L	150-350	1
Platelets low (platelet count decreased)	93	2015-04-22/ -1	Cycle 1 day 1	93	x10E9/L	150-350	1
Platelets low (platelet count decreased)	93	2015-04-30/ 8	Cycle 1 day 8	82	x10E9/L	150-350	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	93	2015-05-07/ 15	Cycle 1 day 15	50	x10E9/L	150-350	2
Platelets low (platelet count decreased)	93	2015-05-14/ 22	Cycle 1 day 22	37	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-05-21/ 29	Cycle 2 day 1	49	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-05-25/ 33	Cycle 2 day 1 unscheduled 1	40	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-06-01/ 40	Cycle 2 day 9 unscheduled 1	32	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-06-08/ 47	Cycle 2 day 16 unscheduled 1	22	x10E9/L	150-350	4
Platelets low (platelet count decreased)	93	2015-06-11/ 50	Cycle 2 day 22	25	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-06-15/ 54	Cycle 2 day 22 unscheduled 1	27	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-06-18/ 57	Cycle 3 day 1	25	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-06-29/ 68	Cycle 3 day 8 unscheduled 1	36	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-07-06/ 75	Cycle 3 day 16 unscheduled 1	37	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-07-16/ 85	Cycle 4 day 1	33	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-07-17/ 86	Cycle 4 day 2	26	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-07-30/ 99	Cycle 4 day 15	20	x10E9/L	150-350	4
Platelets low (platelet count decreased)	93	2015-08-13/ 113	Cycle 4 day 22 unscheduled 1	17	x10E9/L	150-350	4
Platelets low (platelet count decreased)	93	2015-08-20/ 120	Cycle 5 day 1	14	x10E9/L	150-350	4
Platelets low (platelet count decreased)	93	2015-09-03/ 134	Cycle 5 day 15	23	x10E9/L	150-350	4

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	93	2015-09-17/ 148	Cycle 6 day 1	26	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-10-01/ 162	Cycle 6 day 15	25	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-10-15/ 176	Cycle 7 day 1	22	x10E9/L	150-350	4
Platelets low (platelet count decreased)	93	2015-11-12/ 204	Cycle 7 day 22 unscheduled 1	31	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-11-16/ 208	Cycle 7 day 22 unscheduled 2	23	x10E9/L	150-350	4
Platelets low (platelet count decreased)	93	2015-11-19/ 211	Cycle 7 day 22 unscheduled 3	26	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-11-24/ 216	Cycle 7 day 22 unscheduled 4	27	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-11-26/ 218	End of treatment	31	x10E9/L	150-350	3
Platelets low (platelet count decreased)	93	2015-12-03/ 225	End of treatment unscheduled 1	33	x10E9/L	150-350	3

■ Demographics and Baseline Characteristics

□ Country: Japan
□ Study site identifier: JP91743
□ Race: Asian
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): 60.9
□ Baseline height(cm): 158.7
□ Baseline ECOG score: 0

■ Disposition Information

□ Treatment discontinuation: 2015-11-25 Physician Decision

□ Study discontinuation: Subject Ongoing on Study

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
218.82	1117.40	505.00	2015-04-23	2015-11-05	6.47

■ **NARRATIVE TEXT**

被験者 810016 は，7[redacted]歳のアジア人男性で，2008 年 6 月 23 日に初めて病期 I（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，高血圧，左脚ブロック，末梢性浮腫，好中球減少症及び末梢性ニューロパチーであった。ベースラインの ECOG スコアは 0 であった。慢性 B 型肝炎及び深部静脈血栓症の既往歴を有した。

被験者は合計 6 レジメンの前治療を受けていた。レジメン 1 はシクロホスファミド，デキサメタゾン，ドキソルビシン，メルファラン，ビンクリスチン及び ASCT，レジメン 2 及びレジメン 3 はボルテゾミブ及びデキサメタゾン，レジメン 4 はボルテゾミブ，デキサメタゾン及びドキソルビシン，レジメン 5 はボルテゾミブ，デキサメタゾン及びサリドマイド，レジメン 6 はボルテゾミブ，シクロホスファミド，デキサメタゾン，メルファラン及びサリドマイドであった。被験者はレジメン 3，4，5 及び 6 に対して治療抵抗性を示した。

治験組入れ時の併用薬は，アシクロビル，アムロジピン，スルファメトキサゾール／トリメトプリム（Bactrim），エンテカビル水和物及びワルファリンであった。

Day 15～Day 208 に**非重篤な有害事象の Grade 3～4 のリンパ球減少症**，Day 15～Day 216 に **Grade 3～4 の好中球減少症**が複数回発現した（臨床検査値は上記の表を参照）。治験担当医師は，好中球減少症と本剤との因果関係を「多分なし」，デキサメタゾンとの因果関係を「関連なし」，レナリドミドとの因果関係を「ほぼ確実」（Day 162，Day 208 及び Day 216 は「関連なし」）と判断した。また，リンパ球減少症と本剤との因果関係を「関連なし」，デキサメタゾン及びレナリドミドとの因果関係を「ほぼ確実」（Day 208 のレナリドミドとの因果関係は「関連なし」）と判断した。好中球減少症のために，Day 22，Day 29 及び Day 50 に本剤を休薬し，Day 15～Day 21，Day 29～Day 35，Day 48～Day 49，Day 57～Day 70 にレナリドミドを休薬し，その後（サイクル 4 以降）も引き続き休薬した。好中球減少症のためにフィルグラスチムによる治療を実施した。

レナリドミドの投与量は，Day 36～Day 47 は CrCL（54.8 mL/分）のために 10 mg に減量し，Day 71～Day 77 はその他の毒性のために治験実施計画書に従い 5 mg に減量した。

Day 112 に，**非重篤な有害事象の Grade 1 の鼻咽頭炎**（記載語：感冒）が報告され，治験薬との因果関係は「関連なし」と判断された。本事象のために治験薬を休薬し，サイクル 5 の開始を延期した。レボフロキサシンによる治療を実施した。本事象は Day 119 に回復し，Day 120 にサイクル 5 を開始した。

Day 147 に，**非重篤な有害事象の Grade 2 の上気道感染**が報告され，治験薬との因果関係は「関連なし」と判断された。本事象のために，Day 148 の本剤を休薬し，レナリドミドは引き続き休薬した。セファレキシン及び漢方薬（葛根湯）による治療を実施した。本事象は Day 156 に回復した。

Day 200 に，**重篤な有害事象の Grade 3 の肺炎**が報告された。被験者は鼻詰まり感を訴え，Day 204 に入院した。入院時に，咳嗽，右背側の軽度ラ音，咽頭に軽度の発赤が認められ，血圧 91/60 mm Hg，脈拍数 136 bpm，酸素飽和度 88%であった。同日（Day 204）に，**非重篤な有害事象の Grade 1 の発**

熱（体温：38°C）が報告された。本事象の病原体は報告されなかった。治験担当医師は，肺炎とデキサメタゾンとの因果関係を「可能性大」，本剤との因果関係を「多分なし」，レナリドミドとの因果関係を「関連なし」と判断し，発熱と治験薬との因果関係を「関連なし」と判断した。Day 204 の臨床検査では，CRP 25.34 mg/dL（正常範囲：0.0-0.18 mg/dL），IgM 1132.1 mg/dL（正常範囲：33-190 g/dL），ヘマトクリット 16.9%（正常範囲：40.4-51.1%），ヘモグロビン値 55 g/L（Day 204 に非重篤な有害事象の Grade 3 の貧血として報告された）であった（その他の臨床検査値は上記の表を参照）。同日の CT スキャンでは両肺の内側底区に浸潤性陰影が認められた。アセトアミノフェン，セフトリアキソンナトリウム，アミノ酸／電解質／ブドウ糖（ビーフリード），ビタミン B 複合体，ビサコジル及び酸素吸入による治療を実施した。濃厚赤血球も数単位輸血した。発熱は Day 207 に回復した。Day 208 の臨床検査では CRP 5.82 mg/dL，ヘマトクリット 21.2%であった（その他の臨床検査値は上記の表を参照）。

リンパ球減少症は Day 211 に回復した。

肺炎のために医師の判断に従い，Day 217 に治験薬の投与を中止した。レナリドミド，本剤及びデキサメタゾンの最終投与日は，それぞれ Day 77，Day 176 及び Day 197 であった。

Day 218 の ECOG スコアは 2 に悪化した。

Day 225 に好中球減少症，Day 250 に肺炎が回復した。Day 252 に，被験者は退院した。

本報告書（クリニカルカットオフ日の 2016 年 3 月 7 日時点）では，被験者の生存状況を追跡調査中であった。

3) 被験者識別番号 810020

■ REASON FOR NARRATIVE SELECTION

Infections and infestations, Grade 3 or 4

Serious AEs

■ Infections and infestations, Grade 3 or 4 and Serious AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
細菌感染 Bacterial infection	2015-05-11 2015-05-25	14 15	Y 3	Probable Probable PROBABLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
低酸素症 Hypoxia	2015-06-27 2015-07-06	61 10	Y 1	Probable Probable PROBABLE	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
口唇炎 Angular stomatitis	2015-04-23 2015-04-26	-5 4	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
便秘 Constipation	2015-04-14 -	-14 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
皮膚乾燥 Dry skin	2015-05-25 2015-05-28	28 4	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
皮膚乾燥 Dry skin	2015-11-10 -	197 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
味覚異常 Dysgeusia	2015-06-23 -	57 -	N 1	Not related Very likely POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
呼吸困難 Dyspnoea	2015-04-28T11:15 2015-04-28T12:45	1 1	N 1	Probable Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	Y
呼吸困難 Shortness of breath	2015-11-26 -	213 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
ウイルス性腸炎 Enterocolitis viral	2015-10-17 2015-11-19	173 34	N 1	Not related Not related NOT RELATED	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好酸球増加症 Eosinophilia	2015-06-15 2015-06-22	49 8	N 1	Doubtful Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
好酸球増加症 Eosinophilia	2015-07-13 2015-07-21	77 9	N 1	Doubtful Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
しゃっくり Hiccups	2015-05-07 2015-05-08	10 2	N 2	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
しゃっくり	2015-06-10	44	N	Not related	Dose not changed	Daratumumab	Y	N
Hiccups	2015-06-10	1	2	Very likely NOT RELATED	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	
しゃっくり	2015-04-29	2	N	Not related	Dose not changed	Daratumumab	Y	N
Hiccups	2015-04-29	1	2	Very likely NOT RELATED	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	
高血糖	2016-01-20	268	N	Not related	Dose not changed	Daratumumab	N	N
Hyperglycemia	-	-	1	Not related NOT RELATED	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	NOT RECOVERED/NOT RESOLVED	
低リン酸血症	2015-11-09	196	N	Not related	Dose not changed	Daratumumab	N	N
Hypophosphatemia	2015-12-07	29	3	Not related NOT RELATED	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	
低リン酸血症	2016-02-29	308	N	Not related	Dose not changed	Daratumumab	N	N
Hypophosphatemia	-	-	3	Not related NOT RELATED	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	NOT RECOVERED/NOT RESOLVED	
リンパ球減少症	2015-06-15	49	N	Probable	Dose not changed	Daratumumab	N	N
Lymphocyte count decreased	2015-06-22	8	3	Probable POSSIBLE	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	
リンパ球減少症	2015-06-30	64	N	Probable	Dose not changed	Daratumumab	N	N
Lymphocyte count decreased	2015-07-06	7	3	Probable POSSIBLE	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	
リンパ球減少症	2015-06-04	38	N	Probable	Dose not changed	Daratumumab	N	N
Lymphocyte count decreased	2015-06-08	5	3	Probable POSSIBLE	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	
リンパ球減少症	2015-04-30	3	N	Probable	Dose not changed	Daratumumab	N	N
Lymphocyte count decreased	2015-05-07	8	4	Probable POSSIBLE	DOSE NOT CHANGED Dose not changed	Dexamethasone LENALIDOMIDE	RECOVERED/RESOLVED	

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
鼻咽頭炎 Common cold	2015-12-20 2016-01-04	237 16	N 1	Not related Not related NOT RELATED Dose not changed	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
末梢性ニューロパチー Neuropathy peripheral	2015-06-13 -	47 -	N 1	Not related Not related PROBABLE Dose not changed	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
発疹 Upper body rash	2015-05-04 2015-05-11	7 8	N 1	Not related Not related PROBABLE Dose not changed	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Demographics and Baseline Characteristics

□ Country: Japan
□ Study site identifier: JP91213
□ Race: Asian
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 58
□ Baseline height(cm): 169.1
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: Subject Ongoing on Treatment

□ Study discontinuation: Subject Ongoing on Study

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
323.81	1619.80	4830.00	2015-04-28	2016-03-02	10.18

■ NARRATIVE TEXT

被験者 810020 は，6[redacted]歳のアジア人男性で，2005 年 9 月 27 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，肺気腫，高血圧，不眠症，背部痛，夜間頻尿，腎結石症及び上気道感染であった。ベースラインの ECOG スコアは 1 であった。両側性肺炎，帯状疱疹及び脂肪腫の既往歴を有した。スクリーニング時のバイタルサインは，体温 36.8°C，脈拍数 92 bpm 及び血圧 136/68 mm Hg であった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はシクロホスファミド，デキサメタゾン，ドキソルビシン，メルファラン，ビンクリスチン及び ASCT，レジメン 2 はボルテゾミブ，デキサメタゾン及びパノビノスタットであった。

治験組入れ時の併用薬は，アムロジピン，ブロチゾラム，ラベプラゾールナトリウム，calcium/magnesium（Super Cal600-MG300），酸化マグネシウム，オキシコドン，プロクロルペラジン，センノシド A+B／カルシウム，アズレンスルホン酸ナトリウム水和物及びアセトアミノフェンであった。

CrCL 低値（53.7 mL/分）のために，Day 1 からレナリドミドを 10 mg に減量して投与を開始した。

Day 1（2015 年 4 月 28 日）に，**非重篤な有害事象の Grade 1 の呼吸困難**が報告された。治験担当医師は，本事象は IRR であり，本剤との因果関係を「可能性大」，デキサメタゾン又はレナリドミドとの因果関係を「関連なし」と判断した。投与前の血圧は 120/70 mm Hg であった。治験実施計画書に従い前投薬を実施した。本事象のために本剤の投与速度を減速したが，デキサメタゾン又はレナリドミドの処置は実施しなかった。本事象に対する治療は実施せず，発現日に回復した。その後本剤を 19 回投与したが，IRR は再発しなかった。

CrCL が改善したため（64.44 mL/分），Day 4 からレナリドミドを 25 mg に増量したが，CrCL が低下したため（43.68 mL/分），Day 10 に再度 10 mg に減量した。

Day 14 に，**重篤な有害事象の Grade 3 の細菌感染**が報告された。体温は 38.3°C であった。血液培養検査を実施したが，本事象の病原体は報告されなかった。治験担当医師は，本事象は医学的に重大であり，すべての治験薬との因果関係を「可能性大」と判断した。本事象のために Day 15 及び Day 22 に本剤及びデキサメタゾンを休薬し，Day 15～Day 21 にレナリドミドを休薬した。ピペラシリン／タゾバクタム（ゾシン）及びセフェピムによる治療を実施した。本事象は Day 28 に回復した。

CrCL が改善したため（61.60 mL/分），Day 43 からレナリドミドを 25 mg に再度増量した。

Day 61 に，被験者は疲労及び呼吸困難を訴え，酸素飽和度は 93%であった。**重篤な有害事象の Grade 1 の低酸素症**が報告され，被験者は Day 64 に入院した。同日に実施した CT スキャンの結果は正常であった。治験担当医師は，本事象とすべての治験薬との因果関係を「可能性大」と判断した。本事象のために Day 64 にデキサメタゾンを休薬し，Day 64～Day 70 にレナリドミドを休薬した。本剤の処置は実施しなかった。Day 69 の酸素飽和度は 96%であった。本事象は無処置で Day 70 に回復し，被験者は Day 78 に退院した。

本報告書（クリニカルカットオフ日の 2016 年 3 月 7 日時点）では，被験者は治験薬の投与継続中であった。

4) 被験者識別番号 810037

■ **REASON FOR NARRATIVE SELECTION**

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

Second primary malignancies

■ **Discontinuation of study treatment due to AE and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
エプスタイン・バーウイルス関連リンパ増殖性障害 Ebv-positive lymphoproliferative disorder	2015-09-08 -	91 -	Y 3	Probable Probable PROBABLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N	-

■ **Infections and infestations, Grade 3 or 4 and Serious AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
サイトメガロウイルス感染 Cytomegalovirus infection	2015-08-25 2015-09-24	77 31	Y 3	Possible Probable POSSIBLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	VIRAL (CYTOMEGALOVIRUS)

■ Second primary malignancies

Dictionary-Derived Term Reported Term for the Clinical Event	Diagnosis of 2nd Primary Malignancy Diagnosis Date/Time of 2nd Primary Malig	Recurrence of a prior existing malig.? Initial Diagnosis Date	Confirm by pathology diagnosis obtained? Confirmation Method Specimen source or sample	Stage of the disease Staging sytem	Concomitant or Additional Trtmnt Given	Surgery	Radiotherapy	Systemic therapy Specific Regimen	Palliative supportive care provided	Outcome of Event
エプスタイン・バーウイルス関連リンパ増殖性障害 EBV-POSITIVE LYMPHOPROLIFERATIVE DISORDER	EBV-POSITIVE LYMPHOPROLIFERATIVE DISORDER 2015-10-26	N -	Y BIOPSY LYMPH NODE IN ANDOMINAL CAVITY	IV ANN ARBOR ALASSIFICATION	Y	N	N	Y CHOP REGIMEN	N	NOT RECOVERED/ NOT RESOLVED

■ Demographics and Baseline Characteristics

- □ Country: Japan
- □ Study site identifier: JP91223
- □ Race: Asian
- □ Age(yrs): 6[redacted]
- □ Sex: Female
- □ Baseline weight(kg): 57.4
- □ Baseline height(cm): 149.5
- □ Baseline ECOG score: 0

■ Disposition Information

- □ Treatment discontinuation: 2015-09-30 Adverse Event
- □ Study discontinuation: Subject Ongoing on Study

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
165.84	478.00	895.00	2015-06-10	2015-08-26	2.56

■ NARRATIVE TEXT

被験者 810037 は，6[redacted] 歳のアジア人女性で，2010 年 9 月に初めて病期 II（スクリーニング時）の MM と診断され，本剤，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，湿疹及び不眠症であった。ベースラインの ECOG スコアは 0 であった。帯状疱疹，ニューモシスティスカリニ肺炎，胃潰瘍及び血栓の既往歴を有した。

被験者は 1 レジメンの前治療（シクロホスファミド，デキサメタゾン，ドキソルビシン，メルファラン，ビンクリスチン及び ASCT）を受けていた。

治験組入れ時の併用薬は，ブロチゾラム，ベタメタゾンジプロピオン酸エステル，ヘパリン類似物質，betamethasone/gentamicin（Valisone-G）及びフェキソフェナジンであった。

Day 1（2015 年 6 月 10 日）の本剤投与開始から 23 分後に，**非重篤な有害事象の Grade 2 の上気道性喘鳴**が報告され，IRR と判断された。治験担当医師は，本事象と本剤との因果関係を「ほぼ確実」，デキサメタゾン又はレナリドミドとの因果関係を「関連なし」と判断した。投与前の血圧は 123/72 mm Hg であった。治験実施計画書に従い前投薬を実施した。投与開始から 63 分後に，上気道性喘鳴のために本剤の投与を 70 分間中断した。メチルプレドニゾロンコハク酸エステルナトリウムによる治療を実施した。投与中断から 70 分後に，上気道性喘鳴は回復した。投与を再開して終了した。その後本剤を 9 回投与したが，上気道性喘鳴の再発は認められなかった。

レナリドミドの投与量は，非重篤な有害事象の Grade 3 のアラニンアミノトランスフェラーゼ増加のために，Day 20 から 15 mg に減量し，非重篤な有害事象の Grade 1 の腎機能障害のために，Day 43 からは更に 10 mg に減量した。

Day 57 に，ECOG スコアは 1 に悪化した。

Day 77 に，発熱が認められた（体温は未報告）。Day 85 に，下痢及び肝機能障害が認められ（臨床検査値は未報告），血清学的検査ではサイトメガロウイルス抗原血症陽性であった。**重篤な有害事象の Grade 3 のサイトメガロウイルス感染**が報告された（発現日は Day 77）。MM 並びに本剤，レナリドミド及びデキサメタゾンによる免疫抑制がリスク因子と判断された。Day 87 に，被験者は入院した。治験担当医師は，サイトメガロウイルス感染と本剤及びレナリドミドとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「可能性大」と判断した。本事象のために治験薬を休薬した。本剤，レナリドミド及びデキサメタゾンの事象発現前の投与日は，それぞれ Day 71，Day 77 及び Day 78 であり，サイトメガロウイルス感染のためにサイクル 4 を延期した。サイトメガロウイルス感染に対してガンシクロビルによる治療を実施した。アセトアミノフェン，セフェピム，ベンフォチアミン／ビタミン B6／ビタミン B12（ビタメジン）及びミカファンギンも投与した。肝内腫瘍及び全身のリンパ節腫脹が認められた。しかし，リンパ節生検ではエプスタイン・バーウイルス関連リンパ増殖性リンパ腫が確認された。Day 91 に，**重篤な有害事象の Grade 3 のエプスタイン・バーウイルス関連リンパ増殖性障害**が報告された。治験担当医師は，本事象と本剤，レナリドミド及びデキサメタゾンとの因果関係を「可能性大」と判断した。Day 93 の CT スキャンでは腹部肝内病変が認められた。Day 94 及び Day 107 に，サイトメガロウイルス抗原血症は陰性であった。サイトメガロウイルス感染は Day 107 に回復した。Day 108 に，肝病変の生検では明確な結論は得られなかった。

Day 113 に，エプスタイン・バーウイルス関連リンパ増殖性障害のために治験薬の投与を中止した。本剤，レナリドミド及びデキサメタゾンの最終投与日は，それぞれ Day 71，Day 77 及び Day 78 であった。

Day 114 に，ECOG スコアは 2 に悪化した。

Day 132 の腹部リンパ節生検では，ホジキン型のエプスタイン・バーウイルス関連リンパ増殖性障害が確認された。病期 IV と報告された（Ann Arbor 分類）。Day 146 に，シクロホスファミド，ドキソルビシン，ビンクリスチン及びプレドニゾロン（CHOP）による治療を実施した。Day 152 に，一過性の敗血症のために抗生物質を投与した。白血球数は 0/mm^3 であった。Day 153 の CT スキャンでは肝腫瘍及びリンパ節病変の萎縮が認められた。Day 291 まで CHOP を 6 サイクル投与した。

本報告書（クリニカルカットオフ日の 2016 年 3 月 7 日時点）では，被験者の生存状況を追跡調査中であった。エプスタイン・バーウイルス関連リンパ増殖性障害は未回復であった。

(2) Rd 群

1) 被験者識別番号 810024

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-05-19	2015-09-07	112	2015-09-27	132	PROGRESSIVE DISEASE	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
急性腎不全 Acute kidney injury	2015-05-21 2015-09-27	3 130	Y 4	Not related Doubtful PROBABLE	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
傾眠 Somnolence	2015-09-20 -	125 -	Y 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA	-
急性腎不全 Acute kidney injury	2015-09-27 2015-09-27	132 1	Y 5	Not related Doubtful PROBABLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	N FATAL	NA	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-06-03 2015-06-04	16 2	N 2	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
貧血 Anemia	2015-09-09 -	114 -	N 3	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	NA
貧血 Anemia	2015-08-26 2015-09-09	100 15	N 2	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
貧血 Anemia	2015-06-08 2015-06-19	21 12	N 2	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
貧血 Anemia	2015-06-22 2015-07-08	35 17	N 2	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
便秘 Constipation	2015-06-21 -	34 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
多形紅斑 Erythema multiforme	2015-07-09 2015-08-02	52 25	N 2	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
高尿酸血症 Hyperuricemia	2015-06-08 2015-06-12	21 5	N 1	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
不眠症 Insomnia	2015-09-01 2015-09-21	106 21	N 2	Not related Probable NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
不眠症 Insomnia	2015-05-26 2015-05-27	8 2	N 1	Not related Probable NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
不眠症 Insomnia	2015-06-02 2015-07-01	15 30	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
リンパ球減少症 Lymphocytopenia	2015-06-26 2015-06-29	39 4	N 3	Not related Probable PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
メレナ Melena	2015-09-20 2015-09-21	125 2	N 1	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
頚部痛 Neck pain	2015-08-21 -	95 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
肺炎 Pneumonia	2015-08-10 2015-08-26	84 17	N 2	Not related Possible POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
血小板減少症 Thrombocytopenia	2015-09-11 2015-09-14	116 4	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
血小板減少症 Thrombocytopenia	2015-09-09 2015-09-11	114 3	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA
血小板減少症 Thrombocytopenia	2015-09-14 -	119 -	N 4	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	NA
尿閉 Urinary retention	2015-06-17 2015-06-17	30 1	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
嘔吐 Vomiting	2015-06-17 2015-06-17	30 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	NA

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
嘔吐 Vomiting	2015-09-08 2015-09-19	113 12	N 2	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA
創合併症 Wound pain	2015-06-16 2015-06-20	29 5	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	NA

■ Demographics and Baseline Characteristics

- □ Country: Japan
- □ Study site identifier: JP91216
- □ Race: Asian
- □ Age(yrs): 5[redacted]
- □ Sex: Male
- □ Baseline weight(kg): -
- □ Baseline height(cm): 167.5
- □ Baseline ECOG score: 0

■ Disposition Information

- □ Treatment discontinuation: 2015-09-25 Progressive Disease
- □ Study discontinuation: 2015-09-27 Death
- □ Cause of death: Progressive Disease

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	520.00	340.00	2015-05-19	2015-09-07	3.68

■ NARRATIVE TEXT

被験者 810024 は，5[redacted]歳のアジア人男性で，2013 年 8 月 1 日に初めて病期 I（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，胃炎及び末梢性感覚ニューロパチーであった。ベースラインの ECOG スコアは 0 であった。関節リウマチの既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，サリドマイド及び ASCT）を受けていた。

治験組入れ時の併用薬はオメプラゾールであった。

サイクル 1 の Day 1 に，デキサメタゾン 40 mg 及びレナリドミド 25 mg の投与を開始した（CrCL：89 mL/分）。Day 3（2015 年 5 月 21 日）に，被験者は**重篤な有害事象の Grade 4 の急性腎不全**のために入院した［クレアチニン値：315.59 μmol/L（正常範囲：44.2-106.08 μmol/L），血中尿素窒素：39 mg/dL，糸球体濾過率（GFR）：15 mL/分/1.73 m^2］。心エコー検査及び腹部エコー検査では臨床的に重要な所見は認められなかった。治験担当医師は，本事象とデキサメタゾンとの因果関係を「多分なし」，レナリドミドとの因果関係を「可能性大」と判断した。同日，急性腎不全のためにレナリドミドを休薬したが，デキサメタゾンの処置は実施しなかった。フロセミドによる治療を実施した。Day 5 に，尿量は安定していたが，腎機能障害が持続したため（クレアチニン値：728.42 μmol/L，血中尿素窒素：57 mg/dL，GFR：6.0 mL/分/1.73 m^2），血液透析を開始した。Day 8 に，腎機能は改善していなかった（クレアチニン値：8.8 mg/dL，GFR：5.5 mL/分/1.73 m^2）。Day 8 の腎生検では，びまん性糸球体硬化病変，係蹄壁の軽度過形成，小葉間動脈の内膜肥厚，血管周囲のリンパ球浸潤，遠位腎尿細管萎縮，腎尿細管の拡張，硝子性円柱，赤血球円柱，尿細管上皮障害を示唆する近位尿細管上皮の空胞形成，尿細管上皮への単核球の軽度浸潤，並びに腎尿細管及び間質における薬剤誘発性変化を示唆する顕著な間質性浮腫が認められた。急性腎不全はレナリドミドに関連する間質性腎炎による可能性があると腎臓内科から報告された。Day 10 に，CT スキャンを実施した（結果は未報告）。

Day 11 に，腎機能は改善しておらず，治験担当医師は，急性腎不全は遊離軽鎖に直接関係していると判断した。翌日，尿量が減少し，トルバプタンの投与を開始した。Day 14 に，メチルプレドニゾロンコハク酸エステルナトリウムによるステロイドパルス療法を開始した。Day 15 にも腎機能は改善していなかったが，尿量は安定していた。同日，ステロイド療法のためにデキサメタゾンを休薬した。翌日（Day 16）から，急性腎不全のためにレナリドミドを 5 mg に減量して投与を再開した。

Day 21 に，**非重篤な有害事象の Grade 1 の高尿酸血症**が報告された（値は未報告）。本事象は腎不全の続発症であり，デキサメタゾン及びレナリドミドとの因果関係は「多分なし」と判断された。高尿酸血症に対する治験薬の処置は実施しなかった。フェブキソスタットによる治療を実施した。高尿酸血症は Day 25 に回復した。

Day 29 に，持続的携帯型腹膜透析カテーテルを留置した。同日，**非重篤な有害事象の Grade 2 の創合併症**（記載語：創部痛）が報告された。翌日（Day 30）に，**非重篤な有害事象の Grade 2 の尿閉**及び**Grade 1 の嘔吐**が報告された。Day 30 に，尿道カテーテルを留置し，腹膜透析も開始した。ペンタゾシン，ヒドロキシジン，セレコキシブ及びアセトアミノフェンによる治療を実施した。治験担当医師は，これらの事象とデキサメタゾン又はレナリドミドとの因果関係を「関連なし」と判断し，治験薬の処置は実施しなかった。尿閉及び嘔吐は発現日に回復した。Day 31 の ECOG スコアは 1 に悪化した。創合併症は Day 33 に回復した。

Day 37 に，血液透析を中止した。Day 42 に，Kt/V が 0.94 から 0.56 に低下し，MM 又は薬剤が原因と報告された。Day 44 に，被験者は退院した。

Day 58 に，ECOG スコアは 0 に改善した。

Day 113 に，**非重篤な有害事象の Grade 2 の嘔吐**が報告され，翌日には悪心も認められた。

嘔吐と治験薬との因果関係は「関連なし」と判断された。Day 114 から嘔吐のためにレナリドミドを休薬し，嘔吐及び併発した Grade 4 の貧血のためにデキサメタゾンも休薬した。プロクロルペラジンによる治療を実施した。

Day 116 のクレアチニン値は 15.92 mg/dL（Grade 4），GFR は 2.9 mL/分/1.73 m^2 であった。Day 119 に，被験者は追加評価及び急性腎不全悪化の治療のために入院し（クレアチニン値：16.95 mg/dL），血液透析を再開した。翌日のクレアチニン値は 9.77 mg/dL（Grade 4）であった。Day 121 に，被験者は退院した。嘔吐は Day 124 に回復した。

Day 125 に，**重篤な有害事象の Grade 3 の傾眠**が報告された。同日，幻視及び幻聴，間欠性の下腹部痛，嘔吐及びメレナが認められ，出血源を特定するために入院した。入院時のバイタルサインは，心拍数 95 bpm，血圧 131/79 mmHg，体温 37.1°C，酸素飽和度 97%であった。臨床検査では，ヘモグロビン値 7.8 g/dL，補正カルシウム値 10.64 mg/L，クレアチニン値 13.15 mg/dL，血小板数 1.3×10^4/μL であった。ヒドロキシジン及びゾピクロンによる治療を実施した。治験担当医師は，傾眠と治験薬との因果関係を「関連なし」と判断した。傾眠に対する治験薬の処置は実施しなかった。Day 130 に，血清蛋白電気泳動での M 蛋白増加による疾患進行のために治験薬の投与を中止した。デキサメタゾン及びレナリドミドの最終投与日は，それぞれ Day 107 及び Day 112 であった。Day 131 に，発熱，血圧低下，並びに尿毒症及び MM の悪化による意識レベルの低下が認められた。ヘモグロビン値 7.5 g/dL，血小板数 1.6×10^4/μL，クレアチニン値 26.44 mg/dL であった。腹膜透析は継続した。Day 132 に，CT スキャンを実施した（結果は未報告）。同日（Day 132），被験者は急性腎不全及び疾患進行のために死亡した。剖検は実施されなかった。

2) 被験者識別番号 810042

■ REASON FOR NARRATIVE SELECTION

Infections and infestations, Grade 3 or 4

Serious AEs

■ Infections and infestations, Grade 3 or 4; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2016-01-08 2016-01-14	193 7	Y 3	Not related Probable PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N	No

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
アラニンアミノトランスフェラーゼ増加 Alanine aminotransferase increased	2015-08-27 2016-03-10	59 197	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
気管支炎 Bronchitis	2015-06-24 2015-06-30	-6 7	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
便秘 Constipation	2015-07-09 -	10 -	N 2	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
味覚異常 Taste alteration	2015-08-20 -	52 -	N 1	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Dexamethasone Causality-Lenalidomide	Action Taken-Daratumumab Action Taken-Dexamethasone Action Taken-Lenalidomide	Sponsor Study Treatment 1 Other Study Treatment 1 Other Study Treatment 2	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction
γ－グルタミルトランスフェラーゼ増加 GGT increased	2015-08-27 -	59 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N NOT RECOVERED/NOT RESOLVED	N
リンパ球減少症 Lymphocytopenia	2016-01-04 2016-03-10	189 67	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
リンパ球減少症 Lymphocytopenia	2015-11-19 2015-11-26	143 8	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	N RECOVERED/RESOLVED	N
筋痙縮 Cramps in the calves	2015-11-05 -	129 -	N 2	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y NOT RECOVERED/NOT RESOLVED	N
好中球減少症 Neutropenia	2015-11-19 2015-12-03	143 15	N 3	Not related Not related PROBABLE	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N
肺炎 Pneumonia	2016-01-04 2016-01-07	189 4	N 2	Not related Probable PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Dexamethasone LENALIDOMIDE	Y RECOVERED/RESOLVED	N

■ Demographics and Baseline Characteristics

□ Country: Japan
□ Study site identifier: JP91219
□ Race: Asian
□ Age(yrs): 5[redacted]
□ Sex: Male
□ Baseline weight(kg): -
□ Baseline height(cm): 178.1
□ Baseline ECOG score: 0

■ Disposition Information

□ Treatment discontinuation: Subject Ongoing on Treatment

□ Study discontinuation: Subject Ongoing on Study

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Lenalidomide Cumulative Dose (mg) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1440.00	4375.00	2015-06-30	2016-03-03	8.15

■ **NARRATIVE TEXT**

被験者 810042 は，5[redacted]歳のアジア人男性で，2013 年 11 月 26 日に初めて病期 I（スクリーニング時）の MM と診断され，レナリドミド及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，アレルギー性鼻炎及び椎間板突出であった。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，メルファラン及び ASCT）を受けていた。

治験組入れ時の併用薬はなかった。

スクリーニング時（Day −1）のリンパ球数は 0.81×10^9/L（正常範囲：1.5-3.5$\times10^9$/L）及び好中球数は 1.17×10^9/L（正常範囲：2.5-7.5$\times10^9$/L）であった。

Day 143 に，**非重篤な有害事象の Grade 3 の好中球減少症及びリンパ球減少症**が報告された（好中球数：0.75×10^9/L，リンパ球数：0.37×10^9/L）。治験担当医師は，好中球減少症とレナリドミドとの因果関係を「可能性大」，デキサメタゾンとの因果関係を「関連なし」，リンパ球減少症とレナリドミド及びデキサメタゾンとの因果関係を「可能性小」と判断した。Day 143〜Day 156 に，好中球減少症のためにレナリドミドを休薬したが，デキサメタゾンの処置は実施しなかった。好中球減少症に対しフィルグラスチムによる治療を実施した。リンパ球減少症は無処置で Day 150 に回復した（リンパ球数：0.79×10^9/L）。好中球減少症は Day 157 に回復した。

Day 189 に，**非重篤な有害事象の Grade 2 の肺炎**及び **Grade 3 のリンパ球減少症**（リンパ球数：0.24×10^9/L）が報告された。治験担当医師は，肺炎とレナリドミド及びデキサメタゾンとの因果関係を「可能性大」，リンパ球減少症とレナリドミド及びデキサメタゾンとの因果関係を「可能性小」と判断した。同日，インフルエンザ検査を実施し（結果は未入手），胸部 X 線写真では右下肺野に肺炎の浸潤影が認められた。これらの事象に対するデキサメタゾン又はレナリドミドの処置は実施しなかった。肺炎に対しスルバクタム／アンピシリン（スルタミシリン）及びアセトアミノフェンによる治療を実施した。Day 193 に，**肺炎は Grade 3（重篤）**に悪化し，入院を必要とした。肺炎の病原体は報告されなかった。肺炎に対しメロペネム及びブロムヘキシンによる治療を追加した。肺炎は Day 199 に回復し，被験者は退院した。リンパ球減少症は Day 255 に回復した。

本報告書（クリニカルカットオフ日の 2016 年 3 月 7 日時点）では，被験者は治験薬の投与継続中であった。

2.7.6.2　海外臨床第 III 相試験（MMY3004 試験，評価資料：5.3.5.1.2-1）

2.7.6.2.1　概要

2.7.6.2.1.1　計画

(1) 治験の標題

再発又は難治性の多発性骨髄腫（MM）患者を対象とした，ダラツムマブ（以下本剤），ボルテゾミブ及びデキサメタゾンの 3 剤併用療法（DVd 療法）とボルテゾミブ及びデキサメタゾンの 2 剤併用療法（Vd 療法）を比較する第 III 相試験

(2) 治験調整医師

[redacted], [redacted], [redacted]

(3) 公表文献（引用文献）

- Palumbo A, et al. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2016 Aug;375(8):754-66.
- Rajkumar SV, et al. Progress in Myeloma - A Monoclonal Breakthrough. N Engl J Med. 2016 Oct;375(14):1390-2.

(4) 治験実施期間

2014 年 9 月 [redacted] 日（最初の被験者がランダム化された日）～2016 年 1 月 11 日（クリニカルカットオフ日）

(5) 開発の相

第 III 相

(6) 目的

本治験の主要目的は，再発又は難治性の MM 患者を対象として，DVd 療法と Vd 療法の有効性を無増悪生存期間（PFS）によって比較することであった。

主な副次目的は以下のとおりであった：

- 無増悪期間（TTP），全奏効率（ORR）及び全生存期間（OS）を含む臨床アウトカムを評価する。
- Very good partial response（VGPR）以上の奏効率を評価する。
- 奏効持続期間及び奏効到達期間を評価する。
- DVd 療法の安全性及び忍容性を評価する。

・ VGPR 以上を達成した被験者において，微少残存病変（MRD）を評価する。

その他の副次目的は以下のとおりであった：

・ DVd 療法での本剤の薬物動態を評価する。

・ 本剤の免疫原性を評価する。

・ European quality of life 5 dimension 5 level scale（EQ-5D-5L）及び欧州がん研究治療機関（EORTC）の quality of life questionnaire-core 30（QLQ-C30）の患者報告アウトカムを用いて，各療法の有効性を評価する。

・ 高リスク染色体異常［del17p，t(4;14)，t(14;20)］を有する部分集団での DVd 療法の臨床的有効性を評価する。

探索的目的は，本剤の効果を予測するバイオマーカー及び治療抵抗性の潜在的機序を探索することであった。

(7) 治験方法

本治験は，再発又は難治性の MM 患者を対象に，DVd 療法と Vd 療法の有効性を PFS によって比較する第 III 相，ランダム化，非盲検，実薬対照，多施設共同試験であった。約 480 例の被験者を DVd 群又は Vd 群に 1：1 の比でランダムに割り付けた。ランダム化にあたっては，中央検査機関によって判定されたスクリーニング時の国際病期分類の病期（I，II 又は III 期），前治療数（1 レジメン，2 又は 3 レジメン，4 レジメン以上）及びボルテゾミブの前治療歴の有無を層別因子とし，層別因子の各層の割付け比が 1：1 となるように被験者をランダムに割り付けた。

本治験は，スクリーニング期（サイクル 1 Day 1 前 21 日以内），治療期（サイクル 1 Day 1 から治験薬投与中止まで）及び後観察期から構成された。後観察期は，投与中止時来院の直後から被験者の死亡，追跡不能，同意撤回又は治験終了のいずれか早い時点までとした。疾患評価には，M 蛋白の測定，骨髄検査，骨格検査，髄外形質細胞腫の評価及びアルブミン補正血清カルシウムの測定が含まれた。

疾患進行は，治験実施計画書で規定したとおり国際骨髄腫作業部会（IMWG）の治療効果判定規準に基づき評価した。血清及び尿検査は，サイクル 1～8 の規定評価日（±3 日）に 21 日ごとに実施した。サイクル 1 以降，M 蛋白が 0 又は定量不能の場合にのみ免疫固定法による測定を実施した。サイクル 8 終了後（サイクル 9 の開始時），疾患評価として血清 M 蛋白電気泳動，尿中 M 蛋白電気泳動及びアルブミン補正血清カルシウムを，本治験の開始後 18 カ月間はサイクルごと，以降は 2 サイクルごとに測定した。治療効果判定［血液生化学検査に基づく progressive disease（PD）を含む］は 2 回連続して同じ判定でなければならなかった。

主要評価項目である PFS の解析は，295 件の PFS イベント発生後に実施することとした。PFS の主要解析後本治験終了（320 件の死亡が発生した時点と定義）まで，治験実施計画書の規定に従い，本治験継続中の被験者を引き続き観察することとした。独立データモニタリング委員会が，事前に規定した 2 回の中間解析時にデータをレビューした。1 回目の中間解析は，治験薬の投与を 8 週以上受けた又は中止した被験者が 80 例に達した時点で実施し，その時点までに入手可能な本剤併用療法の安全性データは限られているため，包括的な安全性評価とした。2 回目の中間

解析（当該結果を本項に示す）は，計画したイベント件数の 60%に当たる約 177 件の PFS イベント発生時点で実施し，その時点までに累積したデータを安全性及び有効性の累積中間データとした。また，独立データモニタリング委員会は本治験期間中に定期的（被験者が 50 例に達した時点，以降は 6 カ月ごと）に安全性データをレビューすることとした。

(8) 被験者数（計画時及び解析時）

計画時：約 480 例を本治験に組み入れることとした（各群約 240 例）。

解析時：498 例（DVd 群 251 例，Vd 群 247 例）を intent-to-treat（ITT）解析対象集団とした。

(9) 診断及び主な組入れ基準

18 歳以上の男性又は女性で，MM の確定診断を受けており，1 レジメン以上の前治療で奏効［IMWG の治療効果判定規準に基づき治験担当医師が partial response（PR）以上と判定］を達成し，かつ直近のレジメン以降に IMWG の治療効果判定規準に基づいた PD が確認され，Eastern Cooperative Oncology Group（ECOG）の performance status スコアが 0，1 又は 2 である患者を，本治験の対象とした。本剤若しくは他の抗 CD38 療法の前治療歴を有する患者，ボルテゾミブ若しくは ixazomib やカルフィルゾミブなど他のプロテアソーム阻害剤（PI）（治験実施計画書改訂第 1 版で除外基準に追加）に対し治療抵抗性を示す患者，ボルテゾミブに対し忍容性が不良の患者，ランダム化前 2 週間以内若しくは治療薬剤の半減期の 5 倍のいずれか長い期間に MM に対する治療を受けた患者，ランダム化前 12 週間以内に自家造血幹細胞移植（ASCT）を受けた患者，過去に同種幹細胞移植を受けた患者，ランダム化前 3 年以内に悪性腫瘍（MM 以外）の既往のある患者，又は MM による髄膜障害を有する患者は本治験から除外した。

(10) 被験薬，用量及び投与方法，ロット番号

1 サイクルをサイクル 1～8 までは 21 日間，サイクル 9 以降は 28 日間とした。サイクルの開始は，いずれかの治験薬投与（本剤，ボルテゾミブ又はデキサメタゾン）の開始と定義した。すべての治験薬を休薬した場合には，サイクル開始の延期として報告することとした。

本剤 16 mg/kg を，最初の 3 サイクルは 1 週間隔（Day 1，8 及び 15），続いてサイクル 4～8 は 3 週間隔（Day 1），サイクル 9 以降は 4 週間隔（Day 1）で持続静脈内投与した。

本剤のロット番号は以下のとおりであった。

[redacted]

(11) 対照薬，用量及び投与方法，ロット番号

ボルテゾミブ 1.3 mg/m^2 を，各サイクル（21 日間）の Day 1，4，8 及び 11 に皮下投与した。ボルテゾミブは 8 サイクル投与することとした。皮下投与で被験者が注射部位反応を発現した場合は，ボルテゾミブを持続静脈内投与に変更できた。本剤投与日は，ボルテゾミブを本剤投与終了後に投与した。

デキサメタゾン（又は治験実施計画書が推奨する同等量の代替ステロイド）は，総投与量80 mg/週を各サイクル（21 日間）の最初の 2 週間に投与した。ただし，75 歳を超える，過少体重（体格指数：18.5 未満），コントロール不良の糖尿病又はステロイド療法に対する不耐性若しくは有害事象の既往を有する被験者には，デキサメタゾンを 20 mg/週で投与することを可とした。本剤を投与する週では，本剤投与当日，デキサメタゾン 20 mg を本剤投与前に可能な限り静脈内投与することとした。治験実施計画書改訂第 1 版以降は，本剤投与前 1～3 時間以内にデキサメタゾンを前投薬として経口投与することも可能とした。その後，デキサメタゾン 20 mg を Day 2，4 及び 5 に経口投与した。本剤を投与しない週及び Vd 群では最初の 8 サイクルの Day 1，2，4，5，8，9，11 及び 12 に，デキサメタゾン 20 mg を投与した（80 mg/週）。デキサメタゾンは，被験者が疾患進行若しくは許容できない毒性を発現する又はサイクル 8 終了のいずれか早い時点まで投与した。

ボルテゾミブのロット番号は以下のとおりであった。

[redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted]

デキサメタゾンのロット番号は以下のとおりであった。

[redacted], [redacted], [redacted], [redacted], [redacted]

(12) 投与期間

DVd 群にランダム化された被験者は，DVd 療法を最大 8 サイクル受けた。DVd 療法を 8 サイクル実施後，疾患進行若しくは許容できない毒性が認められる又はその他の投与中止基準に該当するまで本剤を継続投与した。Vd 群にランダム化された被験者は，Vd 療法を最大 8 サイクル実施後，疾患進行が認められる又はその他の投与中止基準に該当するまで観察した。

(13) 評価基準

有効性の評価：

治療効果及び PD の判定は，IMWG の治療効果判定規準に従い実施した。疾患評価には，血清及び尿中 M 蛋白の測定，血清遊離軽鎖，骨髄中の形質細胞浸潤，骨病変の評価，髄外形質細胞腫の評価及びアルブミン補正血清カルシウムの測定を用いた。また，生存状況及び次の抗がん剤治療に関する情報を収集した。

薬物動態の評価：

DVd 群の被験者から血液検体を採取し，本剤の薬物動態パラメータとして，本剤投与直前の最低血清中濃度（C_{min}）及び投与終了後の最高血清中濃度（C_{max}）を算出した。

免疫原性の評価：

DVd 群の被験者から検体を採取し，本剤に対する抗体産生について評価した。

バイオマーカーの評価：

全被験者から血液検体及び骨髄穿刺検体を採取し，高リスク染色体異常の部分集団における治療効果を検討し，MRD を評価した。両群を対象としたのは，本剤の有無による被験者間の結果を比較するためであった。

安全性の評価：

有害事象，臨床検査値（血液学的検査及び血液生化学検査），心電図（ECG），バイタルサイン（脈拍，血圧及び体温），身体所見，並びに ECOG の performance status スコアに基づき安全性を評価した。

機能状態及び満足できる生活状態：

機能状態及び満足できる生活状態を EORTC-QLQ-C30 及び EQ-5D-5L を用いて評価した。

医療資源の利用状況：

本治験期間中，治験実施計画書に基づく医療現場及び安全性モニタリングに関連した医療資源の利用状況に関する被験者のデータを，治験担当医師及び治験コーディネーターが電子症例報告書に収集した。

(14) 統計手法

主要な解析対象集団は ITT 解析対象集団とし，ランダム化された全被験者を対象とした。主な副次評価項目である ORR，VGPR 以上の奏効率，奏効持続期間及び奏効到達期間の解析は，奏効評価対象集団を対象に実施した。奏効評価対象集団は MM の確定診断を受け，ベースライン又はスクリーニング来院時に測定可能病変を有し，かつ治験薬の投与を 1 回以上受け，ベースライン後の疾患評価を 1 回以上実施している被験者と定義した。部分集団解析は必要に応じて実施した。安全性は，治験薬が投与された全被験者を対象に評価した。薬物動態の解析は，薬物動態評価対象集団（本剤投与を 1 回以上受け，かつ投与後の検体を有する被験者と定義）を対象に実施した。免疫反応評価対象集団は，本剤投与を 1 回以上受け，本剤に対する抗体検出に適した検体が採取された被験者と定義した。

本治験では，Vd 群における PFS の中央値を 10 カ月と想定し，Vd 群に対して DVd 群が疾患進行又は死亡のリスクを 30%低減する［PFS のハザード比（HR）=0.70］と仮定した場合，DVd 群における PFS の中央値が 14.3 カ月となり，log-rank 検定（有意水準両側 0.05）により，検出力 85%で群間差を検出するには計 295 件の PFS イベントが必要とされた。累積期間 16 カ月に後観察期間 10 カ月間を加えた場合，本治験に必要な総被験者数は約 480 例（各群 240 例）であった。

長期生存観察は，320 件の死亡が認められるまで（ランダム化された被験者の 3 分の 2 が死亡するまで）継続することとした。したがって，本治験では，log-rank 検定（有意水準両側 0.05）により，約 80%の検出力で死亡リスクの 27%の低減（HR=0.73）を検出することとした。

有効性の解析：

治療効果及び PD は，バリデートされたコンピュータ・アルゴリズム判定を用いて IMWG の治療効果判定規準に基づき評価した。主要評価項目である PFS の主要解析には，両群の PFS の分布を比較するため，層別 log-rank 検定を実施した。また，Kaplan-Meier 法を用いて両群の PFS の分布を推定した。治療効果（HR）及びその両側 95%信頼区間（CI）は，治療群のみを説明変数とする層別 Cox 回帰モデルを用いて推定した。両群の治療効果は最初の 24 週では 3 週間隔，それ以降では 4 週間隔で評価した。

TTP 及び OS を含む time-to-event 型の有効性評価項目も同様に解析した。ORR，VGPR 以上の奏効率及びその他の 2 値の評価項目の両群間の比較には，層別 Cochran-Mantel-Haenszel 検定を用

いた。Mantel-Haenszel オッズ比及びその両側 95%CI を示し，治療効果の尺度とした。奏効持続期間は記述的に示し，統計学的な比較は実施しなかった。

本治験では 2 回の中間解析を予定した。1 回目の中間解析は，安全性を評価する目的で，治験薬の投与を 8 週間以上受けた又は中止した被験者が 80 例に到達した時点で実施した。2 回目の中間解析は，安全性及び有効性の中間累積データを評価する目的で，計画された総イベント数の 60%に当たる約 177 件の PFS イベントが累積した時点で実施した。PFS に関し Vd 群に対する DVd 群の優越性を立証するための有意水準は，Lan-DeMets の α 消費法による O'Brien-Fleming 境界を用い，中間解析時点で認められた PFS イベント数に基づき決定した。177 件の PFS イベントが認められたと仮定する場合，この中間解析で消費される α は 0.00762（両側）であった。認められた両側 p 値がこの有意水準を下回る場合，PFS に関し Vd 群に対する DVd 群の優越性が立証されることとした。PFS に関して DVd 群が Vd 群より数値的に劣った場合（認められた HR が Vd 群の優越性を示す >1 の場合），本治験は無益となるため終了する可能性があった。

薬物動態解析：

血清中 daratumumab 濃度は記述統計量を用いて来院ごとに集計し，図示した。薬物動態の評価は，薬物動態評価対象集団を対象に実施した。欠測データは補完しなかった。要約統計量について，定量下限未満の濃度は 0 として取り扱った。投与前に採取した検体の値を C_{min}，投与終了時に採取した検体の値を C_{max} とした。Daratumumab の血清中濃度-時間データの母集団薬物動態解析は別途，母集団薬物動態解析計画書に示し，解析結果も別途報告することとした。

免疫原性解析：

免疫反応評価対象集団を対象に，本剤に対する抗体の発現割合（免疫原性）を要約した。

バイオマーカー解析：

バイオマーカーの検討は，本剤を Vd 療法と併用した際に MRD が減少するか検討するため計画された。ITT 解析対象集団及び奏効評価対象集団を対象に，各群の MRD 陰性率を算出した。

安全性の解析：

有害事象は医薬品規制用語集（MedDRA）version 18.0 に従いコード化した。治療期に発現した全有害事象（ベースライン以降に悪化した有害事象も含む）を解析に含めた。発現した有害事象について被験者の割合を群別に要約した。有害事象，臨床検査値，ECG，バイタルサイン，身体所見及び ECOG の performance status スコアを要約した。死亡例，有害事象による投与中止例，高度の有害事象又は重篤な有害事象の発現例については適宜，要約，一覧表，データセット又は被験者の叙述を示した。投与期間中の臨床検査値の Grade 分類を National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 に基づき示した。

機能状態及び満足できる生活状態：

EORTC-QLQ-C30 サブスケール及び EQ-5D-5L スコアを実施時点ごとに要約した。治療効果と生活の質（QOL）スコアの変化の関係を探索した。

医療資源利用状況：

医療資源利用状況を群別に記述的に要約した。

2.7.6.2.1.2　結果

(1) 対象集団

年齢の中央値は 64 歳で，男性が 57%であった。白人が 87%，アジア人が 5%，黒人又はアフリカ系アメリカ人が 4%であった。ECOG の performance status スコアは多くの被験者（94%）が 0 又は 1 であった。血清中の測定可能病変では，IgG 型が最も多く（53%），次いで IgA 型（22%）であった。MM の初回診断から本治験のランダム化までの期間の中央値は 3.8 年であった。すべての被験者に全身療法による前治療歴があり，61%の被験者に ASCT の前治療歴があった。全身療法の前治療数の中央値は 2 レジメン（範囲：1～10 レジメン）であり，24%の被験者に 3 レジメン以上の前治療歴があった。69%の被験者に PI の前治療歴があり，66%の被験者はボルテゾミブであった。また，76%の被験者に免疫調節薬（IMiD），48%の被験者に PI+IMiD の前治療歴があった。IMiD に対し 33%の被験者が治療抵抗性を示し，28%の被験者がレナリドミドに対し治療抵抗性を示した。32%の被験者が直近の前治療に対し治療抵抗性を示した。人口統計学的特性及び疾患特性について，レナリドミドの前治療歴（DVd 群 36%，Vd 群 49%）を除き，両群間で大きな差はなかった。

(2) 有効性

有効性の結果：

再発又は難治性の MM 患者において，Vd 療法に本剤を上乗せすることによって，臨床アウトカム（PFS）は有意に改善し，DVd 群では Vd 群と比べて疾患進行又は死亡のリスクが 61%低減した（HR=0.39，95%CI：0.28～0.53，p<0.0001）。クリニカルカットオフ日（2016 年 1 月 11 日）時点での観察期間の中央値は DVd 群 7.5 カ月，Vd 群 7.4 カ月であり，PFS の中央値は DVd 群で未到達であったが，Vd 群で 7.2 カ月であった。Kaplan-Meier 法により推定した結果，12 カ月の無増悪生存率は DVd 群 61%，Vd 群 27%であった。PFS の結果は，事前に規定された感度分析及びすべての部分集団解析で一貫していた。

有効性の副次解析結果は，ボルテゾミブ及びデキサメタゾンの標準療法において本剤の上乗せ効果が得られることを裏付けている。TTP は Vd 群に比べて DVd 群で統計学的に有意に延長した（HR=0.30，95%CI：0.21～0.43，p<0.0001）。本剤を上乗せすることにより，ORR（DVd 群 83%，Vd 群 63%，p<0.0001），VGPR 以上の奏効率（DVd 群 59%，Vd 群 29%，p<0.0001）及び complete response（CR）以上の奏効率（DVd 群 19%，Vd 群 9%，p=0.0012）は有意に改善した。奏効持続期間の中央値は，DVd 群では未到達（95%CI 下限：11.5 カ月）であったが，Vd 群で 7.9 カ月であり，本剤の上乗せによって奏効はより持続した。ORR は事前に規定されたすべての部分集団解析で一貫しており，DVd 群で改善が認められた（オッズ比 >1.0）。次の抗がん剤治療開始までの期間は，Vd 群と比べて DVd 群で有意に延長した（HR=0.30，p<0.0001，中央値：DVd 群は未到達，Vd 群 9.8 カ月）。死亡例は計 65 例（DVd 群 29 例，Vd 群 36 例）であり，両群とも OS の中央値に未到達であった。OS の HR は 0.77（95%CI：0.47～1.26，p=0.2975）であった。

MRD は，深い奏効への誘導能を両群間で比較するため，VGPR 以上の奏効を達成した被験者について評価した。10^{-4} 閾値での MRD 陰性率は Vd 群と比べ，DVd 群で有意に高かった（DVd 群 14%，Vd 群 3%，p<0.0001）。

患者報告アウトカム，医療資源利用状況及び医療経済学：

EORTC-QLQ-C30 の Global Health Status／QOL サブスケールにおいて，ベースラインからの平均変化量並びに改善又は悪化までの期間の中央値が両群間で同様であった。EQ-5D-5L の効用値及び visual analog scale のベースラインからの変化量について，両群間に統計学的に有意な差はほぼ全時点で認められず，効用値及び visual analog scale の改善又は悪化までの期間の中央値についても，両群間に統計学的に有意な差は認められなかった。患者報告アウトカムの結果から，本剤の Vd 療法への上乗せは，全般的な健康関連の QOL に有意に悪影響をもたらさないことが示された。

DVd 群の 60%と Vd 群の 45%の被験者が，治験の規定来院以外で入院又は外来を受診した。被験者が最も頻回に外来受診した医療機関はいずれの群も治験実施医療機関であった。最も多かった入院又は外来受診の理由は，DVd 群で治験薬投与（56%），Vd 群で「その他（治験薬投与及び有害事象を除く）」（52%）であった。有害事象のため入院した割合は両群間で同様であった（DVd 群 32%，Vd 群 35%）。

(3) 安全性

本治験の安全性の結果から，再発又は難治性の MM 患者に対して，DVd 療法の安全性プロファイルは許容可能であることが示された。概して，サイクル 1～8 では，有害事象の発現割合は Vd 群と比べて DVd 群で高かった。

DVd 群（243 例）で発現した有害事象は Vd 群（237 例）と同様で，ボルテゾミブの既知の毒性及び本剤単剤療法での既知の毒性を含んだものであり，発現割合が高かった有害事象は，血小板減少症（DVd 群 59%，Vd 群 44%），末梢性感覚ニューロパチー（DVd 群 47%，Vd 群 38%），下痢（DVd 群 32%，Vd 群 22%），貧血（DVd 群 26%，Vd 群 31%）及び疲労（DVd 群 21%，Vd 群 25%）であった。DVd 群で投与中止に至った有害事象の発現割合が低かったことから（DVd 群 7%，Vd 群 9%），本剤の上乗せによる忍容性には問題ないことが示された。Grade 3 又は 4 の有害事象の発現割合は DVd 群で高かった（DVd 群 76%，Vd 群 62%）。Grade 3 又は 4 の有害事象の発現割合が高かった主な要因は，血球減少性の有害事象（DVd 群 54%，Vd 群 40%，そのうち血小板減少症：DVd 群 45%，Vd 群 33%，好中球減少症：DVd 群 13%，Vd 群 4%，リンパ球減少症：DVd 群 10%，Vd 群 3%）が多く認められたためであった。血球減少は早期のサイクル（サイクル 1～3 の本剤 1 週間隔投与）においてより顕著であり，輸血，増殖因子，サイクル遅延及び用量調節により管理可能であった。血小板減少症及び好中球減少症の発現割合は DVd 群で高かったが，治験期間中の出血性イベントの発現割合は低く（DVd 群 7%，Vd 群 4%），Grade 3 又は 4 の感染症（DVd 群 21%，Vd 群 19%，そのうち肺炎は DVd 群 8%，Vd 群 10%），サイクル遅延又は用量調節に至った感染症（DVd 群 34%，Vd 群 28%）の発現割合は，両群間で同様であった。また，治験薬中止に至った感染症（いずれかの治験薬中止：DVd 群 4%，Vd 群 3%，すべての治験薬中止：DVd 群 3%，Vd 群 2%）の発現割合も両群間で同様であった。最終投与後 30 日以内に死亡した被験者数は，両群間で同様であった（各群 5%）。最終投与後 30 日以内の主な死因として最も多く認められたのは，有害事象［DVd 群 11 例（5%），Vd 群 10 例（4%）］であった。転帰が死亡で発現割合が高かった有害事象は，DVd 群では虚血性脳卒中及び呼吸不全（各 2 例），Vd 群では全身健康状態低下（3 例）であった。重篤な有害事象の発現割

合は，DVd 群で高かった（DVd 群 42%，Vd 群 34%）。最も発現割合が高かった重篤な有害事象は肺炎（DVd 群 8%，Vd 群 9%）であった。

本剤投与に関連した infusion related reaction（IRR）は 45%（110 例）の被験者に認められ，IRR のため治験薬投与を中止した被験者は 2 例のみであった。IRR のほとんどは Grade 1 又は 2 であり，9%（21 例）の被験者が Grade 3 の IRR を発現したが，Grade 4 又は 5 の IRR を発現した被験者はいなかった。IRR のほとんど（98%，108/110 例）が本剤初回投与の Day 1 での発現であった。末梢性ニューロパチーが DVd 群 49%，Vd 群 40%の被験者に発現し，そのうち Grade 3 又は 4 の末梢性ニューロパチーが DVd 群 5%，Vd 群 7%の被験者に認められた。DVd 群において，本治験で本剤を単剤で投与した期間中での末梢性ニューロパチーの報告は少なかった（全 Grade：5%，Grade 3 又は 4：0%）。ボルテゾミブの曝露量で調整した解析結果から，DVd 群の末梢性ニューロパチーの発現は，ボルテゾミブの曝露量が Vd 群と比べ DVd 群で多かったことによると考えられた。二次性悪性腫瘍が DVd 群の 6 例（2.4%）及び Vd 群の 1 例（0.4%）に認められた。DVd 群の 6 例中 4 例は本治験薬投与開始後 6 カ月以内に診断されており，治験薬投与以外のリスクファクターも関与している可能性が示唆された。

DVd 療法の安全性プロファイルは，年齢，性別，人種又は肝機能障害による部分集団解析で同様であった。腎機能障害を有する被験者は概して有害事象の発現割合が高かった。

血液学的検査，血液生化学検査，血液凝固系検査及び免疫グロブリンを含む臨床検査値からは，新たな知見は特定されなかった。

(4) 薬物動態，免疫原性及びバイオマーカー

薬物動態評価対象集団での daratumumab 濃度について，中等度の被験者間変動（投与後の血清中濃度における変動係数：0～30%）が認められた。本剤 1 週間隔の投与期間の少なくとも 7 回目投与まで，daratumumab のピーク血清中濃度は継続して増加し，サイクル 3 の Day 1 投与後の最高血清中 daratumumab 濃度の平均値は，初回投与後の 2.7 倍であった。サイクル 3 における残りの 1 週間隔での投与中に更に蓄積された可能性があるが，それ以降の蓄積を確認するための薬物動態の測定を設定していなかった。これまでの本剤単剤療法で実施した曝露状況と治療効果の解析では，1 週間隔投与の投与終了時点での血清中トラフ濃度は ORR に関連していることが示されている。本治験での 1 週間隔で 6 回投与後のサイクル 3 Day 1 投与前の血清中トラフ濃度の平均値は，502.4 μg/mL であった。この血清中トラフ濃度は，先行試験で認められた濃度と同様であった。概して，血清中 daratumumab のトラフ濃度及び C_{max} などの薬物動態は，先行試験で認められた薬物動態と同様であり，Vd 療法との併用は本剤の薬物動態に影響を及ぼさないと考えられる。また，先行の単剤療法試験と同様に，本治験でも本剤に対する抗体が陽性となった被験者はなく，免疫原性のリスクは低いことが示された。

2.7.6.2.1.3　結論

DVd 療法は，1 レジメン以上の前治療歴を有する MM 患者において，Vd 療法と比べ有意に高い有効性を示した。DVd 療法は Vd 療法と比べて，PFS，TTP，ORR 及び MRD 陰性率を統計学的に有意に改善した。DVd 療法の安全性プロファイルは本剤単剤療法及び Vd 療法の既知の安全性プロファイルと同様であり，臨床的に管理可能であった。以上より，1 レジメン以上の前治療

歴を有する再発又は難治性の MM 患者の治療において，DVd 療法の良好なリスクベネフィットプロファイルが示された。

2.7.6.2.2 有害事象

2016 年 1 月 11 日のクリニカルカットオフ日時点での，因果関係を問わない有害事象及び治験薬と関連性がある有害事象をそれぞれ表 2.7.6.2-1 及び表 2.7.6.2-2 に示す。

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］

	Vd n (%)	DVd n (%)
Analysis set: safety	237	243
Total number of subjects with TEAE	226 (95.4%)	240 (98.8%)
MedDRA system organ class/Preferred term		
血液およびリンパ系障害	135 (57.0%)	163 (67.1%)
血小板減少症	104 (43.9%)	143 (58.8%)
貧血	74 (31.2%)	64 (26.3%)
好中球減少症	22 (9.3%)	43 (17.7%)
リンパ球減少症	9 (3.8%)	32 (13.2%)
白血球減少症	11 (4.6%)	19 (7.8%)
発熱性好中球減少症	1 (0.4%)	4 (1.6%)
血液障害	1 (0.4%)	2 (0.8%)
白血球増加症	3 (1.3%)	0
鉄欠乏性貧血	0	1 (0.4%)
傍気管リンパ節腫脹	1 (0.4%)	0
血小板増加症	0	1 (0.4%)
感染症および寄生虫症	126 (53.2%)	164 (67.5%)
上気道感染	43 (18.1%)	60 (24.7%)
肺炎	28 (11.8%)	29 (11.9%)
気管支炎	13 (5.5%)	28 (11.5%)
結膜炎	7 (3.0%)	21 (8.6%)
鼻咽頭炎	9 (3.8%)	17 (7.0%)
帯状疱疹	7 (3.0%)	13 (5.3%)
尿路感染	6 (2.5%)	12 (4.9%)
インフルエンザ	7 (3.0%)	8 (3.3%)
副鼻腔炎	3 (1.3%)	10 (4.1%)
胃腸炎	4 (1.7%)	5 (2.1%)
口腔カンジダ症	5 (2.1%)	4 (1.6%)
ウイルス性気道感染	3 (1.3%)	6 (2.5%)
鼻炎	2 (0.8%)	7 (2.9%)
口腔ヘルペス	2 (0.8%)	6 (2.5%)
麦粒腫	3 (1.3%)	4 (1.6%)
下気道感染	3 (1.3%)	3 (1.2%)
咽頭炎	1 (0.4%)	5 (2.1%)
気管支肺炎	2 (0.8%)	3 (1.2%)
カンジダ感染	3 (1.3%)	2 (0.8%)
敗血症	3 (1.3%)	2 (0.8%)
眼感染	4 (1.7%)	0
感染	3 (1.3%)	1 (0.4%)
口腔真菌感染	2 (0.8%)	2 (0.8%)
中耳炎	1 (0.4%)	3 (1.2%)
蜂巣炎	1 (0.4%)	2 (0.8%)
膀胱炎	0	3 (1.2%)
医療機器関連感染	1 (0.4%)	2 (0.8%)
せつ	1 (0.4%)	2 (0.8%)
肺感染	2 (0.8%)	1 (0.4%)
気道感染	3 (1.3%)	0
皮膚感染	2 (0.8%)	1 (0.4%)
慢性副鼻腔炎	1 (0.4%)	1 (0.4%)
クロストリジウム・ディフィシレ感染	1 (0.4%)	1 (0.4%)
丹毒	0	2 (0.8%)
毛包炎	0	2 (0.8%)
ウイルス性胃腸炎	1 (0.4%)	1 (0.4%)
消化管感染	1 (0.4%)	1 (0.4%)
メタニューモウイルス感染	0	2 (0.8%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
粘膜感染	2 (0.8%)	0
サイトメガロウイルス性肺炎	0	2 (0.8%)
肺敗血症	0	2 (0.8%)
ライノウイルス感染	1 (0.4%)	1 (0.4%)
足部白癬	0	2 (0.8%)
気管気管支炎	1 (0.4%)	1 (0.4%)
腟感染	0	2 (0.8%)
ウイルス性上気道感染	0	2 (0.8%)
頚部膿瘍	0	1 (0.4%)
急性副鼻腔炎	1 (0.4%)	0
細菌感染	1 (0.4%)	0
体部白癬	1 (0.4%)	0
脳膿瘍	1 (0.4%)	0
カンピロバクター胃腸炎	0	1 (0.4%)
海綿静脈洞血栓症	1 (0.4%)	0
細菌性結膜炎	0	1 (0.4%)
細菌性膀胱炎	1 (0.4%)	0
大腸菌性膀胱炎	1 (0.4%)	0
憩室炎	0	1 (0.4%)
赤痢	0	1 (0.4%)
心内膜炎	1 (0.4%)	0
精巣上体炎	1 (0.4%)	0
伝染性紅斑	0	1 (0.4%)
大腸菌性敗血症	1 (0.4%)	0
眼瞼感染	0	1 (0.4%)
真菌感染	0	1 (0.4%)
真菌性食道炎	0	1 (0.4%)
壊疽	1 (0.4%)	0
サルモネラ菌性胃腸炎	0	1 (0.4%)
陰部ヘルペス	0	1 (0.4%)
歯肉炎	0	1 (0.4%)
ヘモフィルス感染	0	1 (0.4%)
単純ヘルペス	1 (0.4%)	0
喉頭炎	0	1 (0.4%)
大葉性肺炎	1 (0.4%)	0
限局性感染	1 (0.4%)	0
爪床感染	1 (0.4%)	0
爪感染	1 (0.4%)	0
ノカルジア症	1 (0.4%)	0
食道カンジダ症	0	1 (0.4%)
眼部単純ヘルペス	1 (0.4%)	0
外耳炎	0	1 (0.4%)
急性中耳炎	0	1 (0.4%)
パラインフルエンザウイルス感染	0	1 (0.4%)
爪囲炎	1 (0.4%)	0
腹膜炎	0	1 (0.4%)
百日咳	0	1 (0.4%)
ニューモシスチス・イロベチイ肺炎	0	1 (0.4%)
肺炎球菌性肺炎	0	1 (0.4%)
穿刺部位感染	1 (0.4%)	0
腎盂腎炎	0	1 (0.4%)
慢性腎盂腎炎	1 (0.4%)	0
ＲＳウイルス感染	0	1 (0.4%)
敗血症性ショック	1 (0.4%)	0
唾液腺炎	0	1 (0.4%)
ブドウ球菌性菌血症	1 (0.4%)	0
ブドウ球菌性咽頭炎	0	1 (0.4%)
ステノトロフォモナス感染	1 (0.4%)	0
皮下組織膿瘍	0	1 (0.4%)
股部白癬	1 (0.4%)	0
白癬感染	1 (0.4%)	0
真菌性舌感染	0	1 (0.4%)
扁桃炎	1 (0.4%)	0
歯膿瘍	1 (0.4%)	0

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
歯感染	0	1 (0.4%)
ウイルス感染	1 (0.4%)	0
ウイルス性咽頭炎	1 (0.4%)	0
ウイルス性ぶどう膜炎	1 (0.4%)	0
外陰腟真菌感染	1 (0.4%)	0
神経系障害	131 (55.3%)	153 (63.0%)
末梢性感覚ニューロパチー	89 (37.6%)	115 (47.3%)
神経痛	26 (11.0%)	33 (13.6%)
浮動性めまい	24 (10.1%)	24 (9.9%)
頭痛	14 (5.9%)	25 (10.3%)
錯感覚	14 (5.9%)	11 (4.5%)
味覚異常	10 (4.2%)	9 (3.7%)
末梢性運動ニューロパチー	5 (2.1%)	8 (3.3%)
振戦	8 (3.4%)	3 (1.2%)
嗜眠	2 (0.8%)	6 (2.5%)
感覚鈍麻	4 (1.7%)	3 (1.2%)
失神	6 (2.5%)	1 (0.4%)
注意力障害	1 (0.4%)	4 (1.6%)
傾眠	3 (1.3%)	2 (0.8%)
健忘	3 (1.3%)	1 (0.4%)
平衡障害	3 (1.3%)	1 (0.4%)
記憶障害	1 (0.4%)	3 (1.2%)
末梢性感覚運動ニューロパチー	2 (0.8%)	2 (0.8%)
ヘルペス後神経痛	2 (0.8%)	2 (0.8%)
失神寸前の状態	1 (0.4%)	3 (1.2%)
異常感覚	1 (0.4%)	2 (0.8%)
下肢静止不能症候群	2 (0.8%)	1 (0.4%)
坐骨神経痛	3 (1.3%)	0
運動失調	2 (0.8%)	0
認知障害	2 (0.8%)	0
虚血性脳卒中	0	2 (0.8%)
第６脳神経麻痺	0	2 (0.8%)
血管性脳症	0	2 (0.8%)
味覚消失	1 (0.4%)	0
無嗅覚	1 (0.4%)	0
自律神経ニューロパチー	1 (0.4%)	0
灼熱感	0	1 (0.4%)
粘膜の灼熱感	1 (0.4%)	0
手根管症候群	1 (0.4%)	0
脳梗塞	0	1 (0.4%)
脳虚血	1 (0.4%)	0
脳血管発作	1 (0.4%)	0
認知症	1 (0.4%)	0
塞栓性脳卒中	0	1 (0.4%)
脳症	1 (0.4%)	0
頭部不快感	0	1 (0.4%)
過眠症	0	1 (0.4%)
味覚減退	0	1 (0.4%)
筋緊張低下	1 (0.4%)	0
企図振戦	0	1 (0.4%)
精神的機能障害	0	1 (0.4%)
代謝性脳症	0	1 (0.4%)
不全単麻痺	1 (0.4%)	0
末梢性ニューロパチー	0	1 (0.4%)
不全対麻痺	0	1 (0.4%)
嗅覚錯誤	1 (0.4%)	0
腓骨神経麻痺	0	1 (0.4%)
精神運動亢進	0	1 (0.4%)
根症候群	0	1 (0.4%)
感覚消失	1 (0.4%)	0
副鼻腔炎に伴う頭痛	0	1 (0.4%)
くも膜下出血	1 (0.4%)	0
一過性脳虚血発作	0	1 (0.4%)
第７脳神経麻痺	0	1 (0.4%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
一般・全身障害および投与部位の状態	123 (51.9%)	131 (53.9%)
疲労	58 (24.5%)	52 (21.4%)
発熱	27 (11.4%)	38 (15.6%)
末梢性浮腫	19 (8.0%)	40 (16.5%)
無力症	37 (15.6%)	21 (8.6%)
浮腫	9 (3.8%)	14 (5.8%)
悪寒	3 (1.3%)	11 (4.5%)
疼痛	5 (2.1%)	9 (3.7%)
インフルエンザ様疾患	7 (3.0%)	6 (2.5%)
注射部位紅斑	7 (3.0%)	6 (2.5%)
全身健康状態低下	6 (2.5%)	2 (0.8%)
倦怠感	2 (0.8%)	6 (2.5%)
胸痛	1 (0.4%)	6 (2.5%)
注射部位反応	2 (0.8%)	4 (1.6%)
胸部不快感	2 (0.8%)	3 (1.2%)
末梢腫脹	2 (0.8%)	3 (1.2%)
顔面浮腫	0	4 (1.6%)
歩行障害	0	4 (1.6%)
状態悪化	3 (1.3%)	0
高熱	2 (0.8%)	1 (0.4%)
注入部位血管外漏出	0	3 (1.2%)
注射部位発疹	1 (0.4%)	2 (0.8%)
全身性浮腫	1 (0.4%)	1 (0.4%)
注入部位紅斑	1 (0.4%)	1 (0.4%)
非心臓性胸痛	1 (0.4%)	1 (0.4%)
カテーテル留置部位疼痛	0	1 (0.4%)
注入部位そう痒感	0	1 (0.4%)
注射部位内出血	1 (0.4%)	0
注射部位炎症	1 (0.4%)	0
注射部位刺激感	0	1 (0.4%)
注射部位浮腫	1 (0.4%)	0
注射部位疼痛	0	1 (0.4%)
限局性浮腫	1 (0.4%)	0
小結節	0	1 (0.4%)
粘膜浮腫	0	1 (0.4%)
異物感	0	1 (0.4%)
医療機器関連の血栓症	1 (0.4%)	0
胃腸障害	110 (46.4%)	143 (58.8%)
下痢	53 (22.4%)	77 (31.7%)
便秘	37 (15.6%)	48 (19.8%)
悪心	26 (11.0%)	34 (14.0%)
嘔吐	9 (3.8%)	26 (10.7%)
上腹部痛	7 (3.0%)	14 (5.8%)
腹痛	11 (4.6%)	9 (3.7%)
消化不良	13 (5.5%)	5 (2.1%)
腹部膨満	8 (3.4%)	9 (3.7%)
腹部不快感	4 (1.7%)	6 (2.5%)
胃食道逆流性疾患	2 (0.8%)	6 (2.5%)
胃炎	2 (0.8%)	4 (1.6%)
口内乾燥	2 (0.8%)	3 (1.2%)
放屁	3 (1.3%)	2 (0.8%)
口内炎	2 (0.8%)	3 (1.2%)
嚥下障害	1 (0.4%)	3 (1.2%)
歯痛	2 (0.8%)	1 (0.4%)
下腹部痛	0	2 (0.8%)
肛門出血	1 (0.4%)	1 (0.4%)
アフタ性口内炎	1 (0.4%)	1 (0.4%)
痔核	2 (0.8%)	0
メレナ	1 (0.4%)	1 (0.4%)
口腔内潰瘍形成	1 (0.4%)	1 (0.4%)
口腔内不快感	1 (0.4%)	1 (0.4%)
口腔障害	1 (0.4%)	1 (0.4%)
口腔内痛	2 (0.8%)	0
慢性膵炎	0	2 (0.8%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
歯の知覚過敏	1 (0.4%)	1 (0.4%)
腹部ヘルニア	0	1 (0.4%)
腹壁障害	0	1 (0.4%)
肛門の炎症	0	1 (0.4%)
肛門そう痒症	1 (0.4%)	0
腹水	1 (0.4%)	0
口唇炎	0	1 (0.4%)
齲歯	0	1 (0.4%)
憩室穿孔	0	1 (0.4%)
十二指腸潰瘍	0	1 (0.4%)
十二指腸炎	0	1 (0.4%)
細菌叢異常症	0	1 (0.4%)
糞塊	1 (0.4%)	0
白色便	0	1 (0.4%)
胃潰瘍	1 (0.4%)	0
びらん性胃炎	0	1 (0.4%)
胃十二指腸炎	0	1 (0.4%)
胃腸障害	1 (0.4%)	0
消化器痛	0	1 (0.4%)
歯肉痛	0	1 (0.4%)
歯肉腫脹	1 (0.4%)	0
舌痛	1 (0.4%)	0
痔出血	0	1 (0.4%)
口の感覚鈍麻	0	1 (0.4%)
イレウス	1 (0.4%)	0
嵌頓臍ヘルニア	1 (0.4%)	0
単径ヘルニア	1 (0.4%)	0
腸閉塞	0	1 (0.4%)
口唇腫脹	0	1 (0.4%)
弛緩歯	0	1 (0.4%)
マロリー・ワイス症候群	1 (0.4%)	0
食道痛	1 (0.4%)	0
口腔粘膜血腫	0	1 (0.4%)
口蓋浮腫	0	1 (0.4%)
膵炎	1 (0.4%)	0
急性膵炎	0	1 (0.4%)
小腸閉塞	0	1 (0.4%)
舌変色	0	1 (0.4%)
舌浮腫	0	1 (0.4%)
舌そう痒症	0	1 (0.4%)
舌潰瘍	1 (0.4%)	0
上部消化管出血	0	1 (0.4%)
呼吸器、胸郭および縦隔障害	77 (32.5%)	130 (53.5%)
咳嗽	30 (12.7%)	58 (23.9%)
呼吸困難	21 (8.9%)	45 (18.5%)
気管支痙攣	1 (0.4%)	23 (9.5%)
鼻出血	12 (5.1%)	12 (4.9%)
口腔咽頭痛	9 (3.8%)	8 (3.3%)
労作性呼吸困難	6 (2.5%)	10 (4.1%)
鼻閉	3 (1.3%)	12 (4.9%)
咽喉刺激感	1 (0.4%)	12 (4.9%)
湿性咳嗽	3 (1.3%)	9 (3.7%)
発声障害	6 (2.5%)	2 (0.8%)
鼻漏	1 (0.4%)	7 (2.9%)
しゃっくり	5 (2.1%)	2 (0.8%)
アレルギー性鼻炎	2 (0.8%)	4 (1.6%)
慢性閉塞性肺疾患	2 (0.8%)	3 (1.2%)
喘鳴	0	5 (2.1%)
喀血	1 (0.4%)	3 (1.2%)
胸水	2 (0.8%)	2 (0.8%)
肺塞栓症	2 (0.8%)	2 (0.8%)
呼吸不全	2 (0.8%)	2 (0.8%)
咽喉絞扼感	0	4 (1.6%)
喘息	0	3 (1.2%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
副鼻腔うっ血	2 (0.8%)	1 (0.4%)
急性肺水腫	1 (0.4%)	1 (0.4%)
アレルギー性咳嗽	0	2 (0.8%)
慢性気管支炎	1 (0.4%)	1 (0.4%)
カタル	0	2 (0.8%)
喉頭浮腫	0	2 (0.8%)
胸膜炎	1 (0.4%)	1 (0.4%)
肺水腫	2 (0.8%)	0
気道うっ血	1 (0.4%)	1 (0.4%)
窒息	0	1 (0.4%)
無気肺	1 (0.4%)	0
気管支閉塞	0	1 (0.4%)
胸水症	0	1 (0.4%)
過換気	0	1 (0.4%)
低換気	1 (0.4%)	0
上気道分泌増加	1 (0.4%)	0
間質性肺疾患	1 (0.4%)	0
肺硬化	1 (0.4%)	0
鼻閉塞	0	1 (0.4%)
器質化肺炎	0	1 (0.4%)
口腔咽頭不快感	0	1 (0.4%)
口腔咽頭腫脹	0	1 (0.4%)
咽頭浮腫	0	1 (0.4%)
胸膜痛	1 (0.4%)	0
誤嚥性肺炎	0	1 (0.4%)
肺胞出血	1 (0.4%)	0
肺動脈血栓症	0	1 (0.4%)
肺出血	0	1 (0.4%)
ラ音	1 (0.4%)	0
呼吸窮迫	0	1 (0.4%)
萎縮性鼻炎	0	1 (0.4%)
低音性連続性ラ音	0	1 (0.4%)
睡眠時無呼吸症候群	0	1 (0.4%)
くしゃみ	0	1 (0.4%)
頻呼吸	0	1 (0.4%)
上気道咳症候群	0	1 (0.4%)
筋骨格系および結合組織障害	87 (36.7%)	111 (45.7%)
背部痛	24 (10.1%)	33 (13.6%)
四肢痛	16 (6.8%)	22 (9.1%)
関節痛	11 (4.6%)	23 (9.5%)
骨痛	14 (5.9%)	14 (5.8%)
筋痙縮	5 (2.1%)	19 (7.8%)
筋骨格系胸痛	5 (2.1%)	16 (6.6%)
筋肉痛	4 (1.7%)	11 (4.5%)
筋骨格痛	3 (1.3%)	11 (4.5%)
脊椎痛	5 (2.1%)	6 (2.5%)
筋力低下	6 (2.5%)	4 (1.6%)
ミオパチー	3 (1.3%)	7 (2.9%)
頚部痛	1 (0.4%)	5 (2.1%)
関節炎	2 (0.8%)	1 (0.4%)
関節腫脹	1 (0.4%)	2 (0.8%)
四肢不快感	2 (0.8%)	1 (0.4%)
変形性関節症	0	3 (1.2%)
顎痛	0	3 (1.2%)
滑液包炎	1 (0.4%)	1 (0.4%)
側腹部痛	0	2 (0.8%)
運動性低下	1 (0.4%)	1 (0.4%)
筋攣縮	2 (0.8%)	0
顎骨壊死	1 (0.4%)	1 (0.4%)
病的骨折	0	2 (0.8%)
腱痛	0	2 (0.8%)
腱炎	1 (0.4%)	1 (0.4%)
骨形成亢進	0	1 (0.4%)
骨病変	0	1 (0.4%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
尾骨痛	1 (0.4%)	0
腱付着部症	1 (0.4%)	0
単径部痛	0	1 (0.4%)
出血性関節症	0	1 (0.4%)
椎間板突出	1 (0.4%)	0
顎障害	1 (0.4%)	0
関節硬直	0	1 (0.4%)
下肢腫瘤	0	1 (0.4%)
筋肉疲労	0	1 (0.4%)
筋緊張	0	1 (0.4%)
骨壊死	1 (0.4%)	0
骨減少症	0	1 (0.4%)
骨粗鬆症	0	1 (0.4%)
多発性関節炎	1 (0.4%)	0
脊柱管狭窄症	1 (0.4%)	0
滑液嚢腫	0	1 (0.4%)
顎関節症候群	1 (0.4%)	0
腱障害	0	1 (0.4%)
代謝および栄養障害	66 (27.8%)	93 (38.3%)
高血糖	18 (7.6%)	21 (8.6%)
食欲減退	12 (5.1%)	22 (9.1%)
低カリウム血症	11 (4.6%)	22 (9.1%)
低カルシウム血症	11 (4.6%)	10 (4.1%)
低リン酸血症	7 (3.0%)	13 (5.3%)
低ナトリウム血症	6 (2.5%)	9 (3.7%)
高カルシウム血症	6 (2.5%)	7 (2.9%)
高尿酸血症	6 (2.5%)	4 (1.6%)
低アルブミン血症	2 (0.8%)	8 (3.3%)
糖尿病	2 (0.8%)	7 (2.9%)
高ナトリウム血症	3 (1.3%)	4 (1.6%)
脱水	3 (1.3%)	3 (1.2%)
低マグネシウム血症	2 (0.8%)	4 (1.6%)
体液貯留	3 (1.3%)	2 (0.8%)
高カリウム血症	2 (0.8%)	3 (1.2%)
脂質異常症	1 (0.4%)	1 (0.4%)
水分過負荷	0	2 (0.8%)
高アミラーゼ血症	0	2 (0.8%)
低血糖症	2 (0.8%)	0
過小食	0	2 (0.8%)
食欲亢進	1 (0.4%)	1 (0.4%)
鉄欠乏	0	2 (0.8%)
代謝性アシドーシス	1 (0.4%)	1 (0.4%)
アシドーシス	0	1 (0.4%)
コントロール不良の糖尿病	0	1 (0.4%)
糖尿病性ケトアシドーシス	1 (0.4%)	0
高リン酸塩血症	0	1 (0.4%)
血液量減少症	0	1 (0.4%)
腫瘍崩壊症候群	0	1 (0.4%)
２型糖尿病	0	1 (0.4%)
ビタミンＢ１２欠乏	0	1 (0.4%)
ビタミンＤ欠乏	1 (0.4%)	0
精神障害	53 (22.4%)	67 (27.6%)
不眠症	35 (14.8%)	41 (16.9%)
落ち着きのなさ	7 (3.0%)	8 (3.3%)
うつ病	5 (2.1%)	8 (3.3%)
激越	5 (2.1%)	4 (1.6%)
不安	6 (2.5%)	3 (1.2%)
易刺激性	4 (1.7%)	3 (1.2%)
錯乱状態	3 (1.3%)	3 (1.2%)
睡眠障害	2 (0.8%)	4 (1.6%)
譫妄	3 (1.3%)	1 (0.4%)
転導性	2 (0.8%)	1 (0.4%)
失見当識	1 (0.4%)	1 (0.4%)
気分動揺	0	2 (0.8%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
感情障害	0	1 (0.4%)
抑うつ気分	0	1 (0.4%)
感情的苦悩	1 (0.4%)	0
多幸気分	1 (0.4%)	0
幻覚	0	1 (0.4%)
リビドー減退	0	1 (0.4%)
精神障害	1 (0.4%)	0
気分変化	0	1 (0.4%)
神経過敏	1 (0.4%)	0
パニック障害	0	1 (0.4%)
妄想症	1 (0.4%)	0
精神的機能代償不全	0	1 (0.4%)
物質誘発性精神病性障害	1 (0.4%)	0
血管障害	32 (13.5%)	52 (21.4%)
高血圧	8 (3.4%)	21 (8.6%)
低血圧	10 (4.2%)	12 (4.9%)
潮紅	3 (1.3%)	5 (2.1%)
血腫	3 (1.3%)	5 (2.1%)
起立性低血圧	4 (1.7%)	3 (1.2%)
深部静脈血栓症	1 (0.4%)	3 (1.2%)
ほてり	1 (0.4%)	3 (1.2%)
血栓症	1 (0.4%)	2 (0.8%)
循環虚脱	2 (0.8%)	0
高血圧クリーゼ	1 (0.4%)	1 (0.4%)
表在性血栓性静脈炎	2 (0.8%)	0
静脈塞栓症	1 (0.4%)	0
充血	0	1 (0.4%)
腹腔内血腫	0	1 (0.4%)
末梢動脈瘤	0	1 (0.4%)
末梢静脈疾患	0	1 (0.4%)
静脈炎	0	1 (0.4%)
静脈硬化症	0	1 (0.4%)
血栓性静脈炎	0	1 (0.4%)
血管拡張	0	1 (0.4%)
四肢静脈血栓症	1 (0.4%)	0
皮膚および皮下組織障害	32 (13.5%)	49 (20.2%)
発疹	7 (3.0%)	13 (5.3%)
多汗症	3 (1.3%)	7 (2.9%)
紅斑	3 (1.3%)	5 (2.1%)
そう痒症	3 (1.3%)	5 (2.1%)
寝汗	2 (0.8%)	4 (1.6%)
斑状丘疹状皮疹	1 (0.4%)	4 (1.6%)
脱毛症	2 (0.8%)	2 (0.8%)
褥瘡性潰瘍	2 (0.8%)	1 (0.4%)
皮膚病変	3 (1.3%)	0
皮膚潰瘍	0	3 (1.2%)
蕁麻疹	0	3 (1.2%)
アレルギー性皮膚炎	0	2 (0.8%)
皮膚乾燥	2 (0.8%)	0
湿疹	0	2 (0.8%)
手掌・足底発赤知覚不全症候群	0	2 (0.8%)
点状出血	2 (0.8%)	0
皮膚反応	1 (0.4%)	1 (0.4%)
水疱	0	1 (0.4%)
血性水疱	0	1 (0.4%)
皮膚嚢腫	0	1 (0.4%)
皮膚炎	1 (0.4%)	0
過剰肉芽組織	1 (0.4%)	0
嵌入爪	1 (0.4%)	0
皮膚粘膜発疹	0	1 (0.4%)
爪線状隆起	1 (0.4%)	0
丘疹	1 (0.4%)	0
光線過敏性反応	0	1 (0.4%)
全身性そう痒症	1 (0.4%)	0

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
紅斑性皮疹	0	1 (0.4%)
全身性皮疹	1 (0.4%)	0
痂皮	0	1 (0.4%)
皮膚障害	1 (0.4%)	0
皮膚剥脱	0	1 (0.4%)
皮膚亀裂	0	1 (0.4%)
皮膚出血	1 (0.4%)	0
皮膚色素過剰	0	1 (0.4%)
皮膚腫瘤	1 (0.4%)	0
顔面腫脹	0	1 (0.4%)
臨床検査	23 (9.7%)	49 (20.2%)
アラニンアミノトランスフェラーゼ増加	10 (4.2%)	17 (7.0%)
アスパラギン酸アミノトランスフェラーゼ増加	5 (2.1%)	12 (4.9%)
体重減少	3 (1.3%)	13 (5.3%)
γ－グルタミルトランスフェラーゼ増加	4 (1.7%)	7 (2.9%)
血中クレアチニン増加	4 (1.7%)	5 (2.1%)
血中アルカリホスファターゼ増加	4 (1.7%)	4 (1.6%)
体重増加	2 (0.8%)	6 (2.5%)
血中乳酸脱水素酵素増加	1 (0.4%)	3 (1.2%)
Ｃ－反応性蛋白増加	1 (0.4%)	1 (0.4%)
活性化部分トロンボプラスチン時間延長	0	1 (0.4%)
血中ホモシステイン増加	1 (0.4%)	0
血中リン減少	0	1 (0.4%)
呼吸音異常	0	1 (0.4%)
心電図ＱＴ間隔異常	0	1 (0.4%)
γ－グルタミルトランスフェラーゼ	0	1 (0.4%)
糸球体濾過率減少	0	1 (0.4%)
グリコヘモグロビン増加	0	1 (0.4%)
深吸気量減少	0	1 (0.4%)
国際標準比増加	0	1 (0.4%)
リパーゼ増加	0	1 (0.4%)
総蛋白増加	1 (0.4%)	0
眼障害	27 (11.4%)	42 (17.3%)
霧視	9 (3.8%)	5 (2.1%)
流涙増加	1 (0.4%)	11 (4.5%)
眼乾燥	6 (2.5%)	5 (2.1%)
複視	1 (0.4%)	3 (1.2%)
眼瞼炎	3 (1.3%)	0
白内障	0	3 (1.2%)
結膜出血	0	3 (1.2%)
結膜浮腫	0	3 (1.2%)
眼刺激	1 (0.4%)	2 (0.8%)
眼そう痒症	2 (0.8%)	1 (0.4%)
視力低下	1 (0.4%)	2 (0.8%)
視力障害	2 (0.8%)	1 (0.4%)
霰粒腫	2 (0.8%)	0
眼脂	1 (0.4%)	1 (0.4%)
眼の障害	0	2 (0.8%)
眼痛	1 (0.4%)	1 (0.4%)
眼充血	0	2 (0.8%)
網膜症	1 (0.4%)	1 (0.4%)
眼精疲労	0	1 (0.4%)
眼瞼痙攣	1 (0.4%)	0
嚢胞様黄斑浮腫	0	1 (0.4%)
眼瞼紅斑	0	1 (0.4%)
眼出血	0	1 (0.4%)
眼瞼浮腫	0	1 (0.4%)
虹彩炎	0	1 (0.4%)
眼部不快感	1 (0.4%)	0
網膜剥離	1 (0.4%)	0
潰瘍性角膜炎	1 (0.4%)	0
傷害、中毒および処置合併症	21 (8.9%)	31 (12.8%)
転倒	5 (2.1%)	6 (2.5%)
挫傷	3 (1.3%)	3 (1.2%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
肋骨骨折	2 (0.8%)	2 (0.8%)
上腕骨骨折	0	3 (1.2%)
四肢損傷	1 (0.4%)	2 (0.8%)
大腿骨骨折	0	2 (0.8%)
股関節部骨折	1 (0.4%)	1 (0.4%)
関節損傷	2 (0.8%)	0
裂傷	1 (0.4%)	1 (0.4%)
肩甲骨骨折	0	2 (0.8%)
創傷	0	2 (0.8%)
アレルギー性輸血反応	0	1 (0.4%)
肛門損傷	1 (0.4%)	0
足関節部骨折	0	1 (0.4%)
節足動物咬傷	0	1 (0.4%)
節足動物刺傷	1 (0.4%)	0
足骨折	0	1 (0.4%)
腰椎骨折	0	1 (0.4%)
筋断裂	0	1 (0.4%)
膝蓋骨骨折	1 (0.4%)	0
眼窩周囲挫傷	0	1 (0.4%)
眼窩周囲血腫	1 (0.4%)	0
処置後出血	0	1 (0.4%)
処置による疼痛	0	1 (0.4%)
恥骨骨折	0	1 (0.4%)
橈骨神経損傷	0	1 (0.4%)
皮膚擦過傷	1 (0.4%)	0
脊椎圧迫骨折	0	1 (0.4%)
脊椎骨折	0	1 (0.4%)
皮下血腫	0	1 (0.4%)
硬膜下血腫	1 (0.4%)	0
胸椎骨折	1 (0.4%)	0
歯の完全脱臼	1 (0.4%)	0
歯牙破折	0	1 (0.4%)
上肢骨折	0	1 (0.4%)
腎および尿路障害	28 (11.8%)	21 (8.6%)
腎機能障害	8 (3.4%)	5 (2.1%)
急性腎不全	4 (1.7%)	4 (1.6%)
尿閉	4 (1.7%)	3 (1.2%)
慢性腎臓病	2 (0.8%)	2 (0.8%)
血尿	1 (0.4%)	2 (0.8%)
夜間頻尿	1 (0.4%)	2 (0.8%)
骨髄腫円柱腎症	1 (0.4%)	1 (0.4%)
中毒性ネフロパシー	2 (0.8%)	0
頻尿	1 (0.4%)	1 (0.4%)
腎不全	2 (0.8%)	0
尿路閉塞	1 (0.4%)	1 (0.4%)
膀胱閉塞	1 (0.4%)	0
尿路結石	1 (0.4%)	0
排尿困難	1 (0.4%)	0
失禁	0	1 (0.4%)
尿意切迫	0	1 (0.4%)
多尿	0	1 (0.4%)
腎仙痛	1 (0.4%)	0
腎臓痛	0	1 (0.4%)
腎尿細管壊死	1 (0.4%)	0
心臓障害	15 (6.3%)	33 (13.6%)
心房細動	4 (1.7%)	11 (4.5%)
心不全	3 (1.3%)	4 (1.6%)
動悸	2 (0.8%)	5 (2.1%)
洞性頻脈	1 (0.4%)	6 (2.5%)
うっ血性心不全	2 (0.8%)	3 (1.2%)
狭心症	1 (0.4%)	2 (0.8%)
上室性頻脈	1 (0.4%)	2 (0.8%)
急性心筋梗塞	0	2 (0.8%)
徐脈	1 (0.4%)	1 (0.4%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
心停止	1 (0.4%)	1 (0.4%)
心原性ショック	1 (0.4%)	1 (0.4%)
心筋梗塞	2 (0.8%)	0
急性冠動脈症候群	0	1 (0.4%)
上室性不整脈	0	1 (0.4%)
心房粗動	0	1 (0.4%)
左脚ブロック	0	1 (0.4%)
冠動脈狭窄	1 (0.4%)	0
期外収縮	1 (0.4%)	0
僧帽弁閉鎖不全症	0	1 (0.4%)
肺動脈弁閉鎖不全症	0	1 (0.4%)
頻脈	0	1 (0.4%)
三尖弁閉鎖不全症	0	1 (0.4%)
心室性不整脈	0	1 (0.4%)
心室性期外収縮	1 (0.4%)	0
耳および迷路障害	4 (1.7%)	21 (8.6%)
回転性めまい	2 (0.8%)	9 (3.7%)
耳鳴	2 (0.8%)	6 (2.5%)
耳痛	0	4 (1.6%)
耳垢栓塞	0	1 (0.4%)
難聴	0	1 (0.4%)
両耳難聴	0	1 (0.4%)
耳不快感	0	1 (0.4%)
耳そう痒症	0	1 (0.4%)
乳突洞滲出液	0	1 (0.4%)
中耳の炎症	0	1 (0.4%)
生殖系および乳房障害	7 (3.0%)	14 (5.8%)
骨盤痛	2 (0.8%)	4 (1.6%)
亀頭包皮炎	1 (0.4%)	2 (0.8%)
良性前立腺肥大症	2 (0.8%)	1 (0.4%)
精巣痛	0	3 (1.2%)
腺筋症	0	1 (0.4%)
乳房圧痛	0	1 (0.4%)
勃起不全	0	1 (0.4%)
生殖器痛	1 (0.4%)	0
月経障害	0	1 (0.4%)
不規則月経	0	1 (0.4%)
陰嚢痛	0	1 (0.4%)
子宮出血	1 (0.4%)	0
内分泌障害	5 (2.1%)	12 (4.9%)
クッシング様症状	3 (1.3%)	7 (2.9%)
副腎機能不全	2 (0.8%)	1 (0.4%)
クッシング症候群	0	2 (0.8%)
甲状腺腫	0	1 (0.4%)
甲状腺機能亢進症	0	1 (0.4%)
肝胆道系障害	5 (2.1%)	9 (3.7%)
高ビリルビン血症	2 (0.8%)	5 (2.1%)
胆嚢炎	0	3 (1.2%)
慢性胆嚢炎	0	1 (0.4%)
胆汁うっ滞	1 (0.4%)	0
胆嚢障害	0	1 (0.4%)
肝アミロイドーシス	1 (0.4%)	0
虚血性肝炎	1 (0.4%)	0
門脈域の炎症	1 (0.4%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4%)	8 (3.3%)
結腸腺癌	0	1 (0.4%)
乳癌	0	1 (0.4%)
再発乳癌	1 (0.4%)	0
胃腸管腺腫	0	1 (0.4%)
脂肪肉腫	0	1 (0.4%)
形質細胞腫	0	1 (0.4%)
皮膚乳頭腫	0	1 (0.4%)
皮膚有棘細胞癌	0	1 (0.4%)

表 2.7.6.2-1 有害事象［MMY3004 試験，安全性解析対象集団］（続き）

	Vd n (%)	DVd n (%)
移行上皮癌	0	1 (0.4%)
子宮平滑筋腫	0	1 (0.4%)
免疫系障害	3 (1.3%)	1 (0.4%)
低γグロブリン血症	1 (0.4%)	1 (0.4%)
季節性アレルギー	2 (0.8%)	0

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02A.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\TSFAE02A.SAS] 05APR2016, 16:03

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
Analysis set: safety	237			243			
Total number of subjects with TEAE related to study treatment	196 (82.7%)	182 (76.8%)	143 (60.3%)	225 (92.6%)	182 (74.9%)	207 (85.2%)	165 (67.9%)
MedDRA system organ class/Preferred term							
神経系障害	111 (46.8%)	108 (45.6%)	32 (13.5%)	134 (55.1%)	24 (9.9%)	129 (53.1%)	27 (11.1%)
末梢性感覚ニューロパチー	84 (35.4%)	84 (35.4%)	3 (1.3%)	115 (47.3%)	7 (2.9%)	115 (47.3%)	5 (2.1%)
神経痛	25 (10.5%)	25 (10.5%)	2 (0.8%)	33 (13.6%)	0	33 (13.6%)	0
浮動性めまい	18 (7.6%)	16 (6.8%)	7 (3.0%)	12 (4.9%)	4 (1.6%)	6 (2.5%)	6 (2.5%)
錯感覚	9 (3.8%)	9 (3.8%)	1 (0.4%)	11 (4.5%)	3 (1.2%)	9 (3.7%)	1 (0.4%)
味覚異常	9 (3.8%)	6 (2.5%)	6 (2.5%)	7 (2.9%)	2 (0.8%)	7 (2.9%)	3 (1.2%)
頭痛	6 (2.5%)	1 (0.4%)	6 (2.5%)	9 (3.7%)	5 (2.1%)	4 (1.6%)	4 (1.6%)
末梢性運動ニューロパチー	5 (2.1%)	5 (2.1%)	0	8 (3.3%)	0	7 (2.9%)	1 (0.4%)
振戦	7 (3.0%)	2 (0.8%)	6 (2.5%)	2 (0.8%)	0	0	2 (0.8%)
嗜眠	2 (0.8%)	2 (0.8%)	2 (0.8%)	5 (2.1%)	0	5 (2.1%)	1 (0.4%)
感覚鈍麻	3 (1.3%)	3 (1.3%)	1 (0.4%)	2 (0.8%)	0	2 (0.8%)	0
平衡障害	3 (1.3%)	3 (1.3%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0
注意力障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.2%)	2 (0.8%)	2 (0.8%)	3 (1.2%)
末梢性感覚運動ニューロパチー	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	0	2 (0.8%)	0
失神寸前の状態	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.2%)	1 (0.4%)	3 (1.2%)	0
記憶障害	0	0	0	3 (1.2%)	2 (0.8%)	3 (1.2%)	3 (1.2%)
下肢静止不能症候群	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
運動失調	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	0	0	0
異常感覚	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
味覚消失	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
無嗅覚	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
自律神経ニューロパチー	1 (0.4%)	1 (0.4%)	0	0	0	0	0
灼熱感	0	0	0	1 (0.4%)	0	0	1 (0.4%)
粘膜の灼熱感	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
脳虚血	1 (0.4%)	0	1 (0.4%)	0	0	0	0
認知障害	1 (0.4%)	0	1 (0.4%)	0	0	0	0
塞栓性脳卒中	0	0	0	1 (0.4%)	0	0	1 (0.4%)
脳症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
頭部不快感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
過眠症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
筋緊張低下	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
企図振戦	0	0	0	1 (0.4%)	0	1 (0.4%)	0
虚血性脳卒中	0	0	0	1 (0.4%)	0	1 (0.4%)	0
精神的機能障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
末梢性ニューロパチー	0	0	0	1 (0.4%)	0	1 (0.4%)	0
嗅覚錯誤	1 (0.4%)	1 (0.4%)	0	0	0	0	0
腓骨神経麻痺	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
ヘルペス後神経痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
精神運動亢進	0	0	0	1 (0.4%)	0	0	1 (0.4%)
一過性脳虚血発作	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
第６脳神経麻痺	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
血管性脳症	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
血液およびリンパ系障害	92 (38.8%)	91 (38.4%)	18 (7.6%)	143 (58.8%)	95 (39.1%)	135 (55.6%)	35 (14.4%)
血小板減少症	80 (33.8%)	80 (33.8%)	7 (3.0%)	129 (53.1%)	73 (30.0%)	123 (50.6%)	10 (4.1%)
貧血	28 (11.8%)	28 (11.8%)	6 (2.5%)	33 (13.6%)	22 (9.1%)	29 (11.9%)	5 (2.1%)
好中球減少症	13 (5.5%)	13 (5.5%)	1 (0.4%)	34 (14.0%)	17 (7.0%)	31 (12.8%)	2 (0.8%)
リンパ球減少症	7 (3.0%)	7 (3.0%)	6 (2.5%)	29 (11.9%)	26 (10.7%)	24 (9.9%)	17 (7.0%)
白血球減少症	8 (3.4%)	8 (3.4%)	0	15 (6.2%)	10 (4.1%)	15 (6.2%)	2 (0.8%)
発熱性好中球減少症	1 (0.4%)	1 (0.4%)	0	2 (0.8%)	2 (0.8%)	2 (0.8%)	0
血液障害	0	0	0	1 (0.4%)	1 (0.4%)	0	0
白血球増加症	1 (0.4%)	0	1 (0.4%)	0	0	0	0

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］
（続き）

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
胃腸障害	72 (30.4%)	59 (24.9%)	41 (17.3%)	100 (41.2%)	50 (20.6%)	70 (28.8%)	44 (18.1%)
下痢	29 (12.2%)	28 (11.8%)	7 (3.0%)	48 (19.8%)	19 (7.8%)	40 (16.5%)	11 (4.5%)
便秘	25 (10.5%)	24 (10.1%)	7 (3.0%)	30 (12.3%)	9 (3.7%)	25 (10.3%)	10 (4.1%)
悪心	11 (4.6%)	11 (4.6%)	7 (3.0%)	25 (10.3%)	16 (6.6%)	14 (5.8%)	9 (3.7%)
嘔吐	5 (2.1%)	4 (1.7%)	1 (0.4%)	18 (7.4%)	12 (4.9%)	4 (1.6%)	4 (1.6%)
消化不良	11 (4.6%)	5 (2.1%)	9 (3.8%)	4 (1.6%)	2 (0.8%)	0	2 (0.8%)
腹痛	5 (2.1%)	5 (2.1%)	4 (1.7%)	6 (2.5%)	0	4 (1.6%)	4 (1.6%)
腹部膨満	5 (2.1%)	1 (0.4%)	4 (1.7%)	5 (2.1%)	1 (0.4%)	1 (0.4%)	5 (2.1%)
上腹部痛	5 (2.1%)	1 (0.4%)	5 (2.1%)	5 (2.1%)	1 (0.4%)	1 (0.4%)	4 (1.6%)
腹部不快感	2 (0.8%)	2 (0.8%)	2 (0.8%)	5 (2.1%)	1 (0.4%)	1 (0.4%)	4 (1.6%)
放屁	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)
胃炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.2%)	0	0	3 (1.2%)
胃食道逆流性疾患	1 (0.4%)	0	1 (0.4%)	3 (1.2%)	0	0	3 (1.2%)
アフタ性口内炎	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	1 (0.4%)
口腔内不快感	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
口内炎	0	0	0	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肛門出血	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
憩室穿孔	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
十二指腸潰瘍	0	0	0	1 (0.4%)	0	0	1 (0.4%)
嚥下障害	0	0	0	1 (0.4%)	1 (0.4%)	0	0
糞塊	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
胃腸障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0
イレウス	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
腸閉塞	0	0	0	1 (0.4%)	0	1 (0.4%)	0
口唇腫脹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
口腔内潰瘍形成	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
口腔障害	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
口腔内痛	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
口蓋浮腫	0	0	0	1 (0.4%)	1 (0.4%)	0	0
膵炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
歯の知覚過敏	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
小腸閉塞	0	0	0	1 (0.4%)	0	1 (0.4%)	0
舌そう痒症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
上部消化管出血	0	0	0	1 (0.4%)	0	0	1 (0.4%)
一般・全身障害および投与部位の状態	65 (27.4%)	54 (22.8%)	40 (16.9%)	96 (39.5%)	59 (24.3%)	64 (26.3%)	62 (25.5%)
疲労	35 (14.8%)	31 (13.1%)	20 (8.4%)	40 (16.5%)	27 (11.1%)	36 (14.8%)	23 (9.5%)
末梢性浮腫	11 (4.6%)	5 (2.1%)	11 (4.6%)	26 (10.7%)	4 (1.6%)	8 (3.3%)	24 (9.9%)
発熱	5 (2.1%)	3 (1.3%)	5 (2.1%)	25 (10.3%)	17 (7.0%)	13 (5.3%)	16 (6.6%)
無力症	16 (6.8%)	14 (5.9%)	9 (3.8%)	11 (4.5%)	6 (2.5%)	9 (3.7%)	8 (3.3%)
浮腫	4 (1.7%)	1 (0.4%)	4 (1.7%)	13 (5.3%)	0	0	13 (5.3%)
悪寒	2 (0.8%)	2 (0.8%)	2 (0.8%)	10 (4.1%)	10 (4.1%)	0	1 (0.4%)
注射部位紅斑	6 (2.5%)	6 (2.5%)	0	6 (2.5%)	0	6 (2.5%)	0
注射部位反応	2 (0.8%)	2 (0.8%)	0	4 (1.6%)	0	4 (1.6%)	0
倦怠感	2 (0.8%)	2 (0.8%)	1 (0.4%)	4 (1.6%)	2 (0.8%)	2 (0.8%)	3 (1.2%)
疼痛	2 (0.8%)	0	2 (0.8%)	4 (1.6%)	4 (1.6%)	1 (0.4%)	2 (0.8%)
胸部不快感	1 (0.4%)	0	1 (0.4%)	2 (0.8%)	2 (0.8%)	0	0
顔面浮腫	0	0	0	3 (1.2%)	2 (0.8%)	2 (0.8%)	1 (0.4%)
歩行障害	0	0	0	3 (1.2%)	0	3 (1.2%)	1 (0.4%)
インフルエンザ様疾患	0	0	0	3 (1.2%)	3 (1.2%)	2 (0.8%)	2 (0.8%)
全身性浮腫	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
注入部位紅斑	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
注射部位発疹	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
高熱	1 (0.4%)	1 (0.4%)	0	0	0	0	0
注入部位そう痒感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
注射部位内出血	1 (0.4%)	1 (0.4%)	0	0	0	0	0
注射部位炎症	1 (0.4%)	1 (0.4%)	0	0	0	0	0
注射部位刺激感	0	0	0	1 (0.4%)	0	1 (0.4%)	0
注射部位浮腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0
注射部位疼痛	0	0	0	1 (0.4%)	0	1 (0.4%)	0
限局性浮腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］
（続き）

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
粘膜浮腫	0	0	0	1 (0.4%)	1 (0.4%)	0	0
末梢腫脹	0	0	0	1 (0.4%)	0	1 (0.4%)	0
感染症および寄生虫症	59 (24.9%)	41 (17.3%)	53 (22.4%)	80 (32.9%)	41 (16.9%)	51 (21.0%)	66 (27.2%)
上気道感染	16 (6.8%)	12 (5.1%)	15 (6.3%)	25 (10.3%)	15 (6.2%)	16 (6.6%)	21 (8.6%)
肺炎	15 (6.3%)	10 (4.2%)	14 (5.9%)	18 (7.4%)	11 (4.5%)	12 (4.9%)	14 (5.8%)
気管支炎	7 (3.0%)	5 (2.1%)	7 (3.0%)	12 (4.9%)	7 (2.9%)	6 (2.5%)	9 (3.7%)
帯状疱疹	5 (2.1%)	4 (1.7%)	3 (1.3%)	8 (3.3%)	4 (1.6%)	8 (3.3%)	6 (2.5%)
結膜炎	2 (0.8%)	1 (0.4%)	1 (0.4%)	9 (3.7%)	4 (1.6%)	5 (2.1%)	4 (1.6%)
副鼻腔炎	2 (0.8%)	2 (0.8%)	2 (0.8%)	6 (2.5%)	2 (0.8%)	3 (1.2%)	5 (2.1%)
口腔カンジダ症	4 (1.7%)	1 (0.4%)	4 (1.7%)	2 (0.8%)	0	0	2 (0.8%)
口腔ヘルペス	2 (0.8%)	2 (0.8%)	1 (0.4%)	4 (1.6%)	0	3 (1.2%)	2 (0.8%)
尿路感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	5 (2.1%)	1 (0.4%)	1 (0.4%)	3 (1.2%)
鼻炎	1 (0.4%)	0	1 (0.4%)	4 (1.6%)	1 (0.4%)	1 (0.4%)	4 (1.6%)
口腔真菌感染	2 (0.8%)	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.8%)
カンジダ感染	2 (0.8%)	0	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
インフルエンザ	2 (0.8%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
敗血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	2 (0.8%)
気管支肺炎	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
せつ	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
胃腸炎	2 (0.8%)	1 (0.4%)	2 (0.8%)	0	0	0	0
消化管感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
麦粒腫	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	0	1 (0.4%)
下気道感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
咽頭炎	0	0	0	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
サイトメガロウイルス性肺炎	0	0	0	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.8%)
急性副鼻腔炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
体部白癬	1 (0.4%)	0	1 (0.4%)	0	0	0	0
蜂巣炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
細菌性結膜炎	0	0	0	1 (0.4%)	1 (0.4%)	0	0
医療機器関連感染	0	0	0	1 (0.4%)	0	0	1 (0.4%)
伝染性紅斑	0	0	0	1 (0.4%)	0	0	1 (0.4%)
眼感染	1 (0.4%)	0	1 (0.4%)	0	0	0	0
眼瞼感染	0	0	0	1 (0.4%)	0	0	1 (0.4%)
毛包炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
真菌感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ウイルス性胃腸炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
陰部ヘルペス	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
単純ヘルペス	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
喉頭炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
大葉性肺炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
肺感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
粘膜感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0
鼻咽頭炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
食道カンジダ症	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
眼部単純ヘルペス	1 (0.4%)	1 (0.4%)	0	0	0	0	0
腹膜炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
百日咳	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肺炎球菌性肺炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肺敗血症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
腎盂腎炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
ＲＳウイルス感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
気道感染	1 (0.4%)	1 (0.4%)	0	0	0	0	0
ウイルス性気道感染	0	0	0	1 (0.4%)	1 (0.4%)	0	0
ライノウイルス感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚感染	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
ブドウ球菌性咽頭炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
足部白癬	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
真菌性舌感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］
（続き）

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
気管気管支炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
腟感染	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
ウイルス性咽頭炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
ウイルス性上気道感染	0	0	0	1 (0.4%)	0	0	1 (0.4%)
ウイルス性ぶどう膜炎	1 (0.4%)	1 (0.4%)	0	0	0	0	0
呼吸器、胸郭および縦隔障害	30 (12.7%)	13 (5.5%)	24 (10.1%)	103 (42.4%)	96 (39.5%)	20 (8.2%)	27 (11.1%)
呼吸困難	10 (4.2%)	5 (2.1%)	8 (3.4%)	36 (14.8%)	32 (13.2%)	4 (1.6%)	6 (2.5%)
咳嗽	7 (3.0%)	2 (0.8%)	7 (3.0%)	33 (13.6%)	27 (11.1%)	6 (2.5%)	14 (5.8%)
気管支痙攣	0	0	0	22 (9.1%)	22 (9.1%)	0	0
咽喉刺激感	1 (0.4%)	0	1 (0.4%)	12 (4.9%)	12 (4.9%)	0	0
鼻閉	0	0	0	11 (4.5%)	11 (4.5%)	0	1 (0.4%)
鼻出血	4 (1.7%)	3 (1.3%)	1 (0.4%)	5 (2.1%)	3 (1.2%)	5 (2.1%)	0
労作性呼吸困難	4 (1.7%)	2 (0.8%)	4 (1.7%)	4 (1.6%)	3 (1.2%)	0	3 (1.2%)
発声障害	4 (1.7%)	0	4 (1.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
喘鳴	0	0	0	5 (2.1%)	5 (2.1%)	1 (0.4%)	1 (0.4%)
口腔咽頭痛	1 (0.4%)	0	1 (0.4%)	3 (1.2%)	2 (0.8%)	1 (0.4%)	2 (0.8%)
アレルギー性鼻炎	0	0	0	4 (1.6%)	3 (1.2%)	1 (0.4%)	1 (0.4%)
鼻漏	0	0	0	4 (1.6%)	4 (1.6%)	0	0
咽喉絞扼感	0	0	0	4 (1.6%)	4 (1.6%)	0	0
しゃっくり	3 (1.3%)	2 (0.8%)	1 (0.4%)	0	0	0	0
湿性咳嗽	1 (0.4%)	0	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.8%)
アレルギー性咳嗽	0	0	0	2 (0.8%)	2 (0.8%)	0	0
喉頭浮腫	0	0	0	2 (0.8%)	2 (0.8%)	0	0
喘息	0	0	0	1 (0.4%)	1 (0.4%)	0	0
慢性気管支炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
胸水症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
鼻閉塞	0	0	0	1 (0.4%)	1 (0.4%)	0	0
器質化肺炎	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
口腔咽頭不快感	0	0	0	1 (0.4%)	1 (0.4%)	0	0
口腔咽頭腫脹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
咽頭浮腫	0	0	0	1 (0.4%)	1 (0.4%)	0	0
胸水	1 (0.4%)	0	1 (0.4%)	0	0	0	0
胸膜炎	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
肺動脈血栓症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肺水腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
呼吸不全	1 (0.4%)	0	1 (0.4%)	0	0	0	0
気道うっ血	0	0	0	1 (0.4%)	1 (0.4%)	0	0
低音性連続性ラ音	0	0	0	1 (0.4%)	1 (0.4%)	0	0
副鼻腔うっ血	1 (0.4%)	0	1 (0.4%)	0	0	0	0
上気道咳症候群	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
精神障害	44 (18.6%)	3 (1.3%)	44 (18.6%)	48 (19.8%)	10 (4.1%)	7 (2.9%)	45 (18.5%)
不眠症	30 (12.7%)	1 (0.4%)	30 (12.7%)	31 (12.8%)	7 (2.9%)	3 (1.2%)	29 (11.9%)
落ち着きのなさ	6 (2.5%)	1 (0.4%)	6 (2.5%)	6 (2.5%)	1 (0.4%)	2 (0.8%)	6 (2.5%)
激越	5 (2.1%)	0	5 (2.1%)	4 (1.6%)	1 (0.4%)	1 (0.4%)	4 (1.6%)
不安	5 (2.1%)	0	5 (2.1%)	2 (0.8%)	0	0	2 (0.8%)
易刺激性	4 (1.7%)	0	4 (1.7%)	3 (1.2%)	0	0	3 (1.2%)
うつ病	3 (1.3%)	0	3 (1.3%)	2 (0.8%)	0	0	2 (0.8%)
錯乱状態	2 (0.8%)	1 (0.4%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	1 (0.4%)
睡眠障害	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	0	0	1 (0.4%)
転導性	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
気分動揺	0	0	0	2 (0.8%)	0	0	2 (0.8%)
感情障害	0	0	0	1 (0.4%)	0	0	1 (0.4%)
感情的苦悩	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
リビドー減退	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
気分変化	0	0	0	1 (0.4%)	0	0	1 (0.4%)
神経過敏	1 (0.4%)	0	1 (0.4%)	0	0	0	0
妄想症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
精神的機能代償不全	0	0	0	1 (0.4%)	0	0	1 (0.4%)
物質誘発性精神病性障害	1 (0.4%)	0	1 (0.4%)	0	0	0	0

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］
（続き）

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
代謝および栄養障害	34 (14.3%)	18 (7.6%)	29 (12.2%)	53 (21.8%)	18 (7.4%)	24 (9.9%)	45 (18.5%)
高血糖	14 (5.9%)	1 (0.4%)	14 (5.9%)	19 (7.8%)	0	1 (0.4%)	19 (7.8%)
食欲減退	7 (3.0%)	7 (3.0%)	5 (2.1%)	11 (4.5%)	6 (2.5%)	9 (3.7%)	6 (2.5%)
低カリウム血症	6 (2.5%)	3 (1.3%)	6 (2.5%)	12 (4.9%)	3 (1.2%)	5 (2.1%)	12 (4.9%)
糖尿病	2 (0.8%)	0	2 (0.8%)	7 (2.9%)	0	0	7 (2.9%)
低リン酸血症	3 (1.3%)	3 (1.3%)	3 (1.3%)	4 (1.6%)	4 (1.6%)	3 (1.2%)	3 (1.2%)
低ナトリウム血症	3 (1.3%)	3 (1.3%)	1 (0.4%)	3 (1.2%)	1 (0.4%)	3 (1.2%)	1 (0.4%)
体液貯留	2 (0.8%)	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.8%)
低アルブミン血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.2%)	1 (0.4%)	1 (0.4%)	2 (0.8%)
高尿酸血症	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
低マグネシウム血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
食欲亢進	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
脱水	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
コントロール不良の糖尿病	0	0	0	1 (0.4%)	0	0	1 (0.4%)
糖尿病性ケトアシドーシス	1 (0.4%)	0	1 (0.4%)	0	0	0	0
水分過負荷	0	0	0	1 (0.4%)	1 (0.4%)	0	0
高カルシウム血症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
高カリウム血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
高ナトリウム血症	0	0	0	1 (0.4%)	1 (0.4%)	0	1 (0.4%)
腫瘍崩壊症候群	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
２型糖尿病	0	0	0	1 (0.4%)	0	0	1 (0.4%)
ビタミンＢ１２欠乏	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
筋骨格系および結合組織障害	24 (10.1%)	16 (6.8%)	14 (5.9%)	45 (18.5%)	12 (4.9%)	28 (11.5%)	23 (9.5%)
四肢痛	7 (3.0%)	7 (3.0%)	2 (0.8%)	10 (4.1%)	2 (0.8%)	10 (4.1%)	3 (1.2%)
筋痙縮	3 (1.3%)	2 (0.8%)	1 (0.4%)	13 (5.3%)	1 (0.4%)	12 (4.9%)	4 (1.6%)
筋肉痛	4 (1.7%)	2 (0.8%)	4 (1.7%)	7 (2.9%)	1 (0.4%)	4 (1.6%)	5 (2.1%)
ミオパチー	2 (0.8%)	0	2 (0.8%)	7 (2.9%)	1 (0.4%)	1 (0.4%)	7 (2.9%)
筋力低下	5 (2.1%)	2 (0.8%)	4 (1.7%)	3 (1.2%)	0	1 (0.4%)	3 (1.2%)
背部痛	3 (1.3%)	1 (0.4%)	3 (1.3%)	4 (1.6%)	4 (1.6%)	0	0
関節痛	1 (0.4%)	0	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
四肢不快感	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0
骨痛	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
筋攣縮	2 (0.8%)	0	2 (0.8%)	0	0	0	0
筋骨格痛	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
関節腫脹	0	0	0	1 (0.4%)	0	0	1 (0.4%)
筋肉疲労	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
筋骨格系胸痛	0	0	0	1 (0.4%)	0	0	1 (0.4%)
頚部痛	0	0	0	1 (0.4%)	0	0	1 (0.4%)
変形性関節症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
骨粗鬆症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
血管障害	18 (7.6%)	7 (3.0%)	15 (6.3%)	34 (14.0%)	23 (9.5%)	12 (4.9%)	20 (8.2%)
高血圧	6 (2.5%)	0	6 (2.5%)	16 (6.6%)	11 (4.5%)	4 (1.6%)	12 (4.9%)
低血圧	3 (1.3%)	2 (0.8%)	1 (0.4%)	5 (2.1%)	5 (2.1%)	1 (0.4%)	1 (0.4%)
起立性低血圧	4 (1.7%)	3 (1.3%)	3 (1.3%)	3 (1.2%)	0	3 (1.2%)	0
潮紅	2 (0.8%)	0	2 (0.8%)	4 (1.6%)	2 (0.8%)	0	2 (0.8%)
ほてり	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.8%)	2 (0.8%)	0	0
循環虚脱	2 (0.8%)	2 (0.8%)	2 (0.8%)	0	0	0	0
深部静脈血栓症	0	0	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)
血腫	0	0	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)
高血圧クリーゼ	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
充血	0	0	0	1 (0.4%)	0	1 (0.4%)	0
静脈炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
血栓性静脈炎	0	0	0	1 (0.4%)	1 (0.4%)	0	0
血栓症	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
血管拡張	0	0	0	1 (0.4%)	1 (0.4%)	0	0
眼障害	18 (7.6%)	10 (4.2%)	13 (5.5%)	27 (11.1%)	15 (6.2%)	8 (3.3%)	12 (4.9%)
霧視	8 (3.4%)	4 (1.7%)	7 (3.0%)	5 (2.1%)	0	0	5 (2.1%)

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］
（続き）

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
流涙増加	0	0	0	8 (3.3%)	6 (2.5%)	2 (0.8%)	1 (0.4%)
眼乾燥	4 (1.7%)	4 (1.7%)	0	1 (0.4%)	0	0	1 (0.4%)
結膜浮腫	0	0	0	3 (1.2%)	3 (1.2%)	0	0
眼瞼炎	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	0	0	0
結膜出血	0	0	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	0
眼脂	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0
眼の障害	0	0	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	1 (0.4%)
眼充血	0	0	0	2 (0.8%)	1 (0.4%)	0	1 (0.4%)
視力障害	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0	1 (0.4%)
白内障	0	0	0	1 (0.4%)	0	0	1 (0.4%)
霰粒腫	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
複視	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
眼刺激	1 (0.4%)	0	1 (0.4%)	0	0	0	0
眼痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0
眼そう痒症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
眼瞼浮腫	0	0	0	1 (0.4%)	1 (0.4%)	0	0
網膜症	0	0	0	1 (0.4%)	0	1 (0.4%)	0
潰瘍性角膜炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
視力低下	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
皮膚および皮下組織障害	10 (4.2%)	7 (3.0%)	6 (2.5%)	28 (11.5%)	20 (8.2%)	11 (4.5%)	9 (3.7%)
多汗症	3 (1.3%)	0	3 (1.3%)	3 (1.2%)	1 (0.4%)	0	2 (0.8%)
発疹	0	0	0	6 (2.5%)	4 (1.6%)	3 (1.2%)	2 (0.8%)
紅斑	1 (0.4%)	1 (0.4%)	0	3 (1.2%)	2 (0.8%)	1 (0.4%)	0
そう痒症	1 (0.4%)	1 (0.4%)	0	3 (1.2%)	3 (1.2%)	0	0
斑状丘疹状皮疹	0	0	0	4 (1.6%)	3 (1.2%)	1 (0.4%)	1 (0.4%)
寝汗	1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	1 (0.4%)	2 (0.8%)
アレルギー性皮膚炎	0	0	0	2 (0.8%)	2 (0.8%)	0	0
湿疹	0	0	0	2 (0.8%)	0	1 (0.4%)	1 (0.4%)
手掌・足底発赤知覚不全症候群	0	0	0	2 (0.8%)	2 (0.8%)	1 (0.4%)	0
脱毛症	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚炎	1 (0.4%)	0	1 (0.4%)	0	0	0	0
皮膚乾燥	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0	0	0
皮膚粘膜発疹	0	0	0	1 (0.4%)	0	1 (0.4%)	0
点状出血	1 (0.4%)	1 (0.4%)	0	0	0	0	0
光線過敏性反応	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
紅斑性皮疹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
皮膚障害	1 (0.4%)	1 (0.4%)	0	0	0	0	0
皮膚剥脱	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
皮膚出血	1 (0.4%)	0	1 (0.4%)	0	0	0	0
皮膚反応	1 (0.4%)	1 (0.4%)	0	0	0	0	0
顔面腫脹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
蕁麻疹	0	0	0	1 (0.4%)	1 (0.4%)	0	0
臨床検査	10 (4.2%)	8 (3.4%)	4 (1.7%)	24 (9.9%)	13 (5.3%)	18 (7.4%)	12 (4.9%)
アラニンアミノトランスフェラーゼ増加	5 (2.1%)	5 (2.1%)	2 (0.8%)	10 (4.1%)	4 (1.6%)	8 (3.3%)	5 (2.1%)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8%)	2 (0.8%)	0	6 (2.5%)	5 (2.1%)	5 (2.1%)	3 (1.2%)
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	1 (0.4%)	0	6 (2.5%)	4 (1.6%)	5 (2.1%)	3 (1.2%)
体重減少	1 (0.4%)	1 (0.4%)	0	6 (2.5%)	3 (1.2%)	5 (2.1%)	0
体重増加	2 (0.8%)	0	2 (0.8%)	5 (2.1%)	0	0	5 (2.1%)
血中クレアチニン増加	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	0	0
血中乳酸脱水素酵素増加	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
血中アルカリホスファターゼ増加	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
心臓障害	7 (3.0%)	6 (2.5%)	5 (2.1%)	17 (7.0%)	8 (3.3%)	6 (2.5%)	11 (4.5%)
心房細動	1 (0.4%)	1 (0.4%)	1 (0.4%)	4 (1.6%)	2 (0.8%)	3 (1.2%)	2 (0.8%)

表 2.7.6.2-2 治験薬と関連性がある有害事象［MMY3004 試験，安全性解析対象集団］
（続き）

	Vd n (%)			DVd n (%)			
	Related to Treatment	Related to BORT	Related to DEX	Related to Treatment	Related to DARA	Related to BORT	Related to DEX
心不全	2 (0.8%)	2 (0.8%)	1 (0.4%)	3 (1.2%)	0	1 (0.4%)	2 (0.8%)
動悸	2 (0.8%)	2 (0.8%)	1 (0.4%)	3 (1.2%)	0	1 (0.4%)	2 (0.8%)
洞性頻脈	0	0	0	4 (1.6%)	3 (1.2%)	0	3 (1.2%)
うっ血性心不全	1 (0.4%)	0	1 (0.4%)	2 (0.8%)	0	1 (0.4%)	2 (0.8%)
急性冠動脈症候群	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
狭心症	1 (0.4%)	0	1 (0.4%)	0	0	0	0
徐脈	0	0	0	1 (0.4%)	1 (0.4%)	0	0
左脚ブロック	0	0	0	1 (0.4%)	0	0	1 (0.4%)
上室性頻脈	0	0	0	1 (0.4%)	1 (0.4%)	0	0
心室性期外収縮	1 (0.4%)	1 (0.4%)	0	0	0	0	0
内分泌障害	3 (1.3%)	0	3 (1.3%)	10 (4.1%)	0	0	10 (4.1%)
クッシング様症状	3 (1.3%)	0	3 (1.3%)	7 (2.9%)	0	0	7 (2.9%)
クッシング症候群	0	0	0	2 (0.8%)	0	0	2 (0.8%)
副腎機能不全	0	0	0	1 (0.4%)	0	0	1 (0.4%)
耳および迷路障害	2 (0.8%)	2 (0.8%)	0	10 (4.1%)	4 (1.6%)	7 (2.9%)	3 (1.2%)
回転性めまい	1 (0.4%)	1 (0.4%)	0	7 (2.9%)	2 (0.8%)	6 (2.5%)	1 (0.4%)
耳鳴	1 (0.4%)	1 (0.4%)	0	1 (0.4%)	0	1 (0.4%)	0
難聴	0	0	0	1 (0.4%)	0	1 (0.4%)	0
耳痛	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
耳そう痒症	0	0	0	1 (0.4%)	1 (0.4%)	0	0
中耳の炎症	0	0	0	1 (0.4%)	0	0	1 (0.4%)
腎および尿路障害	2 (0.8%)	2 (0.8%)	1 (0.4%)	6 (2.5%)	4 (1.6%)	4 (1.6%)	2 (0.8%)
急性腎不全	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
尿閉	0	0	0	2 (0.8%)	1 (0.4%)	2 (0.8%)	1 (0.4%)
慢性腎臓病	0	0	0	1 (0.4%)	1 (0.4%)	0	0
失禁	0	0	0	1 (0.4%)	1 (0.4%)	0	0
中毒性ネフロパシー	1 (0.4%)	1 (0.4%)	0	0	0	0	0
腎機能障害	0	0	0	1 (0.4%)	0	1 (0.4%)	0
傷害、中毒および処置合併症	2 (0.8%)	2 (0.8%)	0	4 (1.6%)	2 (0.8%)	2 (0.8%)	1 (0.4%)
アレルギー性輸血反応	0	0	0	1 (0.4%)	1 (0.4%)	0	0
挫傷	0	0	0	1 (0.4%)	0	1 (0.4%)	0
眼窩周囲血腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0
皮下血腫	0	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
硬膜下血腫	1 (0.4%)	1 (0.4%)	0	0	0	0	0
創傷	0	0	0	1 (0.4%)	0	0	1 (0.4%)
肝胆道系障害	0	0	0	5 (2.1%)	3 (1.2%)	2 (0.8%)	1 (0.4%)
高ビリルビン血症	0	0	0	4 (1.6%)	3 (1.2%)	1 (0.4%)	0
胆嚢炎	0	0	0	1 (0.4%)	0	1 (0.4%)	0
慢性胆嚢炎	0	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
生殖系および乳房障害	1 (0.4%)	1 (0.4%)	0	3 (1.2%)	0	1 (0.4%)	2 (0.8%)
亀頭包皮炎	0	0	0	1 (0.4%)	0	0	1 (0.4%)
勃起不全	0	0	0	1 (0.4%)	0	0	1 (0.4%)
生殖器痛	1 (0.4%)	1 (0.4%)	0	0	0	0	0
精巣痛	0	0	0	1 (0.4%)	0	1 (0.4%)	0
免疫系障害	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
低γグロブリン血症	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)

Keys: Vd = bortezomib-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone; BORT = bortezomib; DEX = dexamethasone; DARA = daratumumab.
Keys: TEAE = treatment-emergent adverse event.
Note: Adverse events are reported using MedDRA version 18.0.
Note: Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE04A.RTF] [JNJ-54767414\MMY3004\DBR_CSR\RE_CSR\PROD\TSFAE04A.SAS] 05APR2016, 16:04

2.7.6.2.3　個別症例の詳細

最終投与後 30 日以内の疾患進行以外の理由による死亡例の詳細経過を以下に示す。治験薬と関連性がある重篤な有害事象の詳細経過は，治験総括報告書【CTD 5.3.5.1.2-1】に示した。

2.7.6.2.3.1　最終投与後 30 日以内の死亡（疾患進行以外の理由による死亡）

(1) DVd 群

1) 被験者識別番号 340015

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-02-16	2015-02-27	12	2015-03-01	14	ADVERSE EVENT	-

■ **Discontinuation of study treatment due to AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
脳梗塞 Cerebral infarct	2015-03-01 2015-03-01	14 1	Y 5	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	U FATAL	N	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
脳梗塞 Cerebral infarct	2015-02-28 2015-02-28	13 1	Y 4	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	U NOT RECOVERED/ NOT RESOLVED	N	-
誤嚥性肺炎 Bronchoaspiration pneumonia	2015-02-28 -	13 -	Y 4	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	U NOT RECOVERED/ NOT RESOLVED	NA	-
脳梗塞 Cerebral infarct	2015-03-01 2015-03-01	14 1	Y 5	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	U FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
下痢 Diarrhea	2015-02-24 2015-02-26	9 3	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

■ Demographics and Baseline Characteristics

- □ Country: Spain
- □ Study site identifier: ES12026
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Female
- □ Baseline weight(kg): 48.3
- □ Baseline height(cm): 150
- □ Baseline ECOG score: 0

■ Disposition Information

□ Treatment discontinuation: 2015-03-01 Adverse Event

□ Study discontinuation: 2015-03-01 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
31.80	160.00	5.16	2015-02-16	2015-02-27	0.39

■ **NARRATIVE TEXT**

被験者 340015 は，7[redacted]歳の白人女性で，2007 年 9 月 11 日に初めて病期 I の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，高血圧，不眠症，右非嵌頓鼠径ヘルニア，蜂巣炎及び喫煙（喫煙者）であった。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，ビンクリスチン，カルムスチン，シクロホスファミド，デキサメタゾン，インターフェロン，prednisone，ドキソルビシン及びメルファラン前処置による ASCT，レジメン 2 はボルテゾミブ，デキサメタゾン及びサリドマイド，レジメン 3 はデキサメタゾン及びレナリドミドであった。

治験組入れ時の併用薬は，オメプラゾール，アスピリン及びゾルピデムであった。

Day 13（2015 年 2 月 28 日）に，被験者は右片麻痺，発語変化及び意識消失のために入院した。身体所見で，傾眠状態及び全失語が認められた。運動指令には応答しなかった。神経学的検査では，右同名性半盲，左方共同偏視，右中枢性顔面麻痺，右上下肢の筋緊張低下，触覚鈍麻，右腕脚の痛覚過敏が認められたが，髄膜刺激症状は認められなかった。National Institutes of Health Stroke Scale スコアは 23 ポイントであった。同日（Day 13）の頭部コンピュータ断層撮影（CT）スキャン所見から，発症後間もない左中脳動脈領域の脳梗塞が示唆された。同日（Day 13）に，**重篤な有害事象として Grade 4 の脳梗塞**及び **Grade 4 の誤嚥性肺炎**（記載語：気管支誤嚥性肺炎）が報告された。治験担当医師は，両事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。両事象に対する治験薬の処置は実施しなかった。酸素療法及び気道陽圧法を施行した。Day 14 に，被験者は脳梗塞のために死亡した。剖検は実施されなかった。本剤，ボルテゾミブ及びデキサメタゾンの最終投与日は，それぞれ Day 8，Day 11 及び Day 12 であった。

死亡時に，誤嚥性肺炎は未回復であった。

2) 被験者識別番号 380007

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-02-03	2015-04-18	75	2015-04-28	85	ADVERSE EVENT	-

■ **Serious AEs; Discontinuation of study treatment due to AE; Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-04-17 2015-04-28	74 12	Y 3	Possible Possible NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	No

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
器質化肺炎 Bilateral fibrinous pneumonia	2015-04-28T14:20 2015-04-28	85 1	Y 5	Possible Possible NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
アラニンアミノトランスフェラーゼ増加 Alanine aminotransferase increased	2015-02-23 2015-04-06	21 43	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
心房粗動 Atrial flutter	2015-04-28 -	85 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
γ－グルタミルトランスフェラーゼ増加 Gamma-glutamyl transpeptidase increased	2015-02-23 -	21 -	N 1	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
高カリウム血症 Hyperkaliemia	2015-04-27 -	84 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
低アルブミン血症 Hypoalbuminemia	2015-03-17T09:35 2015-04-06	43 21	N 2	Probable Probable NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
血小板減少症 Platelet count decreased	2015-03-02 2015-03-10	28 9	N 1	Probable Probable PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
血小板減少症 Platelet count decreased	2015-04-20 2015-04-24	77 5	N 2	Possible Not related POSSIBLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
血小板減少症 Platelet count decreased	2015-03-30 2015-04-06	56 8	N 2	Probable Probable PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血小板減少症 Platelet count decreased	2015-03-10T08:35 2015-03-16	36 7	N 3	Probable Probable PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
血小板減少症 Platelet count decreased	2015-04-16 2015-04-20	73 5	N 1	Possible Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
心室性不整脈 Ventricular arrhytmia	2015-04-28 -	85 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-

■ Hematology Results

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Erythrocytes normal ( )	-	2015-01-20/ -14	Screening	5.1	x10E12/L	4.5-5.9	-
Erythrocytes normal ( )	5	2015-02-03/ 1	Cycle 1 day 1	5	x10E12/L	4.5-5.9	-
Erythrocytes normal ( )	5	2015-02-09/ 7	Cycle 1 day 8	5.05	x10E12/L	4.5-5.9	-
Erythrocytes normal ( )	5	2015-02-16/ 14	Cycle 1 day 15	5.08	x10E12/L	4.5-5.9	-
Erythrocytes normal ( )	5	2015-02-23/ 21	Cycle 2 day 1	5.18	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-03-02/ 28	Cycle 2 day 8	4.45	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-03-10/ 36	Cycle 2 day 15	4.25	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-03-16/ 42	Cycle 3 day 1	3.92	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-03-23/ 49	Cycle 3 day 8	3.93	x10E12/L	4.5-5.9	-

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Erythrocytes low ( )	5	2015-03-30/ 56	Cycle 3 day 15	4	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-04-06/ 63	Cycle 4 day 1	4.18	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-04-16/ 73	Cycle 4 day 11	4.06	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-04-20/ 77	Cycle 4 day 12 unscheduled 1	3.96	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-04-24/ 81	Cycle 4 day 12 unscheduled 2	3.39	x10E12/L	4.5-5.9	-
Erythrocytes low ( )	5	2015-04-27/ 84	Cycle 4 day 12 unscheduled 3	4.29	x10E12/L	4.5-5.9	-
Hemoglobin normal (both within grade 0)	-	2015-01-20/ -14	Screening	160	g/L	135-175	0
Hemoglobin normal (both within grade 0)	155	2015-02-03/ 1	Cycle 1 day 1	155	g/L	135-175	0
Hemoglobin normal (both within grade 0)	155	2015-02-09/ 7	Cycle 1 day 8	157	g/L	135-175	0
Hemoglobin normal (both within grade 0)	155	2015-02-16/ 14	Cycle 1 day 15	152	g/L	135-175	0
Hemoglobin normal (both within grade 0)	155	2015-02-23/ 21	Cycle 2 day 1	160	g/L	135-175	0
Hemoglobin normal (both within grade 0)	155	2015-03-02/ 28	Cycle 2 day 8	138	g/L	135-175	0
Hemoglobin low (anemia)	155	2015-03-10/ 36	Cycle 2 day 15	134	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-03-16/ 42	Cycle 3 day 1	123	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-03-23/ 49	Cycle 3 day 8	123	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-03-30/ 56	Cycle 3 day 15	127	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-04-06/ 63	Cycle 4 day 1	132	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-04-16/ 73	Cycle 4 day 11	129	g/L	135-175	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	155	2015-04-20/ 77	Cycle 4 day 12 unscheduled 1	127	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-04-24/ 81	Cycle 4 day 12 unscheduled 2	108	g/L	135-175	1
Hemoglobin low (anemia)	155	2015-04-27/ 84	Cycle 4 day 12 unscheduled 3	134	g/L	135-175	1
Leukocytes normal (both within grade 0)	-	2015-01-20/ -14	Screening	7.8	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-02-03/ 1	Cycle 1 day 1	8.9	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	8.9	2015-02-09/ 7	Cycle 1 day 8	12.6	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	8.9	2015-02-16/ 14	Cycle 1 day 15	13.2	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-02-23/ 21	Cycle 2 day 1	7.7	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-03-02/ 28	Cycle 2 day 8	7.2	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-03-10/ 36	Cycle 2 day 15	8.2	x10E9/L	4.5-11	0
Leukocytes low (white blood cell decreased)	8.9	2015-03-16/ 42	Cycle 3 day 1	4.3	x10E9/L	4.5-11	1
Leukocytes normal (both within grade 0)	8.9	2015-03-23/ 49	Cycle 3 day 8	7.1	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-03-30/ 56	Cycle 3 day 15	10.4	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-04-06/ 63	Cycle 4 day 1	7.6	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	8.9	2015-04-16/ 73	Cycle 4 day 11	14	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-04-20/ 77	Cycle 4 day 12 unscheduled 1	9.1	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	8.9	2015-04-24/ 81	Cycle 4 day 12 unscheduled 2	9.7	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	8.9	2015-04-27/ 84	Cycle 4 day 12 unscheduled 3	15.3	x10E9/L	4.5-11	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes normal (both within grade 0)	-	2015-01-20/ -14	Screening	3	x10E9/L	1.5-3.5	0
Lymphocytes normal (both within grade 0)	2.9	2015-02-03/ 1	Cycle 1 day 1	2.9	x10E9/L	1.5-3.5	0
Lymphocytes high (both within grade 0)	2.9	2015-02-09/ 7	Cycle 1 day 8	3.8	x10E9/L	1.5-3.5	0
Lymphocytes normal (both within grade 0)	2.9	2015-02-16/ 14	Cycle 1 day 15	3	x10E9/L	1.5-3.5	0
Lymphocytes low (lymphocyte count decreased)	2.9	2015-02-23/ 21	Cycle 2 day 1	0.9	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	2.9	2015-03-02/ 28	Cycle 2 day 8	1.4	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	2.9	2015-03-10/ 36	Cycle 2 day 15	1.2	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	2.9	2015-03-16/ 42	Cycle 3 day 1	0.9	x10E9/L	1.5-3.5	1
Lymphocytes normal (both within grade 0)	2.9	2015-03-23/ 49	Cycle 3 day 8	2.2	x10E9/L	1.5-3.5	0
Lymphocytes normal (both within grade 0)	2.9	2015-03-30/ 56	Cycle 3 day 15	2.3	x10E9/L	1.5-3.5	0
Lymphocytes normal (both within grade 0)	2.9	2015-04-06/ 63	Cycle 4 day 1	2	x10E9/L	1.5-3.5	0
Lymphocytes low (lymphocyte count decreased)	2.9	2015-04-16/ 73	Cycle 4 day 11	1.4	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	2.9	2015-04-20/ 77	Cycle 4 day 12 unscheduled 1	0.9	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	2.9	2015-04-24/ 81	Cycle 4 day 12 unscheduled 2	0.5	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	2.9	2015-04-27/ 84	Cycle 4 day 12 unscheduled 3	0.8	x10E9/L	1.5-3.5	1
Neutrophils normal (neutrophil count decreased)	-	2015-01-20/ -14	Screening	4.1	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-02-03/ 1	Cycle 1 day 1	5.2	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	5.2	2015-02-09/ 7	Cycle 1 day 8	7.7	x10E9/L	2.5-7.5	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils high (neutrophil count decreased)	5.2	2015-02-16/ 14	Cycle 1 day 15	9.1	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-02-23/ 21	Cycle 2 day 1	6.3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-03-02/ 28	Cycle 2 day 8	5.2	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-03-10/ 36	Cycle 2 day 15	6.7	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-03-16/ 42	Cycle 3 day 1	3.1	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-03-23/ 49	Cycle 3 day 8	4.3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-03-30/ 56	Cycle 3 day 15	7.4	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.2	2015-04-06/ 63	Cycle 4 day 1	4.4	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	5.2	2015-04-16/ 73	Cycle 4 day 11	11.9	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	5.2	2015-04-20/ 77	Cycle 4 day 12 unscheduled 1	8.1	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	5.2	2015-04-24/ 81	Cycle 4 day 12 unscheduled 2	8.7	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	5.2	2015-04-27/ 84	Cycle 4 day 12 unscheduled 3	14.3	x10E9/L	2.5-7.5	0
Platelets normal (platelet count decreased)	-	2015-01-20/ -14	Screening	194	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	232	2015-02-03/ 1	Cycle 1 day 1	232	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	232	2015-02-09/ 7	Cycle 1 day 8	169	x10E9/L	150-350	0
Platelets low (platelet count decreased)	232	2015-02-16/ 14	Cycle 1 day 15	120	x10E9/L	150-350	1
Platelets low (platelet count decreased)	232	2015-02-23/ 21	Cycle 2 day 1	104	x10E9/L	150-350	1
Platelets low (platelet count decreased)	232	2015-03-02/ 28	Cycle 2 day 8	94	x10E9/L	150-350	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	232	2015-03-10/ 36	Cycle 2 day 15	44	x10E9/L	150-350	3
Platelets low (platelet count decreased)	232	2015-03-16/ 42	Cycle 3 day 1	138	x10E9/L	150-350	1
Platelets low (platelet count decreased)	232	2015-03-23/ 49	Cycle 3 day 8	137	x10E9/L	150-350	1
Platelets low (platelet count decreased)	232	2015-03-30/ 56	Cycle 3 day 15	68	x10E9/L	150-350	2
Platelets low (platelet count decreased)	232	2015-04-06/ 63	Cycle 4 day 1	145	x10E9/L	150-350	1
Platelets low (platelet count decreased)	232	2015-04-16/ 73	Cycle 4 day 11	82	x10E9/L	150-350	1
Platelets low (platelet count decreased)	232	2015-04-20/ 77	Cycle 4 day 12 unscheduled 1	64	x10E9/L	150-350	2
Platelets normal (platelet count decreased)	232	2015-04-24/ 81	Cycle 4 day 12 unscheduled 2	155	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	232	2015-04-27/ 84	Cycle 4 day 12 unscheduled 3	213	x10E9/L	150-350	0

■ Demographics and Baseline Characteristics

- □ Country: Ukraine
- □ Study site identifier: UA90218
- □ Race: White
- □ Age(yrs): 6[redacted]
- □ Sex: Male
- □ Baseline weight(kg): 99
- □ Baseline height(cm): 174
- □ Baseline ECOG score: 1

■ Disposition Information

- □ Treatment discontinuation: 2015-04-28 Adverse Event
- □ Study discontinuation: 2015-04-28 Death
- □ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
160.49	640.00	19.91	2015-02-03	2015-04-18	2.46

■ **NARRATIVE TEXT**

被験者 380007 は，6[redacted]歳の白人男性で，2013 年 9 月 12 日に初めて病期 I（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，変形性関節症，心不全，高血圧及び心筋梗塞であった。ベースラインの ECOG スコアは 1 であった。心室性期外収縮の既往歴を有した。

被験者は 1 レジメンの前治療（クラリスロマイシン，デキサメタゾン及びサリドマイド）を受けていた。

治験組入れ時の併用薬は，アスピリン／水酸化マグネシウム（Cardiomagnyl），ビソプロロール，ラミプリル／ヒドロクロロチアジド（Ramizes），輸液（Rheosorbilact）及びアロプリノールであった。

Day 1（2015 年 2 月 3 日）の ECG 所見は正常であった。同日の臨床検査値は，白血球数 8.9×10^9/L（正常範囲：4.5-11$\times10^9$/L），リンパ球数 2.9×10^9/L（正常範囲：1.5-3.5$\times10^9$/L），好中球数 5.2×10^9/L（正常範囲：2.5-7.5$\times10^9$/L）及び血小板数 232×10^9/L（正常範囲：150-350$\times10^9$/L）であった。

Day 73 の臨床検査値は，白血球数 14×10^9/L，リンパ球数 1.4×10^9/L，好中球数 11.9×10^9/L 及び血小板数 82×10^9/L であった。Day 74 に，呼吸困難及び発熱（体温：38.3°C）を認め，同日に，**Grade 3 の重篤な有害事象の肺炎**（胸部 X 線写真で確認）のために入院した。本感染は限局的であり，病原体は不明であった。アンブロキソール，フルコナゾール，セフトリアキソン，レボフロキサシン，プロカイン／sulfocamphoric acid（Sulfocamphocain），バンコマイシン，スルファメトキサゾール／トリメトプリム（Bactrim）及びセフェピムによる治療を実施した。治験担当医師は，肺炎と本剤及びボルテゾミブとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「関連なし」と判断した。Day 85 に，本事象のために治験薬の投与を中止した。本剤，ボルテゾミブ及びデキサメタゾンの最終投与日は，それぞれ Day 64，Day 74 及び Day 75 であった。

Day 85 に，被験者の状態が悪化し，**重篤な有害事象の器質化肺炎**（記載語：両側性線維素性肺炎）及び **Grade 3 の非重篤な有害事象の心室性不整脈**及び**心房粗動**が ECG 所見に基づき報告された。治験担当医師は，器質化肺炎と本剤及びボルテゾミブとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「関連なし」と判断し，心室性不整脈及び心房粗動とすべての治験薬との因果関係を「関連なし」と判断した。アミオダロン，エノキサパリン，リドカイン及びフェニレフリンによる治療を実施した。同日（Day 85）に，呼吸が停止し，30 分間蘇生したが回復しなかった。同日（Day 85）に，被験者は器質化肺炎のために死亡した。剖検が実施され，左肺水腫，壊死性ネフローゼ及び内臓の実質ジストロフィーが報告された。また，死因は中毒と報告された。

死亡時に，心室性不整脈及び心房粗動は未回復であった。

3) 被験者識別番号 380063

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-09-07	2015-09-10	4	2015-09-12	6	ADVERSE EVENT	-

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺動脈血栓症 Suspected thromboembolism of pulmonary artery	2015-09-10T14:30 -	4 -	Y 4	Possible Possible POSSIBLE	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
急性冠動脈症候群 Acute coronary syndrom	2015-09-11 2015-09-11	5 1	Y 4	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	-
急性冠動脈症候群 Acute coronary syndrom	2015-09-12 2015-09-12	6 1	Y 5	Possible Possible POSSIBLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	Y FATAL	N	-

■ **Other Adverse Events**

No Other Adverse Events reported

■ **Demographics and Baseline Characteristics**

□ Country: Ukraine
□ Study site identifier: UA90216
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Female
□ Baseline weight(kg): 83
□ Baseline height(cm): 159
□ Baseline ECOG score: 2

■ **Disposition Information**

□ Treatment discontinuation: 2015-09-12 Death

□ Study discontinuation: 2015-09-12 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
16.00	60.00	1.31	2015-09-07	2015-09-10	0.13

■ **NARRATIVE TEXT**

被験者 380063 は，5[redacted] 歳の白人女性で，2011 年 6 月 22 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，背部痛，慢性胆嚢炎，末梢性感覚ニューロパチー，甲状腺新生物，中毒性肝炎及び子宮平滑筋腫であった。ベースラインの ECOG スコアは 2 であった。高血圧の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1，レジメン 2 ともにデキサメタゾン及びサリドマイドであった。

治験組入れ時の併用薬は，flupirtine maleate 及びバラシクロビルであった。

Day 4（2015 年 9 月 10 日）に，被験者は頻呼吸（30～35 回／分）及び発熱を訴え救急救命室を受診した。ECG で洞性頻脈が認められた。同日に，軽度の胸痛（肋骨及び胸骨）が発現し，**重篤な有害事象の Grade 4 の肺動脈血栓症**のために入院した（記載語：肺動脈血栓塞栓症の疑い）。Day 5 の ECG で上室性期外収縮及び頻脈とともに左心室前側壁における急性貫壁性心筋梗塞が認められた。同日の心エコー検査で，中等度の三尖弁閉鎖不全症，右心拡大，中等度の肺高血圧症及び軽度の心嚢液貯留が認められ，胸部 CT スキャンでは，心拡大（心胸郭比：76.5%），圧迫性無気肺を伴う心嚢液貯留，溶骨性病変が認められた。同日に，**重篤な有害事象の Grade 4 の急性冠動脈症候群**が報告された。治験担当医師は，肺動脈血栓症及び急性冠動脈症候群と本剤，ボルテゾミブ及びデキサメタゾンとの因果関係を「可能性小」と判断した。肺動脈血栓症のためにボルテゾミブを休薬した。肺動脈血栓症及び急性冠動脈症候群のためにデキサメタゾンを休薬した。Metamizole，ジフェンヒドラミン，メチルプレドニゾロンコハク酸エステルナトリウム，hetastarch，グルコン酸カルシウム，デキサメタゾン，ヒドロコルチゾンコハク酸エステルナトリウム，プロプラノロール，モルヒネ，エピネフリン，

アトロピン，ドパミン，フロセミド，マンニトール，エノキサパリン及びセフトリアキソンによる治療を実施した。また，酸素及び静脈内輸液を投与した。

Day 5 に，被験者は心肺停止に至り，その後，心肺蘇生及び人工肺換気を開始した。Day 6 に，被験者は急性冠動脈症候群のために死亡した。剖検は実施されなかった。本剤及びボルテゾミブの最終投与日は Day 1，デキサメタゾンは Day 4 であった。

死亡時に，肺動脈血栓症は未回復であった。

4) 被験者識別番号 490039

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-07-17	2015-07-25	9	2015-08-17	32	ADVERSE EVENT	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
高カルシウム血症 Hypercalcemia	2015-08-03T08:12 2015-08-08T08:35	18 6	Y 2	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
鼻出血 Epistaxis	2015-08-05 -	20 -	Y 3	Possible Very likely NOT RELATED	Dose not changed NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
腎機能障害 Creatinine elevation/renaal function impairment	2015-08-05T20:53 2015-08-07T08:29	20 3	Y 1	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
肺出血 Pulmonary bleeding	2015-08-14T22:13 -	29 -	Y 4	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
心原性ショック Cardiac shock	2015-08-16T18:31 -	31 -	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y FATAL	U	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-08-14T16:39 -	29 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
下痢 Diarrhoen	2015-07-01 -	-16 -	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	NA NOT RECOVERED/NOT RESOLVED	NA	-
呼吸困難 Dyspnoe	2015-07-17T11:35 2015-07-17T13:50	1 1	N 2	Very likely Not related NOT RELATED	Drug interrupted NOT APPLICABLE Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	Y	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
筋痙縮 Cramps foot pain	2015-07-17T09:00 2015-07-17	1 1	N 2	Not related Not related NOT RELATED	Dose not changed NOT APPLICABLE Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	U	-
寝汗 Night sweating	2015-07-02 -	-15 -	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	N	-
呼吸窮迫 Respiratory distress	2015-08-14 -	29 -	N 4	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
落ち着きのなさ Restlessness	2015-07-01 -	-16 -	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
血小板減少症 Thrombocytopenia	2015-07-27T10:00 -	11 -	N 4	Doubtful Probable NOT RELATED	Dose not changed DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
回転性めまい Vertigo	2015-07-17T11:35 2015-07-17T13:50	1 1	N 2	Probable Not related NOT RELATED	Drug interrupted NOT APPLICABLE Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	Y	-

■ Hematology/Chemistry Toxicities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Calcium corrected high (hypercalcemia)	2.47	2015-08-03/ 18	Cycle 1 day 15 unscheduled 1	3.01	-	1.9-2.7	2
Calcium corrected high (hypercalcemia)	2.47	2015-08-06/ 21	Cycle 1 day 15 unscheduled 3	3.23	-	1.9-2.7	3
Calcium corrected low (hypocalcemia)	2.47	2015-08-17/ 32	End of treatment	1.84	-	1.9-2.7	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Calcium corrected low (hypocalcemia)	2.47	2015-08-11/ 26	Disease evaluation 1	2.03	mmol/L	2.07-2.64	1
Creatinine high (creatinine increased)	79.56	2015-08-05/ 20	Cycle 1 day 15 unscheduled 2	167.9 6	umol/L	53.04-123.76	1
Creatinine high (creatinine increased)	79.56	2015-08-06/ 21	Cycle 1 day 15 unscheduled 3	176.8	umol/L	53.04-123.76	1
Creatinine high (creatinine increased)	79.56	2015-08-17/ 32	End of treatment	167.9 6	umol/L	53.04-123.76	1
Hemoglobin low (anemia)	135	2015-07-24/ 8	Cycle 1 day 8	129	g/L	135-175	1
Hemoglobin low (anemia)	135	2015-07-27/ 11	Cycle 1 day 11	127	g/L	135-175	1
Hemoglobin low (anemia)	135	2015-07-31/ 15	Cycle 1 day 15	118	g/L	135-175	1
Hemoglobin low (anemia)	135	2015-08-14/ 29	Cycle 1 day 15 unscheduled 5	81	g/L	135-175	2
Platelets low (platelet count decreased)	-	2015-07-01/ -16	Screening	132	x10E9/L	150-350	1
Platelets low (platelet count decreased)	77	2015-07-17/ 1	Cycle 1 day 1	77	x10E9/L	150-350	1
Platelets low (platelet count decreased)	77	2015-07-24/ 8	Cycle 1 day 8	39	x10E9/L	150-350	3
Platelets low (platelet count decreased)	77	2015-07-27/ 11	Cycle 1 day 11	15	x10E9/L	150-350	4
Platelets low (platelet count decreased)	77	2015-07-31/ 15	Cycle 1 day 15	11	x10E9/L	150-350	4
Platelets low (platelet count decreased)	77	2015-08-05/ 20	Cycle 1 day 15 unscheduled 2	11	x10E9/L	150-350	4
Platelets low (platelet count decreased)	77	2015-08-06/ 21	Cycle 1 day 15 unscheduled 3	54	x10E9/L	150-350	2
Platelets low (platelet count decreased)	77	2015-08-13/ 28	Cycle 1 day 15 unscheduled 4	15	x10E9/L	150-350	4
Platelets low (platelet count decreased)	77	2015-08-14/ 29	Cycle 1 day 15 unscheduled 5	12	x10E9/L	150-350	4

■ **Demographics and Baseline Characteristics**

□ Country: Germany
□ Study site identifier: DE00475
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Male
□ Baseline weight(kg): 89
□ Baseline height(cm): 167
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-08-17 Death

□ Study discontinuation: 2015-08-17 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
32.72	120.00	3.84	2015-07-17	2015-07-25	0.30

■ **NARRATIVE TEXT**

被験者 490039 は，5[redacted] 歳の白人男性で，2014 年 4 月 15 日に初めて病期 II（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，筋痙縮（両ふくらはぎ）及び錯感覚（左顔面）であった。ベースラインの ECOG スコアは 0 であった。骨接合（右上腕骨）及び B 型肝炎の既往歴を有した。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン及びメルファラン前処置による ASCT）を受けていた。

治験組入れ時の併用薬は，ラミブジン，パミドロン酸二ナトリウム水和物，パントプラゾールナトリウムセスキ水和物及びゾピクロンであった。

スクリーニング時（Day −16）のクレアチニン値は 1.1 mg/dL（正常範囲：0.6-1.4 mg/dL），血清カルシウム値 2.33 mmol/L（正常範囲：1.9-2.7 mmol/L）であった。Day 1 のヘモグロビン値は 135 g/L（正常範囲：135-175 g/L），血小板数 77×10^9/L（正常範囲：150-350$\times10^9$/L）であった。

Day 1（2015 年 7 月 17 日）の本剤の持続静脈内投与開始から 65 分後に **Grade 2 の非重篤な有害事象の回転性めまい及び呼吸困難**が発現し，IRR と判断された。同日に，**Grade 2 の非重篤な有害事象の筋痙縮**（記載語：筋痙攣・足部痛）が発現した。治験担当医師は，呼吸困難と本剤との因果関係を「ほぼ確実」，回転性めまいと本剤との因果関係を「可能性大」と判断し，両事象とボルテゾミブ及びデキサメタゾンとの因果関係を「関連なし」と判断した。治験担当医師は，筋痙縮と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。投与前の血圧は 120/70 mm Hg であった。被験者は治験実施計画書に従い前投薬を受けていた。本剤の持続静脈内投与開始から 65 分後に，回転性めまい及び呼吸困難のために本剤の投与を 2 時間 15 分間中断した。回転性めまい，呼吸困難及び筋痙縮に対するデキサメタゾンの処置は実施しなかった。呼吸困難及び筋痙縮に対して，metamizole sodium，プレドニゾロン，ラニチジン及び paracetamol による治療を実施した。回転性めまいに対する治療は実施しなかった。投与中断から 1

時間 55 分後の血圧は 124/61 mm Hg であった。20 分後に，呼吸困難及び回転性めまいは回復し，本剤の投与を再開した。同日に，筋痙攣も回復した。本剤の持続静脈内投与は翌日（Day 2）終了した。その後，被験者は本剤を 1 回投与されたが，有害事象として回転性めまい及び呼吸困難の再発は認められなかった。

Day 11 に，**Grade 4 の非重篤な有害事象の血小板減少症**が発現した（血小板数：15×10^9/L）。治験担当医師は，本事象との因果関係について，本剤は「多分なし」，ボルテゾミブは「可能性大」，デキサメタゾンは「関連なし」と判断した。本事象に対する本剤の処置は実施しなかった。本事象のためにボルテゾミブ及びデキサメタゾンを休薬し，休薬前の投与日はそれぞれ Day 8 及び Day 9 であった。Day 15 に，血小板を輸血した。

Day 18 に，**Grade 2 の重篤な有害事象の高カルシウム血症**が発現した（カルシウム値：3.01 μmol/L，正常範囲：1.9-2.7 μmol/L）。治験担当医師は，本事象とボルテゾミブとの因果関係を「ほぼ確実」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。本事象に対する治療も実施しなかった。

Day 20 に，**重篤な有害事象の Grade 3 の鼻出血**及び **Grade 1 の腎機能障害**（クレアチニン値：167.96 μmol/L，正常範囲：53.04-123.76 μmol/L）が発現した。鼻出血は血小板減少症によるものと報告された。Day 21 の腎超音波検査で，閉塞は認められなかった。腎機能障害の鑑別診断には，化学療法に関連した障害，疾患進行及び脱水があった。Day 22 に，被験者は入院した。治験担当医師は，鼻出血との因果関係について，本剤は「可能性小」，ボルテゾミブは「ほぼ確実」，デキサメタゾンは「関連なし」と判断した。また，腎機能障害との因果関係について，ボルテゾミブは「ほぼ確実」，本剤又はデキサメタゾンは「関連なし」と判断した。鼻出血及び腎機能障害に対する治験薬の処置は実施しなかった。補充療法，塩化ナトリウムによる過量輸液，デキサメタゾン及びパミドロン酸による治療を実施した。Day 21 のクレアチニン値は 176.8 μmol/L，カルシウム値は 3.23 μmol/L であった。腎機能障害及び高カルシウム血症は，それぞれ Day 22 及び Day 23 に回復した。

Day 28 に，被験者は退院した。翌日（Day 29）に，被験者は呼吸困難のために再入院した。同日（Day 29）に，CT スキャンで肺に非定型的な浸潤が認められた。気管支鏡検査で大量の肺出血が認められ，**Grade 4 の重篤な有害事象の肺出血**が報告された。血小板数は 12×10^9/L であった。Day 29 に，**Grade 2 の非重篤な有害事象の貧血**も報告された（ヘモグロビン値：81 g/L）。治験担当医師は，肺出血及び貧血と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。肺出血のために本剤を休薬し，Day 8 が本剤の最終投与日であった。本事象のためにボルテゾミブ及びデキサメタゾンを引き続き休薬した。貧血に対する治験薬の処置は実施しなかった。ボリコナゾール及び血小板輸血による治療を実施した。Day 31 に，**重篤な有害事象の心原性ショック**が発現した。治験担当医師は，心原性ショックと本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。レボフロキサシン，アシクロビル，イミペネム，ケタミン，sufentanil，トラネキサム酸及び塩酸ノルエピネフリンによる治療を実施した。被験者は危篤状態にあった。Day 32 に，新鮮凍結血漿，濃厚赤血球，血小板を輸血した。被験者の状態は悪化し，Day 32 に，心原性ショックのために死亡した。剖検は実施されなかった。治験薬の最終投与日は，本剤及びボルテゾミブが Day 8，デキサメタゾンが Day 9 であった。

死亡時に，鼻出血，肺出血，血小板減少症及び貧血は未回復であった。

5) 被験者識別番号 490044

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-07-21	2016-01-09	173	2016-01-11	175	ADVERSE EVENT	-

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
虚血性脳卒中 Ischaemic stroke	2016-01-11T12:30 2016-01-11	175 1	Y 5	Not related Possible NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-07-07 2015-09-21	-14 77	N 1	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event End Date/Time of Adverse Event	Start Date/Time of Adverse Event	AE Duration in Days (N) Standard Toxicity Grade	Serious Event Causality-Dexamethasone	Causality-Daratumumab Causality-Velcade Action Taken-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Other Study Treatment 1	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Outcome of Adverse Event	Concomitant or Additional Trtmnt Given	Infusion Reaction	Pathogen
血腫 Hematoma right foot	2015-10-06 2015-10-13	78 8	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
好中球減少症 Neutrophil count decreased	2015-09-08 2015-09-15	50 8	N 3	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
好中球減少症 Neutrophil count decreased	2015-08-04 2015-09-07	15 35	N 2	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
口腔粘膜血腫 Hematoma left cheek	2015-11-13 -	116 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	N	-
血小板減少症 Platelets decreased	2015-08-04 2015-08-30	15 27	N 3	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
尿路感染 Urinary tract infection	2015-12-01 2015-12-07	134 7	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ Hematology Results

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets normal (platelet count decreased)	-	2015-07-07/ -14	Screening	165	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	193	2015-07-21/ 1	Cycle 1 day 1	193	x10E9/L	150-350	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	193	2015-07-28/ 8	Cycle 1 day 8	129	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2015-08-04/ 15	Cycle 1 day 15	38	x10E9/L	150-350	3
Platelets normal (platelet count decreased)	193	2015-08-31/ 42	Cycle 2 day 1	167	x10E9/L	150-350	0
Platelets low (platelet count decreased)	193	2015-09-08/ 50	Cycle 2 day 8	95	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2015-09-15/ 57	Cycle 2 day 15	39	x10E9/L	150-350	3
Platelets low (platelet count decreased)	193	2015-09-22/ 64	Cycle 3 day 1	123	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2015-09-29/ 71	Cycle 3 day 8	61	x10E9/L	150-350	2
Platelets low (platelet count decreased)	193	2015-10-06/ 78	Cycle 3 day 15	33	x10E9/L	150-350	3
Platelets low (platelet count decreased)	193	2015-10-13/ 85	Cycle 4 day 1	90	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2015-10-23/ 95	Cycle 4 day 11	47	x10E9/L	150-350	3
Platelets low (platelet count decreased)	193	2015-11-03/ 106	Cycle 5 day 1	122	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2015-11-13/ 116	Cycle 5 day 11	42	x10E9/L	150-350	3
Platelets low (platelet count decreased)	193	2015-11-24/ 127	Cycle 6 day 1	98	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2015-12-04/ 137	Cycle 6 day 11	34	x10E9/L	150-350	3
Platelets low (platelet count decreased)	193	2015-12-15/ 148	Cycle 7 day 1	109	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2016-01-05/ 169	Cycle 8 day 1	128	x10E9/L	150-350	1
Platelets low (platelet count decreased)	193	2016-01-11/ 175	Cycle 8 day 5 unscheduled 1	72	x10E9/L	150-350	2

■ **Demographics and Baseline Characteristics**

□ Country: Germany
□ Study site identifier: DE00463
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Female
□ Baseline weight(kg): 62
□ Baseline height(cm): 170
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2016-01-11 Death

□ Study discontinuation: 2016-01-11 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
218.68	1200.00	37.10	2015-07-21	2016-01-09	5.68

■ **NARRATIVE TEXT**

被験者 490044 は，6[redacted] 歳の白人女性で，2008 年 3 月に初めて病期 I（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，薬物不耐症（アスピリン及びリドカイン），片頭痛及び僧帽弁閉鎖不全症であった。ベースラインの ECOG スコアは 0 であった。脳血管発作の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はシクロホスファミド，デキサメタゾン，イダルビシン，サリドマイド及びメルファラン前処置による ASCT，レジメン 2 はカルフィルゾミブ，デキサメタゾン及びレナリドミドであった。

治験組入れ時の併用薬は，クロピドグレル，コレカルシフェロール，パントプラゾールナトリウムセスキ水和物及び塩化カリウムであった。

Day 1 の血小板数は 193×10^9/L（正常範囲：150-350$\times10^9$/L）であった。

Day 175（2016 年 1 月 11 日）に，高度の頭痛が発現し，被験者は昏睡状態に陥った。同日に，集中治療室に入院した。頭部 CT スキャンで広範囲の脳内出血が中大脳動脈領域に認められた。同日（Day 175）に，**重篤な有害事象の虚血性脳卒中**が報告された。同日の血小板数は 72×10^9/L，薬物検査の結果はカンナビノイド陽性であった。同日に，被験者は虚血性脳卒中のために死亡した。剖検は実施されなかった。治験担当医師は，虚血性脳卒中とボルテゾミブとの因果関係を「可能性小」，本剤及びデキサメタゾンとの因果関係を「関連なし」と判断した。本剤，ボルテゾミブ及びデキサメタゾンの最終投与日は，それぞれ Day 169，Day 172 及び Day 173 であった。

6) 被験者識別番号 520005

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-10-05	2015-12-24	81	2015-12-31	88	ADVERSE EVENT	-

■ **Serious AEs / Discontinuation of study treatment due to AE**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
心房細動 Atrial fibrilation	2015-12-30 2015-12-31	87 2	Y 4	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-
うっ血性心不全 Congestive heart failure	2015-12-30 2015-12-31	87 2	Y 4	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-
呼吸不全 Respiratory insufficiency	2015-12-31 2015-12-31	88 1	Y 5	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ Serious AEs/ Infections and infestations, Grade 3 or 4

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Community acquired pneumonia	2015-12-25T09:00 2015-12-30	82 6	Y 4	Not related Possible NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	U RECOVERED/RESOLVED WITH SEQUELAE	N	No

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気管支痙攣 Bronchospams	2015-11-26T20:00 2015-11-26T23:00	53 1	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	U	-
気管支痙攣 Bronchospasm	2015-10-05 2015-10-05	1 1	N 1	Possible Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	Y	-
リンパ球減少症 Lymphocytopenia	2015-10-22 2015-12-31	18 71	N 3	Probable Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
血小板減少症 Trombocytopenia	2015-10-22 2015-11-23	18 33	N 1	Possible Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

■ Demographics and Baseline Characteristics

- □ Country: Mexico
- □ Study site identifier: MX00214
- □ Race: Other
- □ Age(yrs): 6
- □ Sex: Female
- □ Baseline weight(kg): 72
- □ Baseline height(cm): 144
- □ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-12-31 Adverse Event

□ Study discontinuation: 2015-12-31 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
161.51	380.00	20.21	2015-10-05	2015-12-24	2.66

■ **NARRATIVE TEXT**

被験者 520005 は，6[redacted]歳の女性（人種：その他）で，2014 年 8 月 5 日に初めて病期 I（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，酸消化性障害，高血圧及び骨粗鬆症であった。ベースラインの ECOG スコアは 1 であった。その他の既往歴はなかった。

被験者は 1 レジメンの前治療（デキサメタゾン，メルファラン及びサリドマイド）を受けていた。

治験組入れ時の併用薬はなかった。

Day 1（2015 年 10 月 5 日）に，**Grade 1 の非重篤な有害事象の気管支痙攣**が報告され，IRR と判断された。治験担当医師は，本事象と本剤との因果関係を「可能性小」，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。被験者の投与前の血圧は 120/72 mm Hg であった。被験者は治験実施計画書に従い前投薬を受けていた。本剤の持続静脈内投与は，気管支痙攣のために 2 時間中断した。本事象に対するボルテゾミブ又はデキサメタゾンの処置は実施しなかった。本剤の投与中断の 2 時間後に，投与を再開した。気管支痙攣は発現日（Day 1）に回復し，同日に，本剤の持続静脈内投与を終了した。気管支痙攣に対しヒドロコルチゾン，paracetamol 及びメチルプレドニゾロンを投与した。その後，本剤を 9 回投与した。

Day 53 に，**Grade 1 の非重篤な有害事象の気管支痙攣**が報告された。治験担当医師は，本事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。ブデソニドによる治療を実施した。気管支痙攣は発現日（Day 53）に回復した。

Day 82 に，**Grade 4 の重篤な有害事象の肺炎**（記載語：市中感染性肺炎）が報告され，同日に，被験者は救急救命室に入院した。咳嗽，痰，発熱（体温：38°C），喘鳴及び息切れがあった（日付不明）。肺炎の危険因子として，MM と治療による免疫不全症，リンパ球減少症及び冬期が報告された。治験担当医師は，肺炎とボルテゾミブとの因果関係を「可能性小」，本剤又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。本事象に対し抗生物質（薬剤名不明）を投与した。被験者は遠隔地の病院で治療を受けたため追加情報は入手できなか

った。本事象は Day 87 に回復したが後遺症があった。同日（Day 87）に，**Grade 4 の重篤な有害事象の心房細動及びうっ血性心不全**が報告された。治験担当医師は，両事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。心房細動及びうっ血性心不全のために治験薬を休薬した。本剤及びデキサメタゾンの休薬前の投与日は Day 75，ボルテゾミブの休薬前の投与日は Day 81 であった。両事象に対する治療は実施しなかった。翌日（Day 88），被験者は呼吸不全のために死亡した。治験担当医師は，**重篤な有害事象の呼吸不全**と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。剖検は実施されなかった。本剤及びデキサメタゾンの最終投与日は Day 75，ボルテゾミブの最終投与日は Day 81 であった。

7) 被験者識別番号 610025

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-04-13	2015-04-24	12	2015-05-18	36	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
十二指腸潰瘍 Duodenal ulcer	2015-04-25 2015-05-17	13 23	Y 4	Not related Not related PROBABLE	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	-

■ **Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
医療機器関連感染 Device related infection	2015-04-25 -	13 -	N 3	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
急性腎不全 Acute kidney injury	2015-04-20 2015-04-24	8 5	Y 2	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
十二指腸潰瘍 Duodenal ulcer	2015-05-18 2015-05-18	36 1	Y 5	Not related Not related PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
アシドーシス Acidosis	2015-04-25 2015-04-26	13 2	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
アシドーシス Acidosis	2015-04-14 2015-04-24	2 11	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
激越 Agitation	2015-04-17 -	5 -	N 2	Probable Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
貧血 Anemia	2015-04-25 -	13 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
譫妄 Delirium	2015-04-20 -	8 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
浮動性めまい Dizziness	2015-04-22 -	10 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	N	-
嚥下障害 Dysphagia	2015-05 -	19 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
呼吸困難 Dysponea	2015-04-13T12:15 2015-04-13T13:05	1 1	N 2	Probable Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	Y	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
高カリウム血症 Hyperkalemia	2015-04-14 2015-04-26	2 13	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
高ナトリウム血症 Hypernatremia	2015-04-28 -	16 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
低カルシウム血症 Hypocalcemia	2015-04-25 -	13 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
低リン酸血症 Hypophosphatemia	2015-04-28 -	16 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
低血圧 Hypotension	2015-04-20T12:20 2015-04-20T19:30	8 1	N 2	Probable Not related POSSIBLE	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	Y	-
末梢性浮腫 Edema limbs	2015-04-28 -	16 -	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
傾眠 Somnollence	2015-04-22 -	10 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
上室性頻脈 Supraventricular tachycardia	2015-04-25 -	13 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	-
血小板減少症 Platelet count deceased	2015-04-26 2015-05-10	14 15	N 3	Not related Possible NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
上部消化管出血 Upper gastrointestinal hemorrhage	2015-04-25 -	13 -	N 4	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	-
尿路感染 Urinary tract infection	2015-04-20 2015-04-24	8 5	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ Hematology/Chemistry Toxicities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Albumin low (hypoalbuminemia)	-	2015-03-30/ -14	Screening	37	g/L	38-48	1
Albumin low (hypoalbuminemia)	37	2015-04-10/ -3	Cycle 1 day 1	37	g/L	38-48	1
Albumin low (hypoalbuminemia)	37	2015-04-20/ 8	Cycle 1 day 8	36	g/L	38-48	1
Albumin low (hypoalbuminemia)	37	2015-04-25/ 13	Cycle 1 day 12 unscheduled 1	26	g/L	38-48	2
Albumin low (hypoalbuminemia)	37	2015-04-28/ 16	Cycle 1 day 15 unscheduled 1	22	g/L	38-48	2
Creatinine high (creatinine increased)	-	2015-03-30/ -14	Screening	142	umol/L	70-110	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine high (creatinine increased)	156	2015-04-10/ -3	Cycle 1 day 1	156	umol/L	70-110	1
Creatinine high (creatinine increased)	156	2015-04-14/ 2	Cycle 1 day 2	131	umol/L	70-110	1
Creatinine high (creatinine increased)	156	2015-04-20/ 8	Cycle 1 day 8	241	umol/L	70-110	2
Creatinine high (creatinine increased)	156	2015-04-25/ 13	Cycle 1 day 12 unscheduled 1	196	umol/L	70-110	2
Creatinine high (creatinine increased)	156	2015-04-28/ 16	Cycle 1 day 15 unscheduled 1	111	umol/L	70-110	1
Potassium high (hyperkalemia)	5.1	2015-04-10/ -3	Cycle 1 day 1	5.1	mmol/L	3.5-5	1
Potassium high (hyperkalemia)	5.1	2015-04-14/ 2	Cycle 1 day 2	5.6	mmol/L	3.5-5	2
Potassium high (hyperkalemia)	5.1	2015-04-25/ 13	Cycle 1 day 12 unscheduled 1	5.8	mmol/L	3.5-5	2
Urate high (hyperuricemia)	420	2015-04-20/ 8	Cycle 1 day 8	620	umol/L	250-420	4

■ **Hematology Results**

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	-	2015-03-30/ -14	Screening	98	g/L	135-175	2
Hemoglobin low (anemia)	91	2015-04-10/ -3	Cycle 1 day 1	91	g/L	135-175	2
Hemoglobin low (anemia)	91	2015-04-20/ 8	Cycle 1 day 8	118	g/L	135-175	1
Hemoglobin low (anemia)	91	2015-04-26/ 14	Cycle 1 day 12 unscheduled 2	70	g/L	135-175	3
Hemoglobin low (anemia)	91	2015-04-25/ 13	Cycle 1 day 15	67	g/L	135-175	3
Hemoglobin low (anemia)	91	2015-05-10/ 28	Cycle 2 day 5 unscheduled 1	86	g/L	135-175	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes normal (both within grade 0)	-	2015-03-30/ -14	Screening	5	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.4	2015-04-10/ -3	Cycle 1 day 1	5.4	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	5.4	2015-04-20/ 8	Cycle 1 day 8	12.4	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	5.4	2015-04-26/ 14	Cycle 1 day 12 unscheduled 2	13.7	x10E9/L	4.5-11	0
Leukocytes high (both within grade 0)	5.4	2015-04-25/ 13	Cycle 1 day 15	24.9	x10E9/L	4.5-11	0
Leukocytes low (white blood cell decreased)	5.4	2015-05-10/ 28	Cycle 2 day 5 unscheduled 1	3.7	x10E9/L	4.5-11	1

■ Demographics and Baseline Characteristics

□ Country: Australia
□ Study site identifier: AU00144
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 111.5
□ Baseline height(cm): 162.2
□ Baseline ECOG score: 2

■ Disposition Information

□ Treatment discontinuation: 2015-05-18 Adverse Event

□ Study discontinuation: 2015-05-18 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
32.14	160.00	4.87	2015-04-13	2015-04-24	0.39

■ NARRATIVE TEXT

被験者 610025 は，6[redacted] 歳の白人男性で，2011 年 11 月 16 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，肥満，不安，脱水，血中コレステロール値上昇，慢性腎臓病，便秘，うつ病，糖尿病，嚥下障害，疲労，不眠症，高カリウム血症，高血圧，睡眠時無呼吸症候群，骨粗鬆症性骨折，腹痛，末梢性ニューロパチー及びヘルペス後神経

痛であった。ベースラインの ECOG スコアは 2 であった。丹毒，頚部痛，筋骨格系胸痛，筋骨格痛，胸痛，肺炎，末梢血管障害及び呼吸困難の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はシクロホスファミド，デキサメタゾン，サリドマイド及びメルファラン前処置による ASCT，レジメン 2 はボルテゾミブ，シクロホスファミド及びデキサメタゾンであった。

治験組入れ時の併用薬は，アスピリン，アトルバスタチン，スルファメトキサゾール／トリメトプリム（Bactrim），オルメサルタンメドキソミル／ヒドロクロロチアジド（Benicar HCT），Coloxyl with senna，フロセミド，免疫グロブリン，リドカイン，メトホルミン，メサドン，ミルタザピン，インスリンアスパルト，プレガバリン，バラシクロビル，バルプロ酸ナトリウム及びゾレドロン酸であった。

Day −3 のクレアチニン値は 156 µmol/L（正常範囲：70-110 µmol/L），ヘモグロビン値は 91 g/L（正常範囲：135-175 g/L）であった。

Day 1（2015 年 4 月 13 日）の本剤の持続静脈内投与開始から 1 時間 25 分後に，**Grade 2 の非重篤な有害事象の呼吸困難**が発現し，IRR と判断された。治験担当医師は，本事象と本剤との因果関係を「可能性大」，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。投与前の血圧は 129/70 mm Hg であった。被験者は治験実施計画書に従い前投薬を受けていた。本剤の持続静脈内投与開始から 85 分後に，血圧は 148/72 mm Hg となり，呼吸困難のために本剤の投与を中断した。本事象に対するボルテゾミブ又はデキサメタゾンの処置は実施しなかった。本事象に対する治療（詳細不明）を実施した。本剤投与中断の 50 分後に呼吸困難は回復し，投与を再開した。持続静脈内投与は同日（Day 1）に終了した。投与終了の 2 時間 40 分後の血圧は 150/80 mm Hg であった。その後，本剤を 1 回投与したが，呼吸困難は再発しなかった。

Day 8 の本剤投与開始の 1 時間 20 分後に，**Grade 2 の非重篤な有害事象の低血圧**が発現し，IRR と判断された。治験担当医師は，本事象と本剤との因果関係を「可能性大」，ボルテゾミブとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「関連なし」と判断した。投与前の血圧は 126/60 mm Hg であった。被験者は治験実施計画書に従い前投薬を受けていた。本剤の持続静脈内投与開始から 1 時間 20 分後に，低血圧のために投与を中断した。本事象に対するボルテゾミブ又はデキサメタゾンの処置は実施しなかった。塩化ナトリウムを投与した。本剤投与中断の 7 時間 10 分後に，低血圧は回復し，投与を再開した。持続静脈内投与は翌日（Day 9）終了した。投与後の血圧は 115/65 mm Hg であった。

同日（Day 8）の臨床検査値は，糸球体濾過率 32 mL/min，カリウム値 5.6 mmol/L，クレアチニン値 214 µmol/L，尿素値 620 µmol/L（正常範囲：250-420 µmol/L），ヘモグロビン値 118 g/L であった。尿培養により *Enterococcus fecalis* による膀胱炎が示唆された（日付不明）。Day 8 に，**重篤な有害事象の Grade 2 の急性腎不全，非重篤な有害事象の Grade 2 の尿路感染及び Grade 3 の譫妄**が報告された。Day 8 に，被験者は補水療法のために入院した。治験担当医師は，急性腎不全と本剤，ボルテゾミブ及びデキサメタゾンとの因果関係を「可能性小」，尿路感染及び譫妄と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。急性腎不全，譫妄及び尿路感染に対する治験薬の処置は実施しなかった。被験者には塩化ナトリウム，アモキシシリン及びハロペリドールを投与した。Day 12 に，濃厚赤血球を輸血した。同日に，急性腎不全及び尿路感染は回復した。

入院中の Day 13 に，**Grade 3 の非重篤な有害事象の貧血**及び**医療機器関連感染**が報告された（ヘモグロビン値：67 g/L）。Day 14 に，胃内視鏡検査により 2 カ所の大出血を伴う十二指腸潰瘍と凝血塊が認められた。**Grade 4 の重篤な有害事象の十二指腸潰瘍及び Grade 4 の非重篤な有害事象の上部消化管出血**が報告され（Day 13 に発現），被験者は救急治療室に移送された。治験担当医師は，十二指腸潰瘍とデキサメタゾンとの因果関係を「可能性大」，本剤又はボルテゾミブとの因果関係を「関連なし」，上部消化管出血及び医療機器関連感染とデキサメタゾンとの因果関係を「可能性小」，本剤又はボルテゾミブとの因果関係を「関連なし」，貧血と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。治験薬投与は十二指腸潰瘍のために中止し，本剤の中止前の投与日は Day 9，ボルテゾミブ及びデキサメタゾンの中止前の投与日は Day 12 であった。メタラミノール，ミダゾラム，パントプラゾール，ヒドロコルチゾン，ピペラシリン／タゾバクタム（Tazocin），メロペネム，バンコマイシン，トラネキサム酸及びビタミン K による治療を実施した。Day 13～Day 32 に，濃厚赤血球，新鮮凍結血漿，ヒトアルブミン，ヒトプロトロンビン複合体及び血小板を輸血した。Day 14 に，塞栓術を施行した。十二指腸潰瘍の原因としてステロイドの使用が疑われた。Day 35 の臨床検査値は，糸球体濾過率>90 mL/min/1.73 m^2 であった。Day 36 に，被験者は十二指腸潰瘍のために死亡した。剖検は実施されなかった。

死亡時に，譫妄，貧血，上部消化管出血及び医療機器関連感染は未回復であった。

8) 被験者識別番号 700003

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-03-03	2015-03-27	25	2015-04-06	35	ADVERSE EVENT	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
慢性閉塞性肺疾患 Exacerbation of chronic obstructive lung disease	2015-03-10T08:00 2015-03-11T09:30	8 2	Y 4	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
呼吸不全 Respiratory failure due to disease progression	2015-04-05T18:40 2015-04-06	34 2	Y 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
呼吸不全 Respiratory failure due to disease progression	2015-04-06 -	35 -	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-03-02T07:05 2015-03-10T07:00	-1 9	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
貧血 Anemia	2015-03-16 2015-03-23	14 8	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
胸痛 Thorax pain	2015-03-25T11:00 -	23 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	N	-
高血圧 Hypertension	2015-03-10T21:00 2015-03-11T10:10	8 2	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

■ Demographics and Baseline Characteristics

□ Country: Russia
□ Study site identifier: RU00183
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 60
□ Baseline height(cm): 165
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2015-03-27 Progressive Disease

□ Study discontinuation: 2015-04-06 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
48.00	200.00	6.63	2015-03-03	2015-03-27	0.82

■ NARRATIVE TEXT

被験者 700003 は，6[redacted] 歳の白人男性で，2010 年 11 月 22 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，狭心症，高血圧，慢性胆嚢炎，慢性閉塞性肺疾患（ベースラインの FEV1：94%）及び慢性膵炎であった。ベースラインの ECOG スコアは 1 であった。胃潰瘍，肺結核腫及び右肺の部分切除の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，メルファラン及びプレドニゾロン，レジメン 2 はデキサメタゾン，イキサゾミブ及びレナリドミドであった。

治験組入れ時の併用薬は，アスピリン，フェノテロール／イプラトロピウム（Duovent）及び硝酸イソソルビドであった。

Day 8（2015 年 3 月 10 日）に，被験者は呼吸困難を訴えた。胸部 X 線写真では肺炎の徴候は認められなかった。Day 8 に，**Grade 4 の重篤な有害事象の慢性閉塞性肺疾患**（記載語：慢性閉塞性肺疾患の悪化）が報告され，被験者を集中治療室に移送した。同日に，**Grade 3 の非重篤な有害事象の高血圧**が報告された。治験担当医師は，慢性閉塞性肺疾患及び高血圧と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。慢性閉塞性肺疾患のために治験薬を休薬した。本剤，ボルテゾミブ及びデキサメタゾンの休薬前の投与日はそれぞれ Day 1，Day 4 及び Day 5 であった。高血圧に対する治験薬の処置は実施しなかった。被験者には，アミノフィリン，cytoflavin，drotaverine，フロセミド，オメプラゾール，ペントキシフィリン，プロカイン及びトラマドールを投与した。慢性閉塞性肺疾患及び高血圧は Day 9 に回復した。

Day 22 に，被験者の ECOG スコアは 2 に悪化した。

Day 23 に，**Grade 2 の非重篤な有害事象の胸痛**が報告された。治験担当医師は，本事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治験薬の処置は実施しなかった。本事象に対する治療も実施しなかった。

Day 25 に，高カルシウム血症に続発した疾患進行のために治験薬投与を中止した（Day 22 の補正カルシウム値は 3.60 mmol/L，正常範囲：2.07-2.64 mmol/L）。本剤の最終投与日は Day 22，ボルテゾミブ及びデキサメタゾンの最終投与日は Day 25 であった。

Day 26 に，被験者は退院した。

Day 34 に，**Grade 4 の重篤な有害事象の呼吸不全**（記載語：疾患進行による呼吸不全）が報告された。治験担当医師は，本事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治療は実施しなかった。Day 35 に，被験者は呼吸不全のために死亡した。剖検は実施されなかった。

死亡時に，胸痛は未回復であった。

9) 被験者識別番号 700017

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-04-08	2015-09-26	172	2015-10-11	187	ADVERSE EVENT	-

■ **Discontinuation of study treatment due to AE; Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
脊椎骨折 Fracture of the second spinal bone	2015-09-23 -	169 -	Y 3	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	N	-

■ **Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
副鼻腔炎 Bilateral exudative sinusitis	2015-06-05 2015-06-23	59 19	N 3	Not related Not related NOT RELATED	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
全身健康状態低下 General deterioration of condition	2015-10-11 2015-10-11	187 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-07-30 2015-08-04	114 6	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-
貧血 Anemia	2015-07-28 2015-07-30	112 3	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	-
貧血 Anemia	2015-09-17 2015-09-22	163 6	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
貧血 Anemia	2015-06-10 2015-07-03	64 24	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-08-04 2015-08-10	119 7	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	-
貧血 Anemia	2015-08-10 2015-08-14	125 5	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
貧血 Anemia	2015-07-24 2015-07-28	108 5	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-
転倒 Subject fall	2015-09-23 2015-09-23	169 1	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-
高カルシウム血症 Hypercalcemia	2015-08-25T09:20 -	140 -	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
口腔ヘルペス Herpes labialis	2015-06-04 2015-06-10	58 7	N 1	Not related Possible NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ Demographics and Baseline Characteristics

□ Country: Russia
□ Study site identifier: RU00386
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Female
□ Baseline weight(kg): 86
□ Baseline height(cm): 163
□ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-09-26 Adverse Event

□ Study discontinuation: 2015-10-11 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
227.71	1280.00	42.28	2015-04-08	2015-09-26	5.65

■ **NARRATIVE TEXT**

被験者 700017 は，5[redacted]歳の女性で，2009 年 9 月 7 日に初めて病期 II（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，冠動脈疾患及び本態性高血圧症であった。ベースラインの ECOG スコアは 1 であった。その他の既往歴はなかった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，デキサメタゾン，メルファラン及びプレドニゾロン，レジメン 2 はベンダムスチン，ボルテゾミブ及びプレドニゾロンであった。

治験組入れ時の併用薬は，ゾレドロン酸，インダパミド，リシノプリル，エポエチンアルファ，Ringer aguettant，アロプリノール及びスルファメトキサゾール／トリメトプリム（Bactrim）であった。

Day 59（2015 年 6 月 5 日）に，**Grade 3 の非重篤な有害事象の副鼻腔炎**（記載語：両側性滲出性副鼻腔炎）が報告された。治験担当医師は，本事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。治験薬を休薬し，本事象のためにサイクル 4 の開始を延期した。ボルテゾミブ，デキサメタゾン及び本剤の休薬前の投与日はそれぞれ Day 53，Day 54 及び Day 57 であった。アジスロマイシン，myrtol，アセチルシステイン／tuaminoheptane（Rinofluimucil S）及びデキサメタゾン／neomycin／ポリミキシン（Polydexa）による治療を実施した。副鼻腔炎は Day 77 に回復した。同日に，サイクル 4 を開始した。

Day 77 に，ECOG スコアは 2 に悪化したが，Day 140 に 1 に改善し，Day 161 に 2 に悪化した。

Day 169（2015 年 9 月 23 日）に，被験者は**転倒**し，**Grade 2 の非重篤な有害事象**と報告された。同日の CT スキャンでは，頚椎骨組織に不規則な透過性領域，溶骨パターンを伴う硬化性骨破壊回転パターン，歯突起のベースでの第二頚椎（軸椎）の骨折（最大 6.8 mm の前方向にずれ），頚椎の生理的前弯の直線化が認められた。同日（Day 169）に，**Grade 3 の重篤な有害事象の脊椎骨折**（記載語：第二脊椎の骨折）が報告された。治験担当医師は，転倒及び脊椎骨折と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。脊椎骨折は永続的な障害の原因となった。転倒に

対する治験薬の処置は実施しなかった。Day 172 に，脊椎骨折のために治験薬投与を中止した。本剤，ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 161，Day 171 及び Day 172 であった。本事象に対する治療は実施しなかった。

Day 187 に，被験者は全身健康状態低下のために死亡した。治験担当医師は，重篤な有害事象の全身健康状態低下と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。剖検は実施しなかった。

10) 被験者識別番号 700020

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-04-21	2015-04-22	2	2015-04-29	9	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
虚血性脳卒中 Left-side ischemic stroke	2015-04-24T13:00 2015-04-29	4 6	Y 3	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ **Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気管支肺炎 Acute subtotal right-side bronchopneumonia	2015-04-22T09:05 -	2 -	Y 3	Not related Not related NOT RELATED	Dose not changed DRUG WITHDRAWN Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	Unknown

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気管支肺炎 Acute subtotal right-side bronchopneumonia	2015-04-22T09:05 -	2 -	Y 3	Not related Not related NOT RELATED	Dose not changed DRUG WITHDRAWN Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	Unknown
虚血性脳卒中 Left-side ischemic stroke	2015-04-24T13:00 2015-04-29	4 6	Y 3	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
虚血性脳卒中 Left-side ischemic stroke	2015-04-29 -	9 -	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ **Other Adverse Events**

No Other Adverse Events reported

■ **Demographics and Baseline Characteristics**

□ Country: Russia
□ Study site identifier: RU00183
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Male
□ Baseline weight(kg): 88
□ Baseline height(cm): 178
□ Baseline ECOG score: 2

■ **Disposition Information**

□ Treatment discontinuation: 2015-04-29 Adverse Event

□ Study discontinuation: 2015-04-29 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
16.00	40.00	1.29	2015-04-21	2015-04-22	0.07

■ **NARRATIVE TEXT**

被験者 700020 は，5[redacted] 歳の白人男性で，2007 年 12 月 11 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，動脈硬化症及び慢性胆嚢炎であった。ベースラインの ECOG スコアは 2 であった。その他の既往歴はなかった。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，メルファラン及びプレドニゾロン，レジメン 2 はボルテゾミブ，シクロホスファミド及びデキサメタゾン，レジメン 3 はシクロホスファミド，lomustine，メルファラン，プレドニゾロン及びビンクリスチンであった。

治験組入れ時の併用薬はなかった。

Day 2（2015 年 4 月 22 日）に，被験者は発熱，咳嗽及び右胸部の疼痛を訴え，同日の胸部 X 線写真に基づき Grade 3 の**重篤な有害事象の気管支肺炎**（記載語：右肺ほぼ全体の急性気管支肺炎）と診断された。治験担当医師は，気管支肺炎と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象のためにボルテゾミブの投与を中止した。ボルテゾミブの最終投与日は Day 1 であった。本剤又はデキサメタゾンの処置は実施しなかった。気管支肺炎の病原体は不明であった。デキサメタゾン，イミペネム／シラスタチン（Primaxin），エノキサパリンナトリウム，モルヒネ，ヒト免疫グロブリン，アンブロキソール，フェニレフリン及び塩化ナトリウムによる気管支肺炎の治療を実施した。Day 4 に，Grade 3 の**重篤な有害事象の虚血性脳卒中**（記載語：左側部虚血性脳卒中）が報告された。治験担当医師は，虚血性脳卒中と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。治療は，choline alfoscerate，エノキサパリンナトリウム，ジアゼパム，ブドウ糖，塩酸メトクロプラミド，デキサメタゾン，炭酸水素ナトリウム／塩化カリウム／塩化ナトリウム／ブドウ糖（Electrosol），エピネフリン及びフロセミドであった。Day 3，Day 4，Day 5 及

び Day 6 に濃厚赤血球を輸血した。Day 9 に，虚血性脳卒中のために治験薬投与を中止した。本剤及びデキサメタゾンの最終投与日はそれぞれ Day 1 及び Day 2 であった。Day 9 に，被験者は虚血性脳卒中のために死亡した。剖検は実施されなかった。

死亡時に，気管支肺炎は未回復であった。

11) 被験者識別番号 900028

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-05-18	2015-06-01	15	2015-06-12	26	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
心停止 Cardiac arrest	2015-06-12 2015-06-12	26 1	Y 5	Not related Not related NOT RELATED	Drug withdrawn DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-06-10 -	24 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	N	-
貧血 Anemia	2015-05-18T09:38 2015-06-10	1 24	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
転倒 Trip and fall	2015-05-29 2015-05-29	12 1	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
好中球減少症 Neutropenia	2015-06-08T10:00 -	22 -	N 4	Possible Doubtful POSSIBLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	-
睡眠障害 Sleep disorder	2015-06-01T12:00 -	15 -	N 1	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	N	-
血小板減少症 Thrombocytopenia	2015-05-25T12:00 2015-06-01	8 8	N 3	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
血小板減少症 Thrombocytopenia	2015-06-08T08:54 2015-06-10	22 3	N 4	Not related Not related NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ **Demographics and Baseline Characteristics**

□ Country: Turkey
□ Study site identifier: TR00053
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Baseline weight(kg): 58
□ Baseline height(cm): 158
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-06-12 Adverse Event

□ Study discontinuation: 2015-06-12 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
48.00	160.00	5.21	2015-05-18	2015-06-01	0.49

■ **NARRATIVE TEXT**

被験者 900028 は，6[redacted] 歳の白人男性で，2013 年 10 月 10 日に初めて病期 III（スクリーニング時）の MM と診断され，本剤，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，慢性閉塞性肺疾患及び胃炎であった。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド，デキサメタゾン，メルファラン及び prednisone，レジメン 2 はデキサメタゾン，レナリドミド及びメルファラン前処置による ASCT，レジメン 3 はシスプラチン，シクロホスファミド，デキサメタゾン，エトポシド及びポマリドミドであった。

治験組入れ時の併用薬は，パントプラゾールナトリウムセスキ水和物，simeticone，トラネキサム酸及びボリコナゾールであった。

Grade 4 の非重篤な有害事象の好中球減少症［Day 22 の好中球数 0.1×10^9/L（正常範囲：$2.5\text{-}7.5\times10^9$/L）］のために治験薬を休薬した。ボルテゾミブ，デキサメタゾン及び本剤の休薬前の投与日はそれぞれ Day 11，Day 12 及び Day 15 であった。

Day 26（2015 年 6 月 12 日）に，被験者は自宅において呼吸困難及び虚脱状態を突然発現した。救急車で測定した血圧は 80/40 mm Hg で，意識消失の状態で救急救命室に搬送された。被験者は心停止の状態であった。心肺蘇生を施行したが回復しなかった。Day 26 に，被験者は心停止のために死亡した。治験担当医師は，**重篤な有害事象の心停止**と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。ボルテゾミブ，デキサメタゾン及び本剤の最終投与日はそれぞれ Day 11，Day 12 及び Day 15 であった。剖検は実施されなかった。

(2) Vd 群

1) 被験者識別番号 310016

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-05-19	2015-08-12	86	2015-08-22	96	ADVERSE EVENT	-

■ **Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気道感染 Respiratory tract infection	2015-06-04 2015-06-12	17 9	Y 3	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	Unknown

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気道感染 Respiratory tract infection	2015-06-04 2015-06-12	17 9	Y 3	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	Unknown

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気道感染 Respiratory tract infection	2015-06-15 2015-06-18	28 4	Y 2	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	Unknown
不全単麻痺 Paresis left leg	2015-08-10 2015-08-12	84 3	Y 3	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
四肢痛 Pain left leg	2015-08-10 2015-08-12	84 3	Y 3	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
全身健康状態低下 Worsening of conditioning	2015-08-22 2015-08-22	96 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	NA FATAL	NA	-

■ Hematology Results

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	-	2015-04-30/ -19	Screening	107.937	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-05-19/ 1	Cycle 1 day 1	115.992	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-05-26/ 8	Cycle 1 day 8	119.214	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-05-28/ 10	Cycle 1 day 15	114.381	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-06-05/ 18	Cycle 1 day 15 unscheduled 1	114.381	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-06-22/ 35	Cycle 2 day 1	111.159	g/L	135-175	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	115.992	2015-06-29/ 42	Cycle 2 day 8	122.436	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-07-02/ 45	Cycle 2 day 15	107.937	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-07-13/ 56	Cycle 3 day 1	101.493	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-07-21/ 64	Cycle 3 day 8	112.77	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-07-24/ 67	Cycle 3 day 11	112.77	g/L	135-175	1
Hemoglobin low (anemia)	115.992	2015-08-03/ 77	Cycle 4 day 1	93.438	g/L	135-175	2
Leukocytes normal (both within grade 0)	-	2015-04-30/ -19	Screening	5	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-05-19/ 1	Cycle 1 day 1	5.7	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-05-26/ 8	Cycle 1 day 8	6.9	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-05-28/ 10	Cycle 1 day 15	10.6	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-06-05/ 18	Cycle 1 day 15 unscheduled 1	9.9	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-06-22/ 35	Cycle 2 day 1	5.1	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-06-29/ 42	Cycle 2 day 8	10.1	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-07-02/ 45	Cycle 2 day 15	9.9	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-07-13/ 56	Cycle 3 day 1	4.7	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-07-21/ 64	Cycle 3 day 8	6.7	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	5.7	2015-07-24/ 67	Cycle 3 day 11	8.3	x10E9/L	4.5-11	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (white blood cell decreased)	5.7	2015-08-03/ 77	Cycle 4 day 1	4.3	x10E9/L	4.5-11	1
Neutrophils low (neutrophil count decreased)	-	2015-04-30/ -19	Screening	2.4	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	2.5	2015-05-19/ 1	Cycle 1 day 1	2.5	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	2.5	2015-05-26/ 8	Cycle 1 day 8	2.8	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	2.5	2015-05-28/ 10	Cycle 1 day 15	8.3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	2.5	2015-06-05/ 18	Cycle 1 day 15 unscheduled 1	7.2	x10E9/L	2.5-7.5	0
Neutrophils low (neutrophil count decreased)	2.5	2015-06-22/ 35	Cycle 2 day 1	1.9	x10E9/L	2.5-7.5	1
Neutrophils normal (neutrophil count decreased)	2.5	2015-06-29/ 42	Cycle 2 day 8	5.8	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	2.5	2015-07-02/ 45	Cycle 2 day 15	7	x10E9/L	2.5-7.5	0
Neutrophils low (neutrophil count decreased)	2.5	2015-07-13/ 56	Cycle 3 day 1	2.1	x10E9/L	2.5-7.5	1
Neutrophils normal (neutrophil count decreased)	2.5	2015-07-21/ 64	Cycle 3 day 8	5.3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	2.5	2015-07-24/ 67	Cycle 3 day 11	4.9	x10E9/L	2.5-7.5	0
Neutrophils low (neutrophil count decreased)	2.5	2015-08-03/ 77	Cycle 4 day 1	2	x10E9/L	2.5-7.5	1
Platelets normal (platelet count decreased)	-	2015-04-30/ -19	Screening	170	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	198	2015-05-19/ 1	Cycle 1 day 1	198	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	198	2015-05-26/ 8	Cycle 1 day 8	192	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	198	2015-05-28/ 10	Cycle 1 day 15	159	x10E9/L	150-350	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	198	2015-06-05/ 18	Cycle 1 day 15 unscheduled 1	60	x10E9/L	150-350	2
Platelets low (platelet count decreased)	198	2015-06-22/ 35	Cycle 2 day 1	150	x10E9/L	150-350	0
Platelets normal (platelet count decreased)	198	2015-06-29/ 42	Cycle 2 day 8	163	x10E9/L	150-350	0
Platelets low (platelet count decreased)	198	2015-07-02/ 45	Cycle 2 day 15	115	x10E9/L	150-350	1
Platelets low (platelet count decreased)	198	2015-07-13/ 56	Cycle 3 day 1	75	x10E9/L	150-350	1
Platelets low (platelet count decreased)	198	2015-07-21/ 64	Cycle 3 day 8	69	x10E9/L	150-350	2
Platelets low (platelet count decreased)	198	2015-07-24/ 67	Cycle 3 day 11	35	x10E9/L	150-350	3
Platelets low (platelet count decreased)	198	2015-08-03/ 77	Cycle 4 day 1	51	x10E9/L	150-350	2

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
背部痛 Increased back pain	2015-07-07 2015-08-22	50 47	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
便秘 Obstipation	2015-05-22 2015-06-05	4 15	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
譫妄 Delirium	2015-06-07 2015-06-08	20 2	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
転倒 Falling down (due to unknown reason)	2015-06-07 2015-06-07	20 1	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
発熱 Fever	2015-06-15 2015-06-16	28 2	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	N	-
発熱 Fever (intermittant)	2015-06-17 2015-08-22	30 67	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
気道感染 Elevated serum c-reactive protein level (possibly due to respiratory tract infection)	2015-07-13 2015-08-10	56 29	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
傾眠 Drowsiness (due to fever)	2015-06-15 2015-06-15	28 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
血小板減少症 Thrombocytopenia	2015-07-24 -	67 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-

■ Demographics and Baseline Characteristics

- □ Country: Netherlands
- □ Study site identifier: NL00154
- □ Race: White
- □ Age(yrs): 6[redacted]
- □ Sex: Male
- □ Baseline weight(kg): 78
- □ Baseline height(cm): 178
- □ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-08-12 Progressive Disease

□ Study discontinuation: 2015-08-22 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	600.00	19.79	2015-05-19	2015-08-12	2.83

■ **NARRATIVE TEXT**

被験者 310016 は，6[redacted]歳の白人男性で，2007 年 1 月 15 日に初めて病期 II（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，難聴，深部静脈血栓症，不眠症，食欲減退，背部痛，四肢痛（両下肢），両足の末梢性感覚ニューロパチー及び浮腫（両下肢の圧痕浮腫）であった。ベースラインの ECOG スコアは 1 であった。狭心症，四肢損傷，ミオパチー及び肺炎の既往歴を有した。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド，デキサメタゾン，ドキソルビシン及びメルファラン前処置による ASCT，レジメン 2 はデキサメタゾン及びレナリドミド，レジメン 3 はシクロホスファミド，レナリドミド及び prednisone であった。

治験組入れ時の併用薬は，パミドロン酸二ナトリウム，オキシコドン，acenocoumarol，Meroken New 及びゾピクロンであった。

Day 1（2015 年 5 月 19 日）の臨床検査値は，ヘモグロビン値 115.99 g/L（正常範囲：135-175 g/L），血小板数 198×10^9/L（正常範囲：$150\text{-}350\times10^9$/L），白血球数 5.7×10^9/L（正常範囲：$4.5\text{-}11.0\times10^9$/L）及び好中球数 2.5×10^9/L（正常範囲：$2.5\text{-}7.5\times10^9$/L）であった。

Day 17 に，発熱（体温：38.7°C）及び悪寒が発現した。同日に，**Grade 3 の重篤な有害事象の気道感染**が報告された。翌日（Day 18）に，被験者は入院した。Day 18 の臨床検査値は，ヘモグロビン値 114.38 g/L，ヘマトクリット 0.33（正常範囲：0.40-0.52），血小板数 60×10^9/L，白血球数 9.9×10^9/L，好中球数 7.2×10^9/L，単球数 1.6×10^9/L（正常範囲：$0.1\text{-}0.8\times10^9$/L）であった。C-反応性たん白（CRP）値は 30（単位及び正常範囲不明），胸部 X 線写真で右肺に浸潤が認められた（日付不明）。尿検査及び血液培養で特に問題は認められなかった。治験担当医師は，気道感染とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象は限局性で，日和見感染であると判断され，病原体は不明であった。ボルテゾミブ及びデキサメタゾンを休薬し，本事象のためにサイクル 2 の開始を延期した。両剤の休薬前の投与日はそれぞれ Day 11 及び Day 12 であった。セフロキシムによる気道感染の治療を実施した。Day 20 に **Grade 2 の非重篤な有害事象の譫妄**が報告された。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対するボルテゾミブ及びデキサメタゾンの処置は実施しなかった。譫妄は，ハロペリドール投与後の

Day 21 に回復した。気道感染は Day 25 に回復したが後遺症があった。同日（Day 25）に，被験者は退院した。Day 28 に，**Grade 2 の重篤な有害事象の気道感染**及び**非重篤な有害事象の Grade 2 の発熱**（体温：39.9°C）及び **Grade 1 の傾眠**が報告された。同日に，被験者は入院した。Day 28 の臨床検査値は，白血球数 5.1×10^9/L，血小板数 130×10^9/L，好中球数 3.1×10^9/L 及び単球数 0.9×10^9/L，Day 29 のヘモグロビン値 5.6 mmol/L（正常範囲：8.5-10.5 mmol/L），ヘマトクリット 0.27 及び白血球数 2.9×10^9/L であった。治験担当医師は，気道感染，発熱及び傾眠とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。気道感染のためにボルテゾミブ及びデキサメタゾンの休薬は継続した。発熱及び傾眠に対するボルテゾミブ及びデキサメタゾンの処置は実施しなかった。気道感染，発熱及び傾眠に対する治療も実施しなかった。傾眠は発現日（Day 28）に回復した。Day 31 に，被験者は退院した（体温：37.7-38.7°C）。気道感染は Day 31 に回復したが後遺症があった。Day 36 に，サイクル 2 を開始した。同日に，ECOG スコアは 2 に悪化した。Day 56 に，**Grade 2 の非重篤な有害事象の気道感染**［記載語：血清 CRP 値上昇（気道感染が原因の可能性あり）］が報告された。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対するボルテゾミブ及びデキサメタゾンの処置は実施しなかった。気道感染は，アジスロマイシン投与後の Day 84 に回復した。

Day 71～Day 75 に，放射線療法（6×4 Gy，椎骨）を施行した。Day 84 に，**Grade 3 の重篤な有害事象の不全単麻痺**（記載語：左肢の不全麻痺）**及び四肢痛**（記載語：左肢の疼痛）が報告され，同日に入院した。翌日（Day 85）の核磁気共鳴画像スキャンでは椎骨／骨盤に新たな病変が複数認められ，MM の進行が疑われた。治験担当医師は，不全単麻痺及び四肢痛とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。Day 86 に，不全単麻痺及び四肢痛，並びに疾患進行のためにボルテゾミブ及びデキサメタゾンの投与を中止した。ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 85 及び Day 86 であった。これらの事象に対する治療は実施しなかった。Day 86 に，不全単麻痺及び四肢痛は回復し，同日に，被験者は退院した。被験者には苦痛緩和／支援的ケアが施行された。Day 96 に，被験者の状態は悪化し，同日，重篤な有害事象の全身健康状態低下のために死亡した。剖検は実施されなかった。

2) 被験者識別番号 340028

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-06-05	2015-06-15	11	2015-06-17	13	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
敗血症性ショック Septic shock	2015-06-16T15:17 2015-06-17T00:09	12 2	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	Y FATAL	NA	Unknown

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
咳嗽 Cough	2015-06-10 2015-06-15	6 6	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
食欲減退 Hyporexia	2015-06-05 2015-06-17	1 13	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
下痢 Diarrhea	2015-06-13 2015-06-14	9 2	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
腎機能障害 Worsening renal function	2015-06-12 2015-06-17	8 6	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血小板減少症 Thrombopenia	2015-06-16 2015-06-17	12 2	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

■ Hematology/Chemistry Results

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine high (creatinine increased)	129.064	2015-06-05/ 1	Cycle 1 day 1	129.064	umol/L	44.2-106.08	1
Creatinine high (creatinine increased)	129.064	2015-06-16/ 12	End of treatment	347.412	umol/L	44.2-106.08	3
Hemoglobin (anemia)	-	2015-05-26/ -10	Screening	105	g/L	135-175	1
Hemoglobin (anemia)	111	2015-06-05/ 1	Cycle 1 day 1	111	g/L	135-175	1
Hemoglobin (anemia)	111	2015-06-12/ 8	Cycle 1 day 8	111	g/L	135-175	1
Hemoglobin (anemia)	111	2015-06-16/ 12	End of treatment	100	g/L	135-175	1
Leukocytes (both within grade 0)	-	2015-05-26/ -10	Screening	9.7	x10E9/L	4.5-11	0
Leukocytes (both within grade 0)	10.2	2015-06-05/ 1	Cycle 1 day 1	10.2	x10E9/L	4.5-11	0
Leukocytes (both within grade 0)	10.2	2015-06-12/ 8	Cycle 1 day 8	15.8	x10E9/L	4.5-11	0
Leukocytes (both within grade 0)	10.2	2015-06-16/ 12	End of treatment	7.9	x10E9/L	4.5-11	0
Lymphocytes (both within grade 0)	-	2015-05-26/ -10	Screening	2.5	x10E9/L	1.5-3.5	0
Lymphocytes (both within grade 0)	2.5	2015-06-05/ 1	Cycle 1 day 1	2.5	x10E9/L	1.5-3.5	0
Lymphocytes (both within grade 0)	2.5	2015-06-12/ 8	Cycle 1 day 8	2	x10E9/L	1.5-3.5	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes (lymphocyte count decreased)	2.5	2015-06-16/ 12	End of treatment	0.4	x10E9/L	1.5-3.5	3
Neutrophils (neutrophil count decreased)	-	2015-05-26/ -10	Screening	6.3	x10E9/L	2.5-7.5	0
Neutrophils (neutrophil count decreased)	6.8	2015-06-05/ 1	Cycle 1 day 1	6.8	x10E9/L	2.5-7.5	0
Neutrophils (neutrophil count decreased)	6.8	2015-06-12/ 8	Cycle 1 day 8	12.1	x10E9/L	2.5-7.5	0
Neutrophils (neutrophil count decreased)	6.8	2015-06-16/ 12	End of treatment	7.3	x10E9/L	2.5-7.5	0
Platelets (platelet count decreased)	-	2015-05-26/ -10	Screening	249	x10E9/L	150-350	0
Platelets (platelet count decreased)	213	2015-06-05/ 1	Cycle 1 day 1	213	x10E9/L	150-350	0
Platelets (platelet count decreased)	213	2015-06-12/ 8	Cycle 1 day 8	172	x10E9/L	150-350	0
Platelets (platelet count decreased)	213	2015-06-16/ 12	End of treatment	95	x10E9/L	150-350	1

■ Demographics and Baseline Characteristics

□ Country: Spain
□ Study site identifier: ES12025
□ Race: White
□ Age(yrs): 8[redacted]
□ Sex: Male
□ Baseline weight(kg): 60
□ Baseline height(cm): 158
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2015-06-17 Adverse Event

□ Study discontinuation: 2015-06-17 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	140.00	5.30	2015-06-05	2015-06-15	0.36

■ **NARRATIVE TEXT**

被験者 340028 は，8[redacted]歳の白人男性で，2008 年 11 月 17 日に初めて病期 III（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，不安，無力症，アテローム性動脈硬化症，2 型糖尿病，高コレステロール血症，高血圧，低カルシウム血症，末梢性虚血，前立腺障害及び腎不全であった。ベースラインの ECOG スコアは 1 であった。その他の既往歴はなかった。

被験者は 1 レジメンの前治療（ボルテゾミブ及びデキサメタゾン）を受けていた。

治験組入れ時の併用薬は，クロピドグレル，タムスロシン，ビカルタミド，カルシウム／コレカルシフェロール（Osvical D），アスピリン，アトルバスタチン，ビソプロロール，ニトログリセリン，ラニチジン，フルオキセチン及びエポエチンアルファであった。

Day 1（2015 年 6 月 5 日）の臨床検査値は，ヘモグロビン値 111 g/L（正常範囲：135-175 g/L），血小板数 213×10^9/L（正常範囲：150-350×10^9/L），リンパ球数 2.5×10^9/L（正常範囲：1.5-3.5×10^9/L），好中球数 6.8×10^9/L（正常範囲：2.5-7.5×10^9/L），白血球数 10.2×10^9/L（正常範囲：4.5-11×10^9/L）及びクレアチニン値 129.06 µmol/L（正常範囲：44.20-106.08 µmol/L）であった。

Day 8 に，**非重篤な有害事象の Grade 1 の腎機能障害**（記載語：腎機能の悪化）が報告された。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対するボルテゾミブ及びデキサメタゾンの処置及び治療は実施しなかった。

被験者は低血圧のために入院した（日付不明）。Day 9 に下痢及び粘液便，Day 12 に胆汁嘔吐が認められた。血圧は 60/30 mm Hg であった。同日（Day 12）の臨床検査値は，CRP 値 39 mg/L（正常範囲：0-8 mg/L），乳酸値 41 mg/dL（正常範囲：5-20 mg/dL），カリウム値 3.1 mmol/L（正常範囲：3.7-5.4 mmol/L），尿素値 201 mg/dL（正常範囲：10-71 mg/dL），二酸化炭素分圧（炭酸ガス分圧）31 mm Hg（正常範囲：38-50 mm Hg），重炭酸塩値 16.7 mmol/L（正常範囲：23-27 mmol/L），ヘマトクリット 32.3%（正常範囲：40-54%），ヘモグロビン値 100 g/L，血小板数 95×10^9/L，クレアチニン値 347.41 µmol/L，リンパ球数 0.4×10^9/L，好中球数 7.3×10^9/L 及び白血球数 7.9×10^9/L であった。Day 12 に，**重篤な有害事象の敗血症性ショック**が報告された。同日（Day 12）に，ECOG スコアは 4 に悪化した。治験担当医師は，敗血症性ショックとボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。Day 13 に，敗血症性ショックのためにボルテゾミブ及びデキサメタゾンの投与を中止した。ボルテゾミブ及びデキサメタゾンの最終投与日は Day 11 であった。敗血症性ショックの病原体は不明であった。hetastarch，塩化ナトリウム，強心剤及び利尿剤による治療を実施した。被験者は無尿であった。Day 13 に，呼吸停止となり，同日に，敗血症性ショックのために死亡した。剖検は実施されなかった。

3) 被験者識別番号 340031

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-07-07	2015-11-21	138	2015-11-28	145	ADVERSE EVENT	-

■ **Infections and infestations, Grade 3 or 4; Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-10-02 2015-10-09	88 8	Y 3	Not related Probable PROBABLE	Not applicable DOSE REDUCED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	No
気管気管支炎 Acute tracheobronchitis	2015-11-23 2015-11-27	140 5	Y 4	Not related Not related POSSIBLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	No

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気管気管支炎 Acute tracheobronchitis	2015-11-28 2015-11-28	145 1	Y 5	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N FATAL	NA	No

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
腹痛 Abdominal pain	2015-10-07 2015-10-07	93 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
下痢 Diarrhea	2015-11-23 2015-11-28	140 6	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

■ Hematology Results

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes normal (both within grade 0)	-	2015-06-18/ -19	Screening	7.5	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-07-07/ 1	Cycle 1 day 1	7.9	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-07-14/ 8	Cycle 1 day 8	9.3	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-07-28/ 22	Cycle 2 day 1	8.4	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-08-04/ 29	Cycle 2 day 8	7.4	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-08-18/ 43	Cycle 3 day 1	7.2	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-08-28/ 53	Cycle 3 day 11	6.8	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-09-08/ 64	Cycle 4 day 1	5.3	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-09-18/ 74	Cycle 4 day 11	5.7	x10E9/L	4.5-11	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes low (both within grade 0)	7.9	2015-09-29/ 85	Cycle 5 day 1	4.5	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-10-08/ 94	Cycle 5 day 11	6.3	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-10-20/ 106	Cycle 6 day 1	5.2	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-10-30/ 116	Cycle 6 day 11	9.4	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-11-10/ 127	Cycle 7 day 1	8	x10E9/L	4.5-11	0
Leukocytes normal (both within grade 0)	7.9	2015-11-20/ 137	Cycle 7 day 11	9.8	x10E9/L	4.5-11	0
Neutrophils normal (neutrophil count decreased)	-	2015-06-18/ -19	Screening	5	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-07-07/ 1	Cycle 1 day 1	5.3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-07-14/ 8	Cycle 1 day 8	6.3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-07-28/ 22	Cycle 2 day 1	6.4	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-08-04/ 29	Cycle 2 day 8	5.2	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-08-18/ 43	Cycle 3 day 1	5.1	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-08-28/ 53	Cycle 3 day 11	5	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-09-08/ 64	Cycle 4 day 1	3.8	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-09-18/ 74	Cycle 4 day 11	3.2	x10E9/L	2.5-7.5	0
Neutrophils low (neutrophil count decreased)	5.3	2015-09-29/ 85	Cycle 5 day 1	2.4	x10E9/L	2.5-7.5	1
Neutrophils normal (neutrophil count decreased)	5.3	2015-10-08/ 94	Cycle 5 day 11	3	x10E9/L	2.5-7.5	0

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Neutrophils normal (neutrophil count decreased)	5.3	2015-10-20/ 106	Cycle 6 day 1	3	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-10-30/ 116	Cycle 6 day 11	5.9	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-11-10/ 127	Cycle 7 day 1	6	x10E9/L	2.5-7.5	0
Neutrophils normal (neutrophil count decreased)	5.3	2015-11-20/ 137	Cycle 7 day 11	6.7	x10E9/L	2.5-7.5	0
Neutrophils high (neutrophil count decreased)	5.3	2015-11-23/ 140	Cycle 7 day 12 unscheduled 1	22	x10E9/L	2.5-7.5	0

■ Demographics and Baseline Characteristics

- □ Country: Spain
- □ Study site identifier: ES12018
- □ Race: White
- □ Age(yrs): 7[redacted]
- □ Sex: Female
- □ Baseline weight(kg): 71.5
- □ Baseline height(cm): 154
- □ Baseline ECOG score: 1

■ Disposition Information

- □ Treatment discontinuation: 2015-11-28 Death
- □ Study discontinuation: 2015-11-28 Death
- □ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1000.00	30.62	2015-07-07	2015-11-21	4.53

■ NARRATIVE TEXT

被験者 340031 は，7[redacted]歳の白人女性で，2011 年 3 月 28 日に初めて病期 III（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，2 型糖尿病，副甲状腺機能亢進症，腎結石症及び老年認知症であった。ベースラインの ECOG スコアは 1 であった。その他の既往歴はなかった。

被験者は 1 レジメンの前治療（ボルテゾミブ，デキサメタゾン，レナリドミド，メルファラン及び prednisone）を受けていた。

治験組入れ時の併用薬はなかった。

Day 1 に，被験者の好中球数は 5.3×10^9/L（正常範囲：2.5-7.5$\times10^9$/L），白血球数 7.9×10^9/L（正常範囲：4.5-11$\times10^9$/L）であった。

Day 64 に，ECOG スコアは 0 に改善した。

Day 92 に，被験者は **Grade 3 の重篤な有害事象の肺炎**のために入院した。本事象の病因として併発疾患が疑われた。治験担当医師は，肺炎とボルテゾミブ及びデキサメタゾンとの因果関係を「可能性大」と判断した。本事象のためにデキサメタゾン及びボルテゾミブを休薬した。両剤の休薬前の投与日はそれぞれ Day 85 及び Day 86 であった。被験者は，イプラトロピウム臭化物，ピペラシリン／タゾバクタム（Tazocel），レボフロキサシン及び paracetamol を投与された。Day 95 に，肺炎は回復し，同日に，被験者は退院した。Day 106 に，デキサメタゾンによる治療を再開した。同日に，ボルテゾミブによる治療を再開したが，肺炎のために投与量を 1.0 mg/m^2 に減量した。

Day 140 に，被験者は **Grade 4 の重篤な有害事象の気管気管支炎**（記載語：急性気管気管支炎）のために入院した。治験担当医師は，本事象とデキサメタゾンとの因果関係を「可能性小」，ボルテゾミブとの因果関係を「関連なし」と判断した。被験者には，メロペネム，酸素及びレボフロキサシンを投与した。被験者の状態は悪化し，急性呼吸器感染は急性肺水腫へと悪化した。Day 145 に，被験者は気管気管支炎のために死亡した。剖検は実施されなかった。ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 137 及び Day 138 であった。

4) 被験者識別番号 360017

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-02-26	2015-05-08	72	2015-06-03	98	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
心停止 Cardiac arrest	2015-06-03T10:03 2015-06-03	98 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	NA FATAL	NA	-

■ Infections and infestations, Grade 3 or 4

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
胃腸炎 Gastroenteritis	2015-05-10 -	74 -	Y 3	Not related Doubtful POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	NA	Unknown
大腸菌性敗血症 Septicaemia by eschericia coli	2015-05-12 -	76 -	N 4	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y UNKNOWN	NA	-
心内膜炎 Infectious endocarditis	2015-05-21 -	85 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	NA	-
ステノトロフォモナス感染 Stenotrophomonas maltophila infection	2015-05-26 -	90 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	NA	-

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
胃腸炎 Gastroenteritis	2015-05-10 -	74 -	Y 3	Not related Doubtful POSSIBLE	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	NA	Unknown
呼吸不全 Respiratory failure	2015-05-12 -	76 -	Y 4	Not related Not related POSSIBLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N UNKNOWN	NA	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
急性副鼻腔炎 Acute sinusitis maxillaris	2015-03-22 2015-03-30	25 9	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
貧血 Anaemia	2015-03-19 2015-04-29	22 42	N 2	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
貧血 Anaemia	2015-05-07 -	71 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血液障害 Increased lactate dehydrogenase probably of hematological origin	2015-05-07 -	71 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	NA	-
体部白癬 Tinea corporis	2015-03-19 2015-03-26	22 8	N 1	Not related Doubtful PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
骨痛 Worsening of bone pain	2015-04-18 2015-05-04	52 17	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	-
骨痛 Worsening of bone pain	2015-05-04 -	68 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	NA	-
鼻出血 Epistaxis	2015-04-21 2015-04-21	55 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
鼻出血 Epistaxis	2015-04-27 2015-04-27	61 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
鼻出血 Nasal bleeding	2015-03-19 2015-03-19	22 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
リンパ球減少症 Lymphopenia	2015-04-29 2015-05-07	63 9	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
リンパ球減少症 Lymphopenia	2015-05-07 -	71 -	N 4	Not related Probable PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N UNKNOWN	NA	-
悪心 Nausea	2015-04-29 2015-05-04	63 6	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
腎機能障害 Decreased renal function	2015-04-29 -	63 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
皮膚障害 Suffusions on skin	2015-05-04 -	68 -	N 1	Not related Possible NOT RELATED	Not applicable DRUG INTERRUPTED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
上室性頻脈 Supraventricular tachcardia	2015-05-14 2015-05-15	78 2	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
血小板減少症 Thrombocytopenia	2015-04-09 2015-04-29	43 21	N 2	Not related Possible DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
血小板減少症 Thrombocytopenia	2015-04-02 2015-04-09	36 8	N 3	Not related Very likely DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血小板減少症 Thrombocytopenia	2015-05-10 -	74 -	N 4	Not related Possible NOT RELATED	Not applicable DRUG INTERRUPTED Not applicable	Daratumumab Velcade DEXAMETHASONE	Y UNKNOWN	NA	-
血小板減少症 Thrombocytopenia	2015-03-12 2015-03-26	15 15	N 2	Not related Very likely NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
血小板減少症 Thrombocytopenia	2015-04-29 2015-05-10	63 12	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

■ Hematology/Chemistry Toxicities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine high (creatinine increased)	-	2015-02-09/ -17	Screening	116	umol/L	53-100	1
Creatinine high (creatinine increased)	114	2015-02-26/ 1	Cycle 1 day 1	114	umol/L	53-100	1
Creatinine high (creatinine increased)	114	2015-03-19/ 22	Cycle 2 day 1	112	umol/L	53-100	1
Creatinine high (creatinine increased)	114	2015-04-09/ 43	Cycle 3 day 1	109	umol/L	53-100	1
Creatinine high (creatinine increased)	114	2015-04-29/ 63	Cycle 4 day 1	131	umol/L	53-100	1
Creatinine high (creatinine increased)	114	2015-05-07/ 71	Cycle 4 day 8	172	umol/L	53-100	2
Creatinine high (creatinine increased)	114	2015-05-10/ 74	Cycle 4 day 9 unscheduled 1	229	umol/L	53-100	2
Hemoglobin low (anemia)	-	2015-02-09/ -17	Screening	99	g/L	120-160	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	101	2015-02-26/ 1	Cycle 1 day 1	101	g/L	120-160	1
Hemoglobin low (anemia)	101	2015-03-05/ 8	Cycle 1 day 8	103	g/L	120-160	1
Hemoglobin low (anemia)	101	2015-03-12/ 15	Cycle 1 day 15	103	g/L	120-160	1
Hemoglobin low (anemia)	101	2015-03-19/ 22	Cycle 2 day 1	95	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-03-26/ 29	Cycle 2 day 8	89	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-04-02/ 36	Cycle 2 day 15	88	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-04-09/ 43	Cycle 3 day 1	88	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-04-16/ 50	Cycle 3 day 8	101	g/L	120-160	1
Hemoglobin low (anemia)	101	2015-04-23/ 57	Cycle 3 day 15	99	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-04-29/ 63	Cycle 4 day 1	106	g/L	120-160	1
Hemoglobin low (anemia)	101	2015-05-07/ 71	Cycle 4 day 8	96	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-05-10/ 74	Cycle 4 day 9 unscheduled 1	95	g/L	120-160	2
Hemoglobin low (anemia)	101	2015-05-11/ 75	Cycle 4 day 11	82	g/L	120-160	2
Leukocytes low (white blood cell decreased)	-	2015-02-09/ -17	Screening	2.67	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	2.65	2015-02-26/ 1	Cycle 1 day 1	2.65	x10E9/L	4.5-11	2
Leukocytes low (white blood cell decreased)	2.65	2015-05-11/ 75	Cycle 4 day 11	1.33	x10E9/L	4.5-11	3
Lymphocytes low (lymphocyte count decreased)	-	2015-02-09/ -17	Screening	0.42	x10E9/L	1.5-3.5	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low (lymphocyte count decreased)	0.62	2015-02-26/ 1	Cycle 1 day 1	0.62	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.62	2015-03-12/ 15	Cycle 1 day 15	1.1	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.62	2015-03-19/ 22	Cycle 2 day 1	0.65	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.62	2015-03-26/ 29	Cycle 2 day 8	0.77	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.62	2015-04-02/ 36	Cycle 2 day 15	1.12	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.62	2015-04-09/ 43	Cycle 3 day 1	0.71	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.62	2015-04-16/ 50	Cycle 3 day 8	0.89	x10E9/L	1.5-3.5	1
Lymphocytes low (lymphocyte count decreased)	0.62	2015-04-23/ 57	Cycle 3 day 15	0.68	x10E9/L	1.5-3.5	2
Lymphocytes low (lymphocyte count decreased)	0.62	2015-04-29/ 63	Cycle 4 day 1	0.36	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.62	2015-05-07/ 71	Cycle 4 day 8	0.08	x10E9/L	1.5-3.5	4
Lymphocytes low (lymphocyte count decreased)	0.62	2015-05-10/ 74	Cycle 4 day 9 unscheduled 1	0.29	x10E9/L	1.5-3.5	3
Lymphocytes low (lymphocyte count decreased)	0.62	2015-05-11/ 75	Cycle 4 day 11	0.07	x10E9/L	1.5-3.5	4
Neutrophils low (neutrophil count decreased)	-	2015-02-09/ -17	Screening	1.65	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.53	2015-02-26/ 1	Cycle 1 day 1	1.53	x10E9/L	2.5-7.5	1
Neutrophils low (neutrophil count decreased)	1.53	2015-05-11/ 75	Cycle 4 day 11	1.09	x10E9/L	2.5-7.5	2
Platelets low (platelet count decreased)	160	2015-03-05/ 8	Cycle 1 day 8	110	x10E9/L	150-350	1
Platelets low (platelet count decreased)	160	2015-03-12/ 15	Cycle 1 day 15	57	x10E9/L	150-350	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low (platelet count decreased)	160	2015-03-19/ 22	Cycle 2 day 1	82	x10E9/L	150-350	1
Platelets low (platelet count decreased)	160	2015-03-26/ 29	Cycle 2 day 8	51	x10E9/L	150-350	2
Platelets low (platelet count decreased)	160	2015-04-02/ 36	Cycle 2 day 15	47	x10E9/L	150-350	3
Platelets low (platelet count decreased)	160	2015-04-09/ 43	Cycle 3 day 1	68	x10E9/L	150-350	2
Platelets low (platelet count decreased)	160	2015-04-16/ 50	Cycle 3 day 8	58	x10E9/L	150-350	2
Platelets low (platelet count decreased)	160	2015-04-23/ 57	Cycle 3 day 15	50	x10E9/L	150-350	2
Platelets low (platelet count decreased)	160	2015-04-29/ 63	Cycle 4 day 1	47	x10E9/L	150-350	3
Platelets low (platelet count decreased)	160	2015-05-07/ 71	Cycle 4 day 8	27	x10E9/L	150-350	3
Platelets low (platelet count decreased)	160	2015-05-10/ 74	Cycle 4 day 9 unscheduled 1	13	x10E9/L	150-350	4
Platelets low (platelet count decreased)	160	2015-05-11/ 75	Cycle 4 day 11	10	x10E9/L	150-350	4

■ Demographics and Baseline Characteristics

□ Country: Hungary
□ Study site identifier: HU90018
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Female
□ Baseline weight(kg): 71
□ Baseline height(cm): 162
□ Baseline ECOG score: 1

■ Disposition Information

□ Treatment discontinuation: 2015-06-03 Adverse Event

□ Study discontinuation: 2015-06-03 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	560.00	18.09	2015-02-26	2015-05-08	2.37

■ **NARRATIVE TEXT**

被験者 360017 は，6[redacted]歳の白人女性で，2008 年 12 月 9 日に初めて病期 III（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，骨痛，腎機能障害，高血圧及び拘束性肺疾患であった。ベースラインの ECOG スコアは 1 であった。うっ血性心不全，閉塞性気道障害，心房細動及び心嚢液貯留の既往歴を有した。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はシクロホスファミド，デキサメタゾン，サリドマイド及びメルファラン前処置による ASCT，レジメン 2 はボルテゾミブ，メルファラン及びプレドニゾロン，レジメン 3 はデキサメタゾン，イキサゾミブ及びレナリドミドであった。被験者はレジメン 3 の前治療に対して治療抵抗性を示した。

治験組入れ時の併用薬は，パミドロン酸二ナトリウム及びアシクロビルであった。

Day 1（2015 年 2 月 26 日）に，ヘモグロビン値 101 g/L（正常範囲：120-160 g/L），血小板数 160×10^9/L（正常範囲：$150\text{-}350\times10^9$/L），リンパ球数 0.62×10^9/L（正常範囲：$1.5\text{-}3.5\times10^9$/L）及びクレアチニン値 114 μmol/L（正常範囲：53-100 μmol/L）であった。

Day 43 に，ECOG スコアは 2 に悪化した。

Day 63 に，**非重篤な有害事象の Grade 3 のリンパ球減少症及び Grade 2 の腎機能障害**が報告された（リンパ球数：0.36×10^9/L，クレアチニン値：131 μmol/L）。治験担当医師は，両事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。両事象に対するボルテゾミブ及びデキサメタゾンの処置及び治療は実施しなかった。Day 71 に，**リンパ球減少症は Grade 4 に悪化し**（リンパ球数：0.08×10^9/L），**Grade 2 の非重篤な有害事象の貧血及び血液障害**（記載語：おそらく赤血球由来の乳酸デヒドロゲナーゼ増加）が報告された［ヘモグロビン値：96 g/L，乳酸デヒドロゲナーゼ値：1534 U/L（正常範囲：153-463 U/L）］。治験担当医師は，Grade 4 のリンパ球減少症とボルテゾミブ及びデキサメタゾンとの因果関係を「可能性大」，貧血及び血液障害とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。これらの事象に対するボルテゾミブ及びデキサメタゾンの処置及び治療は実施しなかった。

Day 15～Day 73 に，**Grade 2～3 の非重篤な有害事象の血小板減少症**が複数回発現した。Day 74 に，ECOG スコアは 4 に悪化した。同日に，被験者は**Grade 3 の重篤な有害事象の胃腸炎**のために入院した。翌日（Day 75）に，便の *Clostridium difficile* 検査を実施した（結果不明）。治験担当医師は，胃腸炎とボルテゾミブとの因果関係を「多分なし」，デキサメタゾンとの因果関係を「可能性小」と判断した。同日（Day 74）に，**血小板減少症が Grade 4 に悪化した**（血小板数：13×10^9/L）。治験担当医師は，本事象とボルテゾミブとの因果関係を「可能性小」，デキサメタゾンとの因果関係を「関連なし」と判断した。血小板減少症及び胃腸炎のためにボルテゾミブ及びデキサメタゾンを休薬した。ボルテゾミブ及びデキサメタゾンの休薬前の投与日はそれぞれ Day 68，Day 72 であった。Ringer 液と塩化ナトリウムによる胃腸炎の治療を実施した。Day 75 に，血小板を輸血した。胃腸炎の病原体は不明であった。

Day 76 に，被験者は**重篤な有害事象の Grade 4 の呼吸不全**のために集中治療室に移送された。同日に，血液，鼻汁，尿，便及び気管支肺胞細胞の培養検査を実施した（結果不明）。同日に，**非重篤な有害事象の Grade 4 の大腸菌性敗血症**（記載語：*Escherichia coli* による敗血症）も報告された。治験担当医師は，呼吸不全とボルテゾミブとの因果関係を「関連なし」，デキサメタゾンとの因果関係を「可能性小」，大腸菌性敗血症とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。大腸菌性敗血症のためにボルテゾミブ及びデキサメタゾンの休薬を継続した。呼吸不全に対するボルテゾミブ及びデキサメタゾンの処置は実施しなかった。人工呼吸（二相性陽圧喚気）を施行し，ドパミン，ヒト正常免疫グロブリン，メロペネム，ノルエピネフリン及びアミカシンによる治療を実施した。

Day 78 に，**非重篤な有害事象の Grade 2 の上室性頻脈**，Day 85 に，**Grade 3 の心内膜炎**（記載語：感染性心内膜炎），Day 90 に，**Grade 3 のステノトロフォモナス感染**（記載語：ステノトロフォモナス・マルトフィリア感染）が報告された。治験担当医師は，これらの事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。これらの事象に対するボルテゾミブ及びデキサメタゾンの処置は実施しなかった。上室性頻脈は，アミオダロン投与後の Day 79 に回復した。心内膜炎及びステノトロフォモナス感染に対しバンコマイシン及びコリスチンを投与した。

Day 98 に，被験者は心停止となった。心肺蘇生を試みたが回復せず，同日（Day 98）に，被験者は心停止のために死亡した。治験担当医師は，**重篤な有害事象の心停止**とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。心停止の原因として大腸菌性敗血症及びステノトロフォモナス感染が報告された。ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 68 及び Day 72 であった。

死亡時に，血小板減少症，貧血，リンパ球減少症，腎機能障害，血液障害，胃腸炎，呼吸不全，大腸菌性敗血症，心内膜炎及びステノトロフォモナス感染は未回復であった。

5) 被験者識別番号 380019

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-03-05	2015-06-19	107	2015-06-20	108	ADVERSE EVENT	-

■ **Discontinuation of study treatment due to AE; Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺塞栓症 Pulmonary embolism	2015-06-20 2015-06-20	108 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	U FATAL	NA	-

■ **Other Adverse Events**

No Other Adverse Events reported

■ **Demographics and Baseline Characteristics**

- □ Country: Ukraine
- □ Study site identifier: UA90176
- □ Race: White
- □ Age(yrs): 5[redacted]
- □ Sex: Female
- □ Baseline weight(kg): 62.5
- □ Baseline height(cm): 159
- □ Baseline ECOG score: 0

■ **Disposition Information**

- □ Treatment discontinuation: 2015-06-20 Adverse Event
- □ Study discontinuation: 2015-06-20 Death
- □ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	840.00	27.35	2015-03-05	2015-06-19	3.52

■ **NARRATIVE TEXT**

被験者 380019 は，5[redacted] 歳の白人女性で，2013 年 7 月 3 日に初めて病期 II（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，子宮平滑筋腫（結節性びまん性子宮類線維症）及び骨端症であった。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド，デキサメタゾン及びサリドマイド，レジメン 2 はメルファランであった。

治験組入れ時の併用薬はなかった。

Day 106 に，ECOG スコアは 1 に悪化した。

Day 108（2015 年 6 月 20 日）に，被験者は**重篤な有害事象の肺塞栓症**のために突然死亡した。剖検の結果，死因は肺塞栓症であることが確認された。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 106 及び Day 107 であった。

6) 被験者識別番号 380042

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Infections and infestations, Grade 3 or 4

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-06-02	2015-11-19	171	2015-11-27	179	ADVERSE EVENT	-

■ Infections and infestations, Grade 3 or 4

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
精巣上体炎 Left-sided orhiepididimit	2015-08-09 2015-08-31	69 23	Y 3	Not related Doubtful DOUBTFUL	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	No
肺炎 Hospital double pneumonia	2015-08-19 2015-08-31	79 13	Y 4	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	No

■ Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
精巣上体炎 Left-sided orhiepididimit	2015-08-09 2015-08-31	69 23	Y 3	Not related Doubtful DOUBTFUL	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	No
肺炎 Hospital double pneumonia	2015-08-19 2015-08-31	79 13	Y 4	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	No
状態悪化 Worsening of conditdon	2015-11-27 2015-11-27	179 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N FATAL	NA	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-10-26 -	147 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
貧血 Anemia	2015-09-11 2015-10-19	102 39	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
貧血 Anemia	2015-08-27 2015-09-07	87 12	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-08-26 2015-08-26	86 1	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
貧血 Anemia	2015-07-21 2015-08-26	50 37	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
貧血 Anemia	2015-10-19 2015-10-26	140 8	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
肛門出血 Anal hemorrhage	2015-07-18 2015-07-23	47 6	N 1	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	NA RECOVERED/RESOLVED	NA	-
便秘 Constipation	2015-07-18 2015-11-17	47 123	N 1	Not related Doubtful POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
低アルブミン血症 Hypoalbuminemia	2015-06-22 2015-10-06	21 107	N 2	Not related Probable PROBABLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
低アルブミン血症 Hypoalbuminemia	2015-10-23 -	144 -	N 2	Not related Doubtful DOUBTFUL	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
リンパ球減少症 Lymphopenia	2015-11-24 -	176 -	N 3	Not related Possible POSSIBLE	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	NA NOT RECOVERED/NOT RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
リンパ球減少症 Lymphopenia	2015-10-12 2015-10-15	133 4	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
リンパ球減少症 Lymphopenia	2015-09-11 2015-09-21	102 11	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
リンパ球減少症 Lymphopenia	2015-09-21 2015-10-02	112 12	N 1	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
リンパ球減少症 Lymphopenia	2015-07-21 2015-07-24	50 4	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	NA RECOVERED/RESOLVED	NA	-
末梢性運動ニューロパチー Motor polyneuropathy of the lower extremities	2015-10-06 2015-11-05	127 31	N 2	Not related Probable DOUBTFUL	Not applicable DOSE REDUCED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
末梢性感覚ニューロパチー Sensory polyneuropathy of the lower extremities	2015-10-06 2015-11-05	127 31	N 2	Not related Probable DOUBTFUL	Not applicable DOSE REDUCED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
脊柱管狭窄症 Spinal stenosis	2015-11-20 -	172 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event End Date/Time of Adverse Event	Start Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血小板減少症 Thrombocytopenia	2015-09-11 2015-09-21	102 11	N 3	Not related Possible NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
血小板減少症 Thrombocytopenia	2015-11-05 -	157 -	N 1	Not related Possible NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
尿路感染 Infection of the urinary system	2015-10-12 2015-10-26	133 15	N 2	Not related Doubtful DOUBTFUL	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-

■ Demographics and Baseline Characteristics

□ Country: Ukraine
□ Study site identifier: UA00157
□ Race: White
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): 77
□ Baseline height(cm): 159
□ Baseline ECOG score: 2

■ Disposition Information

□ Treatment discontinuation: 2015-11-20 Progressive Disease

□ Study discontinuation: 2015-11-27 Death

□ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	1080.00	33.36	2015-06-02	2015-11-19	5.62

■ **NARRATIVE TEXT**

被験者 380042 は，7[redacted]歳の白人男性で，2012 年 1 月 27 日に初めて病期 II（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，白内障，冠動脈疾患，下肢の不全対麻痺，病的骨折（D11）及びくも膜炎であった。ベースラインの ECOG スコアは 2 であった。慢性咽喉頭炎及び前立腺腺腫（2010 年）の既往歴を有した。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はメルファラン，メチルプレドニゾロン及びサリドマイド，レジメン 2 はシクロホスファミド，デキサメタゾン及びサリドマイド，レジメン 3 はベンダムスチン，デキサメタゾン及びサリドマイドであった。

治験組入れ時の併用薬は，アスピリン，トリメタジジン，アトルバスタチンカルシウム，カルシウム／ビタミン D3（Lekovit Ca）及びプレガバリンであった。

Day 62（2015 年 8 月 2 日）に，被験者は予定された治験薬投与のために入院した。Day 69 に，発熱（体温：38.5°C），疼痛及び左精巣の浮腫，顕微鏡的血尿が認められた。同日に，**Grade 3 の重篤な有害事象の精巣上体炎**（記載語：左側の orhiepididimit）が報告され，Day 70 に腹部及び骨盤の超音波検査によって確認された。本事象のために入院期間を延長した。治験担当医師は，本事象とボルテゾミブ及びデキサメタゾンとの因果関係を「多分なし」と判断した。本事象のためにボルテゾミブ及びデキサメタゾンを休薬した。休薬前の投与日はそれぞれ Day 67 及び Day 68 であった。レボフロキサシン，エタンシラート，メロキシカム，タムスロシン，セフトリアキソンナトリウム，フルコナゾール，オフロキサシン及びジメチルスルホキシドによる治療を実施した。

入院中の Day 79 に，**Grade 4 の重篤な有害事象の肺炎**（記載語：両側性の院内感染肺炎）が報告され，胸部 X 線写真で両肺下部に不均一な浸潤影が認められた。身体所見では，体温 37.8°C，全身状態悪化，酸素飽和度 87%及び両肺下部の水泡音が認められた。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象のためにボルテゾミブ及びデキサメタゾンの投与を引き続き休薬した。アジスロマイシン，セフェピム，アンブロキソール及びナイスタチンによる治療を実施した。Day 88 の胸部 X 線写真では浸潤は認められなかった。精巣上体炎及び肺炎は Day 91 に回復した。Day 92 に，ボルテゾミブ及びデキサメタゾンの投与を再開した。被験者は治験手順のために入院を継続し，Day 105 に退院した。

Day 147 に，両下肢の末梢性運動ニューロパチー及び末梢性感覚ニューロパチーのためにボルテゾミブの投与量を 1 mg/m^2 に減量した。

Day 168 に，ECOG スコアは 3 に悪化した。

Day 172 に，疾患進行のためにボルテゾミブ及びデキサメタゾンの投与を中止した。両剤の最終投与日は，それぞれ Day 170 及び Day 171 であった。

Day 179 に，被験者の状態は悪化し，同日，死亡した。剖検は実施されなかった。

7) 被験者識別番号 550015

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-06-29	2015-08-21	54	2015-09-16	80	ADVERSE EVENT	-

■ **Infections and infestations, Grade 3 or 4; Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-08-23 2015-09-15	56 24	Y 3	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	Unknown

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺炎 Pneumonia	2015-09-16 2015-09-16	80 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y FATAL	NA	No

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-08-20 -	53 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	NA	-
便秘 Constipation	2015-08-16 2015-08-18	49 3	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
高カルシウム血症 Hipercalcemia	2015-07-20 2015-08-10	22 22	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
高カルシウム血症 Hypercalcemia	2015-06-29 2015-07-19	1 21	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
高カリウム血症 Hyperkalemia	2015-08-24 2015-08-24	57 1	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
末梢性感覚ニューロパチー Nueropathy sensorial	2015-07-13 -	15 -	N 1	Not related Probable NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	NA	-
血小板減少症 Platelet count decreased	2015-08-17 -	50 -	N 2	Not related Probable NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	NA	-

■ **Demographics and Baseline Characteristics**

□ Country: Brazil
□ Study site identifier: BR00293
□ Race: Black or african american
□ Age(yrs): 7[redacted]
□ Sex: Male
□ Baseline weight(kg): 63.7
□ Baseline height(cm): 162
□ Baseline ECOG score: 0

■ **Disposition Information**

□ Treatment discontinuation: 2015-09-16 Death

□ Study discontinuation: 2015-09-16 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	480.00	14.54	2015-06-29	2015-08-21	1.77

■ **NARRATIVE TEXT**

被験者 550015 は，7[redacted] 歳の黒人又はアフリカ系アメリカ人男性で，2012 年 8 月 2 日に初めて病期 III（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。既往歴はなかった。ベースラインの ECOG スコアは 0 であった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はデキサメタゾン，メルファラン，prednisone 及びサリドマイド，レジメン 2 はデキサメタゾンであった。

治験組入れ時の併用薬はなかった。

Day 56（2015 年 8 月 23 日）に，**Grade 3 の重篤な有害事象の肺炎**が報告され，入院した。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象のためにボルテゾミブ及びデキサメタゾンを休薬した。両剤の休薬前の投与日はそれぞれ Day 53 及び Day 54 であった。被験者を評価したところ，肺炎の症状が悪化していたため入院を延長した。病原体は不明であった。セフトリアキソン，クラリスロマイシン，フェノテロール，イプラトロピウム臭化物，セフェピム，メロペネム，ミカファンギン，バンコマイシン，フルコナゾール，anidulafungin，アムホテリシン B，スルファメトキサゾール／トリメトプリム（Bactrim），レボフロキサシン，オセルタミビル及びポリミキシン B による肺炎の治療を実施した。

Day 80 に，被験者は肺炎のために死亡した。剖検は実施されなかった。

ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 53 及び Day 54 であった。

8) 被験者識別番号 700023

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Infections and infestations, Grade 3 or 4

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-05-27	2015-07-17	52	2015-07-19	54	ADVERSE EVENT	-

■ **Infections and infestations, Grade 3 or 4**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
海綿静脈洞血栓症 Thrombosis of cavernous sinus	2015-07-10 -	45 -	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/ NOT RESOLVED	NA	-

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺水腫 Pulmonary edema	2015-07-17 2015-07-19	52 3	Y 4	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	N	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
肺水腫 Pulmonary edema	2015-07-19 -	54 -	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N FATAL	NA	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-07-12 2015-07-16	47 5	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	NA	-
貧血 Anemia	2015-06-25 2015-07-03	30 9	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	-
貧血 Anemia	2015-07-09 2015-07-12	44 4	N 1	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-
貧血 Anemia	2015-07-16 -	51 -	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	NA	-
貧血 Anemia	2015-07-03 2015-07-09	38 7	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-06-22 2015-06-25	27 4	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED WITH SEQUELAE	NA	-
複視 Diplopia	2015-07-03 -	38 -	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	N	-
胃腸障害 Entheropathy	2015-06-02 2015-06-22	7 21	N 1	Not related Possible NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
高血圧クリーゼ Hypertensic crisis	2015-07-05T01:00 2015-07-05T01:55	40 1	N 2	Not related Not related POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
腎不全 Renal failure	2015-06-22 -	27 -	N 4	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	NA	-
血小板減少症 Trombocytopenia	2015-07-15 -	50 -	N 4	Not related Possible POSSIBLE	Not applicable DRUG INTERRUPTED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	NA	-
血小板減少症 Trombocytopenia	2015-06-25 2015-07-15	30 21	N 3	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血小板減少症 Trombocytopenia	2015-06-22 2015-06-25	27 4	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	NA	-
尿閉 Urinary retention	2015-07-16T02:00 -	51 -	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-

■ Demographics and Baseline Characteristics

- □ Country: Russia
- □ Study site identifier: RU00267
- □ Race: White
- □ Age(yrs): 4[redacted]
- □ Sex: Male
- □ Baseline weight(kg): 75
- □ Baseline height(cm): 178
- □ Baseline ECOG score: 0

■ Disposition Information

- □ Treatment discontinuation: 2015-07-19 Death
- □ Study discontinuation: 2015-07-19 Death
- □ Cause of death: Adverse Event

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	400.00	11.52	2015-05-27	2015-07-17	1.71

■ NARRATIVE TEXT

被験者 700023 は，4[redacted] 歳の白人男性で，2013 年 4 月 25 日に初めて病期 II（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，周期性高熱，骨痛，腎結石症，動脈硬化症及び動脈性高血圧症であった。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ及びデキサメタゾン，レジメン 2 はボルテゾミブ，デキサメタゾン及び lomustine であった。

治験組入れ時の併用薬は，ビソプロロール，エナラプリル，アシクロビル，アロプリノール，塩化ナトリウム及びアスピリンであった。

Day 27 に，ECOG スコアは 1 に悪化した。

Day 45（2015 年 7 月 10 日）に，**Grade 3 の非重篤な有害事象の海綿静脈洞血栓症**が報告された。治験担当医師は，海綿静脈洞血栓症とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対するボルテゾミブ及びデキサメタゾンの処置及び治療は実施しなかった。

Day 52 に，Grade 4 の**重篤な有害事象の肺水腫**が報告された。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対するボルテゾミブ及びデキサメタゾンの処置は実施しなかった。本事象に対する治療は，フロセミド，プレドニゾロン，methylethylpiridinol succinate，デキサメタゾン，硝酸イソソルビド，プロポフォール及びエピネフリンであった。Day 54 に，被験者は肺水腫のために死亡した。剖検は実施されなかった。ボルテゾミブ及びデキサメタゾンの最終投与日はそれぞれ Day 48 及び Day 52 であった。

死亡時に，海綿静脈洞血栓症は未回復であった。

9) 被験者識別番号 700035

■ REASON FOR NARRATIVE SELECTION

Death within 30 days of last dose

Discontinuation of study treatment due to AE

Serious AEs

■ Death within 30 days of last dose

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-07-13	2015-09-17	67	2015-09-18	68	ADVERSE EVENT	-

■ Discontinuation of study treatment due to AE; Serious AEs

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
脳血管発作 Acute cerebrovascular accident	2015-09-18 2015-09-18	68 1	Y 5	Not related Not related NOT RELATED	Not applicable DRUG WITHDRAWN Drug withdrawn	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ Other Adverse Events

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血 Anemia	2015-07-20 -	8 -	N 3	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/ NOT RESOLVED	N	-
下痢 Diarrhea	2015-08-21 2015-08-24	40 4	N 2	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
鼻出血 Nasal bleeding	2015-07-19 2015-07-19	7 1	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
発熱 Fever	2015-08-19 2015-08-22	38 4	N 1	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
血小板減少症 Platelet count decreased	2015-08-21 2015-09-07	40 18	N 3	Not related Not related NOT RELATED	Not applicable DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

■ **Demographics and Baseline Characteristics**

□ Country: Russia
□ Study site identifier: RU90443
□ Race: White
□ Age(yrs): 5[redacted]
□ Sex: Male
□ Baseline weight(kg): 67
□ Baseline height(cm): 177
□ Baseline ECOG score: 2

■ **Disposition Information**

□ Treatment discontinuation: 2015-09-18 Adverse Event

□ Study discontinuation: 2015-09-18 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	440.00	15.59	2015-07-13	2015-09-17	2.20

■ **NARRATIVE TEXT**

被験者 700035 は，5[redacted] 歳の白人男性で，2005 年 5 月 19 日に初めて病期 III（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，無力症及び背部痛であった。ベースラインの ECOG スコアは 2 であった。その他の既往歴はなかった。

被験者は合計 4 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド，デキサメタゾン，ドキソルビシン，lomustine，メルファラン，プレドニゾロン及びビンクリスチン，レジメン 2 はドキソルビシン，ボルテゾミブ，シクロホスファミド，デキサメタゾン及びビンクリスチン，レジメン 3 はボルテゾミブ，シクロホスファミド，デキサメタゾン，lomustine，メルファラン，プレドニゾロン及びビンクリスチン，レジメン 4 はボルテゾミブ，シクロホスファミド，デキサメタゾン及びメルファランであった。

治験組入れ時の併用薬はなかった。

ECOG スコアは Day 29 に 1 に改善し，Day 57 に 2 に悪化した。Day 68（2015 年 9 月 18 日）に，不全失語症及び意識消失が認められ，同日，**重篤な有害事象である脳血管発作**（記載語：急性脳血管発作）が報告された。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象のためにデキサメタゾン及びボルテゾミブの投与を中止した。両剤の最終投与日はそれぞれ Day 65 及び Day 67 であった。本事象に対する治療は実施しなかった。Day 68 に，被験者は脳血管発作のために死亡した。剖検は実施されなかった。

10) 被験者識別番号 700038

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose

Serious AEs

■ **Death within 30 days of last dose**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2015-08-10	2015-09-10	32	2015-09-13	35	ADVERSE EVENT	-

■ **Serious AEs**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
骨髄腫円柱腎症 Myeloma nephropathy	2015-09-13 2015-09-13	35 1	Y 5	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N FATAL	N	-

■ **Other Adverse Events**

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
気管支炎 Acute bronchitis	2015-08-24 2015-09-11	15 19	N 2	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
下痢 Diarrhea	2015-09-10 -	32 -	N 1	Not related Possible POSSIBLE	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	NA	-

Dictionary-Derived Term Reported Term for the Adverse Event	Start Date/Time of Adverse Event End Date/Time of Adverse Event	AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Sponsor Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
低血圧 Hypotension	2015-09-10T23:30 2015-09-11	32 2	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	NA	-
腎機能障害 Renal function impairment	2015-09-11 -	33 -	N 3	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N NOT RECOVERED/NOT RESOLVED	NA	-
腎機能障害 Worsening of renal function impairment	2015-07-28 2015-09-11	-13 46	N 2	Not related Not related NOT RELATED	Not applicable NOT APPLICABLE Not applicable	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED WITH SEQUELAE	NA	-
血小板減少症 Thrombocytopenia	2015-08-24 2015-08-31	15 8	N 3	Not related Not related NOT RELATED	Not applicable DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	NA	-

■ Hematology/Chemistry Toxicities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine high (creatinine increased)	-	2015-07-28/ -13	Screening	208	umol/L	58-96	2
Creatinine high (creatinine increased)	227.7	2015-08-10/ 1	Cycle 1 day 1	227.7	umol/L	58-96	2
Creatinine high (creatinine increased)	227.7	2015-08-31/ 22	Cycle 2 day 1	243	umol/L	58-96	2
Creatinine high (creatinine increased)	227.7	2015-09-11/ 33	Cycle 2 day 11 unscheduled 1	316.1	umol/L	58-96	3

■ Demographics and Baseline Characteristics

□ Country: Russia
□ Study site identifier: RU00267
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Female
□ Baseline weight(kg): 64
□ Baseline height(cm): 165
□ Baseline ECOG score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2015-09-13 Death

□ Study discontinuation: 2015-09-13 Death

□ Cause of death: Adverse Event

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m^2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
-	300.00	10.24	2015-08-10	2015-09-10	1.05

■ **NARRATIVE TEXT**

被験者 700038 は，6[redacted] 歳の白人女性で，2008 年 8 月 14 日に初めて病期 III（スクリーニング時）の MM と診断され，ボルテゾミブ及びデキサメタゾンを投与する群にランダム割付けされた。治験組入れ時の合併症は，貧血，動脈性高血圧症，動脈硬化症，血管性脳症，骨痛及び腎不全であった。ベースラインの ECOG スコアは 1 であった。その他の既往歴はなかった。

被験者は 1 レジメンの前治療（ボルテゾミブ，シクロホスファミド，デキサメタゾン，ドキソルビシン，メルファラン，プレドニゾロン及びビンクリスチン）を受けていた。

治験組入れ時の併用薬は，アロプリノール，メトクロプラミド，インスリンヒト，塩化カルシウム及びテオフィリンであった。

Day −13（2015 年 7 月 28 日）に，**非重篤な有害事象の Grade 2 の腎機能障害**（記載語：腎機能障害の悪化）が報告された（クレアチニン値：208 µmol/L，正常範囲：58-96 µmol/L）。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。本事象に対する治療は実施しなかった。Day −2 に，慢性透析を開始した。

Day 1 のクレアチニン値は 227.7 µmol/L であったが，Day 22 には 243 µmol/L に上昇した。Day 29 に，慢性透析を中止した。

Day 33 に，**腎機能障害は Grade 3 に悪化した**（クレアチニン値：316.1 µmol/L）。

Day 35 に，被験者は重篤な有害事象の**骨髄腫円柱腎症**のために死亡した。剖検は実施されなかった。治験担当医師は，本事象とボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。ボルテゾミブ及びデキサメタゾンの最終投与日は Day 32 であった。

死亡時に，腎機能障害は未回復であった。

2.7.6.3 海外臨床第 II 相試験（MMY2002 試験，評価資料：5.3.5.2.1-1，5.3.5.2.1-2，5.3.5.2.1-3）

2.7.6.3.1 概要

2.7.6.3.1.1 計画

(1) 治験の標題

3 レジメン以上の前治療歴［プロテアソーム阻害剤（PI）及び免疫調節薬（IMiD）を含む］を有する，又は PI 及び IMiD の両剤に対して治療抵抗性を示す多発性骨髄腫（MM）患者を対象としてダラツムマブ（以下本剤）の有効性及び安全性を検討する非盲検，多施設共同，第 II 相試験

(2) 治験責任医師

[redacted], [redacted], Atlanta, GA

(3) 公表文献（引用文献）

- Lonial S, et al. Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): an open-label, randomised, phase 2 trial. Lancet. 2016 Apr;387(10027):1551-60.
- Rajkumar SV. Daratumumab in multiple myeloma. Lancet. 2016 Apr;387(10027):1490-2.

(4) 治験実施期間

2013 年 9 月 [redacted] 日（最初の被験者の初回来院日）～2015 年 1 月 9 日（主解析のクリニカルカットオフ日）

(5) 開発の相

第 II 相

(6) 目的

本治験の主要目的は，PI 及び IMiD を含む 3 レジメン以上の前治療歴がある，又は PI 及び IMiD の両剤に対して治療抵抗性を示す MM 患者を対象に本剤の有効性を全奏効率［ORR；partial response（PR）以上］によって検討することであった。なお，治療抵抗性は治療に対する反応性がない又は minimal response（MR）以上の奏効に達した患者での治療中止後 60 日以内の進行と定義した。

副次目的は，本剤の安全性及び忍容性，第 II 相及び第 III 相試験用製剤の薬物動態，奏効持続期間，奏効到達期間，本剤投与後の臨床的有用率［stringent complete response（sCR）+ complete response（CR）+ very good partial response（VGPR）+ PR + MR］，無増悪期間（TTP），無増悪生存期間（PFS），全生存期間（OS），薬物動態及び薬力学の評価，本剤に対する治療反応性を

予測するバイオマーカーの探索，並びに本剤に対する抗体産生（免疫原性）を検討することであった。

(7) 治験方法

本治験は 2 パート（Part 1 及び Part 2）で実施した。Part 1 では本剤の至適用量と投与スケジュールを確認するため，Simon のランダム化 2 段階デザインを用いて，被験者を本剤 8 mg/kg を 4 週間隔で投与する群，又は本剤 16 mg/kg を最初の 8 週間は 1 週間隔，その後 16 週間は 2 週間隔，以降は 4 週間隔で投与する群にランダムに割り付けた。各ランダム化群内で，無効な用量スケジュールは早期中止ができるよう，2 段階のデザインを用いた。Part 1 では第 II 相試験用製剤を使用した。Part 2 の目的は，第 III 相試験用製剤を用いて Part 1 で選択された用量の薬物動態，薬力学，有効性及び安全性を評価することであった。

有効性の主解析のため，独立評価委員会（IRC）が 2011 年の国際骨髄腫作業部会（IMWG）の治療効果判定規準に従って，治療効果と progressive disease（PD）を判定した。また，治療効果及び PD をプログラムで判定するため，IMWG の治療効果判定規準を適用したコンピュータ・アルゴリズムを開発した。

(8) 被験者数（計画時及び解析時）

最大 150 例の被験者の登録を計画した（最大で Part 1 に 90 例，Part 2 に 60 例）。本治験では 124 例に本剤が投与され，このうち 8 mg/kg を投与された被験者は 18 例，16 mg/kg を投与された被験者は 106 例であった。

(9) 診断及び主な組入れ基準

MM と診断され，PI 及び IMiD を含む 3 レジメン以上の前治療歴がある，又は PI 及び IMiD の両剤に対して治療抵抗性を示す，18 歳以上の患者を本治験の対象とした。

(10) 被験薬，用量及び投与方法，ロット番号

本剤は無色～淡黄色の液体で，持続静脈内投与用の無菌濃縮液であり，20 mg/mL の濃度で提供された。

Part 1 の Stage 1 では，被験者を以下の 2 投与レジメン（28 日間サイクル）のいずれかにランダムに割り付けた：

A 群：本剤 16 mg/kg：サイクル 1 及び 2 の Day 1，8，15 及び 22（1 週間隔），サイクル 3～6 の Day 1 及び Day 15（2 週間隔），サイクル 7 以降の Day 1（4 週間隔）

B 群：本剤 8 mg/kg：サイクル 1 以降の Day 1（4 週間隔）

Part 1 の Stage 2 又は Part 2 に登録された被験者には本剤 16 mg/kg を投与した。Part 1 では第 II 相試験用製剤を，Part 2 では第 III 相試験用製剤を使用した。

本治験では次のロット番号の製剤を使用した。

第 II 相試験用製剤のロット番号：[redacted]，[redacted]，[redacted]，[redacted]，[redacted]

第 III 相試験用製剤のロット番号：[redacted]

(11) 対照薬，用量及び投与方法，ロット番号

該当なし

(12) 投与期間

治療期はサイクル 1 の Day 1 から疾患進行，許容できない毒性，本剤投与の中止又は同意撤回までとした。後観察期は，本剤の投与中止から被験者の死亡，追跡不能，同意撤回又は治験終了のいずれかが発生するまで継続することとした。

(13) 評価基準

主要評価項目／主解析での治療効果は，2011 年の IMWG の治療効果判定規準を用いて，IRC による判定及びコンピュータ・アルゴリズムによる判定に基づき評価した。当該評価には，ORR，奏効持続期間，奏効到達期間，最良効果，臨床的有用率，TTP，PFS 及び OS が含まれた。安全性の評価は，有害事象，臨床検査値，バイタルサイン，心電図，身体所見及び併用薬の使用状況に基づき実施した。有害事象の重症度は，National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 に従い判定した。血清中 daratumumab 濃度を測定するための薬物動態用検体及び本剤に対する抗体産生を確認するための免疫原性用検体をすべての被験者から採取した。採取した全血検体及び骨髄穿刺検体を用いて，ナチュラルキラー（NK）細胞，T 細胞及び B 細胞を含む免疫表現型を分析した。

(14) 統計手法

主要評価項目である ORR では，sCR，CR，sCR + CR，VGPR，PR，ORR，MR，ORR + MR，stable disease，PD 及び評価不能の治療効果カテゴリーに該当する被験者の数及び割合を投与群別に集計した。これらのカテゴリーごとに両側正確 95%信頼区間（CI）を投与群別に示した。解析は，IRC による判定とコンピュータ・アルゴリズムによる判定の両方に基づいて実施した。ただし，主要な有効性は IRC の判定に基づき要約した。治療効果（PR 以上 vs. 無効）について，IRC による判定とコンピュータ・アルゴリズムによる判定の一致性を検討するため kappa 統計量と 95%CI を算出した。

2.7.6.3.1.2 結果

本項では，[redacted] 年 [redacted] 月 [redacted] 日付の治験総括報告書（2015 年 1 月 9 日クリニカルカットオフ日）のデータに基づいた主解析の結果を示す。

(1) 対象集団

本治験では 124 例に本剤を投与し，このうち 106 例に 16 mg/kg を投与した。Part 1 の Stage 1 終了時点では，18 例に本剤 8 mg/kg が投与され，ORR が治験実施計画書に規定した継続基準を満

たさなかった（ORR が 15%以下であるという帰無仮説が成立した）ため，8 mg/kg 投与レジメンは中止した。8 mg/kg 群の 3 例は 16 mg/kg 群に移行した。当該 3 例は 8 mg/kg 群の解析に含めた。累積した奏効データに基づき，Part 1 の Stage 2 及び Part 2 では 16 mg/kg 群のみ継続した。

以降の結果は本剤 16 mg/kg が投与された被験者 106 例を中心に記載する。これらのほぼすべて（97%）の被験者が本治験登録前の直近の治療に対して抵抗性を示した。年齢の中央値は 63.5 歳，女性が 51%であった。また，白人が 79%，黒人又はアフリカ系アメリカ人が 14%であった。Eastern Cooperative Oncology Group（ECOG）のスコアは，多く（65%）の被験者が 1 であり，スコアが 2 の被験者は 8%であった。被験者の多く（75%）は国際病期分類基準の病期 II 期又は III 期であった。16 mg/kg 群では，初回診断からの期間の中央値は 4.8 年，前治療数の中央値は 5 レジメンであり，3 レジメン以上の前治療歴を有していた被験者の割合は 82%であった。すべての被験者に PI と IMiD の前治療歴があり，直近の PI 及び IMiD の両剤に対して治療抵抗性を示した被験者の割合は 95%であった。また，ポマリドミドに対しては 63%，カルフィルゾミブに対しては 48%，アルキル化剤に対しては 77%の被験者が治療抵抗性を示した。自家造血幹細胞移植歴のある被験者の割合は 80%であった。

すべての被験者（124 例）が本剤を 1 回以上投与された。16 mg/kg 群では，投与サイクル数の中央値は 4 サイクルであり，6 サイクル以上の投与を受けた被験者の割合は 38%であった。最長投与期間は 14.2 カ月であった。相対用量強度の中央値は 100%であった。

(2) 有効性

初回中間解析では，Part 1 の Stage 1 において，8 mg/kg 群の 1 例（6%）及び 16 mg/kg 群の 5 例（31%）に奏効が認められた。したがって，Part 1 の Stage 2 及び Part 2 では 16 mg/kg 群のみ継続した。

本剤 16 mg/kg を投与された被験者のうち 31 例に IRC の判定に基づく PR 以上の奏効が認められた（表 2.7.6.3-1）。ORR は 29%（95%CI：21～39%）であった。3 例（3%）が sCR を達成し，13 例（12%）が VGPR 以上を達成した。

表 2.7.6.3-1 IRC の判定に基づく有効性の要約［MMY2002 試験，全投与解析対象集団］

	16 mg/kg	
	Result	95% CI
Analysis set: all treated	106	-
Overall response (sCR+CR+VGPR+PR), n (%)	31 (29.2%)	(20.8%, 38.9%)
Stringent complete response (sCR), n (%)	3 (2.8%)	(0.6%, 8.0%)
VGPR or better (sCR + CR + VGPR), n (%)	13 (12.3%)	(6.7%, 20.1%)
Clinical benefit (Overall response + MR), n (%)	36 (34.0%)	(25.0%, 43.8%)
Median [a] duration of response (months)	7.4	(5.5, NE)
Median [b] time to response (months)	1.0	-
Median [a] progression-free survival (months)	3.7	(2.8, 4.6)
Median [a] overall survival (months)	NE	(13.7, NE)

a: based on Kaplan-Meier estimate; b : descriptive summary; NE = not estimable

本剤 16 mg/kg を投与された被験者で，迅速かつ持続的な奏効が確認された。奏効到達期間の中央値は 1 カ月，最良効果到達期間の中央値は 1.9 カ月，VGPR 以上到達期間の中央値は 1.8 カ月，奏効持続期間の中央値は 7.4 カ月であった。観察期間の中央値は 9.3 カ月であり，奏効例 31 例中 14 例（45%）が本剤の投与を継続していた。Kaplan-Meier 法で推定した結果，奏効例の 59%

が 6 カ月時点で無増悪であり，12 カ月時点では 38%が無増悪であった。OS は中央値に到達していなかったが，12 カ月生存率の推定値は 65%（95%CI：51～76%）であった。

本剤の奏効の深さ（VGPR 以上の割合が 12%）は sCR 3 例及び VGPR 10 例によって示されており，骨髄中の悪性形質細胞を完全に又はほぼ完全に消失させることができるという他剤とは異なる特徴を示している。ORR は前治療数及び治療抵抗性の状態に関係なく，臨床的に重要な部分集団のいずれにおいても一貫しており，特に，ポマリドミドに対して治療抵抗性を示していた 67 例の ORR は 28%，カルフィルゾミブに対して治療抵抗性を示していた 51 例の ORR は 29%に達した。

(3) 安全性

本剤の単剤療法の忍容性は良好で，有害事象は臨床的に管理可能であり，これは本剤と関連性がある毒性のため投与を中止した被験者がいないことからも示されている。本剤 8 mg/kg と 16 mg/kg の安全性プロファイルは，疾患進行による死亡を除き同様であった。

16 mg/kg 群で発現割合が高かった（20%以上）有害事象は，疲労（40%），貧血（33%），悪心（29%），血小板減少症（26%），好中球減少症（23%），背部痛（22%）及び咳嗽（21%）であった。発現割合が高かった Grade 3 又は 4 の有害事象は，貧血（24%），血小板減少症（19%）及び好中球減少症（12%）であった。発現割合が高かった重篤な有害事象は，全身健康状態低下（5%），肺炎（4%）及び高カルシウム血症（4%）であった。

被験者の 5%が有害事象のために本剤の投与を中止したが，本剤と関連性がある有害事象のために投与を中止した被験者はいなかった。転帰が死亡であった有害事象は，2 例を除きいずれも疾患進行によるものであり，いずれも治験担当医師により本剤と関連性がないと判断された。有害事象のために死亡した 2 例（H1N1 インフルエンザ合併後の心肺不全及び気管支誤嚥性肺炎合併後の全身健康状態低下）は，いずれも治験担当医師により本剤と関連性がないと判断された。

16 mg/kg 群では，本剤の投与に伴う infusion related reaction（IRR）が高頻度（43%，45/106 例）に認められたが，そのほとんど（38%，40/106 例）は Grade 1 又は 2 と判定された軽度～中等度の IRR であった。IRR 発現までの時間の中央値は投与開始後 90 分であった。Grade 3 の IRR が 5%の被験者で報告された。Grade 4 の IRR の報告はなかった。投与中止に至った IRR を発現した被験者はいなかった。16 mg/kg 群では，IRR の多く（87%，80/92 件）が初回投与時，4%（4/92 件）が 2 回目投与時，9%（8/92 件）はそれ以降の投与時での発現であった。

Grade 3 又は 4 の感染症が 10%（12/124 例）で認められ，いずれの被験者も 16 mg/kg 群であった。発熱性好中球減少症の発現はなかった。感染症（すべての Grade）の発現割合に経時的な上昇はみられなかった。感染症のために投与を中止した被験者は 1 例のみ（H1N1 インフルエンザ）であった。16 mg/kg 群では，8%の被験者が投与期間中に顆粒球コロニー刺激因子，フィルグラスチム又はペグフィルグラスチムなどの造血成長因子の投与を受けていた。

本剤の安全性プロファイルは，性別，年齢，人種，腎機能又は肝機能，及び製剤による影響を受けないことが示唆された。

(4) 薬物動態，薬力学，免疫原性

本剤の初回持続静脈内投与後の血清中 daratumumab 濃度の平均値は投与終了時に最高値を示し，その後，2 相性で低下した。初回投与終了時の血清中 daratumumab 濃度の平均値は，16 mg/kg 群が 8 mg/kg 群より約 2.3 倍高く，ほぼ用量に比例していた。本剤 16 mg/kg 投与の最初の 8 週間（1 週間隔投与）の間に daratumumab の蓄積が認められ，1 週間隔投与終了時（サイクル 3 の Day 1）のトラフ濃度の平均値（標準偏差）は 573（331.5）μg/mL であった。16 mg/kg 群では，最終投与 8 週間後においてもほとんどの被験者で血清中 daratumumab 濃度が検出可能であった。

本剤投与後の末梢血中及び骨髄中の総 NK 細胞数及び活性化 NK 細胞数の減少が 8 mg/kg 群及び 16 mg/kg 群の両群で認められ，この減少は投与期間中持続した。NK 細胞数又は NK 細胞の割合の低下と臨床効果との間に関連は認められなかった。

本剤に対する抗体が発現した被験者はおらず，第 II 相及び第 III 相試験用製剤の両剤とも検討された用量では免疫原性のリスクが低いことが示された。

2.7.6.3.1.3　結論

本治験では，再発又は難治性の MM 患者の治療における本剤の単剤療法の有効性及び安全性について以下の主要な結果が示された：

- Part 1 の Stage 1 終了後，本剤 16 mg/kg 投与レジメンは治験実施計画書に規定した継続基準を満たしたが，8 mg/kg 投与レジメンは中止となった。したがって，16 mg/kg が推奨用量となった。
- 16 mg/kg 群では，初回診断からの期間の中央値は 4.8 年であり，前治療数の中央値は 5 レジメンであった。すべての被験者に PI と IMiD の前治療歴があり，直近の PI 及び IMiD の両剤に対して治療抵抗性を示した被験者の割合は 95%であった（ポマリドミドに対しては 63%，カルフィルゾミブに対しては 48%の被験者が治療抵抗性を示した）。アルキル化剤に対しては 77%の被験者が治療抵抗性を示した。自家造血幹細胞移植歴のある被験者の割合は 80%であった。ほぼすべて（97%）の被験者が本治験登録前の直近の治療に対して抵抗性を示した。
- 複数の前治療歴を有する本治験の対象集団において，本剤 16 mg/kg 単剤療法での ORR は 29%，奏効持続期間の中央値は 7.4 カ月であり，明らかな臨床効果が示された。
- ORR は前治療数及び治療抵抗性の状態に関係なく，複数の臨床的に重要な部分集団のいずれにおいても全体集団の ORR と一貫していた。
- 本剤 16 mg/kg 投与による奏効の深さ（sCR 3 例を含む VGPR 以上の割合が 12%）は，単剤としては特筆すべき成績であり，その作用機序のほかに，骨髄中の悪性形質細胞を完全に又はほぼ完全に消失させることができるという作用は，難治性 MM の治療において他剤とは異なる特徴を示している。
- 中央値 9.3 カ月の観察では OS は中央値に到達していなかったが，12 カ月生存率の推定値は 65%（95%CI：51～76%）であった。

- 本剤の単剤療法の忍容性は良好であり，安全性プロファイルも良好で有害事象は臨床的に管理可能であった。主な結果を以下に示す：
  - 本剤 16 mg/kg を投与した被験者で本剤と関連性がある有害事象のために本剤の投与を中止した被験者はいなかった。
  - IRR は高頻度（43%，45/106 例）に発現したが，そのほとんど（38%，40/106 例）は Grade 1 又は 2 であった。16 mg/kg 群では，IRR の多く（87%，80/92 件）が初回投与時，4%（4/92 件）が 2 回目投与時，9%（8/92 件）がそれ以降の投与時での発現であった。
  - 造血成長因子（顆粒球コロニー刺激因子，エリスロポエチン）の使用率は 16 mg/kg 群で 8%と低く，16 mg/kg 群の 23%の被験者が好中球減少症を発現したが，発熱性好中球減少症の発現はなく，Grade 3 又は 4 の感染症を発現した被験者の割合は 10%のみであった。

結論として，本治験のデータから，再発及び難治性の MM 患者の治療において本剤は良好なリスクベネフィットプロファイルを有することが示された。

2.7.6.3.2 補遺

2.7.6.3.2.1 補遺 1（2015 年 6 月 30 日クリニカルカットオフ）

[redacted]年[redacted]月[redacted]日付の治験総括報告書の主解析は，最後の被験者の本剤初回投与から約 8 カ月後である 2015 年 1 月 9 日をクリニカルカットオフ日として実施した。最後の被験者の本剤初回投与から約 12 カ月後である 2015 年 6 月 30 日をクリニカルカットオフ日として，本剤の投与を受けたすべての被験者の生存情報を更新し，治験総括報告書 Addendum 1 を作成した。本項では治験総括報告書 Addendum 1 の結果を示す。

- 2015 年 6 月 30 日のクリニカルカットオフ日時点で，Kaplan-Meier 法で推定した観察期間の中央値は，8 mg/kg 群で 19.1 カ月，16 mg/kg 群で 14.7 カ月であった。
- 死亡した被験者は，8 mg/kg 群では 18 例中 8 例（44%）であった。このうち疾患進行による死亡は 5 例（28%）及びその他の理由による死亡は 3 例（17%）であった。これには初回クリニカルカットオフ日（2015 年 1 月 9 日）以降，新たに認められたその他の理由による死亡 1 例が含まれる。16 mg/kg 群では 106 例中 47 例（44%）が死亡した。このうち疾患進行による死亡は 44 例（42%），有害事象による死亡は 2 例（2%），及びその他の理由による死亡は 1 例（1%）であった。初回クリニカルカットオフ日以降，新たに 16 例が死亡し，このうち疾患進行による死亡は 15 例，その他の理由による死亡は 1 例であった。本剤の最終投与後 30 日以内に死亡した被験者数は，初回カットオフ日から変わらなかった。
- 2015 年 6 月 30 日のクリニカルカットオフ日時点での OS を表 2.7.6.3-2 に示す。8 mg/kg 群及び 16 mg/kg 群で合計 55 例が死亡した。生存していた被験者は 8 mg/kg 群では 10 例（56%），16 mg/kg 群では 59 例（56%）であった。8 mg/kg 群では OS は中央値に到達しておらず，16 mg/kg 群の OS の中央値は 17.5 カ月（95%CI：13.67 カ月～NE）であった。12

カ月生存率の推定値は，8 mg/kg 群及び 16 mg/kg 群でそれぞれ 63%（95%CI：34.9～81.1%）及び 65%（95%CI：54.5～73.1%）であった。

表 2.7.6.3-2 全生存期間（2015 年 6 月 30 日クリニカルカットオフ時点）
［MMY2002 試験，全投与解析対象集団］

	8 mg/kg	16 mg/kg
Analysis set: all treated	18	106
Overall survival		
Number of events (%)	8 (44.4%)	47 (44.3%)
Number of censored (%)	10 (55.6%)	59 (55.7%)
Kaplan-Meier estimate (months)		
25% quantile (95% CI)	7.79 (3.75, 18.50)	7.59 (5.62, 10.58)
Median (95% CI)	NE (7.72, NE)	17.48 (13.67, NE)
75% quantile (95% CI)	NE (18.50, NE)	NE (NE, NE)
6-month overall survival rate % (95% CI)	87.5 (58.6, 96.7)	81.8 (73.0, 88.0)
12-month overall survival rate % (95% CI)	62.5 (34.9, 81.1)	64.7 (54.5, 73.1)

Keys: CI = confidence interval; NE = not estimable.
Percentages are calculated with the number of subjects in each group as denominator.
[TEFOS01.rtf] [JNJ-54767414\MMY2002\DBR_BLA_2015_4MSU\RE_BLA_2015_4MSU\tefos01.sas] 13AUG2015, 16:36
参照元：MMY2002 CSR addendum 1_TEFOS01

2.7.6.3.2.2 補遺 2（[redacted]年[redacted]月[redacted]日クリニカルカットオフ）

最後の被験者の本剤初回投与から約 30 カ月後である[redacted]年[redacted]月[redacted]日をクリニカルカットオフ日として，本剤を投与されたすべての被験者の生存情報及び安全性情報を更新し，治験総括報告書 Addendum 2 を作成した。本項では治験総括報告書 Addendum 2 の結果を示す。

- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点で，本剤の投与を中止した被験者は，16 mg/kg 群では 106 例中 104 例（98%），8 mg/kg 群では 18 例中 17 例（94%）であった。いずれの投与群も主な中止理由は疾患進行で，初回クリニカルカットオフ（2015 年 1 月 9 日）以降，新たに 15 例が疾患進行のために投与を中止した。
- 16 mg/kg 群では，投与サイクル数の中央値は 4 サイクルであり，22 例が 10 サイクル以上，9 例が 20 サイクル以上，2 例が 30 サイクル以上本剤を投与された。最長投与期間は 36.5 カ月であった。8 mg/kg 群では，3 例が 10 サイクル以上，1 例が 20 サイクル以上，1 例が 30 サイクル以上本剤を投与された。すべての被験者での相対用量強度の中央値は 100%であった。
- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点で，Kaplan-Meier 法で推定した観察期間の中央値は，16 mg/kg 群で 31.3 カ月，8 mg/kg 群で 35.6 カ月であった。
- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点での OS を表 2.7.6.3-3 に示す。生存していた被験者は，16 mg/kg 群では 39 例（37%），8 mg/kg 群では 4 例（22%）であった。OS の中央値は，16 mg/kg 群及び 8 mg/kg 群でそれぞれ 18.6 カ月（95%CI：13.7～25.0 カ月）及び 19.5 カ月（95%CI：7.7～26.8 カ月）であった。24 カ月生存率の推定値は，16 mg/kg 群及び 8 mg/kg 群でそれぞれ 40.5%（95%CI：30.7～50.1%）及び 43.8%（95%CI：19.8～65.6%）であった。

表 2.7.6.3-3 全生存期間（[redacted]年[redacted]月[redacted]日クリニカルカットオフ時点）
［MMY2002 試験，全投与解析対象集団］

	8 mg/kg	16 mg/kg
Analysis set: all treated	18	106
Overall survival		
Number of events (%)	14 (77.8%)	67 (63.2%)
Number of censored (%)	4 (22.2%)	39 (36.8%)
Kaplan-Meier estimate (months)		
25% quantile (95% CI)	7.79 (3.75, 18.50)	7.59 (5.62, 10.58)
Median (95% CI)	19.45 (7.72, 26.81)	18.60 (13.67, 25.00)
75% quantile (95% CI)	27.33 (18.50, NE)	NE (28.06, NE)
6-month overall survival rate % (95% CI)	87.5 (58.6, 96.7)	81.8 (73.0, 88.0)
12-month overall survival rate % (95% CI)	62.5 (34.9, 81.1)	64.7 (54.5, 73.1)
18-month overall survival rate % (95% CI)	56.3 (29.5, 76.2)	51.3 (41.1, 60.6)
24-month overall survival rate % (95% CI)	43.8 (19.8, 65.6)	40.5 (30.7, 50.1)

Key: CI = confidence interval; NE = not estimable.
Percentages are calculated with the number of subjects in each group as denominator.
[TEFOS01.RTF] [JNJ-54767414\MMY2002\DBR_CSR_ADDENDUM\RE_CSR_ADDENDUM\PROD\TEFOS01.SAS] 14DEC2016, 15:13
参照元：MMY2002 CSR addendum 2_TEFOS01

- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点で，16 mg/kg 群で発現割合が 20%以上の有害事象のうち，初回クリニカルカットオフ日以降，発現割合が新たに 20%以上となった事象は下痢，鼻閉及び上気道感染（各 21%）であった。また，発現割合が新たに 10%以上となった事象は頭痛（13%）及び筋骨格痛（11%）であった。初回クリニカルカットオフ日以降，新たに認められた重篤な有害事象は気道感染であった。なお，Grade 3 又は 4 の有害事象及び本剤と関連性のある重篤な有害事象の発現割合は初回クリニカルカットオフ日時点と同様であり，また，新たに死亡に至った有害事象は認められなかった。
- 本剤の最終投与後 30 日以内に死亡した被験者数は，初回クリニカルカットオフ日時点とその後 22 カ月経過した今回（[redacted]年[redacted]月[redacted]日）のクリニカルカットオフ日時点で変わらなかった。[redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点で，16 mg/kg 群では 106 例中 67 例（63%）が死亡した。このうち疾患進行による死亡は 59 例（56%），有害事象による死亡は 3 例（3%）及びその他の理由による死亡は 5 例（5%）であった。初回クリニカルカットオフ日以降，新たに 36 例が死亡し，このうち疾患進行による死亡は 30 例，その他の理由による死亡は 5 例及び有害事象による死亡は 1 例であった。8 mg/kg 群では 18 例中 14 例（78%）が死亡した。このうち疾患進行による死亡は 10 例（56%）及びその他の理由による死亡は 4 例（22%）であった。これには初回クリニカルカットオフ日以降，新たに認められた疾患進行による死亡 5 例及びその他の理由による死亡 2 例が含まれた。
- 初回クリニカルカットオフ以降，本剤の全般的な安全性プロファイルに特筆すべき新らたな懸念は認められなかった。

2.7.6.3.3 有害事象

2015 年 1 月 9 日のクリニカルカットオフ日時点での，因果関係を問わない有害事象及び本剤と関連性がある有害事象を表 2.7.6.3-4 に示す。

表 2.7.6.3-4 有害事象及び本剤と関連性がある有害事象

［MMY2002 試験，全投与解析対象集団］

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
Analysis set: all treated	18		106		124	
Total number of subjects with TEAEs	18 (100.0%)	14 (77.8%)	105 (99.1%)	81 (76.4%)	123 (99.2%)	95 (76.6%)
MedDRA system organ class /Preferred term						
一般・全身障害および投与部位の状態	12 (66.7%)	9 (50.0%)	74 (69.8%)	42 (39.6%)	86 (69.4%)	51 (41.1%)
疲労	7 (38.9%)	4 (22.2%)	42 (39.6%)	24 (22.6%)	49 (39.5%)	28 (22.6%)
発熱	5 (27.8%)	4 (22.2%)	17 (16.0%)	4 (3.8%)	22 (17.7%)	8 (6.5%)
悪寒	6 (33.3%)	6 (33.3%)	10 (9.4%)	8 (7.5%)	16 (12.9%)	14 (11.3%)
無力症	2 (11.1%)	0	12 (11.3%)	4 (3.8%)	14 (11.3%)	4 (3.2%)
末梢性浮腫	2 (11.1%)	1 (5.6%)	9 (8.5%)	1 (0.9%)	11 (8.9%)	2 (1.6%)
疼痛	1 (5.6%)	1 (5.6%)	6 (5.7%)	1 (0.9%)	7 (5.6%)	2 (1.6%)
全身健康状態低下	1 (5.6%)	0	5 (4.7%)	0	6 (4.8%)	0
非心臓性胸痛	1 (5.6%)	1 (5.6%)	5 (4.7%)	0	6 (4.8%)	1 (0.8%)
胸痛	0	0	5 (4.7%)	1 (0.9%)	5 (4.0%)	1 (0.8%)
インフルエンザ様疾患	0	0	5 (4.7%)	4 (3.8%)	5 (4.0%)	4 (3.2%)
胸部不快感	1 (5.6%)	1 (5.6%)	2 (1.9%)	2 (1.9%)	3 (2.4%)	3 (2.4%)
注射部位内出血	0	0	3 (2.8%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
全身性浮腫	0	0	2 (1.9%)	0	2 (1.6%)	0
局所腫脹	0	0	2 (1.9%)	0	2 (1.6%)	0
倦怠感	0	0	2 (1.9%)	2 (1.9%)	2 (1.6%)	2 (1.6%)
浮腫	0	0	2 (1.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
腋窩痛	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
医療機器の問題	0	0	1 (0.9%)	0	1 (0.8%)	0
顔面浮腫	0	0	1 (0.9%)	0	1 (0.8%)	0
顔面痛	0	0	1 (0.9%)	0	1 (0.8%)	0
歩行障害	0	0	1 (0.9%)	0	1 (0.8%)	0
低体温	0	0	1 (0.9%)	0	1 (0.8%)	0
注入部位内出血	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
注射部位浮腫	0	0	1 (0.9%)	0	1 (0.8%)	0
注射部位反応	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
限局性浮腫	0	0	1 (0.9%)	0	1 (0.8%)	0
腫瘤	0	0	1 (0.9%)	0	1 (0.8%)	0
恥骨上痛	0	0	1 (0.9%)	0	1 (0.8%)	0
筋骨格系および結合組織障害	10 (55.6%)	5 (27.8%)	64 (60.4%)	14 (13.2%)	74 (59.7%)	19 (15.3%)
背部痛	5 (27.8%)	1 (5.6%)	23 (21.7%)	4 (3.8%)	28 (22.6%)	5 (4.0%)
関節痛	1 (5.6%)	1 (5.6%)	20 (18.9%)	2 (1.9%)	21 (16.9%)	3 (2.4%)
四肢痛	1 (5.6%)	0	18 (17.0%)	2 (1.9%)	19 (15.3%)	2 (1.6%)
筋骨格系胸痛	2 (11.1%)	1 (5.6%)	13 (12.3%)	1 (0.9%)	15 (12.1%)	2 (1.6%)
筋痙縮	2 (11.1%)	1 (5.6%)	9 (8.5%)	4 (3.8%)	11 (8.9%)	5 (4.0%)
筋骨格痛	1 (5.6%)	1 (5.6%)	10 (9.4%)	0	11 (8.9%)	1 (0.8%)
骨痛	0	0	9 (8.5%)	2 (1.9%)	9 (7.3%)	2 (1.6%)
筋肉痛	0	0	5 (4.7%)	1 (0.9%)	5 (4.0%)	1 (0.8%)
単径部痛	0	0	4 (3.8%)	0	4 (3.2%)	0
筋力低下	0	0	2 (1.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
頚部痛	0	0	2 (1.9%)	0	2 (1.6%)	0
病的骨折	0	0	2 (1.9%)	0	2 (1.6%)	0
脊椎痛	0	0	2 (1.9%)	0	2 (1.6%)	0
側腹部痛	1 (5.6%)	1 (5.6%)	0	0	1 (0.8%)	1 (0.8%)
関節可動域低下	0	0	1 (0.9%)	0	1 (0.8%)	0
四肢不快感	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
運動性低下	0	0	1 (0.9%)	0	1 (0.8%)	0

表 2.7.6.3-4 有害事象及び本剤と関連性がある有害事象
［MMY2002 試験，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
筋肉疲労	0	0	1 (0.9%)	0	1 (0.8%)	0
骨炎	0	0	1 (0.9%)	0	1 (0.8%)	0
顎骨壊死	0	0	1 (0.9%)	0	1 (0.8%)	0
顎痛	0	0	1 (0.9%)	0	1 (0.8%)	0
脊柱管狭窄症	0	0	1 (0.9%)	0	1 (0.8%)	0
腱炎	0	0	1 (0.9%)	0	1 (0.8%)	0
血液およびリンパ系障害	12 (66.7%)	8 (44.4%)	61 (57.5%)	33 (31.1%)	73 (58.9%)	41 (33.1%)
貧血	9 (50.0%)	7 (38.9%)	35 (33.0%)	18 (17.0%)	44 (35.5%)	25 (20.2%)
血小板減少症	6 (33.3%)	3 (16.7%)	27 (25.5%)	16 (15.1%)	33 (26.6%)	19 (15.3%)
好中球減少症	1 (5.6%)	1 (5.6%)	24 (22.6%)	11 (10.4%)	25 (20.2%)	12 (9.7%)
白血球減少症	2 (11.1%)	2 (11.1%)	7 (6.6%)	5 (4.7%)	9 (7.3%)	7 (5.6%)
リンパ球減少症	3 (16.7%)	1 (5.6%)	4 (3.8%)	4 (3.8%)	7 (5.6%)	5 (4.0%)
ヘモグロビン血症	0	0	1 (0.9%)	0	1 (0.8%)	0
内出血発生の増加傾向	0	0	1 (0.9%)	0	1 (0.8%)	0
汎血球減少症	0	0	1 (0.9%)	0	1 (0.8%)	0
赤血球凝集	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
胃腸障害	9 (50.0%)	4 (22.2%)	64 (60.4%)	28 (26.4%)	73 (58.9%)	32 (25.8%)
悪心	4 (22.2%)	0	31 (29.2%)	17 (16.0%)	35 (28.2%)	17 (13.7%)
下痢	4 (22.2%)	2 (11.1%)	18 (17.0%)	6 (5.7%)	22 (17.7%)	8 (6.5%)
嘔吐	3 (16.7%)	1 (5.6%)	19 (17.9%)	10 (9.4%)	22 (17.7%)	11 (8.9%)
便秘	2 (11.1%)	0	17 (16.0%)	7 (6.6%)	19 (15.3%)	7 (5.6%)
腹痛	1 (5.6%)	0	8 (7.5%)	0	9 (7.3%)	0
腹部膨満	1 (5.6%)	0	3 (2.8%)	1 (0.9%)	4 (3.2%)	1 (0.8%)
歯痛	0	0	4 (3.8%)	0	4 (3.2%)	0
腹部不快感	1 (5.6%)	0	2 (1.9%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
消化不良	0	0	3 (2.8%)	0	3 (2.4%)	0
放屁	0	0	3 (2.8%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
口の感覚鈍麻	0	0	3 (2.8%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
口内炎	0	0	3 (2.8%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
便失禁	0	0	2 (1.9%)	0	2 (1.6%)	0
歯肉出血	0	0	2 (1.9%)	0	2 (1.6%)	0
口腔内痛	0	0	2 (1.9%)	0	2 (1.6%)	0
上腹部痛	0	0	1 (0.9%)	0	1 (0.8%)	0
水疱性出血性口峡炎	0	0	1 (0.9%)	0	1 (0.8%)	0
アフタ性口内炎	1 (5.6%)	0	0	0	1 (0.8%)	0
大腸炎	0	0	1 (0.9%)	0	1 (0.8%)	0
口内乾燥	1 (5.6%)	1 (5.6%)	0	0	1 (0.8%)	1 (0.8%)
嚥下障害	0	0	1 (0.9%)	0	1 (0.8%)	0
胃炎	1 (5.6%)	0	0	0	1 (0.8%)	0
胃食道逆流性疾患	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
歯肉腫脹	0	0	1 (0.9%)	0	1 (0.8%)	0
痔核	0	0	1 (0.9%)	0	1 (0.8%)	0
大腸閉塞	0	0	1 (0.9%)	0	1 (0.8%)	0
口唇出血	0	0	1 (0.9%)	0	1 (0.8%)	0
口腔内潰瘍形成	0	0	1 (0.9%)	0	1 (0.8%)	0
口腔粘膜変色	0	0	1 (0.9%)	0	1 (0.8%)	0
膵炎	0	0	1 (0.9%)	0	1 (0.8%)	0
口の錯感覚	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
舌苔	0	0	1 (0.9%)	0	1 (0.8%)	0
歯の発育障害	0	0	1 (0.9%)	0	1 (0.8%)	0
歯の障害	0	0	1 (0.9%)	0	1 (0.8%)	0
呼吸器、胸郭および縦隔障害	8 (44.4%)	5 (27.8%)	65 (61.3%)	34 (32.1%)	73 (58.9%)	39 (31.5%)
咳嗽	6 (33.3%)	4 (22.2%)	22 (20.8%)	9 (8.5%)	28 (22.6%)	13 (10.5%)
鼻閉	1 (5.6%)	1 (5.6%)	19 (17.9%)	13 (12.3%)	20 (16.1%)	14 (11.3%)
呼吸困難	3 (16.7%)	2 (11.1%)	16 (15.1%)	8 (7.5%)	19 (15.3%)	10 (8.1%)
口腔咽頭痛	1 (5.6%)	0	9 (8.5%)	2 (1.9%)	10 (8.1%)	2 (1.6%)
労作性呼吸困難	1 (5.6%)	0	8 (7.5%)	2 (1.9%)	9 (7.3%)	2 (1.6%)
湿性咳嗽	1 (5.6%)	1 (5.6%)	8 (7.5%)	2 (1.9%)	9 (7.3%)	3 (2.4%)
鼻出血	0	0	8 (7.5%)	0	8 (6.5%)	0
咽喉刺激感	0	0	7 (6.6%)	7 (6.6%)	7 (5.6%)	7 (5.6%)

表 2.7.6.3-4 有害事象及び本剤と関連性がある有害事象
［MMY2002 試験，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
喘鳴	1 (5.6%)	1 (5.6%)	6 (5.7%)	3 (2.8%)	7 (5.6%)	4 (3.2%)
気管支痙攣	0	0	5 (4.7%)	4 (3.8%)	5 (4.0%)	4 (3.2%)
胸水	1 (5.6%)	0	4 (3.8%)	0	5 (4.0%)	0
くしゃみ	0	0	3 (2.8%)	2 (1.9%)	3 (2.4%)	2 (1.6%)
上気道咳症候群	0	0	3 (2.8%)	0	3 (2.4%)	0
呼吸不全	0	0	2 (1.9%)	0	2 (1.6%)	0
副鼻腔うっ血	0	0	2 (1.9%)	0	2 (1.6%)	0
急性肺水腫	0	0	1 (0.9%)	0	1 (0.8%)	0
発声障害	0	0	1 (0.9%)	0	1 (0.8%)	0
低酸素症	0	0	1 (0.9%)	0	1 (0.8%)	0
上気道分泌増加	0	0	1 (0.9%)	0	1 (0.8%)	0
喉頭浮腫	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
誤嚥性肺炎	0	0	1 (0.9%)	0	1 (0.8%)	0
肺うっ血	0	0	1 (0.9%)	0	1 (0.8%)	0
肺塞栓症	0	0	1 (0.9%)	0	1 (0.8%)	0
肺水腫	0	0	1 (0.9%)	0	1 (0.8%)	0
鼻漏	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
代謝および栄養障害	11 (61.1%)	6 (33.3%)	53 (50.0%)	14 (13.2%)	64 (51.6%)	20 (16.1%)
食欲減退	4 (22.2%)	2 (11.1%)	19 (17.9%)	7 (6.6%)	23 (18.5%)	9 (7.3%)
高カルシウム血症	2 (11.1%)	0	18 (17.0%)	1 (0.9%)	20 (16.1%)	1 (0.8%)
低カリウム血症	4 (22.2%)	0	11 (10.4%)	3 (2.8%)	15 (12.1%)	3 (2.4%)
低ナトリウム血症	6 (33.3%)	2 (11.1%)	7 (6.6%)	3 (2.8%)	13 (10.5%)	5 (4.0%)
高血糖	3 (16.7%)	2 (11.1%)	9 (8.5%)	1 (0.9%)	12 (9.7%)	3 (2.4%)
低マグネシウム血症	2 (11.1%)	0	7 (6.6%)	2 (1.9%)	9 (7.3%)	2 (1.6%)
低アルブミン血症	4 (22.2%)	0	4 (3.8%)	0	8 (6.5%)	0
酵素異常	3 (16.7%)	0	4 (3.8%)	1 (0.9%)	7 (5.6%)	1 (0.8%)
高尿酸血症	2 (11.1%)	0	4 (3.8%)	0	6 (4.8%)	0
高カリウム血症	1 (5.6%)	1 (5.6%)	4 (3.8%)	0	5 (4.0%)	1 (0.8%)
低カルシウム血症	1 (5.6%)	0	3 (2.8%)	0	4 (3.2%)	0
低血糖症	1 (5.6%)	0	1 (0.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
糖尿病	0	0	1 (0.9%)	0	1 (0.8%)	0
体液貯留	1 (5.6%)	1 (5.6%)	0	0	1 (0.8%)	1 (0.8%)
高ナトリウム血症	0	0	1 (0.9%)	0	1 (0.8%)	0
高リン酸塩血症	0	0	1 (0.9%)	0	1 (0.8%)	0
低リン酸血症	1 (5.6%)	0	0	0	1 (0.8%)	0
栄養障害	0	0	1 (0.9%)	0	1 (0.8%)	0
代謝性アシドーシス	1 (5.6%)	0	0	0	1 (0.8%)	0
感染症および寄生虫症	8 (44.4%)	1 (5.6%)	54 (50.9%)	15 (14.2%)	62 (50.0%)	16 (12.9%)
上気道感染	3 (16.7%)	0	19 (17.9%)	3 (2.8%)	22 (17.7%)	3 (2.4%)
鼻咽頭炎	1 (5.6%)	0	8 (7.5%)	1 (0.9%)	9 (7.3%)	1 (0.8%)
肺炎	1 (5.6%)	0	8 (7.5%)	4 (3.8%)	9 (7.3%)	4 (3.2%)
副鼻腔炎	1 (5.6%)	0	7 (6.6%)	3 (2.8%)	8 (6.5%)	3 (2.4%)
尿路感染	0	0	6 (5.7%)	0	6 (4.8%)	0
気管支炎	0	0	4 (3.8%)	0	4 (3.2%)	0
インフルエンザ	2 (11.1%)	0	2 (1.9%)	0	4 (3.2%)	0
大葉性肺炎	0	0	3 (2.8%)	2 (1.9%)	3 (2.4%)	2 (1.6%)
カンジダ感染	1 (5.6%)	1 (5.6%)	1 (0.9%)	1 (0.9%)	2 (1.6%)	2 (1.6%)
結膜炎	0	0	2 (1.9%)	0	2 (1.6%)	0
口腔カンジダ症	0	0	2 (1.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
パラインフルエンザウイルス感染	0	0	2 (1.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
軟部組織感染	0	0	2 (1.9%)	0	2 (1.6%)	0
蜂巣炎	0	0	1 (0.9%)	0	1 (0.8%)	0
医療機器関連感染	0	0	1 (0.9%)	0	1 (0.8%)	0
耳感染	0	0	1 (0.9%)	0	1 (0.8%)	0
胃腸炎	0	0	1 (0.9%)	0	1 (0.8%)	0
ウイルス性胃腸炎	0	0	1 (0.9%)	0	1 (0.8%)	0
性器感染	0	0	1 (0.9%)	0	1 (0.8%)	0
Ｈ１Ｎ１インフルエンザ	0	0	1 (0.9%)	0	1 (0.8%)	0

表 2.7.6.3-4 有害事象及び本剤と関連性がある有害事象
［MMY2002 試験，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
帯状疱疹	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
麦粒腫	0	0	1 (0.9%)	0	1 (0.8%)	0
下気道感染	0	0	1 (0.9%)	0	1 (0.8%)	0
粘膜感染	0	0	1 (0.9%)	0	1 (0.8%)	0
眼部単純ヘルペス	0	0	1 (0.9%)	0	1 (0.8%)	0
口腔ヘルペス	0	0	1 (0.9%)	0	1 (0.8%)	0
爪囲炎	0	0	1 (0.9%)	0	1 (0.8%)	0
レンサ球菌性肺炎	0	0	1 (0.9%)	0	1 (0.8%)	0
腎盂腎炎	0	0	1 (0.9%)	0	1 (0.8%)	0
気道感染	0	0	1 (0.9%)	0	1 (0.8%)	0
敗血症	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
レンサ球菌感染	0	0	1 (0.9%)	0	1 (0.8%)	0
歯感染	0	0	1 (0.9%)	0	1 (0.8%)	0
水痘	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
外陰腟真菌感染	0	0	1 (0.9%)	0	1 (0.8%)	0
神経系障害	10 (55.6%)	5 (27.8%)	37 (34.9%)	12 (11.3%)	47 (37.9%)	17 (13.7%)
浮動性めまい	1 (5.6%)	0	10 (9.4%)	3 (2.8%)	11 (8.9%)	3 (2.4%)
頭痛	1 (5.6%)	1 (5.6%)	10 (9.4%)	4 (3.8%)	11 (8.9%)	5 (4.0%)
末梢性感覚ニューロパチー	1 (5.6%)	1 (5.6%)	6 (5.7%)	2 (1.9%)	7 (5.6%)	3 (2.4%)
感覚鈍麻	1 (5.6%)	0	5 (4.7%)	0	6 (4.8%)	0
味覚異常	2 (11.1%)	2 (11.1%)	3 (2.8%)	2 (1.9%)	5 (4.0%)	4 (3.2%)
振戦	2 (11.1%)	0	3 (2.8%)	1 (0.9%)	5 (4.0%)	1 (0.8%)
傾眠	0	0	4 (3.8%)	0	4 (3.2%)	0
脳症	1 (5.6%)	1 (5.6%)	1 (0.9%)	0	2 (1.6%)	1 (0.8%)
錯感覚	0	0	2 (1.9%)	0	2 (1.6%)	0
失神	1 (5.6%)	0	1 (0.9%)	0	2 (1.6%)	0
無感覚	1 (5.6%)	0	0	0	1 (0.8%)	0
手根管症候群	0	0	1 (0.9%)	0	1 (0.8%)	0
意識レベルの低下	0	0	1 (0.9%)	0	1 (0.8%)	0
知覚過敏	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
嗜眠	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
記憶障害	0	0	1 (0.9%)	0	1 (0.8%)	0
嗅覚錯誤	0	0	1 (0.9%)	0	1 (0.8%)	0
下肢静止不能症候群	0	0	1 (0.9%)	0	1 (0.8%)	0
坐骨神経痛	1 (5.6%)	0	0	0	1 (0.8%)	0
脊髄圧迫	0	0	1 (0.9%)	0	1 (0.8%)	0
第７脳神経麻痺	0	0	1 (0.9%)	0	1 (0.8%)	0
血管障害	8 (44.4%)	4 (22.2%)	25 (23.6%)	5 (4.7%)	33 (26.6%)	9 (7.3%)
高血圧	8 (44.4%)	3 (16.7%)	12 (11.3%)	2 (1.9%)	20 (16.1%)	5 (4.0%)
低血圧	1 (5.6%)	1 (5.6%)	7 (6.6%)	1 (0.9%)	8 (6.5%)	2 (1.6%)
血腫	0	0	4 (3.8%)	0	4 (3.2%)	0
深部静脈血栓症	1 (5.6%)	0	2 (1.9%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
潮紅	0	0	2 (1.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
ほてり	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
レイノー現象	0	0	1 (0.9%)	0	1 (0.8%)	0
四肢静脈血栓症	0	0	1 (0.9%)	0	1 (0.8%)	0
腎および尿路障害	9 (50.0%)	2 (11.1%)	22 (20.8%)	2 (1.9%)	31 (25.0%)	4 (3.2%)
腎機能障害	7 (38.9%)	1 (5.6%)	11 (10.4%)	1 (0.9%)	18 (14.5%)	2 (1.6%)
血尿	2 (11.1%)	0	1 (0.9%)	0	3 (2.4%)	0
尿失禁	2 (11.1%)	1 (5.6%)	1 (0.9%)	0	3 (2.4%)	1 (0.8%)
尿閉	1 (5.6%)	0	2 (1.9%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
排尿困難	0	0	2 (1.9%)	0	2 (1.6%)	0
頻尿	0	0	2 (1.9%)	0	2 (1.6%)	0
高窒素血症	1 (5.6%)	0	0	0	1 (0.8%)	0
膀胱痙縮	1 (5.6%)	0	0	0	1 (0.8%)	0
尿意切迫	1 (5.6%)	0	0	0	1 (0.8%)	0
夜間頻尿	0	0	1 (0.9%)	0	1 (0.8%)	0
蛋白尿	0	0	1 (0.9%)	0	1 (0.8%)	0
腎不全	0	0	1 (0.9%)	0	1 (0.8%)	0
急性腎不全	1 (5.6%)	0	0	0	1 (0.8%)	0
腎静脈血栓症	0	0	1 (0.9%)	0	1 (0.8%)	0

表 2.7.6.3-4 有害事象及び本剤と関連性がある有害事象
［MMY2002 試験，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
尿路閉塞	0	0	1 (0.9%)	0	1 (0.8%)	0
皮膚および皮下組織障害	3 (16.7%)	1 (5.6%)	22 (20.8%)	6 (5.7%)	25 (20.2%)	7 (5.6%)
そう痒症	1 (5.6%)	1 (5.6%)	3 (2.8%)	1 (0.9%)	4 (3.2%)	2 (1.6%)
発疹	1 (5.6%)	0	2 (1.9%)	0	3 (2.4%)	0
斑状丘疹状皮疹	0	0	3 (2.8%)	1 (0.9%)	3 (2.4%)	1 (0.8%)
ざ瘡様皮膚炎	0	0	2 (1.9%)	1 (0.9%)	2 (1.6%)	1 (0.8%)
皮膚乾燥	0	0	2 (1.9%)	0	2 (1.6%)	0
寝汗	0	0	2 (1.9%)	0	2 (1.6%)	0
点状出血	0	0	2 (1.9%)	0	2 (1.6%)	0
斑状皮疹	1 (5.6%)	1 (5.6%)	1 (0.9%)	1 (0.9%)	2 (1.6%)	2 (1.6%)
蕁麻疹	1 (5.6%)	1 (5.6%)	1 (0.9%)	1 (0.9%)	2 (1.6%)	2 (1.6%)
褥瘡性潰瘍	0	0	1 (0.9%)	0	1 (0.8%)	0
皮膚嚢腫	0	0	1 (0.9%)	0	1 (0.8%)	0
湿疹	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
紅斑	0	0	1 (0.9%)	0	1 (0.8%)	0
多汗症	0	0	1 (0.9%)	0	1 (0.8%)	0
爪変色	1 (5.6%)	0	0	0	1 (0.8%)	0
手掌・足底発赤知覚不全症候群	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
色素沈着障害	0	0	1 (0.9%)	0	1 (0.8%)	0
全身性そう痒症	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
丘疹性皮疹	0	0	1 (0.9%)	0	1 (0.8%)	0
皮膚剥脱	0	0	1 (0.9%)	0	1 (0.8%)	0
皮膚色素過剰	0	0	1 (0.9%)	0	1 (0.8%)	0
皮膚潰瘍	0	0	1 (0.9%)	0	1 (0.8%)	0
傷害、中毒および処置合併症	0	0	23 (21.7%)	0	23 (18.5%)	0
挫傷	0	0	5 (4.7%)	0	5 (4.0%)	0
転倒	0	0	5 (4.7%)	0	5 (4.0%)	0
上腕骨骨折	0	0	2 (1.9%)	0	2 (1.6%)	0
腰椎骨折	0	0	2 (1.9%)	0	2 (1.6%)	0
肋骨骨折	0	0	2 (1.9%)	0	2 (1.6%)	0
擦過傷	0	0	1 (0.9%)	0	1 (0.8%)	0
足骨折	0	0	1 (0.9%)	0	1 (0.8%)	0
骨折	0	0	1 (0.9%)	0	1 (0.8%)	0
裂傷	0	0	1 (0.9%)	0	1 (0.8%)	0
肉離れ	0	0	1 (0.9%)	0	1 (0.8%)	0
眼窩周囲挫傷	0	0	1 (0.9%)	0	1 (0.8%)	0
処置による疼痛	0	0	1 (0.9%)	0	1 (0.8%)	0
脊椎圧迫骨折	0	0	1 (0.9%)	0	1 (0.8%)	0
硬膜下血腫	0	0	1 (0.9%)	0	1 (0.8%)	0
腱断裂	0	0	1 (0.9%)	0	1 (0.8%)	0
輸血反応	0	0	1 (0.9%)	0	1 (0.8%)	0
上肢骨折	0	0	1 (0.9%)	0	1 (0.8%)	0
手首関節骨折	0	0	1 (0.9%)	0	1 (0.8%)	0
精神障害	4 (22.2%)	0	19 (17.9%)	2 (1.9%)	23 (18.5%)	2 (1.6%)
不安	0	0	7 (6.6%)	1 (0.9%)	7 (5.6%)	1 (0.8%)
錯乱状態	1 (5.6%)	0	6 (5.7%)	1 (0.9%)	7 (5.6%)	1 (0.8%)
うつ病	1 (5.6%)	0	3 (2.8%)	0	4 (3.2%)	0
激越	0	0	3 (2.8%)	0	3 (2.4%)	0
不眠症	0	0	3 (2.8%)	0	3 (2.4%)	0
譫妄	0	0	2 (1.9%)	0	2 (1.6%)	0
精神状態変化	1 (5.6%)	0	1 (0.9%)	0	2 (1.6%)	0
摂食障害	0	0	1 (0.9%)	0	1 (0.8%)	0
幻覚	0	0	1 (0.9%)	0	1 (0.8%)	0
神経過敏	1 (5.6%)	0	0	0	1 (0.8%)	0
臨床検査	4 (22.2%)	1 (5.6%)	14 (13.2%)	3 (2.8%)	18 (14.5%)	4 (3.2%)
体重減少	3 (16.7%)	1 (5.6%)	5 (4.7%)	1 (0.9%)	8 (6.5%)	2 (1.6%)
体重増加	1 (5.6%)	0	4 (3.8%)	1 (0.9%)	5 (4.0%)	1 (0.8%)
国際標準比増加	0	0	3 (2.8%)	0	3 (2.4%)	0
血中テストステロン減少	0	0	1 (0.9%)	0	1 (0.8%)	0

表 2.7.6.3-4 有害事象及び本剤と関連性がある有害事象
［MMY2002 試験，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
心電図ＱＴ延長	0	0	1 (0.9%)	0	1 (0.8%)	0
心電図異常Ｔ波	0	0	1 (0.9%)	0	1 (0.8%)	0
酸素飽和度異常	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
尿量減少	0	0	1 (0.9%)	0	1 (0.8%)	0
心臓障害	2 (11.1%)	2 (11.1%)	8 (7.5%)	2 (1.9%)	10 (8.1%)	4 (3.2%)
動悸	0	0	4 (3.8%)	1 (0.9%)	4 (3.2%)	1 (0.8%)
頻脈	1 (5.6%)	1 (5.6%)	2 (1.9%)	1 (0.9%)	3 (2.4%)	2 (1.6%)
洞性頻脈	1 (5.6%)	1 (5.6%)	1 (0.9%)	0	2 (1.6%)	1 (0.8%)
狭心症	0	0	1 (0.9%)	0	1 (0.8%)	0
徐脈	0	0	1 (0.9%)	0	1 (0.8%)	0
左脚ブロック	0	0	1 (0.9%)	0	1 (0.8%)	0
うっ血性心不全	0	0	1 (0.9%)	0	1 (0.8%)	0
心肺停止	0	0	1 (0.9%)	0	1 (0.8%)	0
眼障害	1 (5.6%)	0	8 (7.5%)	2 (1.9%)	9 (7.3%)	2 (1.6%)
霧視	0	0	3 (2.8%)	0	3 (2.4%)	0
白内障	1 (5.6%)	0	1 (0.9%)	0	2 (1.6%)	0
眼そう痒症	0	0	2 (1.9%)	2 (1.9%)	2 (1.6%)	2 (1.6%)
眼充血	0	0	2 (1.9%)	0	2 (1.6%)	0
複視	0	0	1 (0.9%)	0	1 (0.8%)	0
眼乾燥	0	0	1 (0.9%)	0	1 (0.8%)	0
睫毛乱生	0	0	1 (0.9%)	0	1 (0.8%)	0
肝胆道系障害	3 (16.7%)	1 (5.6%)	6 (5.7%)	2 (1.9%)	9 (7.3%)	3 (2.4%)
肝機能異常	2 (11.1%)	1 (5.6%)	4 (3.8%)	1 (0.9%)	6 (4.8%)	2 (1.6%)
肝不全	0	0	1 (0.9%)	0	1 (0.8%)	0
脂肪肝	1 (5.6%)	0	0	0	1 (0.8%)	0
高ビリルビン血症	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
黄疸	0	0	1 (0.9%)	0	1 (0.8%)	0
耳および迷路障害	2 (11.1%)	0	3 (2.8%)	1 (0.9%)	5 (4.0%)	1 (0.8%)
耳垢栓塞	1 (5.6%)	0	0	0	1 (0.8%)	0
耳不快感	1 (5.6%)	0	0	0	1 (0.8%)	0
耳の障害	0	0	1 (0.9%)	0	1 (0.8%)	0
耳痛	0	0	1 (0.9%)	0	1 (0.8%)	0
回転性めまい	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)
生殖系および乳房障害	2 (11.1%)	0	3 (2.8%)	0	5 (4.0%)	0
生殖器痛	0	0	1 (0.9%)	0	1 (0.8%)	0
乳頭痛	0	0	1 (0.9%)	0	1 (0.8%)	0
性器浮腫	0	0	1 (0.9%)	0	1 (0.8%)	0
骨盤痛	1 (5.6%)	0	0	0	1 (0.8%)	0
陰茎浮腫	0	0	1 (0.9%)	0	1 (0.8%)	0
前立腺炎	1 (5.6%)	0	0	0	1 (0.8%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (5.6%)	0	2 (1.9%)	0	3 (2.4%)	0
腫瘍疼痛	0	0	2 (1.9%)	0	2 (1.6%)	0
形質細胞性白血病	1 (5.6%)	0	0	0	1 (0.8%)	0
免疫系障害	1 (5.6%)	1 (5.6%)	1 (0.9%)	1 (0.9%)	2 (1.6%)	2 (1.6%)
サイトカイン放出症候群	1 (5.6%)	1 (5.6%)	0	0	1 (0.8%)	1 (0.8%)
季節性アレルギー	0	0	1 (0.9%)	1 (0.9%)	1 (0.8%)	1 (0.8%)

Keys: TEAE = treatment-emergent adverse event.
Adverse events are reported using MedDRA version 17.0.
Percentages are calculated with the number of subjects in each group as denominator.

[TSFAE02A.rtf] [JNJ-54767414\MMY2002\DBR_CSR\RE_CSR\tsfae02a.sas] 13FEB2015, 14:18

2.7.6.3.4 個別症例の詳細

最終投与後 30 日以内の疾患進行以外の理由による死亡例の詳細経過を以下に示す。本剤と関連性がある重篤な有害事象の詳細経過は，治験総括報告書【CTD 5.3.5.2.1-1】及び 2015 年 6 月 30 日クリニカルカットオフ時の安全性更新情報【CTD 5.3.5.3.3】に示した。

2.7.6.3.4.1 最終投与後 30 日以内の死亡（疾患進行以外の理由による死亡）

(1) 被験者識別番号 100054

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose of Daratumumab

Serious Adverse Events

AEs leading to Daratumumab Discontinuation

Infections/infestations, Grade 3 or 4

■ **Death within 30 days of last dose of Daratumumab**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-02-21	2014-03-10	18	2014-04-03	42	ADVERSE EVENT	-

■ **Serious Adverse Events**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
心肺停止 (Cardiovascular respiratory arrest)	2014-04-03/ 2014-04-03	42/ (1)	Y/ 5	Not related/ Not applicable	N Fatal

■ **Serious Adverse Events/AEs leading to Daratumumab Discontinuation/Infections/infestations, Grade 3 or 4**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
H1N1 インフルエンザ (Influenza A virus (RNA) hemagglutinin (subtype H1N1))	2014-03-16/ -	24/ -	Y/ 3	Not related/ Drug withdrawn	Y Not recovered/not resolved

■ **Infections/infestations, Grade 3 or 4**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
肺炎 (Worsening pneumonia)	2014-03-20/ -	28/ -	N/ 3	Not related/ Dose not changed	Y Not recovered/not resolved

■ **Other Adverse Events**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
腹部膨満 (Abdominal bloating)	2014-02-20/ -	-1/ -	N/ 2	Not related/ Not applicable	N Not recovered/not resolved
激越 (Agitation)	2014-02-21/ -	1/ -	N/ 2	Not related/ Dose not changed	Y Not recovered/not resolved
貧血 (Anemia)	2014-02-11/ 2014-02-11	-10/ (1)	N/ 2	Not related/ Not applicable	N Recovered/resolved
貧血 (Anemia)	2014-02-17/ 2014-02-19	-4/ (3)	N/ 2	Not related/ Not applicable	N Recovered/resolved
貧血 (Anemia)	2014-02-23/ 2014-02-23	3/ (1)	N/ 2	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-02-27/ 2014-02-27	7/ (1)	N/ 2	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-03-05/ 2014-03-06	13/ (2)	N/ 2	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-03-14/ 2014-03-23	22/ (10)	N/ 2	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-03-25/ 2014-03-29	33/ (5)	N/ 3	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-03-30/ 2014-03-30	38/ (1)	N/ 2	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-03-31/ 2014-04-02	39/ (3)	N/ 3	Not related/ Dose not changed	N Recovered/resolved
貧血 (Anemia)	2014-04-03/ -	42/ -	N/ 1	Not related/ Not applicable	N Not recovered/not resolved
左脚ブロック (Left anterior fascicular block)	2014-03-09/ -	17/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
悪寒 (Teeth chattering)	2014-03-14/ 2014-03-14	22/ (1)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
錯乱状態 (Intermittent confusion)	2014-02-10/ 2014-03-10	-11/ (29)	N/ 1	Not related/ Not applicable	N Recovered/resolved
錯乱状態 (Increased confusion)	2014-02-22/ 2014-03-10	2/ (17)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
錯乱状態 (Increased confusion)	2014-03-11/ -	19/ -	N/ 3	Not related/ Dose not changed	Y Not recovered/not resolved
挫傷 (Bruising to abdomen)	2014-03-15/ -	23/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
挫傷 (Brusing arms elbows)	2014-03-28/ -	36/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
咳嗽 (Dry non-productive cough)	2014-02-25/ -	5/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
口内乾燥 (Dry mouth)	2014-02-14/ -	-7/ -	N/ 2	Not related/ Not applicable	Y Not recovered/not resolved

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
消化不良 (Heartburn)	2014-02-13/ -	-8/ -	N/ 2	Not related/ Not applicable	Y Not recovered/not resolved
嚥下障害 (Difficulty swallowing)	2014-03-04/ -	12/ -	N/ 2	Not related/ Dose not changed	Y Not recovered/not resolved
呼吸困難 (Shortness of breath)	2014-03-31/ -	39/ -	N/ 2	Not related/ Dose not changed	N Not recovered/not resolved
摂食障害 (Difficulty eating)	2014-03-04/ -	12/ -	N/ 2	Not related/ Dose not changed	Y Not recovered/not resolved
脳症 (Suspected viral encephalopathy)	2014-03-18/ -	26/ -	N/ 3	Not related/ Not applicable	N Not recovered/not resolved
紅斑 (Skin under heels reddened)	2014-03-02/ -	10/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
便失禁 (Fecal incontinence)	2014-03-29/ -	37/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
全身性浮腫 (Increased generalized edema)	2014-03-31/ -	39/ -	N/ 2	Not related/ Dose not changed	N Not recovered/not resolved
高カルシウム血症 (Hypercalcemia)	2014-02-11/ 2014-02-15	-10/ (5)	N/ 1	Not related/ Not applicable	Y Recovered/resolved
高カルシウム血症 (Hypercalcemia)	2014-02-16/ 2014-02-20	-5/ (5)	N/ 2	Not related/ Not applicable	Y Recovered/resolved
高カルシウム血症 (Hypercalcemia)	2014-02-21/ 2014-02-28	1/ (8)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
高カルシウム血症 (Hypercalcemia)	2014-03-03/ 2014-03-04	11/ (2)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
高カルシウム血症 (Hypercalcemia)	2014-03-05/ 2014-03-07	13/ (3)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
高ナトリウム血症 (Hypernatremia)	2014-03-31/ -	39/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
低カリウム血症 (Hypokalemia)	2014-03-19/ 2014-03-19	27/ (1)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
低カリウム血症 (Hypokalemia)	2014-03-22/ 2014-03-27	30/ (6)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
低マグネシウム血症 (Hypomagnesemia)	2014-02-11/ 2014-02-11	-10/ (1)	N/ 1	Not related/ Not applicable	Y Recovered/resolved
低マグネシウム血症 (Hypomagnesemia)	2014-02-15/ 2014-02-15	-6/ (1)	N/ 1	Not related/ Not applicable	N Recovered/resolved
低マグネシウム血症 (Hypomagnesemia)	2014-02-17/ 2014-02-17	-4/ (1)	N/ 1	Not related/ Not applicable	N Recovered/resolved
上気道分泌増加 (Excessive phlegm)	2014-03-26/ -	34/ -	N/ 2	Not related/ Dose not changed	N Not recovered/not resolved
不眠症 (Intermittent insomnia)	2014-02-10/ -	-11/ -	N/ 1	Not related/ Not applicable	Y Not recovered/not resolved

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
筋骨格系胸痛 (Worsening rib pain)	2014-03-22/ -	30/ -	N/ 2	Not related/ Dose not changed	Y Not recovered/not resolved
口腔粘膜変色 (Black areas to the roof of the mouth)	2014-03-20/ -	28/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
骨炎 (Reddened coccyx)	2014-02-28/ -	8/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
疼痛 (Increase in generalized pain)	2014-03-29/ -	37/ -	N/ 2	Not related/ Dose not changed	N Not recovered/not resolved
胸水 (Small right pleural effusion)	2014-02-26/ 2014-03-06	6/ (9)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
肺炎 (Pneumonia)	2014-03-13/ 2014-03-19	21/ (7)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
肺水腫 (Pulmonary edema)	2014-04-01/ -	40/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
発熱 (Fever)	2014-02-25/ 2014-02-27	5/ (3)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
腎機能障害 (Elevated creatinine)	2014-02-10/ 2014-02-11	-11/ (2)	Y/ 1	Not related/ Not applicable	Y Recovered/resolved
腎機能障害 (Elevated creatinine)	2014-02-15/ 2014-02-17	-6/ (3)	N/ 1	Not related/ Not applicable	N Recovered/resolved
腎機能障害 (Elevated creatinine)	2014-02-22/ 2014-02-22	2/ (1)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
腎機能障害 (Elevated creatinine)	2014-03-12/ 2014-03-12	20/ (1)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
腎機能障害 (Elevated creatinine)	2014-03-20/ 2014-03-20	28/ (1)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
洞性頻脈 (Sinus tachycardia)	2014-03-09/ -	17/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
傾眠 (Drowsiness)	2014-02-21/ 2014-03-05	1/ (13)	N/ 1	Not related/ Dose not changed	N Recovered/resolved
傾眠 (Increased drowsiness)	2014-03-06/ -	14/ -	N/ 2	Not related/ Dose not changed	N Not recovered/not resolved
尿失禁 (Urinary incontinence)	2014-02-23/ -	3/ -	N/ 1	Not related/ Dose not changed	N Not recovered/not resolved
喘鳴 (Wheezing)	2014-02-27/ -	7/ -	N/ 1	Not related/ Dose not changed	Y Not recovered/not resolved

■ Hematology/Chemistry Toxicities

Lab Test	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Calcium corrected high (hypercalcemia)	2014-02-10/ -11	Screening	3.325	mmol/L	2.07-2.64	3
Calcium corrected (hypercalcemia)	2014-02-21/ 1	Cycle 1 day 1	3.1006	-	2.223-2.6	3

Lab Test	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Calcium corrected (hypercalcemia)	2014-03-05/ 13	Cycle 1 day 8 unscheduled 2	3.109	-	2.223-2.6	3
Calcium corrected (hypercalcemia)	2014-03-12/ 20	Cycle 1 day 15 unscheduled 1	2.8298	-	2.223-2.6	1
Calcium corrected (hypercalcemia)	2014-03-17/ 25	Cycle 1 day 15 unscheduled 4	2.7182	-	2.223-2.6	1
Calcium, ionized high (hypercalcemia)	2014-02-10/ -11	Screening	1.68	mmol/L	1.09-1.25	3
Creatinine high (creatinine increased)	2014-02-10/ -11	Screening	143	umol/L	50-115	1

■ **Demographics and Baseline Characteristics**

☐ Country: Canada
☐ Sex: Male
☐ Baseline weight(kg): 93
☐ Study site identifier: CA00096
☐ Description of planned arm: Daratumumab 16 mg/kg
☐ Baseline height(cm): 175.3
☐ Race: White
☐ Description of actual arm: Daratumumab 16 mg/kg
☐ Baseline ECOG score: 2
☐ Age(yrs): 7[redacted]

■ **Disposition Information**

☐ Treatment discontinuation: 2014-04-01 Adverse Event

☐ Study discontinuation: 2014-04-03 Death

■ **Summary of Study Medication**

Total Dose Received (mg/kg)	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
48.42	2014-02-21	2014-03-10	0.59

■ **NARRATIVE TEXT**

被験者 100054 は，7[redacted] 歳の白人男性で，2010 年 11 月 22 日に初めて病期 III 期の MM と診断され，本治験の Part 1 の Stage 2（本剤を 16 mg/kg の用量で投与）に組み入れられた。治験組入れ時の合併症は貧血，関節腫脹（両足首），眼挫傷，クッシング症候群，脱水，高カルシウム血症，高血圧，血中乳酸脱水素酵素増加，骨溶解，病的骨折（両肋骨），腎機能障害，鼠径ヘルニア及び 2 型糖尿病であった。スクリーニング時（Day −11）の ECOG スコアは 1 であった。既往歴は，末梢性感覚ニューロパチー（両足及び両下腿），扁平上皮癌及び振戦（両手）であった。ベースラインの血清遊離軽鎖 κ 型値は 117 mg/dL であった。ベースラインの骨髄生検で形質細胞は 15% であった。

被験者は合計 3 レジメンの前治療を受けていた。レジメン 1 はレナリドミド及びデキサメタゾン，レジメン 2 はボルテゾミブ，シクロホスファミド及びデキサメタゾン，レジメン 3 はボルテゾミブ，デキサメタゾン及びシクロホスファミドであった。被験者はレジメン 1 のレナリドミド，並びにレジメン 3 のボルテゾミブ及びアルキル化剤に治療抵抗性を示した。

治験組入れ時の併用薬は，メトホルミン，ガバペンチン，塩化ナトリウム，アミトリプチリン，アスピリン，バラシクロビル，ミネラル補給剤（亜鉛/銅），ラニチジン，アロプリノール，ダルテパリンナトリウム及びスルファメトキサゾールであった。

Day −22（2014 年 1 月 30 日）に，**Grade 3 の高カルシウム血症**が発現した。当該事象は，被験者の本治験への同意前に発現した。高カルシウム血症は，パミドロン酸による治療後 Day −10 に **Grade 1** へ改善した。

Day −11 に，クレアチニン値 143 µmol/L（正常範囲：50-115 µmol/L），補正カルシウム値 3.32 mmol/L（正常範囲：2.07-2.64 mmol/L）が認められ，被験者は **Grade 1 の重篤な有害事象の**

腎機能障害により入院した。同日，**Grade 1 の非重篤な有害事象の錯乱状態**（記載語：間欠性錯乱）を認めた。腎機能障害に対する治療は，塩化ナトリウムを含む水分補給であった。腎機能障害は Day −10 に回復した。Day −6 に，**Grade 1 の非重篤な有害事象の腎機能障害**が報告され（クレアチニン値の報告なし），本事象は Day −4 に無処置で回復した。**高カルシウム血症**は，Day −5 に重症度が Grade 1 から **Grade 2 に**悪化し，本事象はゾレドロン酸による治療後，Day 1 に **Grade 1 へ改善**した。Day 1 に，被験者の ECOG スコアは 2 に悪化した。Day 2 に，**錯乱状態**の重症度は **Grade 2** に悪化（記載語：錯乱の悪化）し，**Grade 1 の非重篤な有害事象の腎機能障害**が報告された（クレアチニン値の報告なし）。治験担当医師は，Grade 1 の高カルシウム血症，Grade 1 の腎機能障害及び Grade 2 の錯乱状態と本剤との因果関係を「関連なし」と判断した。これらの事象に対する本剤の処置は実施しなかった。錯乱状態の治療としてハロペリドールを投与した。腎機能障害は同日（Day 2）に回復した。

入院中の Day 5 に，**Grade 1 の非重篤な有害事象の咳嗽**（記載語：乾性咳嗽）**及び発熱**が発現した。Day 6 に，胸部 X 線写真で少量の右**胸水**が認められ，**Grade 1 の非重篤な有害事象**として報告された。翌日（Day 7），**Grade 1 の非重篤な有害事象の喘鳴**が報告された。治験担当医師は，これらの事象と本剤との因果関係を「関連なし」と判断した。これらの事象に対する本剤の処置は実施しなかった。治療薬はレボフロキサシン，paracetamol 及びサルブタモールであった。発熱及び高カルシウム血症は，それぞれ Day 7 及び Day 8 に回復した。

Day 11 に，**Grade 2 の非重篤な有害事象の高カルシウム血症**が報告され，ゾレドロン酸による治療後 Day 13 に **Grade 1 へ改善した**。同日（Day 13），クレアチニン値は 96 μmol/L であった。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。本事象に対する本剤の処置は実施しなかった。胸水及び Grade 1 の高カルシウム血症は，それぞれ Day 14 及び Day15 に回復した。鼻咽頭スワブ培養検査を Day 15 に実施した（結果の報告なし）。

Day 17 に，**Grade 1 の非重篤な有害事象の左脚ブロック**（記載語：左脚前枝ブロック）**及び洞性頻脈**が発現した。治験担当医師は，両事象と本剤との因果関係を「関連なし」と判断した。これらの事象に対する本剤の処置は実施せず，治療も実施されなかった。

被験者は，Day 18 からオセルタミビルによる予防投与を開始した。

Day 19 に，**錯乱状態**の**重症度**が Grade 2 から **Grade 3 に悪化した**。治療としてオランザピンを投与し，ハロペリドールの投与を継続した。Grade 1 の非重篤な有害事象の腎機能障害が Day 20 に報告され，本事象は無処置で同日に回復した。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断し，本事象に対する本剤の処置は実施しなかった。

Day 21 に，胸部 X 線検査を実施し，**Grade 2 の非重篤な有害事象**の**肺炎**が報告された。翌日（Day 22），**Grade 1 の非重篤な有害事象の悪寒**（記載語：歯がガチガチなる）が報告された。治験担当医師は，両事象と本剤との因果関係を「関連なし」と判断した。これらの事象に対する本剤の処置は実施しなかった。肺炎に対する治療として，イプラトロピウム臭化物及びサルブタモールを投与した。悪寒は発現日当日（Day 22）に無処置で回復した。

Day 24 に，鼻咽頭スワブ培養検査により，インフルエンザ A 型ウイルス（RNA）赤血球凝集素（サブタイプ H1N1）陽性が認められ，**Grade 3 の重篤な有害事象の H1N1 インフルエンザ**が報告された。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。治験担当医師は，H1N1 インフルエンザにより入院期間の延長が必要になったと報告した。本事象の治療

として，スルファメトキサゾール／トリメトプリム（Bactrim）及びスルファメトキサゾールを投与した。

Day 25 に，頭部コンピュータ断層撮影を実施した。Day 26 に，頭部核磁気共鳴画像スキャンを実施し，**Grade 3 の非重篤な有害事象**の**脳症**（記載語：ウイルス性脳症の疑い）が報告された。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。脳症に対する治療は実施しなかった。

Day 28 に，**Grade 1 の非重篤な有害事象の腎機能障害**が発現し，本事象は無処置で同日に回復した。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断し，本事象に対する本剤の処置は実施しなかった。同日，胸部 X 線検査を実施した。**肺炎の重症度は** Grade 2 **から Grade 3 に悪化した**。本事象の治療としてセフトリアキソンを投与した。Day 28，39 及び 41 に実施した血液培養では何も同定されなかった。

Grade 2 の非重篤な有害事象の筋骨格系胸痛（記載語：肋骨痛の悪化），**上気道分泌増加**，**疼痛**（記載語：全身性疼痛の増加）**及び呼吸困難**が，それぞれ Day 30，34，37 及び 39 に発現した。治験担当医師は，これらの事象と本剤との因果関係を「関連なし」と判断した。Day 34 に咽頭吸引を実施した。

Day 40 に，被験者の呼吸困難は悪化した。Day 40 の胸部 X 線写真で被験者の左肺に浸潤影変化の悪化を認め，**Grade 1 の非重篤な有害事象の肺水腫**が報告された。同日（Day 40），脳症のための核磁気共鳴画像スキャンを実施した。本事象の治療として，ピペラシリンナトリウム／タゾバクタムを投与した。

Day 40 に，H1N1 インフルエンザのために本剤の投与を中止した。本剤の最終投与日は Day 18 であった。

Day 42 に，被験者は**心肺停止**により死亡した。剖検は実施しなかった。治験担当医師は，心肺停止と本剤との因果関係を「関連なし」と判断した。

(2) 被験者識別番号 100084

■ **REASON FOR NARRATIVE SELECTION**

Death within 30 days of last dose of Daratumumab

Serious Adverse Events

AEs leading to Daratumumab Discontinuation

Bronchospasm, any grade

■ **Death within 30 days of last dose of Daratumumab**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-04-09	2014-04-09	1	2014-05-06	28	ADVERSE EVENT	-

■ Serious Adverse Events

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
誤嚥性肺炎 (Pneumonia by aspiration)	2014-04-09/ 2014-04-30	1/ (22)	Y/ 3	Not related/ Drug interrupted	Y Recovered/resolved

■ Serious Adverse Events/AEs leading to Daratumumab Discontinuation

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
全身健康状態低下 (General deterioration)	2014-05-06/ -	28/ -	Y/ 5	Not related/ Drug withdrawn	N Fatal

■ Bronchospasm, any grade

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
気管支痙攣 (Bronchospasm)	2014-04-15/ 2014-04-30	7/ (16)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved

■ Other Adverse Events

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
激越 (Agitation)	2014-04-20/ 2014-05-06	12/ (17)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
貧血 (Anemia)	2014-04-10/ 2014-04-12	2/ (3)	N/ 3	Not related/ Dose not changed	Y Recovered/resolved
貧血 (Anemia)	2014-04-13/ -	5/ -	N/ 2	Not related/ Dose not changed	N Not recovered/not resolved
不安 (Anxiety)	2014-04-18/ 2014-05-06	10/ (19)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
錯乱状態 (Confusional syndrome)	2014-04-20/ 2014-05-06	12/ (17)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
医療機器関連感染 (Infection by catheter)	2014-04-11/ 2014-04-13	3/ (3)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
高血糖 (Hyperglycemia)	2014-04-09/ 2014-04-09	1/ (1)	N/ 3	Not related/ Dose not changed	Y Recovered/resolved
高血圧 (Arterial hypertension)	2014-04-25/ 2014-05-06	17/ (12)	N/ 2	Not related/ Dose not changed	Y Recovered/resolved
低カリウム血症 (Hypokalemia)	2014-04-12/ 2014-04-15	4/ (4)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
低カリウム血症 (Hypokalemia)	2014-04-17/ 2014-04-17	9/ (1)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Concomitant or Additional Treatment Given/ Outcome of Adverse Event
低カリウム血症 (Hypokalemia)	2014-04-20/ 2014-04-22	12/ (3)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
発熱 (Fever)	2014-04-11/ 2014-04-13	3/ (3)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
発熱 (Fever)	2014-04-26/ 2014-04-27	18/ (2)	N/ 1	Not related/ Dose not changed	Y Recovered/resolved
気道感染 (Respiratory infection)	2014-04-01/ 2014-04-07	-8/ (7)	N/ 1	Not related/ Not applicable	Y Recovered/resolved

■ **Hematology/Chemistry Toxicities**

Lab Test	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low (anemia)	2014-03-18/ -22	Screening	117	g/L	120-160	1
Hemoglobin low (anemia)	2014-04-08/ -1	Cycle 1 day 1	82	g/L	120-160	2
Hemoglobin low (anemia)	2014-04-10/ 2	Cycle 1 day 1 unscheduled 1	77	g/L	120-160	3
Hemoglobin low (anemia)	2014-04-13/ 5	Cycle 1 day 1 unscheduled 3	89	g/L	120-160	2
Leukocytes low (white blood cell decreased)	2014-03-18/ -22	Screening	3.58	x10E9/L	4.5-11	1
Leukocytes low (white blood cell decreased)	2014-04-13/ 5	Cycle 1 day 1 unscheduled 3	4.04	x10E9/L	4.5-11	1

■ **Demographics and Baseline Characteristics**

☐ Country: Spain
☐ Study site identifier: ES00352
☐ Race: White
☐ Age(yrs): 8[redacted]
☐ Sex: Female
☐ Description of planned arm: Daratumumab 16 mg/kg
☐ Description of actual arm: Daratumumab 16 mg/kg
☐ Baseline weight(kg): 59
☐ Baseline height(cm): 161
☐ Baseline ECOG score: 1

■ **Disposition Information**

☐ Treatment discontinuation: 2014-05-06 Adverse Event

☐ Study discontinuation: 2014-05-06 Death

■ **Summary of Study Medication**

Total Dose Received (mg/kg)	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
1.87	2014-04-09	2014-04-09	0.03

■ **NARRATIVE TEXT**

被験者 100084 は，8[redacted] 歳の白人女性で，2011 年 9 月 23 日に初めて病期 II 期の MM と診断され，本治験の Part 2（本剤を 16 mg/kg の用量で投与）に組み入れられた。治験組入れ時の合併症は，貧血，両側人工股関節の使用及び第 XI 因子欠乏症であった。ベースラインの ECOG スコアは 1 であった。既往歴は胆嚢摘出及び左上腕骨骨折であった。ベースラインの血清 M 蛋白は 2.9 g/dL，尿中 M 蛋白は 512.7 mg/24 時間，骨髄穿刺で形質細胞は 40%であった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はメルファラン，その他の抗がん剤（MLN9708：治験中の PI）及び prednisone，レジメン 2 はデキサメタゾン及びレナリドミドであった。被験者はレジメン 1 の PI 及びアルキル化剤，並びにレジメン 2 のレナリドミドに治療抵抗性を示した。

治験組入れ時の併用薬は，アシクロビル及びアロプリノールであった。

スクリーニング時（Day −22），被験者のヘモグロビン値は 117 g/L（正常範囲：120-160 g/L）であった。

Day −8（2014 年 4 月 1 日）に，**Grade 1 の非重篤な有害事象の気道感染**が報告された。本事象の治療として，アモキシシリン／クラブラン酸カリウム（Augmentin）及びシプロフロキサシンを投与した。本事象は Day −2 に回復した。

Day 1 の本剤の持続静脈内投与中，被験者がジュースを飲んでいたところ，気管支への誤嚥に伴った急性呼吸窮迫症候群が発現した。被験者は集中治療室に移送され，同日，**Grade 3 の重篤な有害事象である誤嚥性肺炎**が報告された。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。投与前のバイタルサインは，血圧 112/64 mm Hg，脈拍数 84 拍/分（bpm）及び体温 36.3°C であった。被験者は治験実施計画書に従い前投薬を受けた。投与開始 90 分後の血圧は 124/74 mm Hg，脈拍数 100 bpm，体温 36.1°C であった。誤嚥性肺炎の発現により，持続静脈内投与は開始 100 分後に中止された。被験者は cisatracurium besylate，フロセミド，ニトログリセリン，ヒドロコルチゾンリン酸エステルナトリウム，ピペラシリンナトリウム／タゾバクタムナトリウム（Tazocel），ミダゾラム，プロポフォールの投与によって鎮静状態となり，挿管を受けた。被験者はその後本剤の投与を受けなかった。

Day 2 に，**Grade 3 の非重篤な有害事象の貧血**が報告された（ヘモグロビン値：77 g/L）。翌日，**非重篤な有害事象の Grade 2 の医療機器関連感染**（記載語：カテーテル感染）**及び Grade 1 の発熱**が報告された。Day 4 に，被験者は血液科に移送され，酸素管理，濃厚赤血球 2 単位の輸血を受けた。**貧血**は Day 5 に **Grade 2** へ改善した（ヘモグロビン値：89 g/L）。Day 7 に，**Grade 2 の非重篤な有害事象の気管支痙攣**が報告された。治験担当医師は，これらすべての事象と本剤との因果関係を「関連なし」と判断した。これらの事象に対する本剤の処置は実施しなかった。肺活量測定検査により 69%の呼吸器機能が示された。これらの事象の治療として，クロラゼプ酸二カリウム，モルヒネ，paracetamol，ピペラシリンナトリウム／タゾバクタムナトリウム，ロラゼパム，アルプラゾラム，テイコプラニン，硫酸マグネシウム，カンレノ酸カリウム，フロセミド，ヒドロコルチゾンリン酸エステルナトリウム，イプラトロピウム臭化物，エノキサパリンナトリウム，イプラトロピウム臭化物／サルブタモール（Combiprasal），ペチジン，メチルプレドニゾロン及びミダゾラムを投与した。発熱及び医療機器関連感染は Day 5 に回復した。Day 9 に濃厚赤血球 2 単位を輸血した。Day 18 に，**Grade 1 の非重篤な有害事象の発熱**が報告された。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。本事象に対する本剤の処置は実施しなかった。本事象の治療として metamizole magnesium を投与した。発熱は Day 19 に回復した。誤嚥性肺炎と気管支痙攣は Day 22 に回復し，被験者は，緩和ケアのために同日退院した。

Day 28 に，被験者は**全身健康状態低下**（疾患進行）による心肺停止により死亡した。治験担当医師は，全身健康状態低下と本剤との因果関係を「関連なし」と判断した。死亡時に，貧血は回復していなかった。

2.7.6.4 海外臨床第 I/II 相試験（GEN501 試験，評価資料：5.3.5.2.2-1，5.3.5.2.2-2，5.3.5.2.2-3）

2.7.6.4.1 概要

2.7.6.4.1.1 計画

(1) 治験の標題

多発性骨髄腫（MM）を対象としたダラツムマブ（以下本剤）の安全性試験－非盲検用量漸増期（Part 1）及び非盲検維持用量期（Part 2）

(2) 治験責任医師

[redacted]; [redacted], Amsterdam, Netherlands

(3) 公表文献（引用文献）

Lokhorst HM, et al. Targeting CD38 with daratumumab monotherapy in multiple myeloma. N Engl J Med. 2015 Sep;373(13):1207-19.

(4) 治験実施期間

2008 年 3 月 [redacted] 日（最初の被験者の初回来院日）～2015 年 1 月 9 日（クリニカルカットオフ日）

(5) 開発の相

第 I／II 相

(6) 目的

本治験の主要目的は，2 レジメン以上の治療に対して抵抗性を示した，又は治療後に再発が認められた，ほかに治療選択肢がない MM 患者を対象に本剤の単剤療法の安全性プロファイルを検討することであった。なお，再発は，前治療に対する初回奏効［minimal response（MR）以上］以降の疾患進行が，治療中止後 60 日を超えて認められたものと定義し，治療抵抗性は，M 蛋白の減少が 25%未満であった，又は治療期間中若しくは治療中止から 60 日以内に疾患進行が認められたものと定義した。

副次目的は，第 II 相及び第 III 相試験用製剤を単回及び反復投与したときの本剤の薬物動態プロファイルの検討，本治験で規定された被験者集団での本剤の単剤療法の有効性評価，今後の試験で使用する安全な用量の確立，前投薬を含む本剤の持続静脈内投与方法の最適化，本剤の免疫原性評価，並びに本剤の作用機序，infusion related reaction（IRR），及び臨床効果に関するバイオマーカーを評価することであった。

(7) 治験方法

本治験は本剤をヒトに初めて投与する臨床試験であり，2 パート（Part 1 及び Part 2）で構成される第 I／II 相非盲検安全性試験であった。Part 1 は用量漸増期であり，Part 2 は維持用量期（Part 1 の結果に基づき用量決定）であった。Part 1 では，本剤の 10 段階の用量レベル（0.005，0.05，0.10，0.50，1，2，4，8，16 及び 24 mg/kg）を順に評価した。

独立データモニタリング委員会は，Part 1 で収集したデータに基づき，8 mg/kg 以上の用量で本治験を進めることを決定した。このため，当初は Part 2 の用量として 8 mg/kg を選択し，前投薬と持続静脈内投与方法が異なる 3 コホート（A，B 及び C）へ被験者を組み入れた。しかし，8 mg/kg では薬物動態パラメータの被験者間のばらつきが大きく，投与期間中に daratumumab が標的である CD38 と十分に結合しない可能性があることが考えられた。そのため，CD38 に対して十分量の daratumumab を曝露させて本剤の有効性を最適化するために，コホート D の用量を 16 mg/kg に変更し，高用量の投与が必要かどうかを検討した。また，より大きなスケールの製造工程で製造される第 III 相試験用製剤（市販用製剤）を評価するコホート E（用量 16 mg/kg）を追加した。

(8) 被験者数（計画時及び解析時）

Part 1 では，用量漸増時での用量レベル数に応じて 26～62 例を登録する計画とした。Part 2 では，独立データモニタリング委員会が安全と判断した Part 1 の用量で最大 80 例を登録する計画とした。合計で最大 112 例の被験者を登録する計画とした。Part 1 で本剤を投与された被験者は 32 例であった。このうち，本剤を 4 mg/kg 未満の用量で投与された被験者は 20 例，4 mg/kg，8 mg/kg，16 mg/kg 及び 24 mg/kg を投与された被験者は各 3 例であった。Part 2 で本剤を投与された被験者は 72 例であった。このうち，本剤 8 mg/kg を投与された被験者は 30 例［コホート A（16 例），コホート B（8 例），コホート C（6 例）］，16 mg/kg を投与された被験者は 42 例［コホート D（20 例），コホート E（22 例）］であった。

(9) 診断及び主な組入れ基準

本治験の対象は，2 レジメン以上の治療に対して抵抗性を示した，又は治療後に再発が認められた，ほかに治療選択肢がない 18 歳以上の MM 患者とした。更に，MM と診断され，測定可能な M 蛋白が存在し，Eastern Cooperative Oncology Group（ECOG）の performance status スコアが 2 以下の患者を対象とした。

(10) 被験薬，用量及び投与方法，ロット番号

本剤は無色～淡黄色の液体で，持続静脈内投与用の無菌濃縮液であり，20 mg/mL の濃度で提供された。Part 1 では，本剤の 10 段階の用量レベル（0.005，0.05，0.10，0.50，1，2，4，8，16 及び 24 mg/kg）を順に評価した。用量が最も低い 2 用量（0.005 mg/kg 及び 0.05 mg/kg）コホートには各 1 例（+ 3 例）を割り付け，残りの 8 用量コホートには 3 例（+ 3 例）を割り付けた。被験者に本剤を 7 回投与し，初回と 2 回目の投与の間には 3 週間のウォッシュアウト期間を設けた。Part 2 のコホート A，B，C では，本剤 8 mg/kg を最初の 8 週間は 1 週間隔，その後 16 週間は 2 週

間隔，以降は 4 週間隔で投与した。コホート D と E では，本剤 16 mg/kg を初回投与後 3 週間のウォッシュアウト期間をおき，続く 7 週間は 1 週間隔，その後 14 週間は 2 週間隔，以降は 4 週間隔で投与した。

本治験で使用した本剤のバルクロット番号は以下のとおりであった。

Part 1：[redacted]

Part 2：[redacted]

また，使用した本剤の包装ロット番号は以下のとおりであった。

Part 1：[redacted]

Part 2：[redacted]

(11) 対照薬，用量及び投与方法，ロット番号

該当なし

(12) 投与期間

Part 1 の総投与期間は 8 週間であった。Part 1 には 44 週間の後観察期間が含まれた。本剤投与中に疾患進行が認められた場合，当該被験者は本治験を中止し，治験担当医師の判断で代替療法を開始することとした。

Part 2 の投与期間は，96 週間又は疾患進行若しくは許容できない毒性が発現するまでの期間とした。Part 2 では，被験者の死亡，追跡不能，同意撤回又は治験終了のいずれかが発生するまで，被験者の生存情報についての追跡を継続することとした。

(13) 評価基準

安全性の評価は，有害事象，臨床検査値，バイタルサイン，心電図（ECG），身体所見及び併用薬の使用状況に基づき実施した。有害事象の重症度は，National Cancer Institute Common Terminology Criteria for Adverse Events に従い判定した。血清中 daratumumab 濃度を測定するための薬物動態用検体及び本剤に対する抗体の産生を確認するための免疫原性用検体をすべての被験者から採取した。採取した全血検体及び骨髄穿刺検体を用いてナチュラルキラー（NK）細胞，T 細胞及び B 細胞を含む免疫表現型を分析した。

治療効果は，2011 年の国際骨髄腫作業部会（IMWG）の MM の治療効果判定規準を用いたコンピュータ・アルゴリズムによる判定に基づき評価した。当該評価には，全奏効率［ORR；partial response（PR）以上を達成した被験者の割合］，奏効持続期間，奏効到達期間及び最良効果到達期間，臨床的有用率［stringent complete response（sCR）+ complete response（CR）+ very good partial response（VGPR）+ PR + MR］，無増悪期間（TTP），無増悪生存期間（PFS），全生存期間（OS），血清／尿中 M 蛋白又は遊離軽鎖の減少及び骨髄中形質細胞の割合の変化が含まれた。

(14) 統計手法

Part 1 と Part 2 の主要目的は安全性の検討であり，統計学的仮説の検定は計画しなかった。有害事象，臨床検査値，バイタルサイン及び ECG 検査結果について安全性を要約した。特に注目すべき有害事象として，IRR，感染症及び寄生虫症，二次性（続発性）悪性腫瘍などを要約した。有効性の主要評価項目は ORR であった。治療効果カテゴリーごとに両側正確 95%信頼区間（CI）を算出した。奏効到達期間，TTP，PFS，奏効持続期間及び OS を含む副次評価項目の推定には Kaplan-Meier 法を用いた。血清／尿中 M 蛋白又は遊離軽鎖のベースラインからの最大変化率（%）について，ベースラインで測定可能であったタイプに基づき，waterfall プロットを作成した。奏効例での骨髄中形質細胞の割合について，ベースラインからベースライン以降の最初の測定値をシフトテーブルに示し，ベースラインからの変化率（%）を図示した。各検体採取時の血清中 daratumumab 濃度を記述統計量を用いて要約し，薬物動態パラメータをノンコンパートメント法を用いて算出した。薬物動態／薬力学の解析は線形混合効果モデルを用いて実施し，ベースライン値で調整／補正した QTc 間隔の変化と，各検体採取時点での血清中 daratumumab 濃度との関連性を検討した。

2.7.6.4.1.2 結果

結果は Part 1 と Part 2 に分けて示す。

(1) Part 1

1) Part 1 の対象集団

Part 1 で本剤を 1 回以上投与された被験者は 32 例であった。本剤を 4 mg/kg 未満の用量で投与された被験者は 20 例［0.005 mg/kg（1 例），0.05 mg/kg（1 例），0.1 mg/kg（6 例），0.5 mg/kg（3 例），1 mg/kg（6 例），2 mg/kg（3 例）］，4 mg/kg，8 mg/kg，16 mg/kg 及び 24 mg/kg を投与された被験者は各 3 例であった。32 例中 15 例が治験を完了し，いずれも本剤を 7 回全量投与された。残りの 17 例（53%）は本剤の投与を中止し，このうち疾患進行による中止が 12 例（38%），有害事象による中止が 5 例（16%）であった。

男性が 23 例（72%）であった。すべての被験者が白人で，年齢の中央値は 61.5 歳であった。ベースラインの ECOG performance status スコアが 1 の被験者は 17 例（53%），0 の被験者は 14 例（44%）であった。MM の初回診断からの期間の中央値は 72.6 カ月であった。多くの被験者（88%，28 例）で MM に対する前治療歴が 4 レジメン以上あった。

2) Part 1 の安全性

本剤の用量を 0.005～24 mg/kg の範囲で検討したが，最大耐量（MTD）には到達しなかった。用量制限毒性は 2 例で認められ，その内訳は 0.1 mg/kg 群の Grade 3 の貧血が 1 例，1.0 mg/kg 群の Grade 3 の肝機能異常（アスパラギン酸アミノトランスフェラーゼの増加）が 1 例であった。Part 1 で発現した有害事象の多くは Grade 1 又は 2 であった。Grade 3 又は 4 の有害事象は 11 例（34%）で発現し，重篤な有害事象は 12 例（38%）で発現した。本剤の投与中止に至った有害事象は 5 例（16%）で発現し，その内訳は気管支痙攣（2 例：2 mg/kg 群の 1 例及び 24 mg/kg 群の 1 例），過敏症（4 mg/kg 群の 1 例），肝機能異常（1 mg/kg 群の 1 例），サイトカイン放出症候群

及び潮紅（0.1 mg/kg 群の 1 例）であった。用量に依存した毒性は認められなかった。本剤の最終投与後 30 日以内に死亡した被験者はいなかった。IRR は 20 例（63%）で発現した。Part 1 のすべての被験者の遊離ヘモグロビン値，ハプトグロビン値，乳酸脱水素酵素値，総ビリルビン値及びヘモグロビン値を解析した結果，溶血反応に一貫したパターンはみられなかった。本剤の安全性プロファイルに基づき，8 mg/kg 以上の用量を Part 2 に採用した。

3) Part 1 の有効性

PR 例は 4 例であり，投与群別では 24 mg/kg 群が 2 例，4 mg/kg 群及び 16 mg/kg 群が各 1 例であった。PR 例 4 例では，骨髄中悪性形質細胞がベースラインよりも減少しており，本剤が骨髄内に浸透し，骨髄中の悪性形質細胞を消失させる作用が示された。

4) Part 1 の薬物動態，免疫原性及び薬力学

Daratumumab 濃度は週 1 回の反復投与に伴って上昇したことから，この投与間隔で蓄積することが確認された。初回投与後の daratumumab の最高血清中濃度（C_{max}）は，1 mg/kg から 24 mg/kg まで用量にほぼ比例して上昇した。初回投与後及び最終投与後の血清中濃度-時間曲線下面積（AUC）は，用量比を上回る増加を示した。本剤の消失は非線形性であり，平均消失半減期（$t_{1/2}$）は用量増加及び反復投与に伴って延長した。平均クリアランス（CL）は，特に 2 mg/kg 以上の投与群で用量増加及び反復投与に伴って低下した。本剤に対する抗体の検査を 22 例で実施した。Part 1 では本剤に対する抗体陽性の被験者はいなかった。NK 細胞の減少は，特に 2 mg/kg 以上の投与群において末梢血中と骨髄中の両方で認められた。

(2) Part 2

1) Part 2 の対象集団

Part 2 で本剤を 1 回以上投与された被験者は 72 例であった。このうち本剤 8 mg/kg を投与された被験者は 30 例［コホート A（16 例），コホート B（8 例），コホート C（6 例）］，16 mg/kg を投与された被験者は 42 例［コホート D／第 II 相試験用製剤（20 例），コホート E／第 III 相試験用製剤（22 例）］であった。本項では本剤 16 mg/kg 群（コホート D + コホート E，42 例）の結果を中心に記載する。

被験者 72 例のうち，48 例（67%）が男性であった。多く（65%）の被験者が白人で，年齢の中央値は 61 歳であった。ベースラインの ECOG performance status スコアはほとんど（71%）の被験者が 1 であった。

16 mg/kg 群（42 例）では，初回診断からの期間の中央値は 69 カ月，前治療数の中央値は 4 レジメン，前治療歴が 4 レジメン以上の被験者は 26 例（62%）であった。全例にプロテアソーム阻害剤（PI）の前治療歴があり，免疫調節薬（IMiD）の前治療歴があった被験者は 40 例（95%）であった。直近の治療に対し抵抗性を示した被験者は 32 例（76%）で，27 例（64%）が PI 及び IMiD の両剤に対して治療抵抗性を示した。16 mg/kg 群の本剤の投与期間の中央値は 5.4 カ月であった。

8 mg/kg 群（30 例）では，初回診断からの期間の中央値は 66 カ月，前治療数の中央値は 4 レジメン，前治療歴が 4 レジメン以上の被験者は 24 例（80%）であった。全例に PI の前治療歴があり，IMiD の前治療歴があった被験者は 29 例（97%）であった。直近の治療に対し抵抗性を示した被験者は 25 例（83%）で，19 例（63%）が PI 及び IMiD の両剤に対して治療抵抗性を示した。8 mg/kg 群の本剤の投与期間の中央値は 2.9 カ月であった。

2) Part 2 の安全性

本剤単剤療法の忍容性は良好であり，安全性プロファイルも良好で有害事象は臨床的に管理可能であった。16 mg/kg 群で発現割合が高かった有害事象は，疲労（41%），アレルギー性鼻炎（24%），鼻咽頭炎（24%），背部痛（24%），咳嗽（21%）及び悪心（21%）であった。
16 mg/kg 群の 14 例（33%）に重篤な有害事象が発現した。発現割合が高かった重篤な有害事象は，肺炎（3 例，7%），交差適合試験不適合（3 例，7%）及び発熱（2 例，5%）であった。交差適合試験不適合が発現した 3 例で，赤血球輸血後に輸血関連反応を発現した被験者はおらず，当該事象はいずれも医学的に重要と判断され，重篤な有害事象として報告された。16 mg/kg 群で Grade 3 又は 4 の有害事象が発現した被験者は 11 例（26%）であった。最も発現割合が高かった Grade 3 又は 4 の有害事象は，白血球減少症，好中球減少症及び肺炎が各 2 例（5%）であった。16 mg/kg 群の 1 例が有害事象（肺炎，本剤と関連性なし）のために本剤の投与を中止し，その後死亡した。本剤と関連性がある有害事象のために死亡した被験者はいなかった。Grade 3 又は 4 の感染症が 16 mg/kg 群の 2 例（5%）で認められた。感染症（すべての Grade）の発現割合に経時的な上昇はみられなかった。発熱性好中球減少症（すべての Grade）は認められなかった。

16 mg/kg 群の 31 例（74%）で IRR が発現した。いずれの IRR も重篤とは判断されず，IRR のために本剤の投与を中止した被験者はいなかった。IRR を発現した被験者のうち，97%が初回投与時，10%が 2 回目投与時，3%がそれ以降の投与時での発現であった。

QTcF 間隔を含む ECG データと本剤の薬物動態／薬力学との関連性を検討した結果，本剤投与後に心拍数の中等度の増加及び QTcF の中程度の延長が確認された。U 波異常，QTcF の>500 ms への延長，又は QTcF の>60 ms のベースラインからの増加が認められた被験者はいなかった。Part 2 で認められた QTcF の軽微な延長は臨床的に重要とは判断されなかった。

本剤の用量 16 mg/kg と 8 mg/kg の安全性プロファイルは同様であった。第 II 相試験用製剤（コホート D）と第 III 相試験用製剤（コホート E）の安全性プロファイルも同様であった。ただし，これらの結果の解釈に際しては，被験者数が少なかったことを考慮に入れなければならない。

3) Part 2 の有効性

16 mg/kg 群の ORR（PR 以上）は 36%（15/42 例，95%CI：22～52%）であった（表 2.7.6.4-1）。2 例（5%）が CR，2 例（5%）が VGPR，11 例（26%）が PR を達成した。

表 2.7.6.4-1 コンピュータ・アルゴリズムに基づく有効性の要約－16 mg/kg 群
［GEN501 試験 Part 2，全投与解析対象集団］

	16 mg/kg	
	Result	95% CI
Analysis set: all treated	42	-
Overall response (sCR+CR+VGPR+PR), n (%)	15 (35.7%)	(21.6%, 52.0%)
Stringent complete response (sCR), n (%)	0	-
VGPR or better (sCR + CR + VGPR), n (%)	4 (9.5%)	(2.7%, 22.6%)
Clinical benefit (Overall response + MR), n (%)	19 (45.2%)	(29.8%, 61.3%)
Median [a] duration of response (months)	NE	(5.6, NE)
Median [b] time to response (months)	0.9	-
Median [a] progression-free survival (months)	5.6	(4.2, 8.1)
Median [a] overall survival (months)	NE	(NE, NE)

a: based on Kaplan-Meier estimate; b : descriptive summary; NE = not estimable

本剤 16 mg/kg を投与された被験者で，迅速かつ持続的な奏効が確認された。奏効到達期間の中央値は 0.92 カ月，最良効果到達期間の中央値は 1.8 カ月，VGPR 以上到達期間の中央値は 0.49 カ月であった。観察期間の中央値は 10.2 カ月であり，奏効持続期間は中央値に到達していなかった。Kaplan-Meier 法で推定した結果，奏効例の 78%が 6 カ月時点で無増悪であり，12 カ月時点では 65%が無増悪であった。OS は中央値に到達していなかったが，12 カ月生存率の推定値は 77%（95%CI：58～88%）であった。

CR 2 例を含む本剤の奏効の深さ（VGPR 以上の割合が 10%）は，骨髄中の悪性形質細胞を完全に又はほぼ完全に消失させることができるという他剤とは異なる特徴を示している。ORR は前治療数及び治療抵抗性の状態に関係なく，臨床的に重要な部分集団のいずれにおいても一貫しており，特に，ポマリドミドに対して治療抵抗性を示していた 15 例の ORR は 33%に達した。

16 mg/kg 群で M 蛋白のデータが評価可能であった 41 例中 33 例（80%）では M 蛋白の減少が認められ，ベースラインからの減少率は 41 例中 19 例（46%）で 50%を上回り，41 例中 10 例（24%）で 90%を上回った。ベースライン以降の骨髄検査データを有する奏効例 13 例では，骨髄中の形質細胞の割合は減少（8 例），又は 5%未満のままであった（5 例）。ベースラインの形質細胞の割合が 10%を超えていた奏効例 5 例中 4 例では，ベースライン以降の骨髄中の形質細胞の割合が 5%未満に正常化した。

8 mg/kg 群の ORR は 10%（3/30 例，95%CI：2～27%）であり，3 例（10%）が PR であった。

4) Part 2 の薬物動態，免疫原性及び薬力学

本剤 16 mg/kg 初回投与後の daratumumab の平均 C_{max} は，8 mg/kg 群の約 2 倍であった。16 mg/kg の投与レジメンにおいて，daratumumab の蓄積が 1 週間隔投与の期間中は持続したが，2 週間隔の投与ではやや低下した。反復投与によって daratumumab の CL が低下し，$t_{1/2}$ は延長した。$t_{1/2}$ の平均値（標準偏差）は，16 mg/kg 初回投与後では 216（104）時間，反復投与後（投与回数の中央値は 13.5 回，範囲：1～24 回）では 255（216）時間であった。本治験の Part 2 で抗体データが得られた 66 例（8 mg/kg 群の 27 例，16 mg/kg 群の 39 例）で，本剤に対する抗体が陽性となった被験者はいなかった。8 mg/kg 群及び 16 mg/kg 群のいずれも本剤投与後に末梢血中及び骨髄中 NK 細胞の大幅な減少が認められた。これらのデータは，NK 細胞が本剤の活性に対して感度の高いバイオマーカーであるという予備的エビデンスを示しており，NK 細胞は CD38 を発現し，

本剤による細胞消失作用を示すという所見を裏付けている。NK 細胞数又は NK 細胞の割合の低下と臨床効果との間に関連は認められなかった。

2.7.6.4.1.3　結論

本治験では，再発又は難治性の MM 患者の治療における本剤の単剤療法について以下の主要な結果が示された：

- 本治験の Part 1 の結果から，Part 2 で本剤の臨床開発を継続することは妥当であると判断された。
  - 本剤の用量を 0.005～24 mg/kg の範囲で検討したが，MTD には到達しなかった。用量制限毒性は 2 例で認められ，その内訳は 0.1 mg/kg 群の Grade 3 の貧血が 1 例，1.0 mg/kg 群の Grade 3 の肝機能異常が 1 例であった。
  - 本剤投与により 4 例に骨髄中悪性形質細胞の減少を伴う PR が認められた。
  - Part 1 で発現した有害事象の多くは Grade 1 又は 2 であった。Grade 3 又は 4 の有害事象は 11 例（34%）で発現した。重篤な有害事象は 12 例（38%）で発現した。用量に依存した毒性は認められなかった。本剤の最終投与後 30 日以内に死亡した被験者はいなかった。
  - 本剤投与による IRR が 20 例（63%）で発現した。Part 1 では，IRR の発現を最小限に抑えるためのさまざまな前投薬及び後投薬（ステロイドなど）を検討した。
- Part 2 の 16 mg/kg 群（42 例）と 8 mg/kg 群（30 例）のいずれにおいても本剤の単剤療法は有効であり，忍容性も良好で有害事象は管理可能であった。主要な結果を以下に示す：
  - Part 2 で本剤を投与された 72 例中，本剤の投与中止に至った有害事象を発現した被験者は 1 例であった。
  - IRR が 72 例中 51 例（71%）で報告され，1%の被験者で Grade 3 の IRR が認められた。Grade 4 の IRR は認められなかった。IRR のために本剤の投与を中止した被験者はいなかった。IRR を発現した被験者の多く（98%）が初回投与時，8%の被験者が 2 回目投与時，6%の被験者がそれ以降の投与時での発現であった。
  - 16 mg/kg 群で造血成長因子を使用した被験者の割合は 12%であり，2%の被験者が本剤投与開始後に使用を開始した。16 mg/kg 群の 12%の被験者が好中球減少症を発現したが，発熱性好中球減少症の報告はなかった。また，Grade 3 又は 4 の感染症又は寄生虫症を発現した被験者は 8%であった。
  - 本剤 16 mg/kg と 8 mg/kg の安全性プロファイルは同様であった。ただし，これらの結果の解釈に際しては，被験者数が少なかったことを考慮に入れなければならない。
  - 16 mg/kg 群では，初回診断からの期間の中央値は 69 カ月，前治療数の中央値は 4 レジメンであった。16 mg/kg 群の全例に PI の前治療歴があり，95%の被験者に IMiD の前治療歴があった。76%の被験者が直近の治療に対して抵抗性を示しており，64%の被験者

が PI 及び IMiD の両剤に対して治療抵抗性を示し，ポマリドミドに対しては 36%，アルキル化剤に対しては 60%の被験者が治療抵抗性を示した。

- 複数の前治療歴を有する本治験の対象集団において，本剤 16 mg/kg 単剤療法の明らかな臨床効果が示された。16 mg/kg 群の ORR は 36%（95%CI：22～52%）であった。2 例が CR，2 例が VGPR，11 例が PR を達成した。8 mg/kg 群の ORR は 10%（95%CI：2～27%）であり，治療効果はいずれも PR であった。
- ORR は前治療数及び治療抵抗性の状態に関係なく，複数の臨床的に重要な部分集団のいずれにおいても全体集団の ORR と一貫していた。
- 本剤 16 mg/kg 投与による奏効の深さ（CR の 2 例を含む VGPR 以上の割合が 10%）は，単剤としては特筆すべき成績であり，その作用機序のほかに，骨髄中の悪性形質細胞を完全に又はほぼ完全に消失させることができるという作用は，難治性 MM の治療において他剤とは異なる特徴を示している。
- 16 mg/kg 群での中央値 10.2 カ月の観察では，OS は中央値に到達していなかったが，12 カ月生存率の推定値は 77%（95%CI：58～88%）であった。

- ORR に基づくと，第 II 相試験用製剤と第 III 相試験用製剤の有効性は同様であることが示された。また，安全性プロファイルも第 II 相試験用製剤と第 III 相試験用製剤で同様であった。ただし，これらの結果の解釈に際しては，被験者数が少なかったことを考慮に入れなければならない。
- 本剤の消失は非線形の薬物動態学的特性を示した。$t_{1/2}$ は用量増加及び反復投与に伴って延長し，2 mg/kg 以上の用量では CL は用量増加及び反復投与に伴って低下した。
- 中央 ECG 解析において再分極異常の所見がなかったこと（QTcF の>60 ms の増加なし，QTcF の>500 ms への延長なし，新たな U 波異常なし），及び本剤に QTcF に影響を及ぼす生物学的機序がないことから，本剤は臨床的に重要な QT 延長を引き起こさないことが示唆された。
- 本治験のいずれの Part でも本剤に対する抗体が陽性となった被験者はいなかった。

2.7.6.4.2 補遺

2.7.6.4.2.1 補遺 1（2015 年 6 月 30 日クリニカルカットオフ）

[redacted]年[redacted]月[redacted]日付の治験総括報告書のクリニカルカットオフ日は 2015 年 1 月 9 日であった。本治験の Part 2 で本剤の投与を受けたすべての被験者の生存情報を，2015 年 6 月 30 日をクリニカルカットオフ日として更新し，治験総括報告書 Addendum 1 を作成した。当該 Addendum では，初回クリニカルカットオフ日（2015 年 1 月 9 日）に管理上の問題で最新の生存データが得られなかった数例の被験者の生存情報も含めた。具体的には，治験実施計画書 Amendment 13 の発効まで，被験者の同意項目に生存情報の収集が含まれていなかったため，初回カットオフに基づくデータベースロック時に 9 例の生存情報が利用できなかった。当該 9 例はいずれも本剤 8 mg/kg を

投与され，生存情報の収集に再同意しておらず，2015 年 1 月 9 日のクリニカルカットオフ前に死亡していた。治験実施計画書 Amendment 13 で拡大用量として 16 mg/kg が選択されたことから，この管理上の問題は 8 mg/kg 群のみへ影響を及ぼした。本項では治験総括報告書 Addendum 1 の結果を示す。

- 2015 年 6 月 30 日のクリニカルカットオフ日時点で，Kaplan-Meier 法で推定した観察期間の中央値は，16 mg/kg 群で 15.2 カ月，8 mg/kg 群で 27.6 カ月であった。
- 死亡した被験者は，16 mg/kg 群では 42 例中 11 例（26%）であった。このうち有害事象による死亡は 1 例（2%），疾患進行による死亡は 8 例（19%）及びその他の理由による死亡は 2 例（5%）であった。これには初回クリニカルカットオフ日（2015 年 1 月 9 日）以降，新たに死亡した 3 例が含まれる。8 mg/kg 群では 30 例中 22 例（73%）が死亡し，これには前述の初回クリニカルカットオフ日に生存情報が利用できなかった 9 例の死亡，及び初回クリニカルカットオフ日以降，新たに死亡した 5 例が含まれる。死亡例 22 例のうち，疾患進行による死亡は 11 例（37%），その他の理由による死亡は 10 例（33%）及び死因が収集できなかった被験者が 1 例（3%）であった。その他の理由による死亡 10 例のうち 6 例は，初回クリニカルカットオフ日に生存情報が利用できなかった被験者であった。本剤の最終投与後 30 日以内に死亡した被験者数は，初回クリニカルカットオフ日から変わらなかった。
- 2015 年 6 月 30 日のクリニカルカットオフ日時点での OS を表 2.7.6.4-2 に示す。16 mg/kg 群では OS は中央値に到達しておらず，8 mg/kg 群の OS の中央値は 18.2 カ月（95%CI：7.5～23.4 カ月）であった。12 カ月生存率の推定値は 8 mg/kg 群及び 16 mg/kg 群でそれぞれ 56%（95%CI：36.8～71.8%）及び 79%（95%CI：62.9～88.2%）であった。

表 2.7.6.4-2 全生存期間の要約（2015 年 6 月 30 日クリニカルカットオフ時点）
［GEN501 試験，全投与解析対象集団］

	8 mg/kg	16 mg/kg
Analysis set: all treated	30	42
Overall survival (months)		
Number of events (%)	22 (73.3%)	11 (26.2%)
Number of censored (%)	8 (26.7%)	31 (73.8%)
Kaplan-Meier estimate		
25% quartile (95% CI)	7.2 (2.5, 9.3)	15.9 (5.9, NE)
Median (95% CI)	18.2 (7.5, 23.4)	NE (19.9, NE)
75% quartile (95% CI)	27.0 (20.4, NE)	NE (19.9, NE)
6-month overall survival rate % (95% CI)	76.7 (57.2, 88.1)	88.1 (73.7, 94.9)
12-month overall survival rate % (95% CI)	56.3 (36.8, 71.8)	78.6 (62.9, 88.2)

Keys: CI = confidence interval; NE=not estimable.
Percentages are calculated with the number of subjects in each group as denominator.
[TEFOS01.rtf] [JNJ-54767414\GEN501\DBR_PART2_BLA_2015_4MSU\RE_PART2_BLA_2015_4MSU\tefos01.sas] 10AUG2015, 13:08
参照元：GEN501 CSR addendum 1_TEFOS01

2.7.6.4.2.2　補遺 2（[redacted]年[redacted]月[redacted]日クリニカルカットオフ）

本治験の Part 2 で本剤を投与されたすべての被験者の生存情報及び安全性情報を，[redacted]年[redacted]月[redacted]日をクリニカルカットオフ日として更新し，治験総括報告書 Addendum 2 を作成した。本項では治験総括報告書 Addendum 2 の結果を示す。なお，8 mg/kg 群では，すべての被験者が初回ク

リニカルカットオフ（2015 年 1 月 9 日）時点で投与を中止していたため，曝露に関する結果及び有害事象の結果は，初回クリニカルカットオフ日時点と変わらなかった。

- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点で，72 例中 67 例（93%）が本剤の投与を中止した。16 mg/kg 群では 42 例中 37 例（88%）が本剤の投与を中止した。主な中止理由は疾患進行で，初回クリニカルカットオフ日以降，新たに 9 例が疾患進行のために投与を中止した。
- 16 mg/kg 群の投与期間の中央値は 5.36 カ月であり，17 例（40%）が 1～6 カ月間，5 例（12%）が 24 カ月以上，4 例（10%）が 30 カ月以上本剤を投与された。最長投与期間は 35.7 カ月であった。相対用量強度の中央値は 99.5%であった。
- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点で，Kaplan-Meier 法で推定した観察期間の中央値は，16 mg/kg 群で 31.77 カ月，8 mg/kg 群で 45.14 カ月であった。
- [redacted]年[redacted]月[redacted]日のクリニカルカットオフ日時点での OS を表 2.7.6.4-3 に示す。16 mg/kg 群では 42 例中 23 例（55%）が生存していた。16 mg/kg 群では OS は中央値に到達しておらず，8 mg/kg 群の OS の中央値は 18.2 カ月（95%CI：7.5～22.6 カ月）であった。16 mg/kg 群の 18 カ月生存率の推定値は 69.0%（95%CI：52.7～80.7%）であり，24 カ月生存率の推定値は，16 mg/kg 群及び 8 mg/kg 群でそれぞれ 59.3%（95%CI：43.0～72.4%）及び 28.1%（95%CI：13.4～44.9%）であった。

表 2.7.6.4-3 全生存期間の要約（[redacted]年[redacted]月[redacted]日クリニカルカットオフ時点）
［GEN501 試験，全投与解析対象集団］

	8 mg/kg	16 mg/kg
Analysis set: all treated	30	42
Overall survival (months)		
Number of events (%)	25 (83.3%)	19 (45.2%)
Number of censored (%)	5 (16.7%)	23 (54.8%)
Kaplan-Meier estimate		
25% quartile (95% CI)	7.2 (2.5, 9.3)	15.9 (5.9, 21.0)
Median (95% CI)	18.2 (7.5, 22.6)	NE (19.9, NE)
75% quartile (95% CI)	25.8 (20.4, NE)	NE (NE, NE)
6-month overall survival rate % (95% CI)	76.7 (57.2, 88.1)	88.1 (73.7, 94.9)
12-month overall survival rate % (95% CI)	56.3 (36.8, 71.8)	78.6 (62.9, 88.2)
18-month overall survival rate % (95% CI)	52.8 (33.6, 68.8)	69.0 (52.7, 80.7)
24-month overall survival rate % (95% CI)	28.1 (13.4, 44.9)	59.3 (43.0, 72.4)

Key: CI = confidence interval; NE=not estimable.
Percentages are calculated with the number of subjects in each group as denominator.

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参照元：GEN501 CSR addendum 2_TEFOS01

- 16 mg/kg 群で発現割合が 20%以上の有害事象のうち，初回クリニカルカットオフ日以降，発現割合が新たに 20%以上となった事象は上気道感染（26%）及び発熱（21%）であった。また，発現割合が新たに 10%以上となった事象は不眠症，霧視，胸痛及び高血糖（各

12%）であった。Grade 3 又は 4 の有害事象及び重篤な有害事象は，初回クリニカルカットオフ日以降，新たに各 2 例に認められた。新たに認められた重篤な有害事象は，細菌性敗血症，帯状疱疹，背部痛，健忘，一過性脳虚血発作及び形質細胞腫であった。なお，本剤と関連性のある重篤な有害事象及び死亡に至った有害事象の発現割合は初回クリニカルカットオフ日時点と同様であった。

- 本剤の最終投与後 30 日以内に死亡した被験者数は，初回クリニカルカットオフ日時点とその後 22 カ月経過した今回（[redacted] 年 [redacted] 月 [redacted] 日）のクリニカルカットオフ日時点で変わらなかった。[redacted] 年 [redacted] 月 [redacted] 日のクリニカルカットオフ日時点で，16 mg/kg 群では 42 例中 19 例（45%）が死亡した。このうち疾患進行による死亡は 14 例（33%），有害事象による死亡は 1 例（2%）及びその他の理由による死亡は 4 例（10%）であった。これには初回クリニカルカットオフ日以降，新たに認められた疾患進行による死亡 9 例及びその他の理由による死亡 2 例が含まれた。8 mg/kg 群では 30 例中 25 例（83%）が死亡した。このうち疾患進行による死亡は 14 例（47%），その他の理由による死亡は 10 例（33%）及び死因不明が 1 例（3%）であった。これには初回クリニカルカットオフ日以降，新たに認められた，疾患進行による死亡 9 例，その他の理由による死亡 7 例及び死因不明の 1 例が含まれた。
- 初回クリニカルカットオフ以降，本剤の全般的な安全性プロファイルに特筆すべき新らたな懸念は認められなかった。

2.7.6.4.3 有害事象

本治験の Part 1 及び Part 2（クリニカルカットオフ日：2015 年 1 月 9 日）で発現した因果関係を問わない有害事象及び本剤と関連性がある有害事象をそれぞれ表 2.7.6.4-4 及び表 2.7.6.4-5 に示す。

表 2.7.6.4-4 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 1，全投与解析対象集団］

	<4 mg/kg		4 mg/kg		8 mg/kg	
	Total	Related	Total	Related	Total	Related
Analysis set: all treated	20		3		3	
Total no. subjects with TEAEs	19 (95.0%)	18 (90.0%)	3 (100.0%)	3 (100.0%)	3 (100.0%)	3 (100.0%)
MedDRA system organ class/Preferred term						
腎および尿路障害	10 (50.0%)	3 (15.0%)	1 (33.3%)	1 (33.3%)	3 (100.0%)	0
蛋白尿	9 (45.0%)	2 (10.0%)	1 (33.3%)	1 (33.3%)	3 (100.0%)	0
頻尿	1 (5.0%)	0	0	0	0	0
腎機能障害	1 (5.0%)	1 (5.0%)	0	0	0	0
一般・全身障害および投与部位の状態	11 (55.0%)	9 (45.0%)	0	0	1 (33.3%)	1 (33.3%)
発熱	8 (40.0%)	6 (30.0%)	0	0	1 (33.3%)	0
インフルエンザ様疾患	3 (15.0%)	3 (15.0%)	0	0	0	0
胸痛	2 (10.0%)	0	0	0	0	0
疲労	2 (10.0%)	2 (10.0%)	0	0	0	0
胸部不快感	0	0	0	0	1 (33.3%)	1 (33.3%)
末梢性浮腫	1 (5.0%)	0	0	0	0	0
胃腸障害	7 (35.0%)	2 (10.0%)	2 (66.7%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
悪心	2 (10.0%)	1 (5.0%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
下痢	1 (5.0%)	0	1 (33.3%)	0	0	0
腹痛	2 (10.0%)	0	0	0	0	0
嘔吐	0	0	1 (33.3%)	0	0	0
便秘	1 (5.0%)	0	0	0	0	0
口内乾燥	1 (5.0%)	1 (5.0%)	0	0	0	0
口唇浮腫	0	0	1 (33.3%)	1 (33.3%)	0	0
口腔内潰瘍形成	1 (5.0%)	0	0	0	0	0
食道炎	0	0	1 (33.3%)	0	0	0
感染症および寄生虫症	6 (30.0%)	0	1 (33.3%)	0	1 (33.3%)	0
鼻咽頭炎	2 (10.0%)	0	0	0	0	0
肺炎	1 (5.0%)	0	0	0	0	0
胃腸炎	1 (5.0%)	0	0	0	0	0
帯状疱疹	1 (5.0%)	0	0	0	0	0
メタニューモウイルス感染	0	0	0	0	1 (33.3%)	0
副鼻腔炎	0	0	1 (33.3%)	0	0	0
上気道感染	0	0	0	0	0	0
尿路感染	0	0	0	0	0	0
ウイルス感染	1 (5.0%)	0	0	0	0	0
外陰部腟カンジダ症	1 (5.0%)	0	0	0	0	0
呼吸器、胸郭および縦隔障害	6 (30.0%)	3 (15.0%)	2 (66.7%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
咳嗽	4 (20.0%)	1 (5.0%)	1 (33.3%)	0	0	0
気管支痙攣	1 (5.0%)	1 (5.0%)	0	0	0	0
発声障害	0	0	0	0	1 (33.3%)	1 (33.3%)
呼吸困難	0	0	1 (33.3%)	1 (33.3%)	0	0
鼻閉	0	0	0	0	0	0
アレルギー性鼻炎	1 (5.0%)	1 (5.0%)	0	0	0	0

表 2.7.6.4-4 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 1，全投与解析対象集団］（続き）

	<4 mg/kg		4 mg/kg		8 mg/kg	
	Total	Related	Total	Related	Total	Related
臨床検査	9 (45.0%)	6 (30.0%)	1 (33.3%)	1 (33.3%)	0	0
心電図ＱＴ延長	5 (25.0%)	3 (15.0%)	0	0	0	0
遊離ヘモグロビン陽性	5 (25.0%)	4 (20.0%)	0	0	0	0
血中クレアチンホスホキナーゼ増加	0	0	1 (33.3%)	1 (33.3%)	0	0
ハプトグロビン減少	1 (5.0%)	1 (5.0%)	0	0	0	0
リンパ球数減少	1 (5.0%)	1 (5.0%)	0	0	0	0
血液およびリンパ系障害	8 (40.0%)	7 (35.0%)	1 (33.3%)	1 (33.3%)	0	0
貧血	4 (20.0%)	4 (20.0%)	0	0	0	0
溶血	3 (15.0%)	3 (15.0%)	0	0	0	0
単球減少症	2 (10.0%)	2 (10.0%)	1 (33.3%)	1 (33.3%)	0	0
血小板減少症	3 (15.0%)	2 (10.0%)	0	0	0	0
リンパ球減少症	2 (10.0%)	2 (10.0%)	0	0	0	0
好中球減少症	1 (5.0%)	1 (5.0%)	0	0	0	0
神経系障害	4 (20.0%)	2 (10.0%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)
浮動性めまい	3 (15.0%)	2 (10.0%)	0	0	0	0
頭痛	1 (5.0%)	0	1 (33.3%)	1 (33.3%)	0	0
末梢性感覚ニューロパチー	0	0	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
感覚鈍麻	1 (5.0%)	0	0	0	0	0
錯感覚	0	0	0	0	1 (33.3%)	1 (33.3%)
筋骨格系および結合組織障害	6 (30.0%)	0	0	0	0	0
関節痛	2 (10.0%)	0	0	0	0	0
背部痛	1 (5.0%)	0	0	0	0	0
骨痛	1 (5.0%)	0	0	0	0	0
脊柱後弯症	1 (5.0%)	0	0	0	0	0
四肢痛	1 (5.0%)	0	0	0	0	0
血管障害	5 (25.0%)	4 (20.0%)	0	0	2 (66.7%)	1 (33.3%)
高血圧	2 (10.0%)	1 (5.0%)	0	0	2 (66.7%)	1 (33.3%)
潮紅	2 (10.0%)	2 (10.0%)	0	0	0	0
低血圧	2 (10.0%)	2 (10.0%)	0	0	0	0
皮膚および皮下組織障害	1 (5.0%)	0	2 (66.7%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
発疹	1 (5.0%)	0	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
そう痒症	0	0	1 (33.3%)	1 (33.3%)	0	0
皮脂欠乏性湿疹	0	0	0	0	0	0
紅斑	0	0	1 (33.3%)	0	0	0
心臓障害	3 (15.0%)	2 (10.0%)	1 (33.3%)	1 (33.3%)	0	0
頻脈	2 (10.0%)	2 (10.0%)	0	0	0	0
心房細動	1 (5.0%)	0	0	0	0	0
動悸	0	0	1 (33.3%)	1 (33.3%)	0	0
上室性期外収縮	1 (5.0%)	1 (5.0%)	0	0	0	0
免疫系障害	2 (10.0%)	2 (10.0%)	1 (33.3%)	1 (33.3%)	0	0
サイトカイン放出症候群	1 (5.0%)	1 (5.0%)	0	0	0	0
過敏症	1 (5.0%)	1 (5.0%)	1 (33.3%)	1 (33.3%)	0	0
代謝および栄養障害	2 (10.0%)	1 (5.0%)	0	0	1 (33.3%)	0
食欲減退	1 (5.0%)	0	0	0	0	0
酵素異常	1 (5.0%)	1 (5.0%)	0	0	0	0
高カルシウム血症	0	0	0	0	1 (33.3%)	0
低ナトリウム血症	1 (5.0%)	0	0	0	0	0
肝胆道系障害	1 (5.0%)	1 (5.0%)	0	0	1 (33.3%)	1 (33.3%)
肝機能異常	1 (5.0%)	1 (5.0%)	0	0	1 (33.3%)	1 (33.3%)
眼障害	1 (5.0%)	0	0	0	0	0
眼充血	1 (5.0%)	0	0	0	0	0

表 2.7.6.4-4 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 1，全投与解析対象集団］（続き）

	<4 mg/kg		4 mg/kg		8 mg/kg	
	Total	Related	Total	Related	Total	Related
傷害、中毒および処置合併症	1 (5.0%)	0	0	0	0	0
脊椎圧迫骨折	1 (5.0%)	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (5.0%)	0	0	0	0	0
皮膚良性新生物	1 (5.0%)	0	0	0	0	0
精神障害	0	0	0	0	0	0
錯乱状態	0	0	0	0	0	0
生殖系および乳房障害	0	0	0	0	0	0
前立腺炎	0	0	0	0	0	0

Keys: TEAE = treatment-emergent adverse event.
Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events were coded using MedDRA Version 17.0.

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	16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
Analysis set: all treated	3		3		32	
Total no. subjects with TEAEs	3 (100.0%)	1 (33.3%)	3 (100.0%)	3 (100.0%)	31 (96.9%)	28 (87.5%)
MedDRA system organ class/Preferred term						
腎および尿路障害	1 (33.3%)	0	1 (33.3%)	1 (33.3%)	16 (50.0%)	5 (15.6%)
蛋白尿	1 (33.3%)	0	1 (33.3%)	1 (33.3%)	15 (46.9%)	4 (12.5%)
頻尿	0	0	0	0	1 (3.1%)	0
腎機能障害	0	0	0	0	1 (3.1%)	1 (3.1%)
一般・全身障害および投与部位の状態	2 (66.7%)	1 (33.3%)	0	0	14 (43.8%)	11 (34.4%)
発熱	2 (66.7%)	1 (33.3%)	0	0	11 (34.4%)	7 (21.9%)
インフルエンザ様疾患	1 (33.3%)	1 (33.3%)	0	0	4 (12.5%)	4 (12.5%)
胸痛	0	0	0	0	2 (6.3%)	0
疲労	0	0	0	0	2 (6.3%)	2 (6.3%)
胸部不快感	0	0	0	0	1 (3.1%)	1 (3.1%)
末梢性浮腫	0	0	0	0	1 (3.1%)	0
胃腸障害	0	0	2 (66.7%)	1 (33.3%)	12 (37.5%)	5 (15.6%)
悪心	0	0	0	0	4 (12.5%)	3 (9.4%)
下痢	0	0	1 (33.3%)	0	3 (9.4%)	0
腹痛	0	0	0	0	2 (6.3%)	0
嘔吐	0	0	1 (33.3%)	1 (33.3%)	2 (6.3%)	1 (3.1%)
便秘	0	0	0	0	1 (3.1%)	0
口内乾燥	0	0	0	0	1 (3.1%)	1 (3.1%)
口唇浮腫	0	0	0	0	1 (3.1%)	1 (3.1%)
口腔内潰瘍形成	0	0	0	0	1 (3.1%)	0
食道炎	0	0	0	0	1 (3.1%)	0
感染症および寄生虫症	2 (66.7%)	0	1 (33.3%)	1 (33.3%)	11 (34.4%)	1 (3.1%)
鼻咽頭炎	0	0	1 (33.3%)	1 (33.3%)	3 (9.4%)	1 (3.1%)
肺炎	1 (33.3%)	0	0	0	2 (6.3%)	0
胃腸炎	0	0	0	0	1 (3.1%)	0
帯状疱疹	0	0	0	0	1 (3.1%)	0
メタニューモウイルス感染	0	0	0	0	1 (3.1%)	0
副鼻腔炎	0	0	0	0	1 (3.1%)	0
上気道感染	1 (33.3%)	0	0	0	1 (3.1%)	0
尿路感染	0	0	1 (33.3%)	0	1 (3.1%)	0
ウイルス感染	0	0	0	0	1 (3.1%)	0
外陰部腟カンジダ症	0	0	0	0	1 (3.1%)	0

表 2.7.6.4-4 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 1，全投与解析対象集団］（続き）

	16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
呼吸器、胸郭および縦隔障害	0	0	2 (66.7%)	2 (66.7%)	11 (34.4%)	7 (21.9%)
咳嗽	0	0	1 (33.3%)	1 (33.3%)	6 (18.8%)	2 (6.3%)
気管支痙攣	0	0	1 (33.3%)	1 (33.3%)	2 (6.3%)	2 (6.3%)
発声障害	0	0	0	0	1 (3.1%)	1 (3.1%)
呼吸困難	0	0	0	0	1 (3.1%)	1 (3.1%)
鼻閉	0	0	1 (33.3%)	1 (33.3%)	1 (3.1%)	1 (3.1%)
アレルギー性鼻炎	0	0	0	0	1 (3.1%)	1 (3.1%)
臨床検査	0	0	0	0	10 (31.3%)	7 (21.9%)
心電図ＱＴ延長	0	0	0	0	5 (15.6%)	3 (9.4%)
遊離ヘモグロビン陽性	0	0	0	0	5 (15.6%)	4 (12.5%)
血中クレアチンホスホキナーゼ増加	0	0	0	0	1 (3.1%)	1 (3.1%)
ハプトグロビン減少	0	0	0	0	1 (3.1%)	1 (3.1%)
リンパ球数減少	0	0	0	0	1 (3.1%)	1 (3.1%)
血液およびリンパ系障害	0	0	0	0	9 (28.1%)	8 (25.0%)
貧血	0	0	0	0	4 (12.5%)	4 (12.5%)
溶血	0	0	0	0	3 (9.4%)	3 (9.4%)
単球減少症	0	0	0	0	3 (9.4%)	3 (9.4%)
血小板減少症	0	0	0	0	3 (9.4%)	2 (6.3%)
リンパ球減少症	0	0	0	0	2 (6.3%)	2 (6.3%)
好中球減少症	0	0	0	0	1 (3.1%)	1 (3.1%)
神経系障害	0	0	0	0	8 (25.0%)	6 (18.8%)
浮動性めまい	0	0	0	0	3 (9.4%)	2 (6.3%)
頭痛	0	0	0	0	2 (6.3%)	1 (3.1%)
末梢性感覚ニューロパチー	0	0	0	0	2 (6.3%)	2 (6.3%)
感覚鈍麻	0	0	0	0	1 (3.1%)	0
錯感覚	0	0	0	0	1 (3.1%)	1 (3.1%)
筋骨格系および結合組織障害	0	0	1 (33.3%)	0	7 (21.9%)	0
関節痛	0	0	0	0	2 (6.3%)	0
背部痛	0	0	1 (33.3%)	0	2 (6.3%)	0
骨痛	0	0	0	0	1 (3.1%)	0
脊柱後弯症	0	0	0	0	1 (3.1%)	0
四肢痛	0	0	0	0	1 (3.1%)	0
血管障害	0	0	0	0	7 (21.9%)	5 (15.6%)
高血圧	0	0	0	0	4 (12.5%)	2 (6.3%)
潮紅	0	0	0	0	2 (6.3%)	2 (6.3%)
低血圧	0	0	0	0	2 (6.3%)	2 (6.3%)
皮膚および皮下組織障害	2 (66.7%)	1 (33.3%)	0	0	6 (18.8%)	3 (9.4%)
発疹	0	0	0	0	3 (9.4%)	2 (6.3%)
そう痒症	1 (33.3%)	1 (33.3%)	0	0	2 (6.3%)	2 (6.3%)
皮脂欠乏性湿疹	1 (33.3%)	0	0	0	1 (3.1%)	0
紅斑	0	0	0	0	1 (3.1%)	0
心臓障害	0	0	0	0	4 (12.5%)	3 (9.4%)
頻脈	0	0	0	0	2 (6.3%)	2 (6.3%)
心房細動	0	0	0	0	1 (3.1%)	0
動悸	0	0	0	0	1 (3.1%)	1 (3.1%)
上室性期外収縮	0	0	0	0	1 (3.1%)	1 (3.1%)
免疫系障害	1 (33.3%)	1 (33.3%)	0	0	4 (12.5%)	4 (12.5%)
サイトカイン放出症候群	1 (33.3%)	1 (33.3%)	0	0	2 (6.3%)	2 (6.3%)
過敏症	0	0	0	0	2 (6.3%)	2 (6.3%)
代謝および栄養障害	0	0	0	0	3 (9.4%)	1 (3.1%)
食欲減退	0	0	0	0	1 (3.1%)	0
酵素異常	0	0	0	0	1 (3.1%)	1 (3.1%)
高カルシウム血症	0	0	0	0	1 (3.1%)	0
低ナトリウム血症	0	0	0	0	1 (3.1%)	0

表 2.7.6.4-4 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 1，全投与解析対象集団］（続き）

	16 mg/kg		24 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
肝胆道系障害	0	0	0	0	2 (6.3%)	2 (6.3%)
肝機能異常	0	0	0	0	2 (6.3%)	2 (6.3%)
眼障害	0	0	0	0	1 (3.1%)	0
眼充血	0	0	0	0	1 (3.1%)	0
傷害、中毒および処置合併症	0	0	0	0	1 (3.1%)	0
脊椎圧迫骨折	0	0	0	0	1 (3.1%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0	1 (3.1%)	0
皮膚良性新生物	0	0	0	0	1 (3.1%)	0
精神障害	1 (33.3%)	0	0	0	1 (3.1%)	0
錯乱状態	1 (33.3%)	0	0	0	1 (3.1%)	0
生殖系および乳房障害	0	0	1 (33.3%)	0	1 (3.1%)	0
前立腺炎	0	0	1 (33.3%)	0	1 (3.1%)	0

Keys: TEAE = treatment-emergent adverse event.
Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events were coded using MedDRA Version 17.0.

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表 2.7.6.4-5 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 2，全投与解析対象集団］

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
Analysis set: all treated	30		42		72	
Total no. subjects with TEAEs	30 (100.0%)	27 (90.0%)	41 (97.6%)	33 (78.6%)	71 (98.6%)	60 (83.3%)
MedDRA system organ class/Preferred term						
呼吸器、胸郭および縦隔障害	23 (76.7%)	20 (66.7%)	28 (66.7%)	26 (61.9%)	51 (70.8%)	46 (63.9%)
アレルギー性鼻炎	12 (40.0%)	12 (40.0%)	10 (23.8%)	10 (23.8%)	22 (30.6%)	22 (30.6%)
咳嗽	6 (20.0%)	3 (10.0%)	9 (21.4%)	6 (14.3%)	15 (20.8%)	9 (12.5%)
呼吸困難	8 (26.7%)	4 (13.3%)	6 (14.3%)	2 (4.8%)	14 (19.4%)	6 (8.3%)
鼻閉	4 (13.3%)	2 (6.7%)	6 (14.3%)	4 (9.5%)	10 (13.9%)	6 (8.3%)
口腔咽頭痛	2 (6.7%)	0	5 (11.9%)	0	7 (9.7%)	0
アレルギー性喉頭炎	3 (10.0%)	3 (10.0%)	1 (2.4%)	1 (2.4%)	4 (5.6%)	4 (5.6%)
咽喉刺激感	1 (3.3%)	0	3 (7.1%)	2 (4.8%)	4 (5.6%)	2 (2.8%)
湿性咳嗽	3 (10.0%)	0	0	0	3 (4.2%)	0
咽喉絞扼感	0	0	3 (7.1%)	3 (7.1%)	3 (4.2%)	3 (4.2%)
鼻出血	2 (6.7%)	0	0	0	2 (2.8%)	0
副鼻腔うっ血	0	0	2 (4.8%)	0	2 (2.8%)	0
アレルギー性咳嗽	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
気管支痙攣	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
慢性閉塞性肺疾患	0	0	1 (2.4%)	0	1 (1.4%)	0
低酸素症	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
喉頭の炎症	1 (3.3%)	0	0	0	1 (1.4%)	0
鼻部障害	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
鼻漏	1 (3.3%)	0	0	0	1 (1.4%)	0
くしゃみ	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
上気道咳症候群	1 (3.3%)	0	0	0	1 (1.4%)	0
一般・全身障害および投与部位の状態	22 (73.3%)	9 (30.0%)	27 (64.3%)	11 (26.2%)	49 (68.1%)	20 (27.8%)
疲労	13 (43.3%)	7 (23.3%)	17 (40.5%)	6 (14.3%)	30 (41.7%)	13 (18.1%)
発熱	13 (43.3%)	3 (10.0%)	7 (16.7%)	1 (2.4%)	20 (27.8%)	4 (5.6%)
悪寒	3 (10.0%)	1 (3.3%)	5 (11.9%)	4 (9.5%)	8 (11.1%)	5 (6.9%)
胸痛	1 (3.3%)	0	4 (9.5%)	1 (2.4%)	5 (6.9%)	1 (1.4%)

表 2.7.6.4-5 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 2，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
末梢性浮腫	3 (10.0%)	1 (3.3%)	2 (4.8%)	0	5 (6.9%)	1 (1.4%)
疼痛	1 (3.3%)	1 (3.3%)	2 (4.8%)	0	3 (4.2%)	1 (1.4%)
顔面浮腫	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
インフルエンザ様疾患	1 (3.3%)	1 (3.3%)	1 (2.4%)	0	2 (2.8%)	1 (1.4%)
非心臓性胸痛	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
無力症	1 (3.3%)	0	0	0	1 (1.4%)	0
胸部不快感	1 (3.3%)	0	0	0	1 (1.4%)	0
局所腫脹	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
倦怠感	0	0	1 (2.4%)	0	1 (1.4%)	0
感染症および寄生虫症	21 (70.0%)	6 (20.0%)	27 (64.3%)	5 (11.9%)	48 (66.7%)	11 (15.3%)
鼻咽頭炎	7 (23.3%)	0	10 (23.8%)	0	17 (23.6%)	0
上気道感染	8 (26.7%)	5 (16.7%)	7 (16.7%)	1 (2.4%)	15 (20.8%)	6 (8.3%)
帯状疱疹	4 (13.3%)	1 (3.3%)	2 (4.8%)	2 (4.8%)	6 (8.3%)	3 (4.2%)
肺炎	3 (10.0%)	0	3 (7.1%)	1 (2.4%)	6 (8.3%)	1 (1.4%)
口腔カンジダ症	3 (10.0%)	1 (3.3%)	1 (2.4%)	0	4 (5.6%)	1 (1.4%)
感染	1 (3.3%)	0	2 (4.8%)	0	3 (4.2%)	0
尿路感染	2 (6.7%)	0	1 (2.4%)	0	3 (4.2%)	0
カンジダ感染	1 (3.3%)	0	1 (2.4%)	1 (2.4%)	2 (2.8%)	1 (1.4%)
膀胱炎	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
単純ヘルペス	0	0	2 (4.8%)	0	2 (2.8%)	0
ＲＳウイルス感染	2 (6.7%)	0	0	0	2 (2.8%)	0
鼻炎	0	0	2 (4.8%)	0	2 (2.8%)	0
副鼻腔炎	0	0	2 (4.8%)	0	2 (2.8%)	0
菌血症	1 (3.3%)	0	0	0	1 (1.4%)	0
気管支炎	0	0	1 (2.4%)	0	1 (1.4%)	0
結膜炎	0	0	1 (2.4%)	0	1 (1.4%)	0
サイトメガロウイルス性脈絡網膜炎	0	0	1 (2.4%)	0	1 (1.4%)	0
耳感染	1 (3.3%)	0	0	0	1 (1.4%)	0
真菌感染	1 (3.3%)	0	0	0	1 (1.4%)	0
胃腸炎	1 (3.3%)	0	0	0	1 (1.4%)	0
真菌性消化管感染	1 (3.3%)	0	0	0	1 (1.4%)	0
インフルエンザ	1 (3.3%)	0	0	0	1 (1.4%)	0
肺感染	1 (3.3%)	0	0	0	1 (1.4%)	0
口腔真菌感染	0	0	1 (2.4%)	0	1 (1.4%)	0
咽頭炎	0	0	1 (2.4%)	0	1 (1.4%)	0
細菌性尿路感染	1 (3.3%)	0	0	0	1 (1.4%)	0
水痘	0	0	1 (2.4%)	0	1 (1.4%)	0
ウイルス性上気道感染	0	0	1 (2.4%)	0	1 (1.4%)	0
筋骨格系および結合組織障害	20 (66.7%)	3 (10.0%)	24 (57.1%)	3 (7.1%)	44 (61.1%)	6 (8.3%)
背部痛	3 (10.0%)	0	10 (23.8%)	1 (2.4%)	13 (18.1%)	1 (1.4%)
骨痛	6 (20.0%)	0	5 (11.9%)	0	11 (15.3%)	0
関節痛	4 (13.3%)	0	5 (11.9%)	0	9 (12.5%)	0
筋肉痛	6 (20.0%)	2 (6.7%)	1 (2.4%)	1 (2.4%)	7 (9.7%)	3 (4.2%)
筋骨格系胸痛	3 (10.0%)	0	3 (7.1%)	0	6 (8.3%)	0
筋骨格痛	2 (6.7%)	0	3 (7.1%)	0	5 (6.9%)	0
四肢痛	0	0	5 (11.9%)	0	5 (6.9%)	0
骨侵食	0	0	1 (2.4%)	0	1 (1.4%)	0
骨病変	0	0	1 (2.4%)	0	1 (1.4%)	0
四肢不快感	1 (3.3%)	0	0	0	1 (1.4%)	0
筋痙縮	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
筋骨格不快感	0	0	1 (2.4%)	0	1 (1.4%)	0
筋骨格硬直	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
ミオパチー	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)

表 2.7.6.4-5 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 2，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
頚部痛	0	0	1 (2.4%)	0	1 (1.4%)	0
骨壊死	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
骨粗鬆症性骨折	1 (3.3%)	0	0	0	1 (1.4%)	0
病的骨折	0	0	1 (2.4%)	0	1 (1.4%)	0
脊柱管狭窄症	0	0	1 (2.4%)	0	1 (1.4%)	0
脊椎痛	0	0	1 (2.4%)	0	1 (1.4%)	0
胃腸障害	16 (53.3%)	8 (26.7%)	20 (47.6%)	6 (14.3%)	36 (50.0%)	14 (19.4%)
下痢	9 (30.0%)	2 (6.7%)	6 (14.3%)	1 (2.4%)	15 (20.8%)	3 (4.2%)
悪心	4 (13.3%)	3 (10.0%)	9 (21.4%)	5 (11.9%)	13 (18.1%)	8 (11.1%)
便秘	4 (13.3%)	1 (3.3%)	4 (9.5%)	0	8 (11.1%)	1 (1.4%)
嘔吐	5 (16.7%)	5 (16.7%)	1 (2.4%)	1 (2.4%)	6 (8.3%)	6 (8.3%)
消化不良	3 (10.0%)	3 (10.0%)	1 (2.4%)	0	4 (5.6%)	3 (4.2%)
口内炎	3 (10.0%)	1 (3.3%)	1 (2.4%)	0	4 (5.6%)	1 (1.4%)
アフタ性口内炎	2 (6.7%)	0	0	0	2 (2.8%)	0
腹痛	0	0	1 (2.4%)	0	1 (1.4%)	0
上腹部痛	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
憩室	0	0	1 (2.4%)	0	1 (1.4%)	0
口内乾燥	1 (3.3%)	0	0	0	1 (1.4%)	0
嚥下障害	1 (3.3%)	0	0	0	1 (1.4%)	0
胃炎	0	0	1 (2.4%)	0	1 (1.4%)	0
胃食道逆流性疾患	0	0	1 (2.4%)	0	1 (1.4%)	0
舌炎	0	0	1 (2.4%)	0	1 (1.4%)	0
舌痛	1 (3.3%)	0	0	0	1 (1.4%)	0
血便排泄	0	0	1 (2.4%)	0	1 (1.4%)	0
神経系障害	13 (43.3%)	6 (20.0%)	12 (28.6%)	2 (4.8%)	25 (34.7%)	8 (11.1%)
浮動性めまい	5 (16.7%)	2 (6.7%)	3 (7.1%)	0	8 (11.1%)	2 (2.8%)
頭痛	3 (10.0%)	1 (3.3%)	4 (9.5%)	1 (2.4%)	7 (9.7%)	2 (2.8%)
末梢性感覚ニューロパチー	5 (16.7%)	2 (6.7%)	0	0	5 (6.9%)	2 (2.8%)
味覚異常	2 (6.7%)	2 (6.7%)	0	0	2 (2.8%)	2 (2.8%)
傾眠	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
意識変容状態	0	0	1 (2.4%)	0	1 (1.4%)	0
知覚過敏	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
神経痛	0	0	1 (2.4%)	0	1 (1.4%)	0
錯感覚	0	0	1 (2.4%)	0	1 (1.4%)	0
下肢静止不能症候群	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
振戦	0	0	1 (2.4%)	0	1 (1.4%)	0
第６脳神経麻痺	1 (3.3%)	0	0	0	1 (1.4%)	0
皮膚および皮下組織障害	10 (33.3%)	5 (16.7%)	11 (26.2%)	2 (4.8%)	21 (29.2%)	7 (9.7%)
多汗症	3 (10.0%)	2 (6.7%)	2 (4.8%)	1 (2.4%)	5 (6.9%)	3 (4.2%)
発疹	4 (13.3%)	2 (6.7%)	1 (2.4%)	0	5 (6.9%)	2 (2.8%)
そう痒症	2 (6.7%)	1 (3.3%)	1 (2.4%)	0	3 (4.2%)	1 (1.4%)
接触性皮膚炎	0	0	2 (4.8%)	1 (2.4%)	2 (2.8%)	1 (1.4%)
寝汗	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
脱毛症	1 (3.3%)	0	0	0	1 (1.4%)	0
皮膚嚢腫	0	0	1 (2.4%)	0	1 (1.4%)	0
薬疹	0	0	1 (2.4%)	0	1 (1.4%)	0
湿疹	0	0	1 (2.4%)	0	1 (1.4%)	0
紅斑	0	0	1 (2.4%)	0	1 (1.4%)	0
乾癬	0	0	1 (2.4%)	0	1 (1.4%)	0
斑状丘疹状皮疹	1 (3.3%)	0	0	0	1 (1.4%)	0
血液およびリンパ系障害	5 (16.7%)	1 (3.3%)	10 (23.8%)	2 (4.8%)	15 (20.8%)	3 (4.2%)
血小板減少症	3 (10.0%)	0	3 (7.1%)	0	6 (8.3%)	0
貧血	2 (6.7%)	1 (3.3%)	3 (7.1%)	0	5 (6.9%)	1 (1.4%)
好中球減少症	0	0	5 (11.9%)	1 (2.4%)	5 (6.9%)	1 (1.4%)
白血球減少症	0	0	4 (9.5%)	2 (4.8%)	4 (5.6%)	2 (2.8%)

表 2.7.6.4-5 有害事象及び本剤と関連性がある有害事象
［GEN501 試験 Part 2，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
眼障害	9 (30.0%)	1 (3.3%)	5 (11.9%)	1 (2.4%)	14 (19.4%)	2 (2.8%)
霧視	2 (6.7%)	0	4 (9.5%)	1 (2.4%)	6 (8.3%)	1 (1.4%)
結膜出血	0	0	1 (2.4%)	0	1 (1.4%)	0
複視	1 (3.3%)	0	0	0	1 (1.4%)	0
眼乾燥	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
眼そう痒症	1 (3.3%)	0	0	0	1 (1.4%)	0
眼部腫脹	1 (3.3%)	0	0	0	1 (1.4%)	0
眼瞼機能障害	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
眼瞼下垂	1 (3.3%)	0	0	0	1 (1.4%)	0
眼瞼発疹	1 (3.3%)	0	0	0	1 (1.4%)	0
光視症	1 (3.3%)	0	0	0	1 (1.4%)	0
視力障害	1 (3.3%)	0	0	0	1 (1.4%)	0
硝子体浮遊物	1 (3.3%)	0	0	0	1 (1.4%)	0
代謝および栄養障害	3 (10.0%)	0	10 (23.8%)	2 (4.8%)	13 (18.1%)	2 (2.8%)
食欲減退	1 (3.3%)	0	4 (9.5%)	2 (4.8%)	5 (6.9%)	2 (2.8%)
高血糖	1 (3.3%)	0	4 (9.5%)	0	5 (6.9%)	0
低マグネシウム血症	0	0	2 (4.8%)	0	2 (2.8%)	0
高カルシウム血症	1 (3.3%)	0	0	0	1 (1.4%)	0
低カリウム血症	0	0	1 (2.4%)	0	1 (1.4%)	0
低ナトリウム血症	0	0	1 (2.4%)	0	1 (1.4%)	0
ビタミンＢ１２欠乏	0	0	1 (2.4%)	0	1 (1.4%)	0
精神障害	5 (16.7%)	0	8 (19.0%)	2 (4.8%)	13 (18.1%)	2 (2.8%)
不眠症	4 (13.3%)	0	4 (9.5%)	0	8 (11.1%)	0
不安	0	0	2 (4.8%)	1 (2.4%)	2 (2.8%)	1 (1.4%)
気分変化	0	0	2 (4.8%)	0	2 (2.8%)	0
激越	1 (3.3%)	0	0	0	1 (1.4%)	0
譫妄	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
うつ病	1 (3.3%)	0	0	0	1 (1.4%)	0
気分動揺	1 (3.3%)	0	0	0	1 (1.4%)	0
傷害、中毒および処置合併症	3 (10.0%)	0	5 (11.9%)	0	8 (11.1%)	0
肋骨骨折	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
骨挫傷	0	0	1 (2.4%)	0	1 (1.4%)	0
挫傷	1 (3.3%)	0	0	0	1 (1.4%)	0
裂傷	0	0	1 (2.4%)	0	1 (1.4%)	0
四肢外傷性切断	1 (3.3%)	0	0	0	1 (1.4%)	0
脊椎圧迫骨折	0	0	1 (2.4%)	0	1 (1.4%)	0
創傷	0	0	1 (2.4%)	0	1 (1.4%)	0
臨床検査	3 (10.0%)	1 (3.3%)	5 (11.9%)	3 (7.1%)	8 (11.1%)	4 (5.6%)
交差適合試験不適合	0	0	3 (7.1%)	3 (7.1%)	3 (4.2%)	3 (4.2%)
体重減少	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
血中クレアチンホスホキナーゼ増加	0	0	1 (2.4%)	0	1 (1.4%)	0
心電図異常Ｑ波	0	0	1 (2.4%)	0	1 (1.4%)	0
心拍数増加	1 (3.3%)	0	0	0	1 (1.4%)	0
国際標準比増加	1 (3.3%)	0	0	0	1 (1.4%)	0
リンパ球数減少	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
血管障害	4 (13.3%)	3 (10.0%)	4 (9.5%)	3 (7.1%)	8 (11.1%)	6 (8.3%)
高血圧	0	0	3 (7.1%)	2 (4.8%)	3 (4.2%)	2 (2.8%)
潮紅	1 (3.3%)	1 (3.3%)	1 (2.4%)	1 (2.4%)	2 (2.8%)	2 (2.8%)
ほてり	2 (6.7%)	1 (3.3%)	0	0	2 (2.8%)	1 (1.4%)
血腫	1 (3.3%)	1 (3.3%)	0	0	1 (1.4%)	1 (1.4%)
表在性静脈炎	0	0	1 (2.4%)	0	1 (1.4%)	0

表 2.7.6.4-5 有害事象及び本剤と関連性がある有害事象

［GEN501 試験 Part 2，全投与解析対象集団］（続き）

	8 mg/kg		16 mg/kg		Total	
	Total	Related	Total	Related	Total	Related
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (6.7%)	0	4 (9.5%)	0	6 (8.3%)	0
基底細胞癌	1 (3.3%)	0	2 (4.8%)	0	3 (4.2%)	0
肛門直腸ヒト乳頭腫ウイルス感染	0	0	1 (2.4%)	0	1 (1.4%)	0
皮膚癌	0	0	1 (2.4%)	0	1 (1.4%)	0
皮膚乳頭腫	1 (3.3%)	0	0	0	1 (1.4%)	0
心臓障害	0	0	3 (7.1%)	1 (2.4%)	3 (4.2%)	1 (1.4%)
心房粗動	0	0	1 (2.4%)	0	1 (1.4%)	0
動悸	0	0	1 (2.4%)	0	1 (1.4%)	0
洞性頻脈	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
耳および迷路障害	1 (3.3%)	0	2 (4.8%)	1 (2.4%)	3 (4.2%)	1 (1.4%)
耳痛	0	0	1 (2.4%)	0	1 (1.4%)	0
耳鳴	0	0	1 (2.4%)	1 (2.4%)	1 (1.4%)	1 (1.4%)
回転性めまい	1 (3.3%)	0	0	0	1 (1.4%)	0
腎および尿路障害	2 (6.7%)	0	1 (2.4%)	0	3 (4.2%)	0
排尿困難	0	0	1 (2.4%)	0	1 (1.4%)	0
腎機能障害	1 (3.3%)	0	0	0	1 (1.4%)	0
尿失禁	1 (3.3%)	0	0	0	1 (1.4%)	0
肝胆道系障害	0	0	2 (4.8%)	1 (2.4%)	2 (2.8%)	1 (1.4%)
肝機能異常	0	0	2 (4.8%)	1 (2.4%)	2 (2.8%)	1 (1.4%)
免疫系障害	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
アレルギー性浮腫	0	0	1 (2.4%)	0	1 (1.4%)	0
過敏症	1 (3.3%)	0	0	0	1 (1.4%)	0
生殖系および乳房障害	1 (3.3%)	0	1 (2.4%)	0	2 (2.8%)	0
血精液症	1 (3.3%)	0	0	0	1 (1.4%)	0
腟出血	0	0	1 (2.4%)	0	1 (1.4%)	0
先天性、家族性および遺伝性障害	0	0	1 (2.4%)	0	1 (1.4%)	0
あざ	0	0	1 (2.4%)	0	1 (1.4%)	0

Keys: TEAE = treatment-emergent adverse event.
Percentages are calculated with the number of subjects in each group as denominator.
Note: Adverse events were coded using MedDRA Version 17.0.

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2.7.6.4.4 個別症例の詳細

最終投与後 30 日以内の疾患進行以外の理由による死亡例の詳細経過を以下に示す。本剤と関連性がある重篤な有害事象の詳細経過は，治験総括報告書【CTD 5.3.5.2.2-1】及び 2015 年 6 月 30 日クリニカルカットオフ時の安全性更新情報【CTD 5.3.5.3.3】に示した。

2.7.6.4.4.1 最終投与後 30 日以内の死亡（疾患進行以外の理由による死亡）

(1) 被験者識別番号 501262

■ **Reasons for narrative selection:** Death within 30 days of last dose of daratumumab; Serious adverse events; AEs leading to daratumumab discontinuation; Infusion-related reactions, Grade 3 or 4

■ **Death within 30 days of last dose of Daratumumab**

Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Study Day of Last Exposure to Treatment	Date of Death	Study Day of Death	Cause of Death	Other Cause of Death
2014-05-09	2014-06-02	25.00	2014-06-14	37.00	ADVERSE EVENT	-

■ **Serious Adverse Events**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Outcome of Adverse Event
骨痛 (Bone pain)	2014-05-23/ 2014-05-28	15/ (6)	Y/ 3	Not related/ Dose not changed	Recovered/resolved
悪心 (Nausea)	2014-05-23/ 2014-05-28	15/ (6)	Y/ 2	Not related/ Dose not changed	Recovered/resolved
骨痛 (Bone pain)	2014-05-31/ 2014-06-01	23/ (2)	Y/ 3	Not related/ Dose not changed	Recovered/resolved

■ **Serious Adverse Events/AEs leading to Daratumumab Discontinuation**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Outcome of Adverse Event
肺炎 (Pneumonia)	2014-06-08/ 2014-06-14	31/ (7)	Y/ 5	Not related/ Drug withdrawn	Fatal

■ **Infusion-related Reactions (IRR), Grade 3 or 4**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Outcome of Adverse Event
高血圧 (Hypertension (IRR))	2014-05-09/ 2014-05-09	1/ (1)	N/ 3	Possible/probable/ Drug interrupted	Recovered/resolved
低酸素症 (Hypoxia (IRR))	2014-05-09/ 2014-05-09	1/ (1)	N/ 3	Possible/probable/ Drug interrupted	Recovered/resolved

■ **Other Adverse Events**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event/ End Date of Adverse Event	Study Day of Start of Adverse Event/ Duration (days)	Serious Event/ Standard Toxicity Grade	Causality/ Action Taken with Study Treatment	Outcome of Adverse Event
意識変容状態 (Altered sensorium)	2014-05-31/ 2014-06-01	23/ (2)	N/ 1	Not related/ Dose not changed	Recovered/resolved
背部痛 (Worsening back pain (IRR))	2014-05-09/ 2014-05-09	1/ (1)	N/ 1	Possible/probable/ Drug interrupted	Recovered/resolved with sequelae
胸痛 (Chest pain possibly due to haziness in lung fields)	2014-05-11/ 2014-05-12	3/ (2)	N/ 2	Not related/ Dose not changed	Recovered/resolved
悪寒 (Rigors (IRR))	2014-05-09/ 2014-05-09	1/ (1)	N/ 1	Possible/probable/ Drug interrupted	Recovered/resolved
便秘 (Constipation)	2014-05-31/ 2014-06-01	23/ (2)	N/ 2	Not related/ Dose not changed	Recovered/resolved
譫妄 (Delirium (IRR))	2014-05-09/ 2014-05-09	1/ (1)	N/ 1	Possible/probable/ Drug interrupted	Recovered/resolved
疲労 (Fatigue)	2014-05-29/ -	21/ -	N/ 2	Possible/probable/ Dose not changed	Not recovered/not resolved
悪心 (Nausea)	2014-05-31/ 2014-06-01	23/ (2)	N/ 2	Not related/ Dose not changed	Recovered/resolved
傾眠 (Somnolence)	2014-05-29/ 2014-06-02	21/ (5)	N/ 3	Not related/ Drug interrupted	Recovered/resolved

■ **Demographics and Baseline Characteristics**

□ Country: USA
□ Study site identifier: 50125
□ Race: White
□ Age(yrs): 6[redacted]
□ Sex: Male
□ Description of actual arm: Schedule E - 16mg/kg
□ Description of planned arm: Schedule E - 16mg/kg
□ Baseline weight(kg): 60.8
□ Baseline height(cm): 171.1
□ Baseline ecog score: 1

■ **Disposition Information**

□ Treatment discontinuation: 2014-06-02 Adverse Event

□ Study discontinuation: 2014-06-14 Adverse Event

■ **Summary of Study Medication**

Total dose received from full infusions (mg/kg)	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of treatment (months)
22.22	2014-05-09	2014-06-02	0.82

■ **NARRATIVE TEXT**

被験者 501262 は，6[redacted] 歳の白人男性で，2009 年 7 月 15 日に初めて病期 III 期の MM と診断され，本治験のコホート E（本剤を 16 mg/kg の用量で投与）に組み入れられた。本治験組入れ時の合併症は体重減少及び背部痛であった。ベースライン時の ECOG スコアは 1 であった。スクリーニング時の血清 M 蛋白は 3.1 g/dL，尿中 M 蛋白は 50 mg/24 時間であった。ベースライン時の骨髄生検で形質細胞は 0%であった。既往歴は虫垂切除，椎骨形成術（3 回），肺炎及び精管切除であった。

被験者は以下の合計 5 レジメンの前治療を受けていた。レジメン 1 はサリドマイド，クラリスロマイシン，デキサメタゾン，レナリドミド，メルファラン及び自家造血幹細胞移植，レジメン 2 はボルテゾミブ，シクロホスファミド及びデキサメタゾン，レジメン 3 はクラリスロマイシン，デキサメタゾン及びポマリドミド，レジメン 4 はボルテゾミブ，デキサメタゾン，レナリドミド

及びパノビノスタット，レジメン 5 はカルフィルゾミブであった。被験者は，レジメン 1 のサリドマイド，レジメン 2 のアルキル化剤，レジメン 3 のポマリドミド，並びにレジメン 4 のレナリドミド及びボルテゾミブに治療抵抗性を示した。

治験組入れ時の併用薬は，スクラルファート，フルドロコルチゾン酢酸エステル，バラシクロビル，ビタミン B 複合体，ヒドロコルチゾン，モルヒネ，オキシコドンであった。

被験者は，Visit 2 に本剤を（1000 mL ではなく）700 mL しか投与されておらず，治験実施計画書からの重大な逸脱として報告された。全量を投与できなかったのは，IRR のために，被験者が投与を受けていたクリニックの就業時間外に投与時間が延長したためであった。

2014 年 5 月 9 日（Day 1）に，**非重篤な有害事象として高血圧及び低酸素症（ともに Grade 3），背部痛，悪寒**及び**譫妄（いずれも Grade 1）が報告された**。治験担当医師は，これらの事象が IRR であり，本剤との因果関係を「関連あり」と判断した。被験者は，前投薬としてメチルプレドニゾロン，paracetamol 及びジフェンヒドラミンの投与を受けた後に，本剤の初回投与を受けた。本剤投与前のバイタルサインは，血圧 130/72 mm Hg，心拍数 89 拍/分（bpm），体温 36.8°C であった。本剤の持続静脈内投与開始から 60 分後に，上記の事象により投与を 90 分間一時中断した。これらの事象に対する治療として，ジフェンヒドラミン，ファモチジン，メチルプレドニゾロン及びペチジンを投与した。本剤投与後（投与終了から 10 分後）のバイタルサインは，体温 37.1°C，心拍数 95 bpm 及び血圧 129/87 mm Hg であった。すべての事象は発現日と同日に回復した。メチルプレドニゾロンを治験実施計画書に従って Day 2 及び Day 3 に投与した。被験者は本剤の追加投与を 1 回受けた。

Day 3 に，**非重篤な有害事象として Grade 2 の胸痛**が報告され，翌日回復した。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。本事象に対する本剤の処置は実施せず，治療も実施しなかった。

Day 15 に，**重篤な有害事象として Grade 3** の進行性**骨痛**及び **Grade 2 の悪心**が報告され，被験者は入院した。治験担当医師は，これらの事象と本剤との因果関係を「関連なし」と判断した。これらの事象に対する本剤の処置は実施しなかった。悪心に対する治療としてプロメタジンを，骨痛に対する治療として鎮痛薬（詳細不明）を投与した。これらの事象は Day 20 に回復した。

Day 21 に，**非重篤な有害事象として Grade 3 の傾眠**が報告されたため，本剤の投与を休薬した。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。治療としてメサドンを投与した。Day 23 に，**重篤な有害事象として Grade 3 の骨痛**の再発が報告された。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。本事象に対する本剤の処置は実施しなかった。骨痛は Day 24 に，傾眠は Day 25 に回復した。本剤の投与は Day 25 に減量して再開した。

Day 31 に，**重篤な有害事象として肺炎**が報告され，翌日，被験者は入院した。治験担当医師は，本事象と本剤との因果関係を「関連なし」と判断した。本事象のために本剤の投与を中止し，最終投与は Day 25 であった。静脈補液（詳細不明）による治療を行った。骨髄腫の進行及び合併症を考慮し，以降の医学的介入の中止が決定された。被験者は退院し，在宅ホスピスサービスを受けることとなった。被験者は，肺炎のため Day 37 に死亡した。

2.7.6.5　国内臨床第 I 相試験（MMY1002 試験，評価資料：5.3.5.2.3-1）

2.7.6.5.1　概要

2.7.6.5.1.1　計画

(1) 治験の標題

再発又は難治性の多発性骨髄腫（MM）を有する日本人患者を対象としたダラツムマブ（以下本剤）の臨床第 I 相試験

(2) 治験実施医療機関

国内 2 施設

(3) 公表文献（引用文献）

なし

(4) 治験実施期間

2014 年 4 月 ■日（最初の被験者の初回来院日）～2015 年 9 月 ■日（最後の被験者の最終観察日）

(5) 開発の相

第 I 相

(6) 目的

本治験の主要目的は，再発又は難治性の MM を有する日本人患者における本剤の安全性及び忍容性を検討することであった。副次目的は，本剤の薬物動態プロファイル及び本剤に対する抗体産生（免疫原性）を検討し，有効性を予備的に検討することであった。また，探索的目的は，本剤に対する治療反応性を予測するバイオマーカーを検討することであった。

(7) 治験方法

本治験は，再発又は難治性の MM を有する日本人患者を対象に本剤の安全性及び忍容性を評価する非盲検，非ランダム化，多施設共同，用量漸増，第 I 相試験であった。なお，再発の定義は，過去に minimal response（MR）以上の奏効があり，疾患進行が治療中止後 60 日を超えて認められ，サルベージ治療の開始が必要となったものとした。治療抵抗性の定義は，初回治療もしくはサルベージ治療に対して反応性がない又は治療中止後 60 日以内に疾患進行したものとした。本治験はスクリーニング期，治療期及び後観察期で構成され，その主な治験スケジュールを以下に示す。

スクリーニング期：

同意取得日から Day −1 までをスクリーニング期（最長 21 日間）とし，選択／除外基準に従い本治験登録のための被験者の適格性を確認した。

治療期：

本剤を Day 1（Week 0）から投与中止に至るまで非盲検で持続静脈内投与した。治療期は 2 つの投与期（第 1 期：投与頻度の高いレジメンで Week 0 から Week 9 まで，第 2 期：第 1 期に比べ投与頻度の低いレジメンで Week 10 から投与中止まで）で構成された。

第 1 期では，本剤を初回投与後 3 週間ウォッシュアウトし，続いて 1 週間隔で Week 8 まで 6 回投与した（計 7 回投与）。本剤初回投与開始時から 4 回目の投与開始直前までの約 5 週間を用量制限毒性（DLT）評価期間とした。DLT 評価期間では，本剤の単回投与後 3 週間及び以降の 1 週間隔で 2 回投与した際の忍容性を評価した。4 回目の投与開始前に被験者から再同意を取得した。

第 2 期では，28 日間（4 週間）を 1 サイクルとし，被験者はサイクルごとに本剤投与を受けた。Week 10 から Week 24 までは 2 週間隔（サイクル 1〜4 で計 8 回），続いてサイクル 5（Week 26）から投与中止まで，4 週間隔で本剤投与を受けた。

本治験では，本剤を 2 用量（8 及び 16 mg/kg）で評価した。2 用量を評価するため，被験者を 2 つのコホート（各コホート 3 例以上）に順に登録した。最初のコホートの被験者には本剤 8 mg/kg を投与し，安全性及び忍容性を確認後，次のコホートで本剤 16 mg/kg を投与した。治験期間中は本剤と関連性がある有害事象を管理するための投与延期を可能とした。また，第 2 期のみ投与延期後の用量調節を可能とした。

被験者は，疾患進行若しくは管理不能な有害事象が認められる，又はその他の中止基準に合致するまで本剤投与を継続した。

後観察期：

投与中止後の 8 週間を後観察期とし，本剤の最終投与後 8 週，被験者の死亡，追跡不能，同意撤回又は治験終了のいずれか早い時点までとした。

(8) 被験者数（計画時及び解析時）

計画時：6〜12 例（各コホート 3 例以上）を組み入れることとした。

登録時：9 例（8 mg/kg 群 4 例，16 mg/kg 群 5 例）が組み入れられた。

解析時：組み入れられた 9 例全例を本治験の解析対象とした。

(9) 診断及び主な組入れ基準

日本人の男性又は女性で，20 歳以上の再発又は難治性の MM 患者を対象とした。また，2 レジメン以上の MM に対する前治療歴があり，国際骨髄腫作業部会（IMWG）の診断規準に基づき症候性骨髄腫と診断され，血清又は尿の M 蛋白検査による測定可能病変を有する患者とした。

(10) 被験薬，用量及び投与方法，ロット番号

本剤は無色～淡黄色の液体で，持続静脈内投与用 6 mL バイアル（含有量 5 mL）中 20 mg/mL の濃度で提供された（ロット番号：[redacted]，[redacted]）。本剤を 2 用量（8 及び 16 mg/kg）で投与した。本剤の投与は 8 mg/kg から開始し，8 mg/kg 群の安全性及び忍容性を確認後に 16 mg/kg の投与を開始した。

(11) 対照薬，用量及び投与方法，ロット番号

該当なし

(12) 投与期間

治療期の第 1 期では，本剤を初回投与後 3 週間ウォッシュアウトし，以降は 1 週間隔で持続静脈内投与した［Week 0 から Week 8 まで（計 7 回投与）］。治療期の第 2 期では Week 10 から Week 24 までは 2 週間隔（計 8 回投与），以降は投与中止又は治験の参加中止に至るまで 4 週間隔で投与を継続した。

(13) 評価基準

薬物動態：

血清中 daratumumab 濃度を検討するため，血清中濃度-時間曲線下面積（AUC），クリアランス（CL），最高血清中濃度（C_{max}），血清中トラフ濃度（C_{trough}），消失半減期（$t_{1/2}$），最高血清中濃度到達時間（t_{max}）及び分布容積（V）を含む薬物動態パラメータをノンコンパートメント解析法により，初回投与後，実際の検体採取時点ごとに算出した。薬物動態評価用の静脈血液検体は，第 1 期の Day 1，4，8，15，22，29，36，43，50，57，60 及び 64，第 2 期のサイクル 1～4 の Day 1 及び 15，サイクル 5 の Day 1，投与中止時並びに後観察来院時に採取した。

免疫原性：

第 1 期の Day 1 及び後観察来院時に本剤に対する抗体を評価した。

バイオマーカー：

バイオマーカー［ナチュラルキラー（NK）細胞及び T 細胞］を評価した。バイオマーカー評価用の血液検体は，第 1 期の Day 1，8，15，22，29，43 及び 57，第 2 期のサイクル 1 及びサイクル 5 の Day 1～4 並びに投与中止時に採取した。

有効性：

有効性の評価は本治験の主要目的ではなかった。副次的有効性評価項目は，全奏効率（ORR），無増悪生存期間（PFS）及び観察期間とした。その他の副次的有効性評価項目は，奏効到達期間，奏効持続期間，無増悪期間（TTP）及び M 蛋白の評価とした。有効性の評価には IMWG の治療効果判定規準に基づく治療効果が含まれた。臨床的有用率［stringent complete response（sCR）＋ complete response（CR）＋ very good partial response（VGPR）＋ partial response（PR）＋ MR］及び ORR（PR 以上）を要約した。

安全性：

有害事象の発現割合，臨床検査値，バイタルサイン，身体所見，心電図，Eastern Cooperative Oncology Group（ECOG）の performance status スコア及び直接／間接クームス試験に基づき安全性を評価した。

DLT：

DLT は，DLT 評価期間中に発現した本剤と関連性がある有害事象のうち，治験実施計画書で規定した infusion related reaction（IRR），血液毒性又は非血液毒性に該当する事象と定義した。

(14)　統計手法

解析対象集団：本治験の評価には以下の解析対象集団を用いた。

- 全投与解析対象集団：本剤投与を 1 回以上受けた被験者で，明記しない限りすべての安全性及び有効性の解析に使用した。
- 奏効評価対象集団：本剤投与を 1 回以上受け，かつ治療期中にベースラインとの比較が可能な疾患評価を受けた被験者
- 薬物動態解析対象集団：本剤投与を 1 回以上受け，かつ治療期中に daratumumab 濃度測定用に採取した検体が 1 検体以上ある被験者
- 免疫原性解析対象集団：本剤投与を 1 回以上受け，かつ治療期中に本剤に対する抗体産生評価用に採取した検体が 1 検体以上ある被験者
- DLT 評価対象集団：全投与解析対象集団の中で用量漸増を決定するための DLT 評価が可能な被験者

解析計画：

- 薬物動態：各検体採取時点の血清中 daratumumab 濃度及び daratumumab の薬物動態パラメータを，記述統計量を用いて要約した。
- 免疫原性：本剤投与を 1 回以上受け，本剤に対する抗体検出に適した検体を有するすべての被験者について本剤に対する抗体の発現割合を要約した。
- バイオマーカー：NK 細胞（CD3−CD16+CD56+）数を来院時点ごとに要約した。
- 有効性：主な副次的有効性評価項目（ORR，PFS 及び観察期間）及びその他の副次的有効性評価項目（奏効到達期間，TTP 及び奏効持続期間）を用量別に要約した。全投与解析対象集団を用いた TTP と PFS の解析を除き，治療効果に関連したすべての解析には奏効評価対象集団を用いた。血清及び尿の M 蛋白（絶対値とベースラインからの変化率）について要約した。
- 安全性：安全性の解析では，全有害事象，死亡例，重篤な有害事象，その他の重要な有害事象（投与中止，投与延期，減量及び投与中断に至った有害事象）及び特に注目すべき有害事象（IRR 並びに感染症及び寄生虫症に分類された有害事象）について要約及び頻度集計を行った。臨床検査値は，クレアチニン，ヘモグロビン，血小板，白血球，好中球及びリンパ球について要約し，シフトテーブル及び時系列のプロット図を用いて示した。臨床

検査値異常は一覧表に示した。本剤の心電図に対する影響については，記述統計量及び頻度集計で評価した。その他の安全性データ（バイタルサイン，身体所見及び直接／間接クームス試験）はすべて一覧表又は表に示した。

2.7.6.5.1.2　結果

(1) 対象集団

スクリーニングが実施された 13 例中 9 例（8 mg/kg 群 4 例，16 mg/kg 群 5 例）が組み入れられ，本剤が投与された。8 mg/kg 群の安全性及び忍容性を確認後，本剤 16 mg/kg の投与を開始した。本剤が投与されたすべての被験者が本剤投与を中止した。本剤が投与された 9 例中 7 例（77.8%）は疾患進行，1 例（11.1%）は治験実施計画書からの逸脱，1 例（11.1%）は投薬規定不遵守のために本剤投与を中止した。

被験者の人口統計学的特性は，2 群間でほぼ同様であった。本剤が投与された 9 例中 5 例（55.6%）は女性，4 例（44.4%）は男性であった。年齢の中央値は 65 歳（範囲：47～73 歳）であった。ベースライン時点で，すべての被験者の ECOG の performance status スコアは 0 又は 1 であった。ほとんどの被験者（8/9 例，88.9%）の MM の病期は I 又は II 期であった。

投与期間の中央値は，全被験者では 5.6 カ月（範囲：0～10.6 カ月），このうち 8 mg/kg 群では 6.3 カ月（範囲：0.7～10.6 カ月），16 mg/kg 群では 2.4 カ月（範囲：0～9.5 カ月）であった。本剤が投与された 9 例中 4 例（44.4%）の投与日数は 183 日間以上であった。本剤の総投与量の中央値は，8 mg/kg 群では 127.1 mg/kg（範囲：16.3～182.1 mg/kg），16 mg/kg 群では 122.7 mg/kg（範囲：16.2～309.7 mg/kg）であった。

(2) 有効性

ORR（PR 以上）は，8 mg/kg 群では 25.0%（1/4 例），16 mg/kg 群では 60.0%（3/5 例）であった。ORR を達成した 4 例はすべて PR であった。Kaplan-Meier 法で推定した PFS の中央値は 8 mg/kg 群では 6.0 カ月，16 mg/kg 群では 9.5 カ月であった。本剤が投与された 9 例中 7 例（8 mg/kg 群 4 例全例，16 mg/kg 群 3/5 例）に疾患進行が認められ，16 mg/kg 群の 2 例は疾患進行に至る前に評価打ち切りとなった。観察期間の中央値は，8 mg/kg 群では 10.5 カ月（範囲：2.3～16.4 カ月），16 mg/kg 群では 9.9 カ月（範囲：1.7～13.2 カ月）であった。

8 mg/kg 群の奏効例 1 例の奏効到達期間は 2.3 カ月であった。16 mg/kg 群の奏効例 3 例の奏効到達期間の中央値は 1.8 カ月（範囲：1.2～1.9 カ月）であった。Kaplan-Meier 法で推定した 8 mg/kg 群の奏効例 1 例の奏効持続期間は 2.8 カ月，16 mg/kg 群の奏効例 3 例の奏効持続期間の中央値は 7.7 カ月であった。Kaplan-Meier 法で推定した TTP の中央値は，8 mg/kg 群では 6.0 カ月，16 mg/kg 群では 9.5 カ月であった。9 例中 5 例（55.6%）に血清 M 蛋白のベースラインからの減少が認められた。

(3) 安全性

有害事象：

本治験では，有害事象及び本剤と関連性がある有害事象が全例で発現した。死亡又は本剤の投与中止に至った有害事象はなかった。また，減量又は休薬に至った有害事象もなかった。いずれの用量でも DLT は認められなかった（DLT 評価対象集団：8 mg/kg 群 3 例，16 mg/kg 群 3 例）。

本剤が投与された 9 例全例（8 mg/kg 群 4 例，16 mg/kg 群 5 例）に血液関連の有害事象が発現した。発現割合が高かった血液関連の有害事象［基本語（PT）］は，リンパ球減少症（8 mg/kg 群 4 例，16 mg/kg 群 5 例），好中球減少症（8 mg/kg 群 2 例，16 mg/kg 群 5 例），白血球減少症（8 mg/kg 群 0 例，16 mg/kg 群 3 例）であった。発現割合が高かった本剤と関連性がある血液関連の有害事象（PT）は，リンパ球減少症（8 mg/kg 群 4 例，16 mg/kg 群 5 例），好中球減少症（8 mg/kg 群 0 例，16 mg/kg 群 5 例），白血球減少症（8 mg/kg 群 0 例，16 mg/kg 群 3 例）であった。有害事象の発現時期については，投与開始後 8 週間に多く，時間の経過（Week 8～24）とともに減少した。

Grade 3 以上の有害事象：

Grade 5 の有害事象は報告されなかった。発現割合が高かった Grade 3 又は 4 の有害事象（PT）は，リンパ球減少症（8 mg/kg 群 2 例，16 mg/kg 群 5 例），好中球減少症（8 mg/kg 群 0 例，16 mg/kg 群 4 例），白血球減少症（8 mg/kg 群 0 例，16 mg/kg 群 3 例）であった。

重篤な有害事象：

9 例中 3 例に重篤な有害事象が発現した。内訳は，血小板減少症が 8 mg/kg 群の 1 例，頭痛及び発熱が 16 mg/kg 群の 1 例，肺炎が 16 mg/kg 群の 1 例であった。頭痛，発熱及び肺炎は回復し，いずれも治験担当医師は本剤との因果関係を「可能性小」と判断した。血小板減少症は回復しておらず，治験担当医師は本剤との因果関係を「関連なし」と判断した。

その他の重要な有害事象：

減量及び休薬に至った有害事象は報告されなかった。8 mg/kg 群の 1 例が非重篤な Grade 2 の上気道感染のため投与を延期した。有害事象による投与中断は，9 例中 2 例（22.2%，各投与群 1 例）に報告された。

特に注目すべき有害事象：

IRR を発現した 4 例（8 mg/kg 群 1/4 例，16 mg/kg 群 3/5 例）のうち，3 例（8 mg/kg 群 1 例，16 mg/kg 群 2 例）は本剤の初回投与後，16 mg/kg 群の 1 例は本剤の 2 回目投与後に IRR を発現した。すべての IRR は Grade 1 又は 2 であった。

感染症及び寄生虫症に分類される有害事象（鼻咽頭炎，膀胱炎，咽頭炎，肺炎，上気道感染及びアデノイド咽頭炎）が 9 例中 5 例（55.6%，8 mg/kg 群 2/4 例，16 mg/kg 群 3/5 例）に発現した。当該 5 例中 16 mg/kg 群の 1 例は重篤な有害事象である Grade 3 の肺炎を発現した。肺炎はその後回復し，治験担当医師は本剤との因果関係を「可能性小」と判断した。

臨床検査値：

9 例中 8 例（88.9%，8 mg/kg 群 3/4 例，16 mg/kg 群 5 例全例）に Grade 3 又は 4 の血液関連の有害事象が発現した。

その他の安全性に関する所見：

本治験では本剤の用量（8 及び 16 mg/kg）とバイタルサイン異常の発現割合との間に一定の傾向は認められなかった。QTcF 若しくは QTcB>500 msec の被験者，QTcF 若しくは QTcB のベースラインからの変化量>60 msec の被験者又は臨床的に重要な心電図異常が認められた被験者はいなかった。間接クームス試験では，9 例中 8 例（88.9%，8 mg/kg 群 4 例全例，16 mg/kg 群 4/5 例）がベースラインで陰性であったが，本剤初回投与後 5 時間以内の時点で陽性を呈した。本剤による血液適合性検査の干渉が，臨床上，輸血処置の判断に影響することはなかった。

(4) 薬物動態，免疫原性及びバイオマーカー

薬物動態：

本剤 16 mg/kg の初回投与後の daratumumab の平均 C_{max} は，8 mg/kg 投与後に比べ約 2～3 倍高かった。16 mg/kg 群は 8 mg/kg 群と比較して平均 $t_{1/2}$ は延長し（8 mg/kg 群 68.163 時間，16 mg/kg 群 407.379 時間），平均 CL 値は低下した（8 mg/kg 群 0.678 mL/h/kg，16 mg/kg 群 0.247 mL/h/kg）。本剤 16 mg/kg 投与レジメンにおいて，1 週間隔で本剤を投与されている間は daratumumab の蓄積が続き，投与間隔が 2 週間，その後 4 週間と長くなるに従い，daratumumab 濃度は徐々に低下した。

免疫原性：

本剤を投与した 9 例全例（8 mg/kg 群 4 例，16 mg/kg 群 5 例）に本剤に対する抗体検査が実施された。本剤に対する抗体陽性を呈した被験者はいなかった。

バイオマーカー：

総 NK 細胞数の顕著な減少が Day 8 に 8 及び 16 mg/kg の両群で認められた。この減少は奏効例か否かにかかわらず，治療期中継続して認められた。

2.7.6.5.1.3 結論

- 本治験では，再発又は難治性の MM を有する日本人患者における本剤 8 及び 16 mg/kg の安全性及び忍容性が確認された。
  - DLT は認められなかった。
  - 検討した用量では，死亡又は本剤の投与中止に至った有害事象はなかった。Grade 3 又は 4 の有害事象は，貧血及び血小板減少症（両事象ともに治験担当医師は本剤との因果関係を「関連なし」と判断した）を除き，すべて回復した。
  - IRR はすべて Grade 1 又は 2 であり一過性であった。
  - QTcF 若しくは QTcB>500 msec の被験者，QTcF 若しくは QTcB のベースラインからの変化量>60 msec の被験者又は臨床的に重要な心電図異常が認められた被験者はいなかった。
  - 臨床上での輸血処置の判断に影響するような，本剤による血液適合性検査の干渉は報告されなかった。

- 本剤 16 mg/kg 投与レジメンにおいて，1 週間隔で本剤を投与されている間は daratumumab の蓄積が続き，投与間隔が 2 週間，その後 4 週間と長くなるに従い，daratumumab 濃度は徐々に低下した。初回投与後の daratumumab の消失は非線形の薬物動態特性を示した。
- 本剤に対する抗体の発現は認められず，本剤の免疫原性リスクは低いことが示唆された。
- 全体の ORR は 44.4%（4/9 例）で，8 mg/kg 群では 25.0%（1/4 例），16 mg/kg 群では 60.0%（3/5 例）であった。
- 本剤投与後に総 NK 細胞数の減少が両群で認められた。この結果から NK 細胞は CD38 を発現することが裏付けられた。

結論として，本治験の結果から，再発又は難治性の MM を有する日本人患者の治療において，本剤が良好なリスクベネフィットプロファイルを有することが示された。

2.7.6.5.2 有害事象

因果関係を問わない有害事象及び本剤と関連性がある有害事象を表 2.7.6.5-1 に示す。

表 2.7.6.5-1 有害事象及び本剤と関連性がある有害事象

［MMY1002 試験，全投与解析対象集団］

	TEAEs			Drug Related TEAEs (Study Drug)[a]		
	8 mg/kg	16 mg/kg	All groups	8 mg/kg	16 mg/kg	All groups
Analysis set: All Treated Analysis Population	4	5	9	4	5	9
Number of subjects with any TEAEs	4 (100.0%)	5 (100.0%)	9 (100.0%)	4 (100.0%)	5 (100.0%)	9 (100.0%)
MedDRA system organ class/preferred term						
感染症および寄生虫症	2 (50.0%)	3 (60.0%)	5 (55.6%)	1 (25.0%)	3 (60.0%)	4 (44.4%)
鼻咽頭炎	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	0	0
膀胱炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
咽頭炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
肺炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
上気道感染	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
アデノイド咽頭炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
血液およびリンパ系障害	4 (100.0%)	5 (100.0%)	9 (100.0%)	4 (100.0%)	5 (100.0%)	9 (100.0%)
リンパ球減少症	4 (100.0%)	5 (100.0%)	9 (100.0%)	4 (100.0%)	5 (100.0%)	9 (100.0%)
好中球減少症	2 (50.0%)	5 (100.0%)	7 (77.8%)	0	5 (100.0%)	5 (55.6%)
白血球減少症	0	3 (60.0%)	3 (33.3%)	0	3 (60.0%)	3 (33.3%)
貧血	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	1 (20.0%)	1 (11.1%)
血小板減少症	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	1 (20.0%)	1 (11.1%)
代謝および栄養障害	1 (25.0%)	2 (40.0%)	3 (33.3%)	1 (25.0%)	0	1 (11.1%)
高カリウム血症	0	1 (20.0%)	1 (11.1%)	0	0	0
低リン酸血症	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
高脂血症	0	1 (20.0%)	1 (11.1%)	0	0	0
神経系障害	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
頭痛	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
呼吸器、胸郭および縦隔障害	0	2 (40.0%)	2 (22.2%)	0	1 (20.0%)	1 (11.1%)
低酸素症	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
アレルギー性鼻炎	0	1 (20.0%)	1 (11.1%)	0	0	0
口腔咽頭痛	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
胃腸障害	1 (25.0%)	1 (20.0%)	2 (22.2%)	0	0	0
便秘	0	1 (20.0%)	1 (11.1%)	0	0	0
悪心	1 (25.0%)	0	1 (11.1%)	0	0	0
皮膚および皮下組織障害	2 (50.0%)	0	2 (22.2%)	2 (50.0%)	0	2 (22.2%)
そう痒症	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
発疹	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
筋骨格系および結合組織障害	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
骨炎	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
腎および尿路障害	1 (25.0%)	0	1 (11.1%)	0	0	0
排尿困難	1 (25.0%)	0	1 (11.1%)	0	0	0
一般・全身障害および投与部位の状態	1 (25.0%)	3 (60.0%)	4 (44.4%)	1 (25.0%)	3 (60.0%)	4 (44.4%)
発熱	1 (25.0%)	3 (60.0%)	4 (44.4%)	1 (25.0%)	3 (60.0%)	4 (44.4%)
悪寒	0	1 (20.0%)	1 (11.1%)	0	1 (20.0%)	1 (11.1%)
臨床検査	1 (25.0%)	1 (20.0%)	2 (22.2%)	1 (25.0%)	0	1 (11.1%)
Ｃ－反応性蛋白増加	1 (25.0%)	0	1 (11.1%)	1 (25.0%)	0	1 (11.1%)
体重減少	0	1 (20.0%)	1 (11.1%)	0	0	0

Key: TEAEs = treatment-emergent adverse events
Note: Adverse Events are coded using MedDRA 18.0.
[a] Adverse events whose causal relationship to the investigational medication were judged as ("possible", "probable", or "very likely") by the investigator.

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2.7.6.5.3 個別症例の詳細

治験期間中の死亡は認められなかった。本剤と関連性がある重篤な有害事象の詳細経過を以下に示す。本剤と関連性がない重篤な有害事象の詳細経過は，治験総括報告書【CTD 5.3.5.2.3-1】に示した。

2.7.6.5.3.1 本剤と関連性がある重篤な有害事象（日本人）

(1) 被験者識別番号 810103

■ **REASON FOR NARRATIVE SELECTION**

Serious adverse events

■ **Serious Adverse Events**

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Trtmnt Given Outcome of Adverse Event
頭痛 (Headache)	2014-08-28 2014-09-01	24 5	Y 2	Possible Dose not changed	Y Recovered/resolved
発熱 (Fever)	2014-08-30 2014-09-25	26 27	Y 1	Possible Dose not changed	N Recovered/resolved

■ **Demographics and Baseline Characteristics**

- □ Country: JPN
- □ Site no.: JP00053
- □ Race: Asian
- □ Age (yrs): 7[redacted]
- □ Sex: Female
- □ Dose level received: 16 mg/kg
- □ Dose level planned: 16 mg/kg
- □ Baseline weight (kg): 43.9
- □ Baseline height (cm): 143.8
- □ Baseline ecog: 1

■ **Disposition Information**

- □ Treatment discontinuation: 2015-04-28 Progressive Disease
- □ Study discontinuation: 2015-06-02 Progressive Disease

■ **Summary of Study Medication**

Total dose (mg/kg)	Start Date Treatment	End Date of Treatment	Treatment duration (months)
272.6	2014-08-05	2015-04-03	8.0

■ **Study Medication**

Dosing Start Date/Time Study Day of Dosing Start Date	Dosing End Date/Time Study Day of Dosing End Date	Dose per Administration (mg/kg)	Reason for Dose Adjustment
2014-08-05t10:16 1	2014-08-05t19:53 1	15.7	-
2014-08-05t12:16 1	2014-08-05t13:38 1	0.0	-
2014-08-26t10:16 22	2014-08-26t17:12 22	15.3	-
2014-09-02t10:10 29	2014-09-02t14:22 29	14.9	-
2014-09-09t10:16 36	2014-09-09t13:50 36	14.2	-
2014-09-16t12:11 43	2014-09-16t15:40 43	13.8	-
2014-09-24t11:00 51	2014-09-24t14:27 51	14.2	-
2014-09-30t10:29 57	2014-09-30t13:58 57	14.9	-
2014-10-14t11:56 71	2014-10-14t15:18 71	14.6	-

Dosing Start Date/Time Study Day of Dosing Start Date	Dosing End Date/Time Study Day of Dosing End Date	Dose per Administration (mg/kg)	Reason for Dose Adjustment
2014-10-28t11:25 85	2014-10-28t14:54 85	14.9	-
2014-11-11t11:40 99	2014-11-11t15:11 99	15.3	-
2014-11-25t11:56 113	2014-11-25t15:24 113	15.3	-
2014-12-09t11:56 127	2014-12-09t15:23 127	15.3	-
2014-12-24t12:49 142	2014-12-24t16:12 142	15.7	-
2015-01-06t12:22 155	2015-01-06t15:51 155	15.7	-
2015-01-20t12:02 169	2015-01-20t15:31 169	15.7	-
2015-02-03t12:33 183	2015-02-03t16:02 183	15.7	-
2015-03-06t11:57 214	2015-03-06t15:22 214	15.7	-
2015-04-03t12:24 242	2015-04-03t15:49 242	15.7	-

■ Pre-infusion Medications

Type of Medication/ Standardized Medication Name	Start Date/Time of Medication Study Day of Start of Medication	Total Daily Dose/Unit	Dosing Frequency per Interval/Route of Administration
Glucocorticoids/ methylprednisolone	2014-10-14t11:12 71	60 mg	Once/intravenous
Anilides/ paracetamol	2014-10-14t11:12 71	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-10-14t11:12 71	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-10-28t10:44 85	60 mg	Once/intravenous
Anilides/ paracetamol	2014-10-28t10:44 85	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-10-28t10:44 85	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-11-11t10:36 99	60 mg	Once/intravenous
Anilides/ paracetamol	2014-11-11t10:36 99	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-11-11t10:36 99	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-11-25t11:08 113	60 mg	Once/intravenous
Anilides/ paracetamol	2014-11-25t11:08 113	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-11-25t11:08 113	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-12-09t11:05 127	60 mg	Once/intravenous
Anilides/ paracetamol	2014-12-09t11:05 127	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-12-09t11:05 127	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-12-24t12:00 142	60 mg	Once/intravenous
Anilides/ paracetamol	2014-12-24t12:00 142	600 mg	Once/oral

Type of Medication/ Standardized Medication Name	Start Date/Time of Medication Study Day of Start of Medication	Total Daily Dose/Unit	Dosing Frequency per Interval/Route of Administration
Aminoalkyl ethers/ diphenhydramine	2014-12-24t12:00 142	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-01-06t11:31 155	60 mg	Once/intravenous
Anilides/ paracetamol	2015-01-06t11:31 155	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2015-01-06t11:31 155	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-01-20t11:17 169	60 mg	Once/intravenous
Anilides/ paracetamol	2015-01-20t11:17 169	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2015-01-20t11:17 169	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-02-03t11:40 183	60 mg	Once/intravenous
Anilides/ paracetamol	2015-02-03t11:40 183	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2015-02-03t11:40 183	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-03-06t11:07 214	60 mg	Once/intravenous
Anilides/ paracetamol	2015-03-06t11:07 214	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2015-03-06t11:07 214	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-04-03t11:36 242	60 mg	Once/intravenous
Anilides/ paracetamol	2015-04-03t11:36 242	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2015-04-03t11:36 242	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-08-05t09:34 1	100 mg	Once/intravenous
Anilides/ paracetamol	2014-08-05t09:35 1	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-08-05t09:35 1	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-08-26t09:32 22	100 mg	Once/intravenous
Anilides/ paracetamol	2014-08-26t09:33 22	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-08-26t09:33 22	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-02t09:27 29	60 mg	Once/intravenous
Anilides/ paracetamol	2014-09-02t09:30 29	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-09-02t09:30 29	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-09t09:35 36	60 mg	Once/intravenous
Anilides/ paracetamol	2014-09-09t09:35 36	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-09-09t09:35 36	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-16t11:28 43	60 mg	Once/intravenous

Type of Medication/ Standardized Medication Name	Start Date/Time of Medication Study Day of Start of Medication	Total Daily Dose/Unit	Dosing Frequency per Interval/Route of Administration
Anilides/ paracetamol	2014-09-16t11:29 43	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-09-16t11:29 43	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-24t10:14 51	60 mg	Once/intravenous
Anilides/ paracetamol	2014-09-24t10:15 51	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-09-24t10:15 51	50 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-30t09:45 57	60 mg	Once/intravenous
Anilides/ paracetamol	2014-09-30t09:45 57	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-09-30t09:45 57	50 mg	Once/oral

■ Post-infusion Medications

Type of Medication/ Standardized Medication Name	Start Date/Time of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose/Unit	Dosing Frequency per Interval/Route of Administration
Glucocorticoids/ methylprednisolone	2014-10-14 71	2014-10-15 72	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-10-28 85	2014-10-29 86	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-11-11 99	2014-11-12 100	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-11-25 113	2014-11-26 114	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-12-09 127	2014-12-10 128	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-12-24 142	2014-12-25 143	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-01-06 155	2015-01-07 156	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-01-20 169	2015-01-21 170	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-02-03 183	2015-02-04 184	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-03-06 214	2015-03-07 215	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2015-04-03 242	2015-04-04 243	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-08-05 1	2014-08-06 2	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-08-26 22	2014-08-27 23	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-02 29	2014-09-03 30	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-09 36	2014-09-10 37	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-16 43	2014-09-17 44	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-24 51	2014-09-25 52	20 mg	Once/oral
Glucocorticoids/ methylprednisolone	2014-09-30 57	2014-10-01 58	20 mg	Once/oral

■ Other Adverse Events

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Trtmnt Given Outcome of Adverse Event
悪寒 (Chills)	2014-08-05 2014-08-05	1 1	N 2	Probable Drug interrupted	Y Recovered/resolved
頭痛 (Headache)	2014-08-05 2014-08-05	1 1	N 2	Probable Drug interrupted	Y Recovered/resolved
低酸素症 (Hypoxia)	2014-08-05 2014-08-05	1 1	N 2	Probable Drug interrupted	Y Recovered/resolved
口腔咽頭痛 (Pain in the throat)	2014-08-05 2014-08-05	1 1	N 2	Probable Drug interrupted	Y Recovered/resolved
発熱 (Fever)	2014-08-05 2014-08-05	1 1	N 2	Probable Drug interrupted	Y Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-08-06 2014-08-08	2 3	N 4	Probable Dose not changed	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-08-08 2014-09-29	4 53	N 3	Probable Dose not changed	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-08-12 2014-08-20	8 9	N 3	Probable Dose not changed	N Recovered/resolved
好中球減少症 (Neutropenia)	2014-08-12 2014-09-01	8 21	N 2	Possible Dose not changed	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-08-25 2014-09-01	21 8	N 3	Probable Dose not changed	N Recovered/resolved
頭痛 (Headache)	2014-09-04 2014-10-17	31 44	N 2	Possible Dose not changed	Y Recovered/resolved
体重減少 (Weight loss)	2014-09-07 2014-09-29	34 23	N 1	Doubtful Dose not changed	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-09-29 -	56 -	N 2	Probable Dose not changed	N Not recovered/not resolved

■ Medical History

Dictionary-Derived Term (Reported Term for the Medical History)	Past or Current?
白内障 (Cataract)	Past
脊椎圧迫骨折 (Cervical vertebral conpression fracture)	Past
下痢 (Diarrhea)	Past
不眠症 (Insomnia)	Past
末梢性感覚ニューロパチー (Peripheral sensory neuropathy)	Past
脊椎圧迫骨折 (Thoracic spine compression fracture)	Past
脊椎圧迫骨折 (Cervical vertebral conpression fracture)	Current
下痢 (Diarrhea)	Current
不眠症 (Insomnia)	Current
末梢性感覚ニューロパチー (Peripheral sensory neuropathy)	Current

Dictionary-Derived Term (Reported Term for the Medical History)	Past or Current?
脊椎圧迫骨折 (Thoracic spine compression fracture)	Current

■ Disease History

Date of initial MM Diagnosis	Stage of MM	Staging Method
2003-01	1	International staging system

■ Concomitant Medication

Standardized Medication Name (Reported Name)	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Indication	Dose/Unit	Dosing Frequency per Interval/Route of Administration
Bactrim (Daiphen)	2014-08-05 1	Ongoing -	Prophylaxis	1 tablet	Qd/oral
Hydrocortisone (Hydrocortone)	2014-08-05 1	2014-08-05 1	Adverse event	100 mg	Qd/intravenous
Oxygen (Oxygen)	2014-08-05 1	2014-08-05 1	Adverse event	2000 ml	Once/nasal
Valaciclovir hydrochloride (Valtrex)	2014-08-05 1	Ongoing -	Prophylaxis	500 mg	Qd/oral
Febuxostat (Feburic)	2014-08-05 1	Ongoing -	Prophylaxis	20 mg	Qd/oral
Omeprazole (Omeprazole)	2014-08-05 1	Ongoing -	Prophylaxis	10 mg	Qd/oral
Rasburicase (Rasuritek)	2014-08-05 1	2014-08-05 1	Prophylaxis	7.5 mg	Qd/intravenous
Zoledronic acid (Zometa)	2014-08-06 2	2014-08-06 2	Other- m.m	4 mg	Qd/intravenous
Paracetamol (Calonal)	2014-08-28 24	2014-10-16 73	Adverse event	400 mg	Prn/oral
Levofloxacin (Cravit)	2014-09-06 33	2014-09-08 35	Other- suspected of infection	500 mg	Qd/oral

■ Prior MM Therapy

Line of Regimen	Standardized Medication Name (Reported Name)	Med. Start Date	Med. End Date	Dose/Unit/ Frequency	Number of Cycles	Best Response to Therapy	Date of Progression
1	Vincristine (Vincrisstine)	2003-01-08	2003-02-06	-/-/-	1	SD	-
1	Doxorubicin (Doxorubicin)	2003-01-08	2003-02-06	-/-/-	1	SD	-
1	Prednisolone (Prednisolone)	2003-01-08	2003-02-06	-/-/-	1	SD	-
2	Ranimustine (Cymerin)	2003-02-07	2003-03-19	-/-/-	-	SD	-
2	Vincristine sulfate (Oncovin)	2003-02-07	2003-03-19	-/-/-	-	SD	-
2	Melphalan (Alkeran)	2003-02-07	2003-03-19	-/-/-	-	SD	-
2	Dexamethasone (Dexamethasone)	2003-02-07	2003-03-19	-/-/-	-	SD	-
2	Prednisolone (Prednisolone)	2003-02-07	2003-03-19	-/-/-	-	SD	-
3	Thalidomide (Thalidomide)	2003-03-20	2012-01	-/-/-	-	PR	-
4	Lenalidomide (Revlimid)	2012-01	2014-07-17	-/-/-	-	U	2014-05-23

Line of Regimen	Standardized Medication Name (Reported Name)	Med. Start Date	Med. End Date	Dose/Unit/ Frequency	Number of Cycles	Best Response to Therapy	Date of Progression
4	Dexamethasone (Dexamethasone)	2012-01	2014-07-17	-/-/-	-	U	2014-05-23
4	Clarithromycin (Clarithromycin)	2012-01	2014-07-17	-/-/-	-	U	2014-05-23

■ Hematology/Chemistry Toxicities

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine increased	2014-08-20 16	Period 1, day 15	51.272	Umol/l	44.2-106.08	1
Creatinine increased	2014-09-01 28	Period 1, day 29	52.156	Umol/l	44.2-106.08	1
Creatinine increased	2014-09-08 35	Period 1, day 36	53.924	Umol/l	44.2-106.08	1
Creatinine increased	2015-01-06 155	Cycle 4, day 1	51.272	Umol/l	44.2-106.08	1
Creatinine increased	2015-01-20 169	Cycle 4, day 15	53.04	Umol/l	44.2-106.08	1
Creatinine increased	2015-02-03 183	Cycle 5, day 1	57.46	Umol/l	44.2-106.08	1
Creatinine increased	2015-03-06 214	Cycle 6, day 1	60.996	Umol/l	44.2-106.08	1
Creatinine increased	2015-04-03 242	Cycle 7, day 1	60.996	Umol/l	44.2-106.08	1
Creatinine increased	2015-04-28 267	Eot	63.648	Umol/l	44.2-106.08	1
Hemoglobin decreased	2014-07-22 -14	Screening	111	G/l	115-150	1
Hemoglobin decreased	2014-08-06 2	Period 1, day 2	94	G/l	115-150	2
Hemoglobin decreased	2014-08-08 4	Period 1, day 4	103	G/l	115-150	1
Hemoglobin decreased	2014-08-12 8	Period 1, day 8	107	G/l	115-150	1
Hemoglobin decreased	2014-08-20 16	Period 1, day 15	112	G/l	115-150	1
Hemoglobin decreased	2014-08-25 21	Period 1, day 22	108	G/l	115-150	1
Hemoglobin decreased	2014-09-01 28	Period 1, day 29	110	G/l	115-150	1
Hemoglobin decreased	2014-09-16 43	Period 1, day 43	108	G/l	115-150	1
Hemoglobin decreased	2014-09-24 51	Period 1, day 50	102	G/l	115-150	1
Hemoglobin decreased	2014-09-29 56	Period 1, day 57	99	G/l	115-150	2
Hemoglobin decreased	2014-10-14 71	Cycle 1, day 1	114	G/l	115-150	1
Hemoglobin decreased	2014-11-11 99	Cycle 2, day 1	111	G/l	115-150	1
Hemoglobin decreased	2014-11-25 113	Cycle 2, day 15	109	G/l	115-150	1
Hemoglobin decreased	2014-12-09 127	Cycle 3, day 1	112	G/l	115-150	1
Hemoglobin decreased	2014-12-24 142	Cycle 3, day 15	107	G/l	115-150	1

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin decreased	2015-01-06 155	Cycle 4, day 1	112	G/l	115-150	1
Hemoglobin decreased	2015-04-28 267	Eot	112	G/l	115-150	1
Leukocytes decreased	2014-07-22 -14	Screening	2.9	X10e9/l	3.7-8	2
Leukocytes decreased	2014-08-04 -1	Period 1, day 1	2.7	X10e9/l	3.7-8	2
Leukocytes decreased	2014-08-08 4	Period 1, day 4	3.6	X10e9/l	3.7-8	1
Leukocytes decreased	2014-08-12 8	Period 1, day 8	1.8	X10e9/l	3.7-8	3
Leukocytes decreased	2014-08-20 16	Period 1, day 15	2.1	X10e9/l	3.7-8	2
Leukocytes decreased	2014-08-25 21	Period 1, day 22	1.6	X10e9/l	3.7-8	3
Leukocytes decreased	2014-09-01 28	Period 1, day 29	2.8	X10e9/l	3.7-8	2
Leukocytes decreased	2014-09-08 35	Period 1, day 36	2.8	X10e9/l	3.7-8	2
Leukocytes decreased	2014-09-16 43	Period 1, day 43	2.2	X10e9/l	3.7-8	2
Leukocytes decreased	2014-09-24 51	Period 1, day 50	2.1	X10e9/l	3.7-8	2
Leukocytes decreased	2014-09-29 56	Period 1, day 57	3.4	X10e9/l	3.7-8	1
Neutrophils decreased	2014-07-22 -14	Screening	1.421	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-08-04 -1	Period 1, day 1	1.5282	X10e9/l	1.665-6.4	1
Neutrophils decreased	2014-08-12 8	Period 1, day 8	1.1736	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-08-20 16	Period 1, day 15	1.4112	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-08-25 21	Period 1, day 22	1.104	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-09-16 43	Period 1, day 43	1.6236	X10e9/l	1.665-6.4	1
Neutrophils decreased	2014-09-24 51	Period 1, day 50	1.659	X10e9/l	1.665-6.4	1
Lymphocytes decreased	2014-08-04 -1	Period 1, day 1	0.9207	X10e9/l	0.999-3.44	1
Lymphocytes decreased	2014-08-06 2	Period 1, day 2	0.11	X10e9/l	0.999-3.44	4
Lymphocytes decreased	2014-08-08 4	Period 1, day 4	0.2916	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-08-12 8	Period 1, day 8	0.333	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-08-20 16	Period 1, day 15	0.4998	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-08-25 21	Period 1, day 22	0.336	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-01 28	Period 1, day 29	0.252	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-08 35	Period 1, day 36	0.28	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-16 43	Period 1, day 43	0.3564	X10e9/l	0.999-3.44	3

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes decreased	2014-09-24 51	Period 1, day 50	0.273	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-29 56	Period 1, day 57	0.5984	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-10-14 71	Cycle 1, day 1	0.5358	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-10-28 85	Cycle 1, day 15	0.7448	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-11-11 99	Cycle 2, day 1	0.6683	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-11-25 113	Cycle 2, day 15	0.8372	X10e9/l	0.999-3.44	1
Lymphocytes decreased	2014-12-09 127	Cycle 3, day 1	0.798	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-12-24 142	Cycle 3, day 15	0.608	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2015-01-06 155	Cycle 4, day 1	0.7546	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2015-01-20 169	Cycle 4, day 15	0.7176	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2015-02-03 183	Cycle 5, day 1	0.8624	X10e9/l	0.999-3.44	1
Lymphocytes decreased	2015-03-06 214	Cycle 6, day 1	0.7595	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2015-04-03 242	Cycle 7, day 1	0.779	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2015-04-28 267	Eot	0.6806	X10e9/l	0.999-3.44	2

■ ECOG Performance Status

Date of ECOG Assessment Study Day	Visit	ECOG score
2014-07-22 -14	Screening	1
2014-08-05 1	Period 1, day 1	1
2014-08-25 21	Period 1, day 22	1
2014-09-09 36	Period 1, day 36	1
2014-09-30 57	Period 1, day 57	1
2015-04-28 267	Eot	0

■ NARRATIVE TEXT

被験者 810103 は，7[redacted]歳のアジア人女性で，2003 年 1 月に初めて MM（病期 I 期）と診断され，本剤を 16 mg/kg の用量で投与するコホートに組み入れられた。治験組入れ時の合併症は，頚椎及び胸椎の圧迫骨折，下痢，不眠症及び末梢性感覚ニューロパチーであった。ベースラインの ECOG スコアは 1 であった。白内障の既往歴があった。被験者は以下の合計 4 レジメンの前治療を受けていた。レジメン 1 はドキソルビシン，プレドニゾロン及びビンクリスチン（最良効果：stable disease），レジメン 2 はデキサメタゾン，メルファラン，プレドニゾロン，ラニムスチン及びビンクリスチン（最良効果：stable disease），レジメン 3 はサリドマイドのみ（最良効果：PR），レジメン 4 はクラリスロマイシン，デキサメタゾン及びレナリドミド（最良効果：不明）

であった。被験者はレジメン 2 のアルキル化剤とレジメン 4 のレナリドミドに対して治療抵抗性を示した。治験組入れ時の併用薬は，レバミピド，ブロチゾラム，塩酸ロペラミド，ロキソプロフェンナトリウム及びアセトアミノフェンであった。

Day 1（2014 年 8 月 5 日，本剤の初回投与日）に，非重篤な有害事象として Grade 2 の悪寒，頭痛，低酸素症，口腔咽頭痛及び発熱が発現した。治験担当医師は，この一連の事象は IRR であり，本剤との因果関係を「可能性大」と判断した。被験者には前投薬としてメチルプレドニゾロン，ジフェンヒドラミン及びアセトアミノフェンを投与した後に本剤を初回投与した。投与前のバイタルサインは，体温 37°C，心拍数 69 拍/分（bpm）及び血圧 110/48 mm Hg であった。上記の事象が発現したため，本剤投与開始から約 2 時間後に投与を約 1.5 時間中断した。被験者にヒドロコルチゾン及び酸素による治療を実施した。同日，スルファメトキサゾール／トリメトプリム（ダイフェン），フェブキソスタット，オメプラゾール，バラシクロビル及びラスブリカーゼを併用した。本剤投与後（投与終了 2 時間後）のバイタルサインは，体温 36.5°C，心拍数 84 bpm 及び血圧 110/55 mm Hg であった。上記の事象は発現当日（Day 1）に回復した。治験実施計画書に従い Day 1 及び Day 2 に後投薬としてメチルプレドニゾロンを投与した。その後，被験者に本剤を 17 回投与した。

Day 2～56 に Grade 2～4 のリンパ球減少症，Day 8 及び Day 21 に Grade 3 の白血球減少症が発現した（白血球及びリンパ球数については上記の表を参照）。治験担当医師は，これらすべての事象と本剤との因果関係を「可能性大」と判断した。これらの事象に対する本剤の処置は実施しなかった。白血球減少症は，それぞれ Day 16 及び Day 28 に無処置で回復した。

Day 24（本剤の 2 回目投与の 2 日後）に，重篤な有害事象として Grade 2 の頭痛が発現し，被験者は同日入院した。頭痛の特徴は「体中に電気が流れている又はピリピリする感じ」であった。Day 26 の頭部コンピューター断層撮影（CT）で異常所見は認められなかった。Day 26（本剤の 2 回目投与の 4 日後）に，入院期間の延長に至った重篤な有害事象として Grade 1 の発熱（体温：37.0～37.4°C）が発現した。治験担当医師は，頭痛及び発熱と本剤との因果関係を「可能性小」と判断した。これらの事象に対する本剤の処置は実施しなかった。頭痛の治療のためアセトアミノフェンを投与した。頭痛は Day 28 に回復した。Day 31（本剤の 3 回目投与の 2 日後）に，非重篤な有害事象として Grade 2 の頭痛が発現した。治験担当医師は，本事象と本剤との因果関係を「可能性小」と判断した。本事象に対する本剤の処置は実施しなかった。アセトアミノフェンの投与は継続した。Day 33 に，被験者の体温が 38.0°C に上昇した。血液培養検査の結果は陰性であった。レボフロキサシンを投与した。Day 35 の腰椎穿刺の結果，単核球数は 10 であり，髄膜炎を示唆する明らかな所見はなかったが，無菌性髄膜炎の可能性は否定できなかった。発熱は Day 52 に回復し（体温 36.5°C），同日，被験者は退院した。頭痛は Day 74 に回復した。

Day 267 に，疾患進行のため本剤投与を中止した。本剤の最終投与日は Day 242 であった（被験者には本剤を合計 18 回投与した）。Day 302 に，被験者は疾患進行のため本治験を中止した。本報告時点で Grade 2 のリンパ球減少症は未回復であった。

(2) 被験者識別番号 810104

■ REASON FOR NARRATIVE SELECTION

Serious adverse events

■ Serious Adverse Events

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Trtmnt Given Outcome of Adverse Event
肺炎 (Pneumonia)	2014-09-24 2014-11-05	15 43	Y 3	Possible Not applicable	Y Recovered/resolved

■ Demographics and Baseline Characteristics

□ Country: JPN
□ Site no.: JP00053
□ Race: Asian
□ Age (yrs): 6[redacted]
□ Sex: Male
□ Dose level received: 16 mg/kg
□ Dose level planned: 16 mg/kg
□ Baseline weight (kg): 58.2
□ Baseline height (cm): 162.2
□ Baseline ecog: 0

■ Disposition Information

□ Treatment discontinuation: 2014-09-17 Protocol Violation

□ Study discontinuation: 2014-11-12 Protocol Violation

■ Summary of Study Medication

Total dose (mg/kg)	Start Date Treatment	End Date of Treatment	Treatment duration (months)
16.2	2014-09-10	2014-09-10	0.0

■ Study Medication

Dosing Start Date/Time Study Day of Dosing Start Date	Dosing End Date/Time Study Day of Dosing End Date	Dose per Administration (mg/kg)	Reason for Dose Adjustment
2014-09-10t10:16 1	2014-09-10t17:25 1	16.2	-

■ Pre-infusion Medications

Type of Medication/ Standardized Medication Name	Start Date/Time of Medication Study Day of Start of Medication	Total Daily Dose/Unit	Dosing Frequency per Interval/Route of Administration
Glucocorticoids/ methylprednisolone	2014-09-10t09:33 1	100 mg	Once/intravenous
Anilides/ paracetamol	2014-09-10t09:35 1	600 mg	Once/oral
Aminoalkyl ethers/ diphenhydramine	2014-09-10t09:35 1	50 mg	Once/oral

■ Post-infusion Medications

Type of Medication/ Standardized Medication Name	Start Date/Time of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose/Unit	Dosing Frequency per Interval/Route of Administration
Glucocorticoids/ methylprednisolone	2014-09-10 1	2014-09-11 2	20 mg	Once/oral

■ Other Adverse Events

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Trtmnt Given Outcome of Adverse Event
リンパ球減少症 (Lymphocytopenia)	2014-09-11 2014-09-12	2 2	N 2	Probable Dose not changed	N Recovered/resolved
高カリウム血症 (Hyperpotassemia)	2014-09-14 -	5 -	N 1	Not related Dose not changed	Y Not recovered/not resolved
貧血 (Anemia)	2014-09-23 2014-09-24	14 2	N 2	Possible Not applicable	N Recovered/resolved

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Trtmnt Given Outcome of Adverse Event
血小板減少症 (Thrombocytopenia)	2014-09-23 2014-09-25	14 3	N 2	Probable Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-09-24 2014-10-06	15 13	N 3	Probable Not applicable	N Recovered/resolved
貧血 (Anemia)	2014-09-25 2014-10-02	16 8	N 2	Probable Not applicable	Y Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-09-25 2014-09-26	16 2	N 1	Probable Not applicable	N Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-09-25 2014-09-28	16 4	N 3	Probable Not applicable	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-09-26 2014-09-30	17 5	N 3	Probable Not applicable	Y Recovered/resolved
好中球減少症 (Neutropenia)	2014-09-26 2014-09-29	17 4	N 1	Possible Not applicable	N Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-09-28 2014-09-30	19 3	N 4	Probable Not applicable	Y Recovered/resolved
好中球減少症 (Neutropenia)	2014-09-29 2014-09-30	20 2	N 3	Probable Not applicable	Y Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-09-30 2014-10-01	21 2	N 3	Probable Not applicable	N Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-10-01 2014-10-02	22 2	N 4	Probable Not applicable	Y Recovered/resolved
貧血 (Anemia)	2014-10-02 2014-10-05	23 4	N 3	Probable Not applicable	Y Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-10-02 2014-10-03	23 2	N 3	Probable Not applicable	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-10-03 2014-10-05	24 3	N 2	Probable Not applicable	N Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-10-03 2014-10-05	24 3	N 4	Probable Not applicable	Y Recovered/resolved
貧血 (Anemia)	2014-10-05 2014-10-06	26 2	N 2	Probable Not applicable	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-10-05 2014-10-06	26 2	N 3	Probable Not applicable	Y Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-10-05 2014-10-06	26 2	N 3	Possible Not applicable	Y Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-06 2014-10-08	27 3	N 4	Probable Not applicable	N Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-10-06 2014-10-08	27 3	N 2	Possible Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-08 2014-10-10	29 3	N 3	Probable Not applicable	N Recovered/resolved
血小板減少症 (Thrombocytopenia)	2014-10-08 2014-11-04	29 28	N 3	Possible Not applicable	Y Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-10-10 2014-10-14	31 5	N 2	Probable Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-10 2014-10-14	31 5	N 4	Possible Not applicable	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-10-14 2014-10-24	35 11	N 3	Doubtful Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-14 2014-10-17	35 4	N 2	Possible Not applicable	N Recovered/resolved

Dictionary-Derived Term (Reported Term for the Adverse Event)	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Trtmnt Given Outcome of Adverse Event
リンパ球減少症 (Lymphocytopenia)	2014-10-17 2014-10-20	38 4	N 3	Probable Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-20 2014-10-27	41 8	N 2	Probable Not applicable	N Recovered/resolved
白血球減少症 (Leukocytopenia)	2014-10-24 2014-11-12	45 20	N 2	Doubtful Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-27 2014-10-30	48 4	N 1	Probable Not applicable	N Recovered/resolved
リンパ球減少症 (Lymphocytopenia)	2014-10-30 2014-11-04	51 6	N 2	Probable Not applicable	N Recovered/resolved

■ Medical History

Dictionary-Derived Term (Reported Term for the Medical History)	Past or Current?
便秘 (Constipation)	Past
糖尿病 (Diabetes)	Past
末梢性ニューロパチー (Peripheral neuropathy)	Past
便秘 (Constipation)	Current
糖尿病 (Diabetes)	Current
末梢性ニューロパチー (Peripheral neuropathy)	Current

■ Disease History

Date of initial MM Diagnosis	Stage of MM	Staging Method
2010-09	3	International staging system

■ Concomitant Medication

Standardized Medication Name (Reported Name)	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Indication	Dose/Unit	Dosing Frequency per Interval/Route of Administration
Febuxostat (Feburic)	2014-09-10 1	Ongoing -	Prophylaxis	20 mg	Qd/oral
Bactrim (Daiphen)	2014-09-10 1	2014-09-11 2	Prophylaxis	1 tablet	Qd/oral
Valaciclovir (Valaciclovir)	2014-09-10 1	Ongoing -	Prophylaxis	500 mg	Qd/oral
Bactrim (Daiphen)	2014-09-11 2	2014-09-14 5	Adverse event	12 tablet	Tid/oral
Bactrim (Daiphen)	2014-09-14 5	2014-09-29 20	Adverse event	6 tablet	Tid/oral
Sodium polystyrene sulfonate (Kayexalate)	2014-09-14 5	Ongoing -	Adverse event	19.62 g	Tid/oral
Sennoside a+b (Cennaride)	2014-09-16 7	Ongoing -	Medical history	12 mg	Prn/oral
Sodium picosulfate (Laxodete)	2014-09-16 7	Ongoing -	Medical history	-	-/oral
Voriconazole (Vfend)	2014-09-16 7	2014-09-16 7	Adverse event	600 mg	Bid/oral

Standardized Medication Name (Reported Name)	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Indication	Dose/Unit	Dosing Frequency per Interval/Route of Administration
Voriconazole (Vfend)	2014-09-17 8	2014-09-29 20	Adverse event	400 mg	Bid/oral
Sodium picosulfate (Laxodete)	2014-09-21 12	Ongoing -	Medical history	5-45 gtt	Prn/oral
Paracetamol (Calonal)	2014-09-22 13	Ongoing -	Adverse event	400 mg	Prn/oral
Meropenem (Meropenem)	2014-09-22 13	2014-10-14 35	Adverse event	1000 mg	Bid/intravenous
Norepinephrine (Nor adrenalin)	2014-09-23 14	2014-10-01 22	Adverse event	-	-/intravenous
Sennoside a+b calcium (Pursenid)	2014-09-24 15	Ongoing -	Medical history	12 mg	Prn/oral
New lecicarbon (New lecicarbon)	2014-09-26 17	Ongoing -	Medical history	1 other	Prn/rectal
Bactrim (Daiphen)	2014-09-29 20	Ongoing -	Adverse event	4-12 tablet	Tid/oral
Prednisolone (Prednisolone)	2014-09-29 20	Ongoing -	Adverse event	5-60 mg	Qd/oral
Amphotericin b, liposome (Ambisome)	2014-09-29 20	Ongoing -	Adverse event	150 mg	Qd/intravenous
Filgrastim (Gran)	2014-09-29 20	2014-09-30 21	Adverse event	75 ug	Qd/subcutaneous
Vancomycin (Vancomycin)	2014-10-01 22	2014-10-02 23	Adverse event	2000 mg	Bid/intravenous
Amino acids nos w/copper/electrolytes nos/glu (Elneopa)	2014-10-02 23	2014-10-06 27	Adverse event	1000 ml	Qd/intravenous
Albumin human (Albumin)	2014-10-03 24	2014-10-05 26	Adverse event	50 ml	Qd/intravenous
Vancomycin (Vancomycin)	2014-10-03 24	2014-10-06 27	Adverse event	1000 mg	Qd/intravenous
Insulin human (Humulinr)	2014-10-03 24	2014-10-20 41	Medical history	2-12 other	Prn/subcutaneous
Furosemide (Furosemide)	2014-10-04 25	2014-10-05 26	Adverse event	20 mg	Qd/intravenous
Magnesium oxide (Maglax)	2014-10-04 25	Ongoing -	Medical history	330-1980 mg	Prn/oral
Filgrastim (Gran)	2014-10-05 26	2014-10-05 26	Adverse event	75 ug	Once/subcutaneous
Furosemide (Furosemide)	2014-10-06 27	2014-10-07 28	Adverse event	10 mg	Qd/intravenous
Vancomycin (Vancomycin)	2014-10-07 28	2014-10-14 35	Adverse event	1500 mg	Qd/intravenous
Amino acids nos w/copper/electrolytes nos/glu (Elneopa)	2014-10-07 28	2014-10-09 30	Adverse event	1000 ml	Qd/intravenous
Indometacin (Catlep)	2014-10-08 29	Ongoing -	Other- mm	-	-/topical
Amino acids nos w/copper/electrolytes nos/glu (Elneopa)	2014-10-10 31	2014-10-13 34	Adverse event	1500 ml	Qd/intravenous

■ Prior MM Therapy

Line of Regimen	Standardized Medication Name (Reported Name)	Med. Start Date	Med. End Date	Dose/Unit/ Frequency	Number of Cycles	Best Response to Therapy	Date of Progression
1	Dexamethasone (Dexamethasone)	2010-11-02	2012-10-24	-/-/-	-	PR	2012-10-10
1	Cyclophosphamide (Endoxan)	2010-11-02	2012-10-24	-/-/-	1	PR	2012-10-10
1	Bortezomib (Velcade)	2010-11-02	2012-10-24	-/-/-	21	PR	2012-10-10
2	Lenalidomide (Revlimid)	2012-10-24	2013-11-12	-/-/-	-	CR	2014-08-20
2	Dexamethasone (Lenadex)	2012-10-24	2013-11-12	-/-/-	-	CR	2014-08-20
2	Dexamethasone (Lenadex)	2012-10-24	2013-11-12	-/-/-	2	CR	2014-08-20
2	Bortezomib (Velcade)	2012-10-24	2013-11-12	-/-/-	2	CR	2014-08-20
2	Dexamethasone sodium phosphate (Dexart)	2012-10-24	2013-11-12	-/-/-	3	CR	2014-08-20
2	Bortezomib (Velcade)	2012-10-24	2013-11-12	-/-/-	3	CR	2014-08-20
2	Cyclophosphamide (Endoxan)	2012-10-24	2013-11-12	-/-/-	5	CR	2014-08-20

■ Hematology/Chemistry Toxicities

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Creatinine increased	2014-08-25 -16	Screening	94.588	Umol/l	44.2-106.08	1
Creatinine increased	2014-09-12 3	Period 1, day 4	91.052	Umol/l	44.2-106.08	1
Creatinine increased	2014-09-14 5	Period 1, day 4 unscheduled 1	112.268	Umol/l	44.2-106.08	1
Creatinine increased	2014-09-17 8	Period 1, day 8	118.456	Umol/l	44.2-106.08	1
Creatinine increased	2014-09-19 10	Eot	122.876	Umol/l	44.2-106.08	1
Hemoglobin decreased	2014-08-25 -16	Screening	115	G/l	130-165	1
Hemoglobin decreased	2014-09-09 -1	Period 1, day 1	105	G/l	130-165	1
Hemoglobin decreased	2014-09-11 2	Period 1, day 2	105	G/l	130-165	1
Hemoglobin decreased	2014-09-12 3	Period 1, day 4	104	G/l	130-165	1
Hemoglobin decreased	2014-09-17 8	Period 1, day 8	122	G/l	130-165	1
Hemoglobin decreased	2014-09-19 10	Eot	107	G/l	130-165	1
Hemoglobin decreased	2014-09-23 14	Eot unscheduled 1	96	G/l	130-165	2
Hemoglobin decreased	2014-09-24 15	Eot unscheduled 2	101	G/l	130-165	1
Hemoglobin decreased	2014-09-25 16	Eot unscheduled 3	92	G/l	130-165	2

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin decreased	2014-09-26 17	Eot unscheduled 4	87	G/l	130-165	2
Hemoglobin decreased	2014-09-28 19	Eot unscheduled 5	89	G/l	130-165	2
Hemoglobin decreased	2014-09-29 20	Eot unscheduled 6	82	G/l	130-165	2
Hemoglobin decreased	2014-09-30 21	Eot unscheduled 7	97	G/l	130-165	2
Hemoglobin decreased	2014-10-01 22	Eot unscheduled 8	99	G/l	130-165	2
Hemoglobin decreased	2014-10-02 23	Eot unscheduled 9	73	G/l	130-165	3
Hemoglobin decreased	2014-10-03 24	Eot unscheduled 10	79	G/l	130-165	3
Hemoglobin decreased	2014-10-05 26	Eot unscheduled 11	81	G/l	130-165	2
Hemoglobin decreased	2014-10-06 27	Eot unscheduled 12	104	G/l	130-165	1
Hemoglobin decreased	2014-10-08 29	Eot unscheduled 13	115	G/l	130-165	1
Hemoglobin decreased	2014-10-10 31	Eot unscheduled 14	101	G/l	130-165	1
Hemoglobin decreased	2014-10-14 35	Eot unscheduled 15	89	G/l	130-165	2
Hemoglobin decreased	2014-10-17 38	Post tmt week 4	82	G/l	130-165	2
Hemoglobin decreased	2014-10-20 41	Post tmt week 4 unscheduled 1	85	G/l	130-165	2
Hemoglobin decreased	2014-10-24 45	Post tmt week 4 unscheduled 2	77	G/l	130-165	3
Hemoglobin decreased	2014-10-27 48	Post tmt week 4 unscheduled 3	81	G/l	130-165	2
Hemoglobin decreased	2014-10-30 51	Post tmt week 4 unscheduled 4	80	G/l	130-165	2
Hemoglobin decreased	2014-11-04 56	Post tmt week 4 unscheduled 5	77	G/l	130-165	3
Hemoglobin decreased	2014-11-12 64	Post tmt week 8	90	G/l	130-165	2
Platelets decreased	2014-08-25 -16	Screening	109	X10e9/l	130-400	1
Platelets decreased	2014-09-09 -1	Period 1, day 1	106	X10e9/l	130-400	1
Platelets decreased	2014-09-11 2	Period 1, day 2	98	X10e9/l	130-400	1
Platelets decreased	2014-09-12 3	Period 1, day 4	107	X10e9/l	130-400	1
Platelets decreased	2014-09-17 8	Period 1, day 8	120	X10e9/l	130-400	1
Platelets decreased	2014-09-19 10	Eot	99	X10e9/l	130-400	1
Platelets decreased	2014-09-23 14	Eot unscheduled 1	66	X10e9/l	130-400	2
Platelets decreased	2014-09-24 15	Eot unscheduled 2	52	X10e9/l	130-400	2
Platelets decreased	2014-09-25 16	Eot unscheduled 3	49	X10e9/l	130-400	3
Platelets decreased	2014-09-26 17	Eot unscheduled 4	37	X10e9/l	130-400	3

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets decreased	2014-09-28 19	Eot unscheduled 5	19	X10e9/l	130-400	4
Platelets decreased	2014-09-29 20	Eot unscheduled 6	17	X10e9/l	130-400	4
Platelets decreased	2014-09-30 21	Eot unscheduled 7	29	X10e9/l	130-400	3
Platelets decreased	2014-10-01 22	Eot unscheduled 8	21	X10e9/l	130-400	4
Platelets decreased	2014-10-02 23	Eot unscheduled 9	26	X10e9/l	130-400	3
Platelets decreased	2014-10-03 24	Eot unscheduled 10	21	X10e9/l	130-400	4
Platelets decreased	2014-10-05 26	Eot unscheduled 11	36	X10e9/l	130-400	3
Platelets decreased	2014-10-06 27	Eot unscheduled 12	50	X10e9/l	130-400	2
Platelets decreased	2014-10-08 29	Eot unscheduled 13	28	X10e9/l	130-400	3
Platelets decreased	2014-10-10 31	Eot unscheduled 14	25	X10e9/l	130-400	3
Platelets decreased	2014-10-14 35	Eot unscheduled 15	49	X10e9/l	130-400	3
Platelets decreased	2014-10-17 38	Post tmt week 4	29	X10e9/l	130-400	3
Platelets decreased	2014-10-20 41	Post tmt week 4 unscheduled 1	26	X10e9/l	130-400	3
Platelets decreased	2014-10-24 45	Post tmt week 4 unscheduled 2	30	X10e9/l	130-400	3
Platelets decreased	2014-10-27 48	Post tmt week 4 unscheduled 3	31	X10e9/l	130-400	3
Platelets decreased	2014-10-30 51	Post tmt week 4 unscheduled 4	39	X10e9/l	130-400	3
Platelets decreased	2014-11-04 56	Post tmt week 4 unscheduled 5	55	X10e9/l	130-400	2
Platelets decreased	2014-11-12 64	Post tmt week 8	89	X10e9/l	130-400	1
Leukocytes decreased	2014-09-25 16	Eot unscheduled 3	3	X10e9/l	3.7-8	1
Leukocytes decreased	2014-09-26 17	Eot unscheduled 4	1.9	X10e9/l	3.7-8	3
Leukocytes decreased	2014-09-28 19	Eot unscheduled 5	1.7	X10e9/l	3.7-8	3
Leukocytes decreased	2014-09-29 20	Eot unscheduled 6	1.3	X10e9/l	3.7-8	3
Leukocytes decreased	2014-10-03 24	Eot unscheduled 10	2.5	X10e9/l	3.7-8	2
Leukocytes decreased	2014-10-05 26	Eot unscheduled 11	1.1	X10e9/l	3.7-8	3
Leukocytes decreased	2014-10-10 31	Eot unscheduled 14	2.4	X10e9/l	3.7-8	2
Leukocytes decreased	2014-10-14 35	Eot unscheduled 15	1.9	X10e9/l	3.7-8	3
Leukocytes decreased	2014-10-17 38	Post tmt week 4	1.8	X10e9/l	3.7-8	3
Leukocytes decreased	2014-10-20 41	Post tmt week 4 unscheduled 1	1.5	X10e9/l	3.7-8	3
Leukocytes decreased	2014-10-24 45	Post tmt week 4 unscheduled 2	2.3	X10e9/l	3.7-8	2

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Leukocytes decreased	2014-10-27 48	Post tmt week 4 unscheduled 3	2.1	X10e9/l	3.7-8	2
Leukocytes decreased	2014-10-30 51	Post tmt week 4 unscheduled 4	2.2	X10e9/l	3.7-8	2
Leukocytes decreased	2014-11-04 56	Post tmt week 4 unscheduled 5	2.8	X10e9/l	3.7-8	2
Neutrophils decreased	2014-09-26 17	Eot unscheduled 4	1.596	X10e9/l	1.665-6.4	1
Neutrophils decreased	2014-09-29 20	Eot unscheduled 6	0.858	X10e9/l	1.665-6.4	3
Neutrophils decreased	2014-10-14 35	Eot unscheduled 15	1.1818	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-10-17 38	Post tmt week 4	1.116	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-10-20 41	Post tmt week 4 unscheduled 1	0.5685	X10e9/l	1.665-6.4	3
Neutrophils decreased	2014-10-24 45	Post tmt week 4 unscheduled 2	1.1753	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-10-27 48	Post tmt week 4 unscheduled 3	1.05	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-10-30 51	Post tmt week 4 unscheduled 4	1.3068	X10e9/l	1.665-6.4	2
Neutrophils decreased	2014-11-04 56	Post tmt week 4 unscheduled 5	1.442	X10e9/l	1.665-6.4	2
Lymphocytes decreased	2014-09-11 2	Period 1, day 2	0.7455	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-09-24 15	Eot unscheduled 2	0.256	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-25 16	Eot unscheduled 3	0.36	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-26 17	Eot unscheduled 4	0.266	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-29 20	Eot unscheduled 6	0.364	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-09-30 21	Eot unscheduled 7	0.348	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-10-01 22	Eot unscheduled 8	0.245	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-10-02 23	Eot unscheduled 9	0.259	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-10-03 24	Eot unscheduled 10	0.3375	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-10-06 27	Eot unscheduled 12	0.192	X10e9/l	0.999-3.44	4
Lymphocytes decreased	2014-10-08 29	Eot unscheduled 13	0.2255	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-10-10 31	Eot unscheduled 14	0.156	X10e9/l	0.999-3.44	4
Lymphocytes decreased	2014-10-14 35	Eot unscheduled 15	0.5643	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-10-17 38	Post tmt week 4	0.324	X10e9/l	0.999-3.44	3
Lymphocytes decreased	2014-10-20 41	Post tmt week 4 unscheduled 1	0.714	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-10-24 45	Post tmt week 4 unscheduled 2	0.7774	X10e9/l	0.999-3.44	2
Lymphocytes decreased	2014-10-27 48	Post tmt week 4 unscheduled 3	0.8274	X10e9/l	0.999-3.44	1

Lab Test	Date of Specimen Collection Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes decreased	2014-10-30 51	Post tmt week 4 unscheduled 4	0.7238	X10e9/l	0.999-3.44	2

■ ECOG Performance Status

Date of ECOG Assessment Study Day	Visit	ECOG score
2014-08-25 -16	Screening	0
2014-09-10 1	Period 1, day 1	0
2014-09-17 8	Eot	0

■ NARRATIVE TEXT

被験者 810104 は，6[redacted]歳のアジア人男性で，2010 年 9 月に初めて MM（病期 III 期）と診断され，本剤を 16 mg/kg の用量で投与するコホートに組み入れられた。治験組入れ時の合併症は，便秘，糖尿病及び末梢性ニューロパチーであった。ベースラインの ECOG スコアは 0 であった。既往歴の報告はなかった。被験者は以下の合計 2 レジメンの前治療を受けていた。レジメン 1 はボルテゾミブ，シクロホスファミド及びデキサメタゾン（最良効果：PR），レジメン 2 はボルテゾミブ，シクロホスファミド，デキサメタゾン，デキサメタゾンリン酸エステルナトリウム及びレナリドミド（最良効果：CR）であった。治験組入れ時の併用薬は，イミプラミン，メコバラミン，オメプラゾール，オキシコドン，プレガバリン及びシタグリプチンであった。

Day −13（2014 年 8 月 28 日）に，ニューモシスティス肺炎の可能性を示唆する CT スキャン所見及び *Aspergillus* 抗原陽性（+1.1）を示す臨床検査結果に基づき，重篤な有害事象として Grade 2 の肺炎が発現した。本事象は，本剤の初回投与後に，臨床的に肺炎が疑われる所見が過去にないか確認した結果，診断，報告されたものである。被験者は本剤の投与を開始するために入院した。本剤投与開始前の酸素飽和度は 85～90%で，呼吸困難及び発熱は認められなかった。Day 1 に本剤を投与し，酸素 2 L を併用した。同日，バラシクロビル及びスルファメトキサゾール／トリメトプリム（ダイフェン）も投与した。Day 2 の血液検査で *Candida* 及び *Aspergillus* の抗原が陽性であった。被験者に更にポリスチレンスルホン酸ナトリウム及びボリコナゾールを追加した。Day 8 の CT スキャンでは両肺野に高吸収域が認められ，すりガラス様陰影は完全に消失しており，被験者の状態の改善が示唆された。しかし，経過観察のため入院期間は延長された。同日（Day 8）に，治験実施計画書からの逸脱（治験開始前のニューモシスティス肺炎の疑い）のため本剤投与を中止し，Day 1 の投与が本剤の最終投与であった（被験者への本剤の投与は 1 回のみであった）。Day 13 に，被験者の体温は 38.8°C，酸素飽和度は 81%であった。酸素 3 L を投与し，メロペネム及びアセトアミノフェンの投与を開始した。Day 14 に，被験者の体温は 40°C に上昇し，呼吸状態が悪化し，血圧は 80/50 mm Hg と低く，その後更に 70 mm Hg 台まで低下した。ノルアドレナリンの投与を開始し，血圧は安定した。Day 15 に，重篤な有害事象の肺炎が Grade 3 に悪化した。治験担当医師は，本事象と本剤との因果関係を「可能性小」と判断した。Day 17 に，非重篤な有害事象として Grade 1 の好中球減少症が発現し，Day 20 に Grade 3 に悪化した（好中球数については上記の表を参照）。治験担当医師は，Grade 1 の好中球減少症と本剤との因果関係を「可能性小」，Grade 3 の好中球減少症と本剤との因果関係を「可能性大」と判断した。被験者は，Day 16～45 に Grade 1～3 の白血球減少症，Day 2～51 に Grade 1～4 のリンパ

球減少症，Day 14～29 に Grade 2～4 の血小板減少症をそれぞれ数件発現した（白血球数，リンパ球数及び血小板数については上記の表を参照）。治験担当医師は，Day 35 及び Day 45 の白血球減少症と本剤との因果関係を「多分なし」，Day 31 及び Day 35 のリンパ球減少症並びに Day 26，Day 27 及び Day 29 の血小板減少症と本剤との因果関係を「可能性小」と判断した以外は，すべての白血球減少症，リンパ球減少症及び血小板減少症と本剤との因果関係を「可能性大」と判断した。肺炎の悪化は血球減少症（特にリンパ球減少症）が原因と判断した。しかし，白血球減少症，リンパ球減少症及び血小板減少症は，いずれも本剤の初回投与後に発現した。Day 19 に，喀痰検体を採取し，*Enterococcus faecium* が検出された。Day 20 の CT スキャンでは，両肺にすりガラス様陰影が認められ，異型肺炎と確定診断された。同日の臨床検査で *Aspergillus* 抗原レベルの上昇が認められた。これらの事象に対する治療として，フィルグラスチム，アムホテリシン B，スルファメトキサゾール／トリメトプリム（ダイフェン），プレドニゾロン，アミノ酸／銅／電解質／グルコース（エルネオパ），人血清アルブミン，バンコマイシン及びフロセミドを投与した。貧血と血小板減少症に対する治療として，濃厚赤血球輸血と濃厚血小板輸血を数回実施した。好中球減少症は Day 21 に回復した。Day 25 に，被験者は呼吸苦を訴えた。酸素飽和度は 90%で発熱はなかった。胸部 X 線検査で両肺の上肺野と中肺野に広がる「陰影」が認められた。Day 28 に，呼吸状態は改善し，酸素飽和度は 96%に上昇した。Day 30 及び Day 41 の臨床検査で，*Aspergillus* 抗原は陰性であった（Day 41 のシアル化糖鎖抗原 KL-6 値は 2,978 IU/L）。アムホテリシン B の投与を中止した。Day 42 の臨床検査でサイトメガロウイルス陽性となり，ガンシクロビルを投与した。Day 42 の胸部 CT 検査では両肺野の改善が認められた（肺炎領域の減少）。Day 56 の臨床検査で，シアル化糖鎖抗原 KL-6 値が 2,145 IU/L に低下し，サイトメガロウイルス検査の結果は陰性であった。同日（Day 56）に，被験者は退院した。リンパ球減少症及び血小板減少症は Day 56，肺炎及び白血球減少症はそれぞれ Day 57 及び Day 64 に回復した。

被験者は，最後の有害事象 2 事象（肺炎及び白血球減少症）が回復した後の Day 64 に，治験実施計画書からの逸脱のために本治験を中止した。

2.7.6.6　国内臨床第 Ib 相試験（MMY1005 試験，評価資料：5.3.5.2.4-1）

2.7.6.6.1　概要

2.7.6.6.1.1　計画

(1) 治験の標題

再発又は難治性の多発性骨髄腫（MM）を有する日本人患者を対象に，ダラツムマブ（以下本剤）をボルテゾミブ及びデキサメタゾンと併用投与（DVd）する第 Ib 相試験

(2) 治験実施医療機関

国内 5 施設

(3) 公表文献（引用文献）

なし

(4) 治験実施期間

2015 年 8 月 ■ 日（最初の被験者の初回来院日）～2016 年 6 月 3 日（クリニカルデータカットオフ日，最後の被験者のサイクル 6 Day 1 完了日）

(5) 開発の相

第 Ib 相

(6) 目的

本治験の主要目的は，再発又は難治性の MM の日本人患者を対象に DVd 療法の忍容性及び安全性を検討することであった。

副次目的は以下のとおりであった。

- DVd 療法での本剤の薬物動態を評価する。
- 本剤の免疫原性を評価する。
- 全奏効率（ORR）を評価する。
- Complete response（CR）以上の奏効を達成した被験者の割合を評価する。
- Very good partial response（VGPR）以上の奏効を達成した被験者の割合を評価する。
- 奏効到達期間を評価する。

探索的目的は以下のとおりであった。

- 本剤の効果を予測するバイオマーカーを探索する。
- 奏効持続期間を評価する。

(7) 治験方法

本治験は，再発又は難治性の MM の日本人患者を対象として，DVd 療法の安全性及び忍容性を検討する，非盲検，非ランダム化，多施設共同，第 Ib 相試験であった。本治験では，少なくとも 6 例の被験者を組み入れる予定であった。

本治験はスクリーニング期，治療期及び後観察期から構成された。治験期間及び重要な治験手順を以下に記載する。

スクリーニング期：

スクリーニング期はサイクル 1 Day 1 まで（最長 21 日間）とした。スクリーニング手順は，疾患評価，臨床検査及び妊娠検査を除き，サイクル 1 Day 1 前 21 日以内に実施することとした。血清及び尿検査は，サイクル 1 Day 1 前 14 日以内に実施することとした。サイクル 1 Day 1 前 42 日以内に疾患の定期的なフォローアップとして全骨格検査及び放射線による形質細胞腫の評価が実施されている場合，サイクル 1 Day 1 前 42 日以内に骨髄穿刺／生検が実施されている場合は，これらの結果を使用可能とした。サイクル 1 Day 1 前 7 日以内に尿又は血清妊娠検査を実施した。スクリーニングで脱落した被験者の状態が変化した場合，治験依頼者が承認すれば再スクリーニング可能とした。

治療期：

治療期はサイクル 1 Day 1 の治験薬（本剤，ボルテゾミブ又はデキサメタゾン）投与から治験薬の投与中止までとした。

サイクル 1～8 は 21 日間サイクルとした。サイクル 9 以降は 28 日間サイクルとした。用量制限毒性（DLT）評価期間は，本剤の初回投与からサイクル 1 の終了（サイクル 2 Day 1 の本剤投与前の安全性評価を含む）までとした。

本剤 16 mg/kg を，最初の 3 サイクルは 1 週間隔（Day 1，8 及び 15），サイクル 4～8 は 3 週間隔（Day 1）で持続静脈内投与した。サイクル 9 以降は 4 週間隔の Day 1 に本剤 16 mg/kg を持続静脈内投与した。各被験者の投与量は，小数点第 1 位を四捨五入した体重（kg）に基づいて算出した。本剤の投与量の再計算は，ベースラインからの体重の変化が 10%未満であれば不要とした。本剤投与の際は，infusion related reaction（IRR）のリスク軽減のため，前投薬及び（必要に応じて）後投薬を実施した。本剤の投与は，疾患進行若しくは許容できない毒性が認められる又はその他の投与中止基準に該当するまで継続することとした。

ボルテゾミブ 1.3 mg/m^2 を各 21 日間サイクルの Day 1，4，8 及び 11 に皮下投与した。ボルテゾミブの投与はサイクル 8 までとした。注射部位反応が認められた被験者には，ボルテゾミブを静脈内投与した。

デキサメタゾン 20 mg を，ボルテゾミブを投与する最初の 8 サイクル（サイクル 1～3 を除く）の Day 1，2，4，5，8，9，11 及び 12 に経口投与した。サイクル 1～3 では，Day 15 にもデキサメタゾン 20 mg を前投薬として投与した。本剤投与日は，デキサメタゾン 20 mg を前投薬として静脈内投与又は静脈内投与できない場合は経口投与した。75 歳を超える，過少体重（体格指数：18.5 未満），コントロール不良の糖尿病を有する，又はステロイド療法に対する不耐性若しくは有害事象の既往を有する被験者には，デキサメタゾンを 20 mg/週で投与した。

有害事象，臨床検査値異常及び臨床効果を詳細に観察するため，治療期のサイクル 1 の Day 1 から Day 8 まで被験者を入院させた。必要に応じて，診察及び臨床検査を追加実施した。疾患進

行が確認された場合は，治験薬の投与を中止し，被験者は中止時来院後に後観察期へ移行することとした。

治験参加の同意を撤回した又は追跡不能となった被験者を除き，中止時来院は，治験薬の最終投与から 4 週間（±3 日）後又は次の治療開始前の可能な限り早期に実施した。次の治療が開始される前に可能な限り中止時来院を実施した。被験者が中止時来院のために治験実施医療機関に来院できない場合，治験薬の最終投与後 30 日以内に発現した有害事象に関する情報を収集した。

後観察期：

後観察期は，中止時来院の直後から，治験薬の最終投与から 8 週後，死亡，追跡不能，治験参加の同意撤回又は治験終了のいずれか早い時点までとした。薬物動態評価用及び免疫原性評価用の検体を後観察期に採取した。

(8) 被験者数（計画時及び解析時）

被験者	**Vd+本剤（16 mg/kg）** 被験者数（割合）
計画	6 以上，20 以下
組入れ	8
治験薬投与	8 (100.0%)
有効性解析対象（奏効評価対象集団）	8 (100.0%)
安全性解析対象（安全性解析対象集団）	8 (100.0%)
薬物動態解析対象（薬物動態評価対象集団）	8 (100.0%)
免疫原性評価対象（免疫原性評価対象集団）	5 (62.5%)
DLT 評価対象（DLT 評価対象集団）	8 (100.0%)

DLT：用量制限毒性

(9) 診断及び主な組入れ基準

症候性骨髄腫［国際骨髄腫作業部会（IMWG）診断規準］と診断され，20 歳以上の日本人の男性及び妊娠していない女性で，MM に対して 1 レジメン以上の前治療歴があり，直近のレジメンの投薬中又は投薬後に IMWG 治療効果判定規準に基づく治験担当医師の奏効判定により progressive disease（PD）が確認されている患者を本治験の対象とした。患者は血清若しくは尿中 M 蛋白又は血清遊離軽鎖（FLC）に基づく測定可能病変を有することとした。

(10)　被験薬，用量及び投与方法，ロット番号

本剤は無色～淡黄色で，20 mg/mL の無菌濃縮液としてバイアルに充填され，提供された（ロット番号：[redacted]）。静脈内投与前に，発熱性物質を含まない滅菌生理食塩水（0.9% NaCl）で希釈した。

ボルテゾミブは 1.3 mg/m^2 の用量で治験担当医師が皮下投与した。注射部位反応が認められた被験者には，ボルテゾミブを静脈内投与した。

デキサメタゾン 20 mg は，使い切りバイアル又は経口投与用錠剤として，治験担当医師の処方に従い提供した。

(11) 対照薬，用量及び投与方法，ロット番号

該当なし

(12) 投与期間

治療期は，サイクル 1 Day 1 の治験薬（本剤，ボルテゾミブ又はデキサメタゾン）投与から治験薬の投与中止までとした。サイクル 1～8 は 21 日間サイクルとした。サイクル 9 以降は 28 日間サイクルとした。

(13) 評価基準

薬物動態：

血清中 daratumumab の薬物動態パラメータとして，最低血清中濃度（C_{min}）及び最高血清中濃度（C_{max}）を算出した。本剤の薬物動態を評価するための血液検体をサイクル 1，3，6，9 及び 12 の Day 1，中止時及び後観察期に採取した。

免疫原性：

本剤に対する抗体を，サイクル 1 Day 1 の投与前，中止時及び後観察期に評価した。

バイオマーカー：

バイオマーカー（ナチュラルキラー細胞及び T 細胞）の評価を実施した。バイオマーカー評価用の血液検体は，サイクル 1，2，3 及び 8 並びに中止時に採取した。

有効性：

有効性は本治験の主要目的ではなかったが，有効性評価項目として，ORR［partial response（PR）以上］及び奏効到達期間（本剤の初回投与から最初に PR 以上の判定規準に合致した有効性評価までの期間）を評価した。その他の有効性評価項目は，奏効持続期間，無増悪期間（TTP），無増悪生存期間（PFS），全生存期間（OS），血清及び尿中 M 蛋白の変化とした。有効性評価として IMWG の治療効果判定規準に基づく治療効果を検討した。奏効［stringent complete response（sCR），CR，VGPR 及び PR］が認められた被験者の割合及び臨床的有用率［sCR + CR + VGPR + PR + minimal response（MR）］を要約した。

安全性：

有害事象，臨床検査値，バイタルサイン，身体所見，心電図（ECG）及び Eastern Cooperative Oncology Group（ECOG）の performance status に基づき安全性を評価した。初回用量である本剤 16 mg/kg の用量での DVd 療法の忍容性については，治験評価委員会が検討して判断した。

DLT：

DLT は，DLT 評価期間に発現した本剤と関連性がある有害事象のうち，治験実施計画書で規定した IRR，血液学的毒性又は非血液学的毒性に該当する事象と定義した。

(14) 統計手法

解析対象集団

- 全投与解析対象集団：本剤の投与を 1 回以上受けた被験者で，明記しない限り，安全性解析対象集団としてすべての安全性解析及び有効性解析に使用した。

・ 奏効評価対象集団：本剤の投与を 1 回以上受け，かつ治療期中にベースラインとの比較が可能な疾患評価を受けた被験者

・ 薬物動態評価対象集団：本剤の投与を 1 回以上受け，かつ投与後に daratumumab 濃度データが 1 つ以上得られた被験者

・ 免疫原性評価対象集団：本剤の投与を 1 回以上受け，かつ投与後に本剤に対する免疫原性データが 1 つ以上得られた被験者

・ DLT 評価対象集団：全投与解析対象集団の中で用量漸増を決定するための DLT 評価が可能な被験者

解析計画

薬物動態：各検体採取時点の血清中 daratumumab 濃度（C_{max} 及び C_{min}）を記述統計量を用いて要約した。

免疫原性：本剤投与を 1 回以上受け，本剤に対する抗体検出に適した検体を有する被験者において，本剤に対する抗体の発現割合を要約した。

バイオマーカー：CD3+CD4+，CD3+CD8+，CD3-CD16+CD56+及び CD19+の値を来院時点ごとに要約した。

有効性：ORR，奏効到達期間及びその他の有効性評価項目［奏効持続期間，無増悪期間（TTP），PFS，OS，血清及び尿中 M 蛋白の変化］を要約した。奏効に関連したすべての解析には奏効評価対象集団を用いた。

安全性：安全性の解析では，すべての有害事象，死亡，重篤な有害事象，その他の重要な有害事象（投与中止，投与延期，減量及び投与中断に至った有害事象）及び特に注目すべき有害事象（IRR，感染症及び寄生虫症）について記述統計量及び発現割合を算出した。有害事象の重症度は，National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 に従い判定した。臨床検査値は，クレアチニン濃度，ヘモグロビン濃度，血小板数，白血球数，好中球数及びリンパ球数について，シフトテーブル及び経時プロット図を用いて要約した。臨床検査値異常は一覧表に示した。本剤の ECG に対する影響を記述統計量及び頻度集計で評価した。その他の安全性データ（バイタルサイン及び身体所見）は一覧表又は表に示した。

2.7.6.6.1.2 結果

(1) 対象集団

本治験は日本の 5 施設で実施した。2016 年 6 月 3 日（最後の被験者がサイクル 6 Day 1 を完了）のクリニカルデータカットオフ日時点で，8 例が組み入れられ，すべての被験者に本剤が 1 回以上投与された。クリニカルデータカットオフ日時点で，治験薬が投与された 8 例中 7 例（87.5%）は投与を継続中であり，1 例（12.5%）は有害事象の前立腺癌のために治験薬の投与を中止していた。本治験を中止した被験者はいなかった。治験薬の投与期間の中央値は 5.34 カ月（範囲：4.3～8.9 カ月）であった。

人口統計学的特性

年齢の中央値は 74.5 歳（範囲：54～82 歳）であり，4 例（50.0%）は 75 歳以上であった。6 例（75.0%）は男性であった。体重の平均値（標準偏差）は 57.40（10.281）kg，体表面積の平均値（標準偏差）は 1.583（0.1859）m^2 であった。ベースラインの ECOG スコアはいずれの被験者も 0 又は 1 であった。

ベースライン疾患特性

免疫蛍光検査により 4 例（50.0%）が IgG 型，2 例（25.0%）が IgA 型，2 例（25.0%）がκ軽鎖型の骨髄腫を有していた。血清中に測定可能病変を有した被験者は 5 例（62.5%）で，IgG が最も多く（3 例，37.5%），次いで IgA（2 例，25.0%）であった。測定可能病変が尿中のみであった被験者は 1 例（12.5%）で，残りの 2 例（25.0%）の測定可能病変は血清 FLC のみであった。ほとんど（7 例，87.5%）の被験者は病期 I 期であった。すべての被験者が MM に対する前治療を 1 又は 2 レジメン受けていた。4 例（50.0%）はボルテゾミブの前治療を受けていた。初回診断から治験薬初回投与までの期間の中央値は 3.74 年（範囲：2.3～11.5 年）であった。

前治療及び併用療法

すべての被験者に MM に対する全身療法の前治療歴があった。2 例（25.0%）は自家造血幹細胞移植歴があった。前治療数は 6 例（75.0%）が 2 レジメンであった。ボルテゾミブの前治療歴が 4 例（50.0%），免疫調節薬であるレナリドミド及びサリドマイドの前治療歴が各 3 例（37.5%）にあった。アルキル化剤の前治療歴が 7 例（87.5%）にあった。すべての被験者に全身用副腎皮質ステロイドの前治療歴があった。治験参加前に MM に関連する手術又は放射線療法を受けた被験者はいなかった。

治験実施計画書からの逸脱

治験実施計画書からの重要な逸脱が 3 例（37.5%）で報告された。3 例中 2 例の逸脱は，ボルテゾミブの規定外の用法・用量レジメンでの投与であった。ボルテゾミブの 1 週間隔投与への変更は，末梢性ニューロパチーが認められた場合にのみ許容していたが，1 例では，サイクル 1 中に認められた Grade 4 の血小板減少症のため，サイクル 2 Day 1（DLT 評価の終了後）からボルテゾミブを 1 週間隔で投与された。別の 1 例も，サイクル 1 に認められた血液毒性のため，サイクル 2 Day 1 からボルテゾミブを 1 週間隔で投与された。残り 1 例の逸脱は，併用禁止療法（DLT 評価期間中の血小板輸血）の実施であった。

(2) 有効性

DVd 療法の効果

8 例全例で DVd 療法の奏効評価が可能であった。ORR（PR 以上）は 100.0%であり，sCR 及び CR が各 1 例（12.5%），VGPR が 2 例（25.0%），PR が 4 例（50.0%）であった。クリニカルデータカットオフ日時点で PD と判定された被験者はいなかった。初回奏効（PR 以上）到達期間の中央値は 0.9 カ月（95%信頼区間：0.8～1.5 カ月）であった。

その他の有効性

奏効持続期間：

クリニカルデータカットオフ日時点での奏効持続期間の中央値は，4.06 カ月（範囲：3.5～8.1 カ月）であった。

M 蛋白：

ベースライン時に血清 M 蛋白は 5 例で測定可能であった。血清 M 蛋白の平均値はすべての測定時点でベースラインから経時的に減少し，ベースラインからの減少率は Week 24 が最大であり，その中央値は 90.0%（範囲：80.0～100.0%）であった。5 例全例で血清 M 蛋白の減少が認められ，ベースラインからの最大減少率は，いずれの被験者も 50%以上であった。このうち 3 例（3/5 例，60.0%）の最大減少率は 90%以上であり，うち 1 例（1/5 例，20.0%）は 100%であった。

ベースライン時の測定可能病変が尿中 M 蛋白のみであった 1 例では，ベースライン以降に尿中 M 蛋白は検出されなかった。ベースライン時の測定可能病変が血清 FLC のみであった 2 例では，血清 FLC 値の involved FLC と uninvolved FLC の差（dFLC）の減少が認められた。dFLC のベースラインからの最大減少率は，2 例ともに 90.0%以上であった。

(3) 安全性

8 例全例に有害事象が発現した。クリニカルデータカットオフ日時点までに死亡した被験者はいなかった。

有害事象

発現割合が高かった有害事象（基本語）は，血小板減少症（7 例，87.5%）及びリンパ球減少症（5 例，62.5%）であった。これらの事象は，いずれも治験薬と関連性があると治験担当医師によって判断された。

Grade 3 以上の有害事象

Grade 5 の有害事象は認められなかった。8 例全例で Grade 3 又は 4 の有害事象が発現した。発現割合が高かった Grade 3 又は 4 の有害事象（基本語）は，血小板減少症（6 例，75.0%）及びリンパ球減少症（5 例，62.5%）であった。Grade 4 の血小板減少症が 3 例（37.5%），Grade 4 のリンパ球減少症が 1 例（12.5%）で発現した。

重篤な有害事象

重篤な有害事象が 3 例（37.5%）で発現し，その内訳は帯状疱疹，鼻咽頭炎及び前立腺癌（各 1 例，12.5%）であった。このうち帯状疱疹及び鼻咽頭炎は治験薬と関連性があると判断された。

その他の重要な有害事象

1 例が前立腺癌（重篤な有害事象）のために治験薬の投与を中止した。本事象は治験薬と関連性がないと判断された。

サイクルの遅延又は投与調節に至った有害事象が 8 例全例で発現し，血小板減少症によるものが最も多かった（4 例，50.0%）。

特に注目すべき有害事象

IRR が 5 例（62.5%）に発現した。すべての IRR が初回投与時に発現し，Grade 1 又は 2 であった。発現割合が高かった IRR は，低酸素症，喘鳴及び悪寒（各 2 例，25.0%）であった。IRR 発現までの時間の中央値は 85.0 分（範囲：20.0～184.0 分）で，すべての IRR が発現後 24 時間以内に消失した。

血球減少に関連する有害事象が 8 例全例に発現した。発現割合が高かった血球減少に関連する有害事象は，血小板減少症（7 例，87.5%）及びリンパ球減少症（5 例，62.5%）であった。ほとんどの被験者（7 例，87.5%）で認められた血球減少に関連する有害事象は Grade 3 又は 4 であっ

た。血小板減少症が発現した 7 例のうち，4 例（57.1%）は本事象のために治験薬の投与調節又はサイクルの遅延に至り，1 例は出血を伴う血小板減少症が発現して DLT と判定され，別の 1 例では Grade 1 の皮下出血が認められた。

Grade 3 又は 4 の感染症及び寄生虫症が 2 例（25.0%）で発現し，その内訳は帯状疱疹及び鼻咽頭炎（各 1 例，12.5%）で，いずれも重篤な有害事象として報告された。予防的な抗ウイルス剤投与を受けた 7 例中 4 例で感染症が発現し，1 例で日和見感染が発現した。予防的な抗菌薬投与を受けた 5 例中 3 例で感染症が発現したが，日和見感染は認められなかった。

DLT

3 件の DLT イベント［Grade 3 の血小板減少症，Grade 3 のγ－グルタミルトランスフェラーゼ増加及び Grade 3 のアスパラギン酸アミノトランスフェラーゼ（AST）増加］が 2 例（25.0%）に認められた。血小板減少症の DLT は血小板輸血を要した。DLT のために治験薬の投与を中止した被験者はいなかった。治験評価委員会が DLT をレビューした結果，本剤 16 mg/kg と Vd 療法の併用は安全かつ忍容性があると判断された。

臨床検査値

平均ヘモグロビン濃度はベースラインからサイクル 8 Day 11 までおおむね安定しており，変動は軽微（20 g/L 以内）であった（各測定時点の評価可能被験者数 5～8 例）。平均血小板数は，各サイクルの Day 1 に急激に減少し，その後急激に回復した。この変動は最初の 2 サイクルで顕著で，臨床検査の基準値下限（LLN）である 130×10^9/L 未満を示した。平均白血球数及び好中球数は，サイクル 2 の Day 1 に急激に減少し，サイクル 2 Day 15 にベースライン値へ回復した。その後，平均白血球数及び好中球数の変動はサイクル 8 Day 11 まで軽微で，LLN である白血球数 3.7×10^9/L 及び好中球数 1.665×10^9/L を上回る値で安定して推移した（各測定時点の評価可能被験者数 5～8 例）。平均リンパ球数の急激な減少がサイクル 1 Day 8 に認められたが，徐々に増加してサイクル 3 Day 15 にはベースライン値へ回復した。その後，平均リンパ球数の変動はサイクル 8 Day 11 まで軽微で，LLN である 0.999×10^9/L を上回る値で安定して推移した（各測定時点の評価可能被験者数 5～8 例）。

平均 AST 値及びアラニンアミノトランスフェラーゼ値は，サイクル 2 Day 1 でベースラインから上昇したが，それぞれの基準値上限である 38.0 U/L 及び 43.0 U/L 未満の値であった。その後，平均 AST 値及びアラニンアミノトランスフェラーゼ値は，それぞれサイクル 4 及びサイクル 5 の Day 1 に低下が認められ，クリニカルデータカットオフ日時点までベースライン値未満のままであった。血清クレアチニン濃度は，サイクル 8 までほぼベースライン値のまま維持された（各測定時点の評価可能被験者数 6～8 例）。

その他の安全性所見

クリニカルデータカットオフ日時点まで，ECG 又はバイタルサインの臨床的に重要な異常は認められなかった。

(4) 薬物動態，免疫原性及びバイオマーカー

薬物動態

8 例全例でサイクル 6 Day 1 までの薬物動態評価が可能であった。初回投与後（サイクル 1 Day 1 の投与後）の daratumumab ピーク濃度の平均値（標準偏差）は 354.10（61.757）μg/mL で

あった。本剤 1 週間隔の投与期間の少なくとも 7 回目投与（1 週間隔投与での最後の薬物動態検体採取時点）まで，daratumumab のピーク濃度は継続して増加し，サイクル 3 の Day 1 投与後の daratumumab ピーク濃度の平均値（標準偏差）は 864.98（167.806）μg/mL であり，初回投与後に比べて 2.4 倍増加した。本剤を 1 週間隔で 6 回投与した後のサイクル 3 Day 1 投与前のトラフ濃度の平均値（標準偏差）は 512.87（137.972）μg/mL であった。サイクル 6 Day 1 投与前のトラフ濃度の平均値（標準偏差）は 536.05（144.480）μg/mL であった。サイクル 1 Day 1 からサイクル 6 Day 1 までの daratumumab の平均 C_{max}（標準偏差）は 937.25（160.965）μg/mL，平均 C_{min}（標準偏差）は 350.75（63.539）μg/mL であった。

免疫原性

本剤の初回投与後に本剤に対する抗体が評価された被験者は 5 例であった。治験期間中に本剤に対する抗体が陽性となった被験者はいなかった。

バイオマーカー

全血を用いたバイオマーカーの分析を，ベースライン（サイクル 1 Day 1），サイクル 2，3 及び 8 の Day 1 に実施した。CD3-CD16+CD56+細胞レベルは，すべての測定時点でベースラインから減少した。同様の傾向が，CD3+CD4+細胞及び CD19+細胞でも認められた。CD3+CD8+リンパ球に変動は認められなかった。

2.7.6.6.1.3　結論

1 レジメン以上の前治療歴を有する再発又は難治性の MM の日本人患者における DVd 療法（本剤 16 mg/kg）の忍容性が認められた。また，本治験の結果から，当該患者集団での DVd 療法（本剤 16 mg/kg）の良好な安全性及び有効性プロファイルが示された。

2.7.6.6.2 有害事象

2016 年 6 月 3 日のクリニカルデータカットオフ日時点での，因果関係を問わない有害事象及び治験薬と関連性がある有害事象をそれぞれ表 2.7.6.6-1 及び表 2.7.6.6-2 に示す。

表 2.7.6.6-1 有害事象［MMY1005 試験，安全性解析対象集団］

	Vd + Daratumumab (16 mg/kg) n (%)
Analysis set: Safety	8
Total number of subjects with TEAE	8 (100.0%)
MedDRA system organ class/Preferred term	
血液およびリンパ系障害	8 (100.0%)
血小板減少症	7 (87.5%)
リンパ球減少症	5 (62.5%)
貧血	3 (37.5%)
白血球減少症	3 (37.5%)
好中球減少症	3 (37.5%)
一般・全身障害および投与部位の状態	5 (62.5%)
疲労	3 (37.5%)
悪寒	2 (25.0%)
歩行障害	1 (12.5%)
末梢性浮腫	1 (12.5%)
発熱	1 (12.5%)
感染症および寄生虫症	5 (62.5%)
鼻咽頭炎	2 (25.0%)
気管支炎	1 (12.5%)
帯状疱疹	1 (12.5%)
インフルエンザ	1 (12.5%)
代謝および栄養障害	5 (62.5%)
高血糖	3 (37.5%)
脱水	2 (25.0%)
低カリウム血症	2 (25.0%)
低リン酸血症	1 (12.5%)
神経系障害	5 (62.5%)
異常感覚	3 (37.5%)
頭痛	1 (12.5%)
神経痛	1 (12.5%)
末梢性感覚ニューロパチー	1 (12.5%)
ヘルペス後神経痛	1 (12.5%)
胃腸障害	4 (50.0%)
便秘	2 (25.0%)
下痢	2 (25.0%)
胃炎	2 (25.0%)
腹部膨満	1 (12.5%)
上腹部痛	1 (12.5%)
消化不良	1 (12.5%)
悪心	1 (12.5%)
胃肉芽腫	1 (12.5%)
嘔吐	1 (12.5%)

表 2.7.6.6-1 有害事象［MMY1005 試験，安全性解析対象集団］（続き）

	Vd + Daratumumab (16 mg/kg) n (%)
臨床検査	4 (50.0%)
血中乳酸脱水素酵素増加	3 (37.5%)
体重減少	3 (37.5%)
アラニンアミノトランスフェラーゼ増加	1 (12.5%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (12.5%)
血圧上昇	1 (12.5%)
血中尿素増加	1 (12.5%)
Ｃ－反応性蛋白増加	1 (12.5%)
細胞マーカー増加	1 (12.5%)
フィブリン分解産物増加	1 (12.5%)
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)
サーファクタントプロテイン増加	1 (12.5%)
呼吸器、胸郭および縦隔障害	4 (50.0%)
低酸素症	2 (25.0%)
喘鳴	2 (25.0%)
発声障害	1 (12.5%)
口腔咽頭不快感	1 (12.5%)
口腔咽頭痛	1 (12.5%)
皮膚および皮下組織障害	4 (50.0%)
皮膚嚢腫	1 (12.5%)
皮膚炎	1 (12.5%)
紅斑	1 (12.5%)
皮下出血	1 (12.5%)
全身性皮疹	1 (12.5%)
眼障害	2 (25.0%)
眼精疲労	1 (12.5%)
霧視	1 (12.5%)
筋骨格系および結合組織障害	2 (25.0%)
筋力低下	1 (12.5%)
ミオパチー	1 (12.5%)
精神障害	2 (25.0%)
短時間睡眠	1 (12.5%)
不眠症	1 (12.5%)
耳および迷路障害	1 (12.5%)
片耳難聴	1 (12.5%)
肝胆道系障害	1 (12.5%)
薬物性肝障害	1 (12.5%)
傷害、中毒および処置合併症	1 (12.5%)
凍瘡	1 (12.5%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (12.5%)
前立腺癌	1 (12.5%)
血管障害	1 (12.5%)
高血圧	1 (12.5%)
低血圧	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population as denominator.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE02.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE02.SAS] 28SEP2016, 04:13

表 2.7.6.6-2 治験薬と関連性がある有害事象［MMY1005 試験，安全性解析対象集団］

	Vd + Daratumumab (16 mg/kg) n (%)			
	Related to Treatment	Related to Daratumumab	Related to Bortezomib	Related to Dexamethasone
Analysis set: Safety	8			
Subjects with drug-related TEAE	8 (100.0%)	7 (87.5%)	8 (100.0%)	8 (100.0%)
MedDRA system organ class/Preferred term				
血液およびリンパ系障害	8 (100.0%)	7 (87.5%)	8 (100.0%)	5 (62.5%)
血小板減少症	7 (87.5%)	6 (75.0%)	7 (87.5%)	1 (12.5%)
リンパ球減少症	5 (62.5%)	5 (62.5%)	4 (50.0%)	5 (62.5%)
白血球減少症	3 (37.5%)	3 (37.5%)	3 (37.5%)	0
好中球減少症	3 (37.5%)	3 (37.5%)	3 (37.5%)	0
貧血	2 (25.0%)	1 (12.5%)	2 (25.0%)	1 (12.5%)
胃腸障害	4 (50.0%)	2 (25.0%)	2 (25.0%)	3 (37.5%)
便秘	2 (25.0%)	1 (12.5%)	2 (25.0%)	2 (25.0%)
胃炎	2 (25.0%)	1 (12.5%)	1 (12.5%)	2 (25.0%)
腹部膨満	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
上腹部痛	1 (12.5%)	0	0	1 (12.5%)
下痢	1 (12.5%)	0	1 (12.5%)	0
消化不良	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
悪心	1 (12.5%)	1 (12.5%)	0	0
嘔吐	1 (12.5%)	1 (12.5%)	0	0
感染症および寄生虫症	4 (50.0%)	4 (50.0%)	4 (50.0%)	4 (50.0%)
気管支炎	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
帯状疱疹	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
インフルエンザ	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
鼻咽頭炎	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
代謝および栄養障害	4 (50.0%)	0	1 (12.5%)	4 (50.0%)
高血糖	3 (37.5%)	0	0	3 (37.5%)
低カリウム血症	2 (25.0%)	0	0	2 (25.0%)
脱水	1 (12.5%)	0	1 (12.5%)	0
呼吸器、胸郭および縦隔障害	4 (50.0%)	4 (50.0%)	1 (12.5%)	1 (12.5%)
低酸素症	2 (25.0%)	2 (25.0%)	0	0
喘鳴	2 (25.0%)	2 (25.0%)	0	0
発声障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
口腔咽頭不快感	1 (12.5%)	1 (12.5%)	0	0
口腔咽頭痛	1 (12.5%)	1 (12.5%)	0	0
一般・全身障害および投与部位の状態	3 (37.5%)	3 (37.5%)	3 (37.5%)	2 (25.0%)
疲労	3 (37.5%)	2 (25.0%)	3 (37.5%)	2 (25.0%)
悪寒	2 (25.0%)	2 (25.0%)	0	0
発熱	1 (12.5%)	1 (12.5%)	0	0
臨床検査	3 (37.5%)	3 (37.5%)	3 (37.5%)	2 (25.0%)
体重減少	2 (25.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)
アラニンアミノトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0	0
血中乳酸脱水素酵素増加	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
血圧上昇	1 (12.5%)	1 (12.5%)	0	0
血中尿素増加	1 (12.5%)	0	1 (12.5%)	0
Ｃ－反応性蛋白増加	1 (12.5%)	1 (12.5%)	0	0

表 2.7.6.6-2 治験薬と関連性がある有害事象［MMY1005 試験，安全性解析対象集団］

（続き）

	Vd + Daratumumab (16 mg/kg) n (%)			
	Related to Treatment	Related to Daratumumab	Related to Bortezomib	Related to Dexamethasone
細胞マーカー増加	1 (12.5%)	0	1 (12.5%)	0
フィブリン分解産物増加	1 (12.5%)	1 (12.5%)	0	0
γ－グルタミルトランスフェラーゼ増加	1 (12.5%)	1 (12.5%)	0	1 (12.5%)
サーファクタントプロテイン増加	1 (12.5%)	0	1 (12.5%)	0
神経系障害	3 (37.5%)	2 (25.0%)	3 (37.5%)	2 (25.0%)
異常感覚	2 (25.0%)	2 (25.0%)	2 (25.0%)	2 (25.0%)
頭痛	1 (12.5%)	1 (12.5%)	0	0
神経痛	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
末梢性感覚ニューロパチー	1 (12.5%)	0	1 (12.5%)	0
皮膚および皮下組織障害	3 (37.5%)	1 (12.5%)	3 (37.5%)	1 (12.5%)
皮膚炎	1 (12.5%)	0	1 (12.5%)	0
紅斑	1 (12.5%)	0	1 (12.5%)	0
全身性皮疹	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
眼障害	2 (25.0%)	2 (25.0%)	2 (25.0%)	2 (25.0%)
眼精疲労	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
霧視	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
筋骨格系および結合組織障害	2 (25.0%)	0	0	2 (25.0%)
筋力低下	1 (12.5%)	0	0	1 (12.5%)
ミオパチー	1 (12.5%)	0	0	1 (12.5%)
精神障害	2 (25.0%)	1 (12.5%)	1 (12.5%)	2 (25.0%)
短時間睡眠	1 (12.5%)	0	0	1 (12.5%)
不眠症	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
耳および迷路障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
片耳難聴	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
肝胆道系障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
薬物性肝障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	0
傷害、中毒および処置合併症	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
凍瘡	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
血管障害	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)
高血圧	1 (12.5%)	1 (12.5%)	0	0
低血圧	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)

Keys: Vd = bortezomib-dexamethasone; TEAE = treatment-emergent adverse event.
Note: Percentages calculated with the number of subjects in safety population in ‘Related to Treatment’ column as denominator.
Note: Adverse events related to study treatments are adverse events with a relationship to study treatments of very likely, probably or possible.
Note: Adverse events are coded using MedDRA version 18.0.

[TSFAE06.RTF] [JNJ-54767414\MMY1005\DBR_CSR\RE_CSR\PROD\TSFAE06.SAS] 28SEP2016, 04:15

2.7.6.6.3　個別症例の詳細

クリニカルデータカットオフ日時点までに，治験薬の最終投与後 30 日以内の死亡は認められなかった。治験薬と関連性がある重篤な有害事象の詳細経過を以下に示す。治験薬と関連性がない重篤な有害事象の詳細経過は，治験総括報告書【CTD 5.3.5.2.4-1】に示した。

2.7.6.6.3.1　治験薬と関連性がある重篤な有害事象（日本人）

(1) 被験者識別番号 810102

■ **REASON FOR NARRATIVE SELECTION**

Serious AEs

■ **Serious AEs**

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
帯状疱疹	Herpes zoster	2016-04-17 2016-04-26	83 10	Y 3	Probable Probable PROBABLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	VIRAL (HERPES ZOSTER)

■ **Demographics and Baseline Characteristics**

□ Country: JPN
□ Study site identifier: JP10001
□ Race: Asian
□ Age(yrs): 7
□ Sex: Female
□ Baseline weight(kg): 45
□ Baseline height(cm): 150.5
□ Baseline ecog score: 0

■ **Disposition Information**

□ Treatment discontinuation: Subject Ongoing on Treatment
□ Study discontinuation: Subject Ongoing on Study
□ Cause of death: (No Death)

■ Summary of Study Medication

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
189.19	638.20	25.98	2016-01-26	2016-06-03	4.27

■ Pre-infusion Medications

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dosing Frequency Per Interval/Route of Administration
Diphenhydramine	diphenhydramine	2016-01-26 1	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-01-26 1	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-02-02 8	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-02-02 8	- -	800mg	Once /oral
Dexamethasone	dexamethasone	2016-02-09 15	- -	19.8mg	Once /intravenous
Diphenhydramine	diphenhydramine	2016-02-09 15	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-02-09 15	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-02-19 25	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-02-19 25	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-02-26 32	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-02-26 32	- -	800mg	Once /oral
Dexamethasone	dexamethasone	2016-03-04 39	- -	19.8mg	Once /intravenous
Diphenhydramine	diphenhydramine	2016-03-04 39	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-03-04 39	- -	800mg	Once /oral

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dosing Frequency Per Interval/Route of Administration
Diphenhydramine	diphenhydramine	2016-03-11 46	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-03-11 46	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-03-18 53	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-03-18 53	- -	800mg	Once /oral
Dexamethasone	dexamethasone	2016-03-25 60	- -	19.8mg	Once /intravenous
Diphenhydramine	diphenhydramine	2016-03-25 60	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-03-25 60	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-04-01 67	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-04-01 67	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-05-13 109	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-05-13 109	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2016-06-03 130	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-06-03 130	- -	800mg	Once /oral

■ **Other Adverse Events**

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
胃炎	Gastritis	2016-02-18 -	24 -	N 2	Not related Not related POSSIBLE	Dose not changed DOSE NOT CHANGED Dose reduced	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
リンパ球減少症	Lymphopenia	2016-01-27 2016-01-29	2 3	N 3	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
リンパ球減少症	Lymphopenia	2016-02-19 2016-02-23	25 5	N 3	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
リンパ球減少症	Lymphopenia	2016-03-04 2016-03-11	39 8	N 3	Possible Possible POSSIBLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
末梢性浮腫	Leg edema	2016-03-20 -	55 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
ヘルペス後神経痛	Post herpetic neuralgia	2016-05-03 -	99 -	N 2	Not related Not related NOT RELATED	Dose not changed DOSE NOT CHANGED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-

■ Medical History

Dictionary-Derived Term (Reported Term for the Medical History)	Past or Current?
腱石灰化 (Calcific tendinitis)	Current
筋痙縮 (Cramps in the calves)	Current
高脂血症 (Hyperlipemia)	Current
不眠症 (Insomnia)	Current
腰部脊柱管狭窄症 (Lumber spinal stenosis)	Current
感覚鈍麻 (Numbness in feet)	Current
骨粗鬆症 (Osteoporosis)	Current
頻尿 (Pollakiuria)	Current
腱鞘炎 (Tenosvnovitis)	Current

■ Concomitant Medication

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dose Form	Dosing Frequency Per Interval/Route of Administration	Indication
ALENDRONATE SODIUM	BONALON TABLET	- -	- -	35mg	TABLET	QS /ORAL	MEDICAL HISTORY
ALFACALCIDOL	TOYOFAROL CAPSULES	- -	- -	0.1ug	CAPSULE	QD /ORAL	MEDICAL HISTORY
ASPARTATE CALCIUM	CALCIUM L-ASPARTATE HYDRATE	- -	- -	200mg	TABLET	BID /ORAL	MEDICAL HISTORY
FLAVOXATE HYDROCHLORIDE	BLADDERON TABLETS	- -	- -	200mg	TABLET	TID /ORAL	MEDICAL HISTORY
LIMAPROST ALFADEX	LIMAPROST ALFADEX	- -	- -	5ug	TABLET	TID /ORAL	MEDICAL HISTORY

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dose Form	Dosing Frequency Per Interval/Route of Administration	Indication
MECOBALAMIN	MECOBALAMIN	- -	- -	200ug	TABLET	TID /ORAL	MEDICAL HISTORY
OMEPRAZOLE	OMEPRAL TABLETS	- -	- -	20mg	TABLET	QD /ORAL	MEDICAL HISTORY
SHAKUYAKUKANZOTO	SHAKUYAKUKANZOTO	- -	- -	2.5g	POWDER	BID /ORAL	MEDICAL HISTORY
SIMVASTATIN	SIMVASTATIN	- -	- -	5mg	TABLET	QD /ORAL	MEDICAL HISTORY
PARACETAMOL	CALONAL	- -	2016-04-18 84	400mg	TABLET	PRN /ORAL	MEDICAL HISTORY
BIFIDOBACTERIUM BIFIDUM	LACB(BIFIDOBACTERIUM)	2016-02-03 9	- -	1g	POWDER	TID /ORAL	OTHER
ACICLOVIR	ACICLOVIR	2016-02-05 11	- -	200mg	TABLET	QD /ORAL	PROPHYLAXIS
ZOPICLONE	AMOBAN	2016-02-05 11	- -	7.5mg	TABLET	QD /ORAL	MEDICAL HISTORY
PROTON PUMP INHIBITORS	TAKECAB TABLET	2016-03-17 52	2016-03-23 58	20mg	TABLET	QD /ORAL	ADVERSE EVENT
FUROSEMIDE	FUROSEMIDE	2016-03-22 57	2016-04-01 67	40mg	TABLET	QD /ORAL	ADVERSE EVENT
PROTON PUMP INHIBITORS	TAKECAB TABLET	2016-03-24 59	- -	10mg	TABLET	QD /ORAL	ADVERSE EVENT
FUROSEMIDE	FUROSEMIDE	2016-04-02 68	- -	40mg	TABLET	PRN /ORAL	ADVERSE EVENT
PARACETAMOL	CALONAL	2016-04-19 85	- -	400mg	TABLET	PRN /ORAL	ADVERSE EVENT
ACICLOVIR	ACICLOVIR	2016-04-19 85	2016-04-19 85	250mg	INJECTION	QD /INTRAVENOUS	ADVERSE EVENT
ACICLOVIR	ACICLOVIR	2016-04-20 86	2016-04-25 91	250mg	INJECTION	TID /INTRAVENOUS	ADVERSE EVENT
PREGABALIN	LYRICA	2016-04-21 87	2016-05-05 101	75mg	CAPSULE	BID /ORAL	ADVERSE EVENT
ACICLOVIR	ACICLOVIR	2016-04-26 92	2016-04-26 92	250mg	INJECTION	QD /INTRAVENOUS	ADVERSE EVENT

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dose Form	Dosing Frequency Per Interval/Route of Administration	Indication
LOXOPROFEN SODIUM	LOXONIN	2016-05-06 102	2016-05-09 105	60mg	TABLET	PRN /ORAL	ADVERSE EVENT
OXYCODONE HYDROCHLORIDE	OXINORM (OXYCODONE HYDROCHLORIDE HYDRATE)	2016-05-09 105	- -	2.5mg	POWDER	PRN /ORAL	ADVERSE EVENT
OXYCODONE HYDROCHLORIDE	OXYCONTIN	2016-05-09 105	- -	5mg	TABLET	BID /ORAL	ADVERSE EVENT

■ Prior Systemic Therapies for Multiple Myeloma

Group ID	Standardized Medication Name	Start Date/Time of Medication	End Date/Time of Medication	Best Response	Transplant Related	Progress/Relapse Date for Prior Sys Ther
1	INVESTIGATIONAL DRUG	2013-05-08	2013-10-22	MR	Not transplant related	-
1	MELPHALAN	2013-05-08	2013-10-22	MR	Not transplant related	-
1	PREDNISOLONE	2013-05-08	2013-10-22	MR	Not transplant related	-
2	MELPHALAN	2013-10-23	2015-02-23	VGPR	Not transplant related	2015-08-11
2	PREDNISOLONE	2013-10-23	2015-02-23	VGPR	Not transplant related	2015-08-11
2	THALIDOMIDE	2013-10-23	2015-02-23	VGPR	Not transplant related	2015-08-11

■ Hematology/Chemistry Toxicities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Alanine aminotransferase high	18	2016-02-19/ 25	Cycle 2 day 1	67	U/L	5-40	1
Albumin low	-	2016-01-13/ -13	Screening	37	g/L	38-50	1
Albumin low	38	2016-02-19/ 25	Cycle 2 day 1	37	g/L	38-50	1
Albumin low	38	2016-03-11/ 46	Cycle 3 day 1	35	g/L	38-50	1
Aspartate aminotransferase high	23	2016-02-19/ 25	Cycle 2 day 1	57	U/L	10-40	1
Hemoglobin low	125	2016-02-01/ 7	Cycle 1 day 8	110	g/L	115-150	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low	125	2016-03-04/ 39	Cycle 2 day 15	112	g/L	115-150	1
Hemoglobin low	125	2016-03-11/ 46	Cycle 3 day 1	110	g/L	115-150	1
Hemoglobin low	125	2016-03-18/ 53	Cycle 3 day 8	110	g/L	115-150	1
Hemoglobin low	125	2016-04-12/ 78	Cycle 4 day 11	113	g/L	115-150	1
Lymphocytes low	1.437	2016-01-27/ 2	Cycle 1 day 2	0.327	x10E9/L	0.999-3.44	3
Lymphocytes low	1.437	2016-02-09/ 15	Cycle 1 day 15	0.778	x10E9/L	0.999-3.44	2
Lymphocytes low	1.437	2016-02-19/ 25	Cycle 2 day 1	0.448	x10E9/L	0.999-3.44	3
Lymphocytes low	1.437	2016-02-26/ 32	Cycle 2 day 8	0.705	x10E9/L	0.999-3.44	2
Lymphocytes low	1.437	2016-03-04/ 39	Cycle 2 day 15	0.487	x10E9/L	0.999-3.44	3
Lymphocytes low	1.437	2016-03-11/ 46	Cycle 3 day 1	0.709	x10E9/L	0.999-3.44	2
Lymphocytes low	1.437	2016-03-18/ 53	Cycle 3 day 8	0.522	x10E9/L	0.999-3.44	2
Lymphocytes low	1.437	2016-03-25/ 60	Cycle 3 day 15	0.636	x10E9/L	0.999-3.44	2
Lymphocytes low	1.437	2016-04-01/ 67	Cycle 4 day 1	0.579	x10E9/L	0.999-3.44	2
Lymphocytes low	1.437	2016-05-13/ 109	Cycle 5 day 1	0.98	x10E9/L	0.999-3.44	1
Magnesium low	0.8228	2016-05-13/ 109	Cycle 5 day 1	0.7405	mmol/L	0.7817-1.0696	1
Platelets low	211	2016-02-09/ 15	Cycle 1 day 15	114	x10E9/L	130-400	1
Platelets low	211	2016-03-04/ 39	Cycle 2 day 15	91	x10E9/L	130-400	1
Platelets low	211	2016-03-25/ 60	Cycle 3 day 15	96	x10E9/L	130-400	1

■ **ECOG Performance Status**

Date of ECOG Assessment/ Study Day	Visit	ECOG score
2016-01-05/ -21	Screening	0
2016-01-26/ 1	Cycle 1 day 1	0
2016-02-19/ 25	Cycle 2 day 1	0
2016-03-11/ 46	Cycle 3 day 1	0
2016-04-01/ 67	Cycle 4 day 1	0
2016-05-13/ 109	Cycle 5 day 1	0
2016-06-03/ 130	Cycle 6 day 1	0

■ **On-study Transfusions**

No On-study Transfusions reported

■ **NARRATIVE TEXT**

被験者 810102 は，7[redacted]歳のアジア人女性で，2013 年 4 月 23 日に初めて病期 I（スクリーニング時）の MM と診断され，本治験で本剤，デキサメタゾン及びボルテゾミブの投与を受けた。治験組入れ時の合併症は，腱石灰化，筋痙縮，高脂血症，不眠症，腰部脊柱管狭窄症，感覚鈍麻，骨粗鬆症，頻尿及び腱鞘炎であった。ベースラインの ECOG スコアは 0 であった。その他の既往歴はなかった。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 は治験薬，メルファラン及びプレドニゾロン，レジメン 2 はメルファラン，プレドニゾロン及びサリドマイドであった。

治験組入れ時の併用薬は，アレンドロン酸ナトリウム，アルファカルシドール，アスパラギン酸カルシウム，フラボキサート，リマプロストアルファデクス，メコバラミン，オメプラゾール，芍薬甘草湯，シンバスタチン及びアセトアミノフェンであった。

Day 11 からアシクロビルの予防的投与を実施した。Day 83（2016 年 4 月 17 日）に，背部痛が認められた。Day 85 に，被験者は**帯状疱疹**と診断されて入院し，本事象は **Grade 3 の重篤な有害事象**として報告された（発現日 Day 83）。入院時の帯状疱疹は右胸部から背部に及んだ。胸部 X 線検査，ECG 並びに血液及び尿検査を実施したが，臨床的に重要な結果は認められなかった。帯状疱疹に対して，アシクロビル，アセトアミノフェン及びプレガバリ

ンによる治療を実施した。治験担当医師は，帯状疱疹と本剤，ボルテゾミブ及びデキサメタゾンとの因果関係を「可能性大」と判断した。Day 88 に発疹が褐色化し，Day 90 に，被験者は顔面浮腫，右耳痛及び咽喉痛を訴えた。帯状疱疹のために，本剤，ボルテゾミブ及びデキサメタゾンを休薬した。Day 92 に，帯状疱疹の発疹は痂皮化し，アシクロビルの院内投与を中止した。帯状疱疹は回復し，顔面浮腫，右耳痛及び咽喉痛は Day 92 に軽快した。同日に，被験者は経口アシクロビルを処方され退院した。

Day 99 に，**非重篤な有害事象の Grade 2 のヘルペス後神経痛**が報告され，治験担当医師は本事象と本剤，ボルテゾミブ又はデキサメタゾンとの因果関係を「関連なし」と判断した。ヘルペス後神経痛のためにデキサメタゾンを休薬したが，本剤及びボルテゾミブの処置は実施しなかった。ヘルペス後神経痛に対し，ロキソプロフェンナトリウム及びオキシコドンによる治療を実施した。Day 130 からデキサメタゾンの投与を再開した。本報告書（クリニカルデータカットオフ日の 2016 年 6 月 3 日時点）では，ヘルペス後神経痛は未回復で，被験者は治験薬の投与継続中であった。

(2) 被験者識別番号 810201

■ REASON FOR NARRATIVE SELECTION

Serious AEs

■ Serious AEs

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
鼻咽頭炎	Infection(common cold)	2015-12-19 2015-12-23	53 5	Y 3	Possible Possible POSSIBLE	Drug interrupted DRUG INTERRUPTED Drug interrupted	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	No

■ Demographics and Baseline Characteristics

- □ Country: JPN
- □ Study site identifier: JP10002
- □ Race: Asian
- □ Age(yrs): 8[redacted]
- □ Sex: Male
- □ Baseline weight(kg): 71.7
- □ Baseline height(cm): 168.5
- □ Baseline ecog score: 0

■ Disposition Information

□ Treatment discontinuation: Subject Ongoing on Treatment

□ Study discontinuation: Subject Ongoing on Study

□ Cause of death: (No Death)

■ **Summary of Study Medication**

Daratumumab Cumulative Dose (mg/kg) Within Time Period	Dexamethasone Cumulative Dose (mg) Within Time Period	Velcade Cumulative Dose (mg/m2) Within Time Period	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Duration of Treatment (Months)
213.40	298.00	31.11	2015-10-28	2016-05-17	6.67

■ **Pre-infusion Medications**

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dosing Frequency Per Interval/Route of Administration
Diphenhydramine	diphenhydramine	2015-10-28 1	- -	50mg	Once /oral
Paracetamol	paracetamol	2015-10-28 1	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2015-11-04 8	- -	50mg	Once /oral
Paracetamol	paracetamol	2015-11-04 8	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2015-11-24 28	- -	50mg	Once /oral
Paracetamol	paracetamol	2015-11-24 28	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2015-12-01 35	- -	50mg	Once /oral
Paracetamol	paracetamol	2015-12-01 35	- -	800mg	Once /oral
Diphenhydramine	diphenhydramine	2015-12-15 49	- -	50mg	Once /oral
Paracetamol	paracetamol	2015-12-15 49	- -	800mg	Once /oral
Dexamethasone	dexamethasone	2015-12-29 63	- -	19.8mg	Qd /intravenous
Diphenhydramine	diphenhydramine	2015-12-29 63	- -	50mg	Qd /oral

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dosing Frequency Per Interval/Route of Administration
Paracetamol	paracetamol	2015-12-29 63	- -	800mg	Qd /oral
Diphenhydramine	diphenhydramine	2016-01-05 70	- -	50mg	Qd /oral
Paracetamol	paracetamol	2016-01-05 70	- -	800mg	Qd /oral
Diphenhydramine	diphenhydramine	2016-01-26 91	- -	50mg	Qd /oral
Paracetamol	paracetamol	2016-01-26 91	- -	800mg	Qd /oral
Diphenhydramine	diphenhydramine	2016-02-16 112	- -	50mg	Qd /oral
Paracetamol	paracetamol	2016-02-16 112	- -	800mg	Qd /oral
Diphenhydramine	diphenhydramine	2016-03-08 133	- -	50mg	Qd /oral
Paracetamol	paracetamol	2016-03-08 133	- -	800mg	Qd /oral
Diphenhydramine	diphenhydramine	2016-03-29 154	- -	50mg	Qd /oral
Paracetamol	paracetamol	2016-03-29 154	- -	800mg	Qd /oral
Dexamethasone	dexamethasone	2016-04-19 175	- -	19.8mg	Qd /intravenous
Diphenhydramine	diphenhydramine	2016-04-19 175	- -	50mg	Qd /oral
Paracetamol	paracetamol	2016-04-19 175	- -	800mg	Qd /oral
Dexamethasone	dexamethasone	2016-05-17 203	- -	19.8mg	Once /intravenous
Diphenhydramine	diphenhydramine	2016-05-17 203	- -	50mg	Once /oral
Paracetamol	paracetamol	2016-05-17 203	- -	800mg	Once /oral

■ **Other Adverse Events**

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
貧血	Anemia	2015-11-17 2015-11-24	21 8	N 2	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
貧血	Anemia	2015-12-19 2016-02-02	53 46	N 2	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
紅斑	Redness(left arm)	2015-11-01 -	5 -	N 1	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERING/RESOLVING	N	-
紅斑	Redness(right arm)	2015-10-30 -	3 -	N 1	Not related Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERING/RESOLVING	N	-
低カリウム血症	Hypokalemia	2015-11-17 2015-12-01	21 15	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-
低カリウム血症	Hypokalemia	2016-01-05 2016-01-26	70 22	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
低カリウム血症	Hypokalemia	2016-01-26 2016-02-02	91 8	N 1	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
低カリウム血症	Hypokalemia	2016-02-02 2016-02-05	98 4	N 3	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/RESOLVED	N	-

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
低カリウム血症	Hypokalemia	2016-02-05 -	101 -	N 2	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y NOT RECOVERED/NOT RESOLVED	N	-
低カリウム血症	Hypokalmia	2015-12-01 2015-12-08	35 8	N 2	Not related Not related VERY LIKELY	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
低リン酸血症	Hypophosphatemia	2015-12-19 2016-01-26	53 39	N 2	Doubtful Doubtful DOUBTFUL	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
白血球減少症	White blood cell decreased	2015-11-04 2015-11-17	8 14	N 2	Probable Probable NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
白血球減少症	White blood cell decreased	2016-01-05 2016-01-15	70 11	N 2	Probable Doubtful NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
白血球減少症	White blood cell decreased	2016-02-02 2016-02-16	98 15	N 2	Probable Doubtful NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
リンパ球減少症	Lymphocyte count decreased	2015-10-29 2015-11-02	2 5	N 3	Probable Probable PROBABLE	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-
好中球減少症	Neutrophilic count decreased	2015-11-11 2015-11-17	15 7	N 2	Probable Probable NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/RESOLVED	N	-

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
好中球減少症	Neutrophilic count decreased	2016-01-05 2016-01-15	70 11	N 1	Probable Probable NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
好中球減少症	Neutrophilic count decreased	2016-02-23 2016-02-26	119 4	N 2	Probable Probable NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2015-10-29 2015-11-04	2 7	N 1	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2015-11-04 2015-11-11	8 8	N 2	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2015-12-01 2015-12-08	35 8	N 1	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2015-12-08 2015-12-15	42 8	N 3	Possible Very likely NOT RELATED	Drug interrupted DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2015-12-21 2015-12-29	55 9	N 2	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2016-01-15 2016-01-26	80 12	N 3	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Start Relative Day AE Duration in Days (N)	Serious Event Standard Toxicity Grade	Causality-Daratumumab Causality-Velcade Causality-Dexamethasone	Action Taken-Daratumumab Action Taken-Velcade Action Taken-Dexamethasone	Sponsor Study Treatment 1 Other Study Treatment 2 Other Study Treatment 1	Concomitant or Additional Trtmnt Given Outcome of Adverse Event	Infusion Reaction	Pathogen
血小板減少症	Thrombocytopenia	2016-02-02 2016-02-05	98 4	N 2	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2016-02-05 2016-02-16	101 12	N 3	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2016-02-23 2016-02-26	119 4	N 2	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2016-02-26 2016-03-08	122 12	N 3	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2016-03-18 2016-03-29	143 12	N 3	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia	2016-04-08 2016-04-19	164 12	N 3	Possible Very likely NOT RELATED	Dose not changed DOSE NOT CHANGED Dose not changed	Daratumumab Velcade DEXAMETHASONE	N RECOVERED/ RESOLVED	N	-
血小板減少症	Thrombocytopenia with bleeding(left temporal region)	2015-11-11 2015-11-17	15 7	N 3	Possible Very likely NOT RELATED	Drug interrupted DOSE REDUCED Dose not changed	Daratumumab Velcade DEXAMETHASONE	Y RECOVERED/ RESOLVED	N	-

■ Medical History

Dictionary-Derived Term (Reported Term for the Medical History)	Past or Current?
大動脈瘤 (An aortic aneurysm(chest))	Current
狭心症 (Angina pectoris)	Current
Ｂ型肝炎コア抗体陽性 (Anti-hbc antibody (positive))	Past
脳梗塞 (Asymptomatic cerebral infarction)	Current
ジルベール症候群 (Blood bilirubin increased(gilbert's syndrome))	Current
認知障害 (Cognitive disturbance)	Current
高脂血症 (Hyperlipidemia)	Current
高血圧 (Hypertension)	Current
不眠症 (Insomnia)	Current

■ Concomitant Medication

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dose Form	Dosing Frequency Per Interval/Route of Administration	Indication
ATORVASTATIN	ATORVASTATIN	- -	- -	10mg	TABLET	QD /ORAL	MEDICAL HISTORY
DOXAZOSIN	DOXAZOSIN	- -	- -	4mg	TABLET	QD /ORAL	MEDICAL HISTORY
SHAKUYAKUKANZOTO	SHAKUYAKU KANZOTO	- -	- -	2.5g	POWDER	TID /ORAL	PROPHYLAXIS
RAMELTEON	ROZEREM	- -	2015-11-01 5	8mg	TABLET	QD /ORAL	MEDICAL HISTORY
CILNIDIPINE	ATELEC	- -	2015-11-10 14	10mg	TABLET	BID /ORAL	MEDICAL HISTORY

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dose Form	Dosing Frequency Per Interval/Route of Administration	Indication
ACETYLSALICYLIC ACID	BAYASPIRIN	- -	2015-11-12 16	100mg	TABLET	QD /ORAL	MEDICAL HISTORY
FAMOTIDINE	FAMOTIDINE	- -	2015-12-19 53	20mg	TABLET	QD /ORAL	PROPHYLAXIS
TRICHLORMETHIAZIDE	FLUITRAN	- -	2016-04-19T07:30 175	2mg	TABLET	QD /ORAL	MEDICAL HISTORY
CILNIDIPINE	CILNIDIPINE	2015-11-11 15	- -	10mg	TABLET	BID /ORAL	MEDICAL HISTORY
POTASSIUM CHLORIDE	K-SUPPLY	2015-11-24 28	2015-12-07 41	1200mg	TABLET	BID /ORAL	ADVERSE EVENT
FAMOTIDINE	FAMOTIDINE IV	2015-12-19 53	2015-12-20 54	20mg	INJECTION	QD /INTRAVENOUS	PROPHYLAXIS
IMMUNOGLOBULIN HUMAN NORMAL	KENKETU GLOVENIN-I	2015-12-19 53	2015-12-20 54	5000mg	INJECTION	QD /INTRAVENOUS	ADVERSE EVENT
PARACETAMOL	ACETAMINOPHENE	2015-12-19 53	2015-12-20 54	400mg	TABLET	PRN /ORAL	ADVERSE EVENT
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	SOLDEM 3A	2015-12-19 53	2015-12-21 55	500mL	INJECTION	TID /INTRAVENOUS	ADVERSE EVENT
HALOPERIDOL	SERENACE	2015-12-19 53	2015-12-22T22:15 56	2.5mg	INJECTION	PRN /INTRAVENOUS	PROPHYLAXIS
CEFOZOPRAN HYDROCHLORIDE	FIRSTCIN	2015-12-19 53	2015-12-23 57	1000mg	INJECTION	BID /INTRAVENOUS	ADVERSE EVENT
CEFDINIR	CEFDINIR	2015-12-23 57	2015-12-29T18:00 63	100mg	CAPSULE	TID /ORAL	ADVERSE EVENT
FAMOTIDINE	FAMOTIDINE OD	2015-12-30 64	- -	20mg	TABLET	QD /ORAL	PROPHYLAXIS
POTASSIUM CHLORIDE	K-SUPPLY	2016-02-02 98	2016-02-05T07:30 101	1200mg	TABLET	BID /ORAL	ADVERSE EVENT

Standardized Medication Name	Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	End Date of Medication Study Day of End of Medication	Total Daily Dose	Dose Form	Dosing Frequency Per Interval/Route of Administration	Indication
POTASSIUM CHLORIDE	K-SUPPLY	2016-02-05 101	- -	1200mg	TABLET	BID /ORAL	ADVERSE EVENT
LOXOPROFEN SODIUM	LOXOPROFEN SODIUM TAPE	2016-04-19 175	- -	100mg	TAPE	PRN /TOPICAL	OTHER
TRICHLORMETHIAZIDE	TRICHLORMETHIAZIDE	2016-04-20 176	- -	2mg	TABLET	QD /ORAL	MEDICAL HISTORY

■ Prior Systemic Therapies for Multiple Myeloma

Group ID	Standardized Medication Name	Start Date/Time of Medication	End Date/Time of Medication	Best Response	Transplant Related	Progress/Relapse Date for Prior Sys Ther
1	MELPHALAN	2010-11-02	2012-02-29	PR	Not transplant related	2011-06-23
1	PREDNISOLONE	2010-11-02	2012-02-29	PR	Not transplant related	2011-06-23
1	THALIDOMIDE	2010-11-02	2012-02-29	PR	Not transplant related	2011-06-23
2	DEXAMETHASONE	2012-03-01	2015-08-19	PR	Not transplant related	2015-06-25
2	LENALIDOMIDE	2012-03-01	2015-08-19	PR	Not transplant related	2015-06-25

■ Hematology/Chemistry Toxicities

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Bilirubin high	-	2015-10-14/ -14	Screening	29.07	umol/L	3.42-17.1	2
Bilirubin high	27.36	2015-10-28/ 1	Cycle 1 day 1	27.36	umol/L	3.42-17.1	2
Bilirubin high	27.36	2015-11-04/ 8	Cycle 1 day 8	23.94	umol/L	3.42-17.1	1
Bilirubin high	27.36	2015-11-11/ 15	Cycle 1 day 15	30.78	umol/L	3.42-17.1	2
Bilirubin high	27.36	2015-11-17/ 21	Cycle 1 day 15 unscheduled 01	35.91	umol/L	3.42-17.1	2
Bilirubin high	27.36	2015-11-24/ 28	Cycle 2 day 1	23.94	umol/L	3.42-17.1	1
Bilirubin high	27.36	2015-12-01/ 35	Cycle 2 day 8	32.49	umol/L	3.42-17.1	2
Bilirubin high	27.36	2015-12-08/ 42	Cycle 2 day 15	30.78	umol/L	3.42-17.1	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Bilirubin high	27.36	2015-12-15/ 49	Cycle 3 day 1	29.07	umol/L	3.42-17.1	2
Bilirubin high	27.36	2015-12-19/ 53	Cycle 3 day 4 unscheduled 01	42.75	umol/L	3.42-17.1	2
Bilirubin high	27.36	2016-01-05/ 70	Cycle 4 day 1	32.49	umol/L	3.42-17.1	2
Bilirubin high	27.36	2016-01-26/ 91	Cycle 5 day 1	30.78	umol/L	3.42-17.1	2
Bilirubin high	27.36	2016-02-16/ 112	Cycle 6 day 1	25.65	umol/L	3.42-17.1	1
Bilirubin high	27.36	2016-03-08/ 133	Cycle 7 day 1	30.78	umol/L	3.42-17.1	2
Bilirubin high	27.36	2016-03-29/ 154	Cycle 8 day 1	25.65	umol/L	3.42-17.1	1
Bilirubin high	27.36	2016-04-19/ 175	Cycle 9 day 1	35.91	umol/L	3.42-17.1	2
Bilirubin high	27.36	2016-05-17/ 203	Cycle 10 day 1	37.62	umol/L	3.42-17.1	2
Calcium corrected	2.2691	2015-11-24/ 28	Cycle 2 day 1	2.2192	-	2.2434-2.7445	1
Calcium corrected	2.2691	2015-12-19/ 53	Cycle 3 day 4 unscheduled 01	2.2188	-	2.2434-2.7445	1
Calcium corrected	2.2691	2016-01-26/ 91	Cycle 5 day 1	2.1696	-	2.2434-2.7445	1
Calcium corrected	2.2691	2016-02-16/ 112	Cycle 6 day 1	2.1696	-	2.2434-2.7445	1
Calcium corrected	2.2691	2016-03-08/ 133	Cycle 7 day 1	2.1703	-	2.2434-2.7445	1
Calcium corrected	2.2691	2016-03-29/ 154	Cycle 8 day 1	2.1204	-	2.2434-2.7445	1
Calcium corrected	2.2691	2016-04-19/ 175	Cycle 9 day 1	2.1949	-	2.2434-2.7445	1
Creatinine high	106.08	2015-11-11/ 15	Cycle 1 day 15	114.92	umol/L	53.04-106.08	1
Hemoglobin low	-	2015-10-14/ -14	Screening	116	g/L	135-180	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low	108	2015-10-28/ 1	Cycle 1 day 1	108	g/L	135-180	1
Hemoglobin low	108	2015-11-04/ 8	Cycle 1 day 8	106	g/L	135-180	1
Hemoglobin low	108	2015-11-11/ 15	Cycle 1 day 15	105	g/L	135-180	1
Hemoglobin low	108	2015-11-17/ 21	Cycle 1 day 15 unscheduled 01	96	g/L	135-180	2
Hemoglobin low	108	2015-11-24/ 28	Cycle 2 day 1	101	g/L	135-180	1
Hemoglobin low	108	2015-12-01/ 35	Cycle 2 day 8	114	g/L	135-180	1
Hemoglobin low	108	2015-12-08/ 42	Cycle 2 day 15	110	g/L	135-180	1
Hemoglobin low	108	2015-12-15/ 49	Cycle 3 day 1	104	g/L	135-180	1
Hemoglobin low	108	2015-12-19/ 53	Cycle 3 day 4 unscheduled 01	94	g/L	135-180	2
Hemoglobin low	108	2015-12-21/ 55	Cycle 3 day 8	88	g/L	135-180	2
Hemoglobin low	108	2015-12-29/ 63	Cycle 3 day 15	99	g/L	135-180	2
Hemoglobin low	108	2016-01-05/ 70	Cycle 4 day 1	96	g/L	135-180	2
Hemoglobin low	108	2016-01-15/ 80	Cycle 4 day 11	94	g/L	135-180	2
Hemoglobin low	108	2016-01-26/ 91	Cycle 5 day 1	99	g/L	135-180	2
Hemoglobin low	108	2016-02-02/ 98	Cycle 5 day 8	101	g/L	135-180	1
Hemoglobin low	108	2016-02-05/ 101	Cycle 5 day 11	104	g/L	135-180	1
Hemoglobin low	108	2016-02-16/ 112	Cycle 6 day 1	101	g/L	135-180	1
Hemoglobin low	108	2016-02-26/ 122	Cycle 6 day 11	111	g/L	135-180	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Hemoglobin low	108	2016-03-08/ 133	Cycle 7 day 1	107	g/L	135-180	1
Hemoglobin low	108	2016-03-18/ 143	Cycle 7 day 11	107	g/L	135-180	1
Hemoglobin low	108	2016-03-29/ 154	Cycle 8 day 1	107	g/L	135-180	1
Hemoglobin low	108	2016-04-08/ 164	Cycle 8 day 11	108	g/L	135-180	1
Hemoglobin low	108	2016-04-19/ 175	Cycle 9 day 1	104	g/L	135-180	1
Hemoglobin low	108	2016-05-17/ 203	Cycle 10 day 1	115	g/L	135-180	1
Leukocytes low	12.8	2015-11-04/ 8	Cycle 1 day 8	2.9	x10E9/L	3.5-9	2
Leukocytes low	12.8	2015-11-11/ 15	Cycle 1 day 15	2.6	x10E9/L	3.5-9	2
Leukocytes low	12.8	2016-01-05/ 70	Cycle 4 day 1	2.7	x10E9/L	3.5-9	2
Leukocytes low	12.8	2016-02-02/ 98	Cycle 5 day 8	2.6	x10E9/L	3.5-9	2
Leukocytes low	12.8	2016-02-05/ 101	Cycle 5 day 11	2.9	x10E9/L	3.5-9	2
Leukocytes low	12.8	2016-03-18/ 143	Cycle 7 day 11	3.3	x10E9/L	3.5-9	1
Leukocytes low	12.8	2016-04-08/ 164	Cycle 8 day 11	3	x10E9/L	3.5-9	1
Lymphocytes low	-	2015-10-14/ -14	Screening	0.55	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2015-10-29/ 2	Cycle 1 day 1 unscheduled 01	0.274	x10E9/L	0.84-3.96	3
Lymphocytes low	2.048	2015-11-02/ 6	Cycle 1 day 4 unscheduled 01	0.585	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2015-11-04/ 8	Cycle 1 day 8	0.609	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2015-11-11/ 15	Cycle 1 day 15	0.676	x10E9/L	0.84-3.96	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Lymphocytes low	2.048	2015-11-17/ 21	Cycle 1 day 15 unscheduled 01	0.792	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2015-11-24/ 28	Cycle 2 day 1	0.798	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2016-02-05/ 101	Cycle 5 day 11	0.696	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2016-03-18/ 143	Cycle 7 day 11	0.66	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2016-04-08/ 164	Cycle 8 day 11	0.54	x10E9/L	0.84-3.96	2
Lymphocytes low	2.048	2016-04-19/ 175	Cycle 9 day 1	0.735	x10E9/L	0.84-3.96	2
Magnesium low	-	2015-10-14/ -14	Screening	0.6171	mmol/L	0.7405-0.9462	1
Magnesium low	0.7817	2016-01-26/ 91	Cycle 5 day 1	0.6994	mmol/L	0.7405-0.9462	1
Magnesium low	0.7817	2016-03-08/ 133	Cycle 7 day 1	0.6994	mmol/L	0.7405-0.9462	1
Magnesium low	0.7817	2016-03-29/ 154	Cycle 8 day 1	0.6994	mmol/L	0.7405-0.9462	1
Magnesium low	0.7817	2016-04-19/ 175	Cycle 9 day 1	0.6994	mmol/L	0.7405-0.9462	1
Magnesium low	0.7817	2016-05-17/ 203	Cycle 10 day 1	0.6994	mmol/L	0.7405-0.9462	1
Neutrophils low	9.728	2015-11-11/ 15	Cycle 1 day 15	1.404	x10E9/L	1.54-6.21	2
Neutrophils low	9.728	2016-01-05/ 70	Cycle 4 day 1	1.512	x10E9/L	1.54-6.21	1
Neutrophils low	9.728	2016-02-23/ 119	Cycle 6 day 8	1.488	x10E9/L	1.54-6.21	2
Phosphate low	1.001	2015-12-19/ 53	Cycle 3 day 4 unscheduled 01	0.6781	mmol/L	0.8073-1.4531	2
Phosphate low	1.001	2016-01-05/ 70	Cycle 4 day 1	0.6458	mmol/L	0.8073-1.4531	2
Platelets low	133	2015-10-29/ 2	Cycle 1 day 1 unscheduled 01	120	x10E9/L	125-370	1

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low	133	2015-11-04/ 8	Cycle 1 day 8	65	x10E9/L	125-370	2
Platelets low	133	2015-11-11/ 15	Cycle 1 day 15	25	x10E9/L	125-370	3
Platelets low	133	2015-11-17/ 21	Cycle 1 day 15 unscheduled 01	89	x10E9/L	125-370	1
Platelets low	133	2015-12-01/ 35	Cycle 2 day 8	88	x10E9/L	125-370	1
Platelets low	133	2015-12-08/ 42	Cycle 2 day 15	36	x10E9/L	125-370	3
Platelets low	133	2015-12-15/ 49	Cycle 3 day 1	99	x10E9/L	125-370	1
Platelets low	133	2015-12-19/ 53	Cycle 3 day 4 unscheduled 01	79	x10E9/L	125-370	1
Platelets low	133	2015-12-21/ 55	Cycle 3 day 8	67	x10E9/L	125-370	2
Platelets low	133	2015-12-29/ 63	Cycle 3 day 15	110	x10E9/L	125-370	1
Platelets low	133	2016-01-15/ 80	Cycle 4 day 11	49	x10E9/L	125-370	3
Platelets low	133	2016-01-26/ 91	Cycle 5 day 1	79	x10E9/L	125-370	1
Platelets low	133	2016-02-02/ 98	Cycle 5 day 8	58	x10E9/L	125-370	2
Platelets low	133	2016-02-05/ 101	Cycle 5 day 11	42	x10E9/L	125-370	3
Platelets low	133	2016-02-16/ 112	Cycle 6 day 1	89	x10E9/L	125-370	1
Platelets low	133	2016-02-23/ 119	Cycle 6 day 8	64	x10E9/L	125-370	2
Platelets low	133	2016-02-26/ 122	Cycle 6 day 11	49	x10E9/L	125-370	3
Platelets low	133	2016-03-08/ 133	Cycle 7 day 1	90	x10E9/L	125-370	1
Platelets low	133	2016-03-18/ 143	Cycle 7 day 11	44	x10E9/L	125-370	3

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Platelets low	133	2016-03-29/ 154	Cycle 8 day 1	104	x10E9/L	125-370	1
Platelets low	133	2016-04-08/ 164	Cycle 8 day 11	41	x10E9/L	125-370	3
Platelets low	133	2016-04-19/ 175	Cycle 9 day 1	100	x10E9/L	125-370	1
Platelets low	133	2016-05-17/ 203	Cycle 10 day 1	112	x10E9/L	125-370	1
Potassium low	-	2015-10-14/ -14	Screening	3.6	mmol/L	3.7-5	2
Potassium low	3.3	2015-10-28/ 1	Cycle 1 day 1	3.3	mmol/L	3.7-5	2
Potassium low	3.3	2015-11-04/ 8	Cycle 1 day 8	3	mmol/L	3.7-5	2
Potassium low	3.3	2015-11-11/ 15	Cycle 1 day 15	3	mmol/L	3.7-5	2
Potassium low	3.3	2015-11-17/ 21	Cycle 1 day 15 unscheduled 01	2.8	mmol/L	3.7-5	3
Potassium low	3.3	2015-11-24/ 28	Cycle 2 day 1	2.9	mmol/L	3.7-5	3
Potassium low	3.3	2015-12-15/ 49	Cycle 3 day 1	3.6	mmol/L	3.7-5	2
Potassium low	3.3	2015-12-19/ 53	Cycle 3 day 4 unscheduled 01	3.1	mmol/L	3.7-5	2
Potassium low	3.3	2015-12-21/ 55	Cycle 3 day 4 unscheduled 02	3	mmol/L	3.7-5	2
Potassium low	3.3	2015-12-29/ 63	Cycle 3 day 15	3	mmol/L	3.7-5	2
Potassium low	3.3	2016-01-05/ 70	Cycle 4 day 1	2.9	mmol/L	3.7-5	3
Potassium low	3.3	2016-01-26/ 91	Cycle 5 day 1	3.1	mmol/L	3.7-5	2
Potassium low	3.3	2016-02-02/ 98	Cycle 5 day 8	2.9	mmol/L	3.7-5	3
Potassium low	3.3	2016-02-05/ 101	Cycle 5 day 11	3	mmol/L	3.7-5	2

Lab Test	Baseline Value	Date of Specimen Collection/ Study Day	Visit	Result	Unit	Normal Range	Analysis Toxicity Grade
Potassium low	3.3	2016-02-16/ 112	Cycle 6 day 1	3.5	mmol/L	3.7-5	2
Potassium low	3.3	2016-03-08/ 133	Cycle 7 day 1	3.1	mmol/L	3.7-5	2
Potassium low	3.3	2016-03-29/ 154	Cycle 8 day 1	3	mmol/L	3.7-5	2
Potassium low	3.3	2016-04-19/ 175	Cycle 9 day 1	3.1	mmol/L	3.7-5	2
Potassium low	3.3	2016-05-17/ 203	Cycle 10 day 1	3	mmol/L	3.7-5	2
Sodium high	146	2016-01-26/ 91	Cycle 5 day 1	149	mmol/L	134-147	1
Sodium high	146	2016-03-08/ 133	Cycle 7 day 1	148	mmol/L	134-147	1
Sodium high	146	2016-05-17/ 203	Cycle 10 day 1	149	mmol/L	134-147	1

■ ECOG Performance Status

Date of ECOG Assessment/ Study Day	Visit	ECOG score
2015-10-08/ -20	Screening	0
2015-10-28/ 1	Cycle 1 day 1	0
2015-11-24/ 28	Cycle 2 day 1	0
2015-12-15/ 49	Cycle 3 day 1	0
2016-01-05/ 70	Cycle 4 day 1	1
2016-01-26/ 91	Cycle 5 day 1	1
2016-02-16/ 112	Cycle 6 day 1	1
2016-03-08/ 133	Cycle 7 day 1	1

Date of ECOG Assessment/ Study Day	Visit	ECOG score
2016-03-29/ 154	Cycle 8 day 1	1
2016-04-19/ 175	Cycle 9 day 1	1
2016-05-17/ 203	Cycle 10 day 1	1

■ **On-study Transfusions**

Date (Study Day)	Sequence Number	Name of Procedure	Indication
2015-11-11 (15)	1	PLATELETS TRANSFUSION	ADVERSE EVENT

■ **NARRATIVE TEXT**

被験者 810201 は，8[redacted]歳のアジア人男性で，治験組入れの約 5 年前に初めて病期 I（スクリーニング時）の MM と診断され，本治験で本剤，デキサメタゾン及びボルテゾミブの投与を受けた。治験組入れ時の合併症は，大動脈瘤，狭心症，脳梗塞，ジルベール症候群，認知障害，高脂血症，高血圧及び不眠症であった。ベースラインの ECOG スコアは 0 であった。B 型肝炎コア抗体陽性の既往歴を有した。

被験者は合計 2 レジメンの前治療を受けていた。レジメン 1 はメルファラン，プレドニゾロン及びサリドマイド，レジメン 2 はデキサメタゾン及びレナリドミドであった。

治験組入れ時の併用薬は，アトルバスタチン，ドキサゾシン，芍薬甘草湯，ラメルテオン，シルニジピン，アスピリン，ファモチジン及びトリクロルメチアジドであった。

Day 53（2015 年 12 月 19 日）に，38.8°C の発熱と咳嗽が認められ，歩行が困難であった。同日に，被験者は感染症管理のために入院した。感染病巣は不明であったが，ウイルス感染の可能性が考えられた。Day 53 の酸素飽和度は 93%であった。被験者は**鼻咽頭炎［記載語：感染（感冒）］**と診断され，本事象は **Grade 3 の重篤な有害事象**として報告された。治験担当医師は，鼻咽頭炎の原因は免疫不全であり，本剤，ボルテゾミブ及びデキサメタゾンとの因果関係を「可能性小」と判断した。セフォゾプラン，人免疫グロブリン，アセトアミノフェン及び炭水化物（詳細不明）／塩化カリウム／ナトリウムによる治療を実施した。鼻咽頭炎のために，本剤，ボルテゾミブ及びデキサメタゾンを休薬した。Day 54 に熱は下がり，体温は 36.4°C から 37.5°C の間であった。体温は Day 55 に 36.9°C，Day 56 に 37°C 及び 36.6°C であった。Day 57 に平熱となり，健康状態は良好であった。同日に，鼻咽頭炎は回復し，被験者は退院した。Day 63 から本剤の投与を再開し，Day 70 からボルテゾミブ及びデキサメタゾンの投与を再開した。

Day 70 に，ECOG スコアは 1 に悪化した。本報告書（クリニカルデータカットオフ日の 2016 年 6 月 3 日時点）では，被験者は治験薬の投与継続中であった。

2.7.6.7　海外臨床第 I/II 相試験（GEN503 試験，参考資料：5.3.5.4.1-1）

2.7.6.7.1　概要

2.7.6.7.1.1　計画

(1) 治験の標題

再発又は難治性の多発性骨髄腫（MM）患者を対象として，ダラツムマブ（以下本剤）とレナリドミド及びデキサメタゾンの併用療法（DRd 療法）の安全性を検討する非盲検，多施設共同，用量漸増，第 I/II 相試験

(2) 治験調整医師

[redacted] – [redacted], Vejle, Denmark

(3) 公表文献（引用文献）

Plesner T, et al. Phase 1/2 study of daratumumab, lenalidomide, and dexamethasone for relapsed multiple myeloma. Blood. 2016 Oct;128(14):1821-8.

(4) 治験実施期間

2012 年 6 月 [redacted] 日（最初の被験者の初回来院日）～2015 年 10 月 2 日（主解析のデータカットオフ日）。

主解析は実施済であるが，治験継続中の被験者は，限定した評価スケジュールにて治験薬の投与を継続している。

(5) 開発の相

第 I／II 相

(6) 目的

本治験の主要目的は，再発又は難治性の MM 患者を対象に，レナリドミド及びデキサメタゾンと併用時の本剤の安全性プロファイルを確立することであった。副次目的は，レナリドミド及びデキサメタゾンと併用時の本剤の有効性及び薬物動態を評価し，本剤の免疫原性を評価することであった。

(7) 治験方法

本治験は，再発又は難治性の MM 患者の治療として本剤とレナリドミド及びデキサメタゾンを併用投与する非盲検，多施設共同，第 I/II 相試験であった。第 I 相部分は用量漸増期であり，本剤 4 用量（2，4，8 及び 16 mg/kg）とレナリドミド及びデキサメタゾンの併用療法を標準的な 3＋3 デザインを用いて評価した。用量漸増は，集積された安全性データをレビューした独立デー

タモニタリング委員会の勧告に基づいて，治験依頼者が決定した。第 II 相部分の推奨用量（RP2D）として 16 mg/kg を選択した。第 II 相部分は維持用量期であり，RP2D の安全性及び有効性を更に探索するデザインとした。第 II 相部分では，本剤 16 mg/kg を 1000 mL で約 6 時間（標準）又は 500 mL で約 3 時間かけて持続静脈内投与し，標準より短い持続投与時間も検討した。被験者の前治療数に関する選択基準は，第 I 相部分では 2 レジメン以上 4 レジメン以下，第 II 相部分では 1 レジメン以上と設定した。

(8) 被験者数（計画時及び解析時）

第 I 相部分の用量漸増に用いる用量レベル数に応じて 42～58 例を登録する計画とした。本治験には合計 45 例の被験者が登録され，このうち第 I 相部分に登録された被験者は 13 例，第 II 相部分に登録された被験者は 32 例であった。第 I 相部分の 13 例（本剤 2，4 及び 16 mg/kg コホートで各 3 例，8 mg/kg コホートで 4 例）が DRd 療法を受けた。第 II 相部分は 32 例全例が DRd 療法（本剤 16 mg/kg）を受け，このうち 21 例は標準的な投与時間，11 例は標準より短い時間で本剤の投与を受けた。

(9) 診断及び主な組入れ基準

本治験では，18 歳以上で，測定可能な M 蛋白が存在し，Eastern Cooperative Oncology Group のスコアが 0，1 又は 2 の患者を対象とした。第 II 相部分では，1 レジメン以上の前治療で partial response（PR）以上を達成しており，最終レジメン以後に疾患進行のエビデンスが記録されている患者も対象とした。本剤の初回持続静脈内投与前 12 週間以内に同種造血幹細胞移植若しくは自家造血幹細胞移植（ASCT）を受けた，過去にレナリドミドを中止した若しくはレナリドミドに対して治療抵抗性を示す，又はレナリドミドが禁忌であることが判明している患者は除外することとした。

(10)　被験薬，用量及び投与方法，ロット番号

第 I 相部分及び第 II 相部分のいずれも，DRd 療法を 28 日間サイクルで投与した。本剤をサイクル 1 及び 2 の Day 1，8，15 及び 22（1 週間隔），サイクル 3～6 の Day 1 及び 15（2 週間隔），サイクル 7 以降の Day 1（4 週間隔）に投与した。レナリドミドは 25 mg を各サイクルの Day 1～21 に経口投与し，デキサメタゾンは 1 週間に合計 40 mg を静脈内投与又は経口投与した。

本治験用として 6 生産ロット（ロット番号：[redacted]，[redacted]，[redacted]，[redacted]，[redacted]及び[redacted]）の本剤が提供された。

レナリドミド及びデキサメタゾンは市販ロットから提供された。

(11)　対照薬，用量及び投与方法，ロット番号

該当なし

(12) 投与期間

本治験はスクリーニング期，治療期及び後観察期で構成された。治療期中の本剤の各投与サイクルは 28 日間であった。被験者は，許容できない毒性又は疾患進行のいずれかが発現するまで DRd 療法を受けることとした。被験者の生存，新たな癌の発現及び新たな MM に対する治療を調査するため，レナリドミドの最終投与後 3 年間（6 カ月間隔）追跡することとした。

(13) 評価基準

本剤の安全性プロファイルは，有害事象の発現割合，死亡例，臨床検査値，バイタルサイン，身体所見，心電図の結果から評価した。有効性評価は国際骨髄腫作業部会（IMWG）の治療効果判定規準を用いて実施し，骨髄の評価，血清中 IgA，M 及び G（M 蛋白），尿中 M 蛋白，血清中遊離軽鎖比などの臨床検査値の評価並びに予後因子（第 I 相部分のみ），骨格検査，形質細胞腫及び髄外疾患の評価を含めた。血清中 daratumumab 濃度を測定するための薬物動態検体及び本剤に対する抗体産生を評価するための免疫原性検体は，すべての被験者から採取した。バイオマーカーの評価は全血及び骨髄穿刺検体で実施し，ナチュラルキラー（NK）細胞の分析を含めた。

(14) 統計手法

安全性に関して，有害事象は要約し，臨床検査データは要約し，記述的統計量を算出した。安全性解析は安全性解析対象集団を対象に行った。心電図の結果は QT 評価解析対象集団を用いて要約した。本治験の有効性の主要評価項目は全奏効率（ORR；PR 以上の被験者の割合）とし，stringent complete response（sCR），complete response（CR），sCR + CR，very good partial response（VGPR），PR，ORR，minimal response（MR），ORR + MR，stable disease，progressive disease（PD）及び評価不能の各治療効果カテゴリーの被験者数及び割合を集計した。有効性の主な副次評価項目は，無増悪期間（TTP），奏効持続期間，無増悪生存期間（PFS），奏効到達期間及び全生存期間（OS）であった。有効性のその他の評価項目には，血清／尿中 M 蛋白又は遊離軽鎖の減少及び骨髄中形質細胞の変化が含まれた。有効性の評価は intent-to-treat（ITT）集団を対象に実施し，治験実施計画書に適合した集団で確認した。

2.7.6.7.1.2 結果

安全性及び有効性の結果は第 I 相部分と第 II 相部分に分けて示す。

(1) 第 I 相部分

1) 第 I 相部分の対象集団

本剤の 4 コホート（2，4，8 及び 16 mg/kg）全体で 13 例が DRd 療法を受けた。ほとんどの被験者（10 例，77%）は男性で，すべての被験者（13 例，100%）が白人であった。前治療数の中央値は 3 レジメンであった。MM の初回診断からの期間の中央値は 4 年であった。12 例（92%）にプロテアソーム阻害剤及び免疫調節薬の前治療歴があった（ただし，異なる治療レジメンの一部としてこれらの薬剤を投与された場合が含まれた）。9 例（69%）に ASCT の前治療歴があった。データカットオフ時点で，6 例（46%）が治験薬の投与を中止し，中止理由は 4 例（31%）が疾患進行（治験担当医師の評価に基づく），2 例（15%）が有害事象［2 mg/kg 群の QTc 延長

（治験薬と関連性なし）が 1 例，8 mg/kg 群の血小板減少症及び好中球減少症（本剤及びレナリドミドと関連性あり）が 1 例］のためであった。

2) 第 I 相部分の安全性

13 例全例で有害事象が発現し，全例で治験薬と関連性がある有害事象が発現した。すべてのコホートで発現割合が高かった有害事象（基本語）は，好中球減少症及び筋痙縮（各 10 例，77%），下痢（9 例，69%），便秘，疲労及び鼻咽頭炎（各 8 例，62%）であった。最も発現割合が高かった Grade 3 又は 4 の有害事象は好中球減少症（9 例，69%）であった。そのほとんど（6/9 例，67%）は Grade 3 であり，成長因子による治療及び／又はレナリドミドの減量によって管理可能であった。有害事象のために死亡した被験者はいなかった。8 例（62%）に重篤な有害事象が認められ，5 例（39%）に治験薬と関連性がある重篤な有害事象が認められた。1 例に本剤と関連性があると考えられた重篤な失神が認められた。5 例（39%）に infusion related reaction（IRR）が認められた。いずれも Grade 1 又は 2 の IRR であり，治験薬の投与中止に至った IRR は認められなかった。用量制限毒性は認められなかった。第 I 相部分での安全性の結果と単剤療法試験である MMY2002 試験及び GEN501 試験の有効性，安全性及び薬物動態の結果を合わせると，16 mg/kg が今後の試験に使用する本剤の至適用量であることが示され，本治験の RP2D として選択した。

3) 第 I 相部分の有効性

有効性解析では，13 例中 11 例（85%）で最良効果が PR 以上であり，5 例は sCR，4 例は VGPR であった。DRd 療法を受けた被験者は，初回奏効への到達が迅速（1～2 カ月）であった。深い奏効が本剤の用量にかかわらず認められた。

(2) 第 II 相部分

1) 第 II 相部分の対象集団

32 例が DRd 療法（本剤 16 mg/kg）を受けた。被験者の多く（22 例，69%）は男性で，ほとんど（31 例，97%）が白人であった。前治療数の中央値は 2 レジメンであった。MM の初回診断からの期間の中央値は 3 年であった。21 例（66%）はプロテアソーム阻害剤及び免疫調節薬の前治療歴があった（ただし，異なる投与レジメンの一部としてこれらの薬剤を投与された場合が含まれた）。25 例（78%）は ASCT の前治療歴があった。11 例（34%）はレナリドミドの前治療歴があり，このうち 1 例はレナリドミドに対して治療抵抗性を示した。28 例（88%）はボルテゾミブの前治療歴があり，このうち 5 例はボルテゾミブに対して治療抵抗性を示した。

データカットオフ時点で，10 例（31%）は治験薬の投与を中止し，中止理由は 5 例（16%）が疾患進行（治験担当医師の評価に基づく），3 例（9%）が有害事象（胃腺癌，ウイルス性肺炎及び咽頭浮腫が各 1 例），2 例（6%）が治験担当医師の判断であった。

32 例全例が治験薬を 1 回以上投与された。相対用量強度の中央値は，本剤及びレナリドミドが 96%を上回っていた。デキサメタゾンの相対用量強度は算出しなかった。

2) 第 II 相部分の安全性

32 例全例で有害事象が発現し，全例で治験薬と関連性がある有害事象が発現した。3 例（9%）に治験薬の投与中止に至る有害事象が発現し，内訳は，胃腺癌（すべての治験薬と関連性なし），喉頭浮腫（本剤と関連性あり）及びウイルス性肺炎（すべての治験薬と関連性あり）が各 1 例であった。発現割合が高かった（40%超）有害事象（基本語）は，好中球減少症（27 例，84%），咳嗽（16 例，50%），筋痙縮及び下痢（各 14 例，44%）であった。最も発現割合が高かった Grade 3 又は 4 の有害事象は好中球減少症（25 例，78%）で，その全例でレナリドミドと関連性があり，そのほとんど（17/25 例，68%）は Grade 3 であり，成長因子による治療及び／又はレナリドミドの減量によって管理可能であった。第 II 相部分中に 1 例がウイルス性肺炎（すべての治験薬と関連性あり）のため治験薬の最終投与後 30 日以内に死亡した。16 例（50%）に重篤な有害事象が認められ，10 例（31%）に治験薬と関連性がある重篤な有害事象が認められた。治験薬と関連性がある重篤な有害事象が認められた 10 例中 6 例は，本剤と関連性があると判断された。

表 2.7.6.7-1 有害事象の概要［GEN503 試験 第 II 相部分，安全性解析対象集団］

	16 mg/kg Dara + Len/Dex
Analysis set: safety	32
Any TEAE	32 (100.0%)
Study Drug-related	32 (100.0%)
Dara-related	28 (87.5%)
Len-related	30 (93.8%)
Dex-related	29 (90.6%)
Any serious TEAE	16 (50.0%)
Study Drug-related	10 (31.3%)
Dara-related	6 (18.8%)
Len-related	7 (21.9%)
Dex-related	6 (18.8%)
Maximum severity of any TEAE	
Grade 1	0
Grade 2	4 (12.5%)
Grade 3	17 (53.1%)
Grade 4	10 (31.3%)
Grade 5	1 (3.1%)
Treatment Discontinuation Due to TEAE[a]	3 (9.4%)
Study Drug-related	2 (6.3%)
Dara-related	2 (6.3%)
Len-related	1 (3.1%)
Dex-related	1 (3.1%)
Death due to TEAE[b]	1 (3.1%)
Study Drug-related	1 (3.1%)
Dara-related	1 (3.1%)
Len-related	1 (3.1%)
Dex-related	1 (3.1%)

Keys: TEAE=treatment-emergent adverse event, Dara=Daratumumab, Len/Dex=Lenalidomide/Dexamethasone
[a] Adverse events reported as the reason for treatment discontinuation on the end of treatment CRF page.
[b] Death due to adverse event on the death CRF page.
Percentages are calculated with the number of subjects in each group as denominator.
[TSFAE01P2.rtf] [JNJ-54767414\GEN503\DBR_CSR\RE_CSR\tsfae01p2.sas] 18JAN2016, 21:48

被験者の約半数（18 例，56%）に IRR が認められ，IRR の発現割合は，本剤を標準的な投与時間（約 6 時間）で投与を受けた被験者（10/21 例，48%）よりも短い投与時間（約 3 時間）で投与を受けた被験者（8/11 例，73%）で高かった。発現した IRR のほとんど（16/18 例，89%）は Grade 1 又は 2 であり，IRR 発現例の全例で初回投与中に IRR が発現した。Grade 3 の IRR が 2 例

（6%）に認められ，このうち 1 例は標準的な投与時間で投与を受けた被験者で，高血圧が発現した。別の 1 例は短い投与時間で投与を受けた被験者で，初回投与中に喉頭浮腫が発現したため入院し，治験薬の投与を中止した。その他の IRR で治験薬の投与中止や入院に至ったものはなかった。Grade 4 の IRR は認められなかった。

ほとんどの被験者（24 例，75%）で感染症及び寄生虫症に分類される有害事象が認められた。最も発現割合が高かった事象は上気道感染（8 例，25%）であった。

DRd 療法の毒性は管理可能であり，安全性上新たに懸念となるようなものはなかった。

3) 第 II 相部分の有効性

32 例中 26 例（81%）は最良効果が PR 以上であり，8 例（25%）は sCR，3 例（9%）は CR，9 例（28%）は VGPR であった。

表 2.7.6.7-2 コンピュータ・アルゴリズムに基づく最良効果
［GEN503 試験 第 II 相部分，ITT 解析対象集団］

	16 mg/kg Dara + Len/Dex	
	n (%)	95% CI for %
Analysis set: ITT	32	
Best response		
Stringent complete response (sCR)	8 (25.0%)	(11.5%, 43.4%)
Complete response (CR)	3 (9.4%)	(2.0%, 25.0%)
Very good partial response (VGPR)	9 (28.1%)	(13.7%, 46.7%)
Partial response (PR)	6 (18.8%)	(7.2%, 36.4%)
Minimal response (MR)	2 (6.3%)	(0.8%, 20.8%)
Stable disease (SD)	3 (9.4%)	(2.0%, 25.0%)
Progressive disease (PD)	0	
Not evaluable (NE)	1 (3.1%)	(0.1%, 16.2%)
Overall response (sCR+CR+VGPR+PR)	26 (81.3%)	(63.6%, 92.8%)
Clinical benefit (Overall response + MR)	28 (87.5%)	(71.0%, 96.5%)
VGPR or better (sCR + CR + VGPR)	20 (62.5%)	(43.7%, 78.9%)
CR or better (sCR + CR)	11 (34.4%)	(18.6%, 53.2%)

Keys: CI=exact confidence interval, Dara=Daratumumab, Len/Dex=Lenalidomide/Dexamethasone
Note: Response was assessed by computerized algorithm, based on international Uniform Response Criteria Consensus Recommendations.
Note: Percentages are calculated with the number of subjects in each group as denominator.
[TEFRSP01P2A.rtf] [JNJ-54767414\GEN503\DBR_CSR\RE_CSR\TEFRSP01P2A.sas] 18JAN2016, 21:50

DRd 療法を受けた被験者で，迅速かつ持続的な奏効が確認された。初回奏効到達期間の中央値は 1 カ月であった。データカットオフ時点で，Kaplan-Meier 法で推定した奏効持続期間の中央値は未到達であったが，奏効例の 91%が 12 カ月時点で無増悪であった。データカットオフ時点で，PD が 7 例（22%，コンピュータ・アルゴリズムに基づく）に認められた。Kaplan-Meier 法で推定した TTP 及び PFS の中央値は未到達であったが，18 カ月時点の無増悪生存率の推定値は 72%であった。OS の中央値は未到達であり，18 カ月生存率の推定値は 90%であった。

すべての被験者で，M 蛋白のベースラインからの顕著な減少が認められ，30 例（94%）ではベースラインから 50%以上減少し，24 例（75%）ではベースラインから 90%以上減少した。奏効例のうち，ベースライン時及びベースライン後の評価時の 2 時点で骨髄中形質細胞が測定された被験者（20 例）では，骨髄中の悪性形質細胞が完全又はほぼ完全に消失した（残存している形質細胞が 5%未満）。

全般的に DRd 療法を受けた被験者は，初回奏効への到達が迅速であり，前治療に対して抵抗性を示した被験者でも深い奏効が認められた。

(3) 薬物動態，免疫原性及びバイオマーカー

本剤 16 mg/kg 投与時（第 II 相部分）において，サイクル 3 Day 1 投与後の血清中 daratumumab のピーク濃度は，初回投与後のピーク濃度に比べて 3 倍程度高値を示し，本剤の週 1 回，8 週間投与に伴う継続した蓄積が認められた。本剤の初回投与後の daratumumab の最高血清中濃度（C_{max}）は，本剤の用量 2～16 mg/kg にほぼ比例して上昇した（第 I 相部分）。本剤の初回投与後の 0 時間から最終定量可能時間までの血清中濃度-時間曲線下面積（AUC_{last}）は，本剤の消失に標的介在性のクリアランスの関与が示唆されていることに一致して，用量比を上回る増加を示した。

第 I 相部分及び第 II 相部分のいずれも本剤に対する抗体陽性の被験者はなく，免疫原性リスクが低いことが示された。

本剤単剤療法と同様，DRd 療法を受けた後に，NK 細胞の減少が末梢血中及び骨髄中のいずれにおいても認められた。これらの結果から，NK 細胞が CD38 を発現していること及び NK 細胞が本剤の活性を反映するバイオマーカーであることが示された。

2.7.6.7.1.3　結論

本治験から，再発又は難治性の MM 患者の治療における，DRd 療法の安全性及び有効性について以下の主要な結果が示された：

- 第 I 相部分に用量制限毒性は認められず，検討した本剤の最高用量（16 mg/kg）は良好な安全性プロファイルを有することが示され，RP2D として選択された。
- 第 II 相部分では，DRd 療法（本剤 16 mg/kg）の忍容性は良好であり，有害事象は管理可能であった。主要な結果を以下に示す：
  - 治験薬の投与中止に至った有害事象が認められた被験者は 3 例のみであった。
  - 最も発現割合が高かった（27 例，84%）有害事象は好中球減少症であり，レナリドミド療法で既知の有害事象であった。そのほとんど（17/27 例，63%）は Grade 3 であり，レナリドミドの減量及び／又は成長因子による治療によって管理可能であった。Grade 3 以上の感染症及び寄生虫症に分類される有害事象が認められた被験者は 5 例であった。
  - IRR は約半数（18 例，56%）の被験者で認められた。初回投与時に標準的な投与時間で投与を受けた被験者よりも，短い投与時間で投与を受けた被験者で IRR の発現割合が高かったことから，今後の試験で本剤の初回投与時に時間を短縮した投与レジメンを用いることは適切ではないと考えられた。発現した IRR のほとんど（16/18 例，89%）は Grade 1 又は 2 であり，主に初回投与中に発現した。短い投与時間で投与を受けた 1 例に認められた喉頭浮腫の IRR を除き，治験薬の投与中止や入院に至った IRR はなかった。
  - DRd 療法の毒性は管理可能であり，安全性上新たに懸念となるようなものはなかった。

- ORR は 81%であった。PFS の中央値は未到達であったが，18 カ月時点での無増悪生存率の推定値は 72%であった。OS の中央値は未到達であり，18 カ月生存率の推定値は 90%であった。データカットオフ時点で，32 例中 22 例が治験実施計画書に従って治験薬の投与を継続していた。
- 奏効の深さ（sCR 8 例を含む VGPR 以上の割合が 63%）は，悪性形質細胞評価が可能であった全例で骨髄中の悪性形質細胞が完全に又はほぼ完全に消失したこと及び M 蛋白の顕著な低下（被験者の 75%でベースラインから 90%以上の減少）と合わせて，特筆すべきことであった。これらの結果は，再発又は難治性の MM 患者を対象として，DRd 療法（本剤 16 mg/kg）をレナリドミド及びデキサメタゾンの併用療法（Rd 療法）と比較する第 III 相試験の実施を支持するものであった。
- 治療効果の迅速な発現も認められ，初回奏効到達期間の中央値は 1 カ月であり，最良効果到達期間の中央値は 6 カ月であった。

- 本治験の主要採血ポイントでの daratumumab 濃度は，同じ投与スケジュールで実施した単剤療法試験と同様であったことから，レナリドミド及びデキサメタゾンの投与が daratumumab の薬物動態に対して臨床的に重要な影響を及ぼす可能性は低いことが示された。

結論として，本治験の結果から，再発又は難治性の MM 患者の治療において，DRd 療法（本剤 16 mg/kg）は良好なリスクベネフィットプロファイルを有することが示された。

2.7.6.8　海外臨床第 Ib 相試験（MMY1001 試験，参考資料：5.3.5.4.2-1）

2.7.6.8.1　概要

2.7.6.8.1.1　計画

(1) 治験の標題

多発性骨髄腫（MM）患者を対象にダラツムマブ（以下本剤）と他の治療レジメンとの併用療法を検討する非盲検，多施設共同，第 Ib 相試験

(2) 治験調整医師

[redacted]; [redacted], Atlanta, GA

(3) 公表文献（引用文献）

なし

(4) 治験実施期間

2014 年 3 月 [redacted] 日～[redacted]年 [redacted]月 [redacted]日（クリニカルカットオフ日）

(5) 開発の相

第 Ib 相

(6) 目的

本治験の主要目的は，MM 患者を対象に，本剤を様々な治療レジメンと併用したとき［本剤とボルテゾミブ及びデキサメタゾン（DVd），本剤とボルテゾミブ，メルファラン及び prednisone（DVMP），本剤とボルテゾミブ，サリドマイド及びデキサメタゾン（DVTd），本剤とポマリドミド及びデキサメタゾン（DPd）］の安全性，忍容性（用量制限毒性の評価を含む）及び投与レジメンを評価することであった。

副次目的は，様々な治療レジメンと併用したときの本剤の薬物動態，本剤と併用したときの様々な治療レジメン（ボルテゾミブ，サリドマイド及びポマリドミド）の薬物動態，本剤の免疫原性を評価すること，並びに complete response（CR）率及び全奏効率（ORR）［partial response（PR）以上］を含む臨床的有効性アウトカム，奏効持続期間及び奏効到達期間を評価し，次の抗骨髄腫療法を実施するまでの期間を検討することであった。

探索的目的は，免疫細胞に対する本剤の効果を評価し，すべての被験者において治療効果を予測する潜在的バイオマーカーを検討し，本剤とポマリドミド及びデキサメタゾン（Pd）を併用された被験者において微小残存病変を評価することであった。

なお，治験実施計画書改訂 5 版で，新たに 2 レジメン［本剤とカルフィルゾミブ及びデキサメタゾン（DKd）並びに本剤とカルフィルゾミブ，レナリドミド及びデキサメタゾン（DKRd）］

が追加された。本申請のクリニカルカットオフ時点で当該 2 レジメンは被験者の組入れ中であったことから，本項では DPd，DVd，DVMP 及び DVTd の 4 レジメンについて主に記載する。

(7) 治験方法

本治験は，MM と初めて診断された患者又は前治療歴を有する患者を対象に，本剤を様々な治療レジメンと併用したときの安全性，忍容性及び投与レジメンを評価する非盲検，非ランダム化，多施設共同，第 Ib 相試験であった。本剤と併用する治療レジメンは，MM と初めて診断された被験者では Vd，VMP 又は VTd，前治療歴を有する被験者では Pd とした。被験者の治療レジメンへの割当ては，ランダム化手法を用いず，治験担当医師の判断及び治療レジメンの組入れ状況に基づいて実施された。併用した治療レジメンは，いずれも添付文書又は標準的な投与方法に従って投与した。すべての治療レジメンで，本剤を持続静脈内投与した。

本治験は，スクリーニング期，治療期及び後観察期で構成された。スクリーニング期は，投与開始前 28 日以内とした。治療期は，初回投与日から最長約 1 年間（DVd，DVMP 及び DVTd レジメン），疾患進行（DPd レジメン）又はその他の中止基準（追跡不能，同意撤回，死亡，治験依頼者による治験終了）に該当するまでのいずれかとした。後観察期は，被験者が治験薬の投与を中止し，投与中止時来院を終了してから治験終了（最後の被験者の本剤初回投与から約 15 カ月後を想定）までとした。

(8) 被験者数（計画時及び解析時）

約 190 例（DVd レジメン 6 例，DVMP 及び DVTd レジメン各約 12 例，DPd レジメン最大 100 例，DKd レジメン 20 例，DKRd レジメン最大 40 例）を登録することとした。

クリニカルカットオフ時では，133 例が解析対象となった（DVd レジメン 6 例，DVMP 及び DVTd レジメン各 12 例，DPd レジメン 103 例）。

DKd レジメン（計画被験者数：20 例）及び DKRd レジメン（計画被験者数：最大 40 例）は被験者の組入れ中であった。

(9) 診断及び主な組入れ基準

すべての治療レジメンに共通した主な適格基準は，18 歳以上，測定可能病変を有する MM と確定診断された Eastern Cooperative Oncology Group（ECOG）performance status スコアが 0，1 又は 2 の患者とした。DVd 及び DVTd レジメンでは，移植の適否にかかわらず MM と初めて診断された患者を対象とした。DVMP レジメンでは，MM と初めて診断され，高用量化学療法による造血幹細胞移植の適応とならない患者を対象とした。DPd レジメンでは，過去に 2 レジメン以上の抗骨髄腫療法を受け，再発又は難治性（直近の治療期間中又は治療終了から 60 日以内に疾患進行が認められたものと定義）の MM と診断され，かつ過去の連続する 2 サイクル以上でレナリドミドとボルテゾミブを別々に投与された患者を対象とした。

臨床検査値の適格基準は，好中球数≥1.0×10^9/L，アスパラギン酸アミノトランスフェラーゼ≤2.5×基準値上限（ULN），アラニンアミノトランスフェラーゼ≤2.5×ULN とした。スクリーニング期のクレアチニン・クリアランス（推算値）の適格基準は，DVd 及び DVTd レジメンでは

≥20 mL/分/1.73 m^2，DVMP レジメンでは≥40 mL/分/1.73 m^2，DPd レジメンでは≥45 mL/分/1.73 m^2 とした。加えて，DVd，DVMP 及び DVTd レジメンではヘモグロビン≥7.5 g/dL，総ビリルビン≤1.5×ULN，補正血清カルシウム<14 mg/dL，血小板数>50×10^9/L，DPd レジメンではヘモグロビン≥8 g/dL，総ビリルビン≤2.0 mg/dL，補正血清カルシウム<14 mg/dL，血小板数>50×10^9/L とした。

(10) 被験薬，用量及び投与方法，ロット番号

本剤は透明～乳白色，無色～淡黄色の液体で，持続静脈内投与用の無菌濃縮液として提供された。持続静脈内投与の際は，発熱性物質を含まない滅菌生理食塩液（0.9% NaCl）で本剤を希釈し，1000 mL（初回投与のみ）又は 500 mL に調製した。

本治験用として提供された本剤のロット番号は以下のとおりであった。

[redacted]

併用するボルテゾミブ，デキサメタゾン，サリドマイド，prednisone，メルファラン及びポマリドミドは，最新の添付文書及び標準的な投与方法に従って投与した。

ボルテゾミブのロット番号は[redacted]であった。

デキサメタゾン，サリドマイド，prednisone，メルファラン及びポマリドミドは，各治験実施医療機関で調達した。

DVd 及び DVTd レジメン：

21 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8 及び 15），サイクル 3 以降は 3 週間隔（Day 1）で投与した。デキサメタゾン 20 mg をサイクル 1～2 は Day 1，2，4，5，8，9，15 及び 16 に，サイクル 3～4 は Day 1，2，4，5，8，9，11 及び 12 に，サイクル 5 以降は Day 1，2，8 及び 9 に静脈内投与又は経口投与した。ボルテゾミブ 1.3 mg/m^2 をサイクル 1～4 は Day 1，4，8 及び 11 に，サイクル 5 以降は Day 1 及び 8 に皮下投与した。DVTd レジメンでは，上記に加えてサリドマイド 100 mg/日を 21 日間連日経口投与した。

DVMP レジメン：

42 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1 は 1 週間隔（Day 1，8，15，22，29 及び 36），サイクル 2 以降は 3 週間隔（Day 1 及び 22）で投与した。Prednisone 60 mg/m^2 を Day 1～4 に静脈内投与又は経口投与した。ボルテゾミブ 1.3 mg/m^2 をサイクル 1 は Day 1，4，8，11，22，25，29 及び 32 に，サイクル 2 以降は Day 1，8，22 及び 29 に皮下投与した。メルファラン 9 mg/m^2 を Day 1～4 に経口投与した。

DPd レジメン：

28 日間を 1 サイクルとし，本剤 16 mg/kg をサイクル 1～2 は 1 週間隔（Day 1，8，15 及び 22），サイクル 3～6 は 2 週間隔（Day 1 及び 15），サイクル 7 以降は 4 週間隔（Day 1）で投与した。デキサメタゾンは 1 週間に合計 40 mg を静脈内投与又は経口投与した。75 歳を超える被験者には，デキサメタゾンを 20 mg/週で投与することを可とした。ポマリドミド 4 mg/日を Day 1～21 に経口投与した。

(11) 対照薬，用量及び投与方法，ロット番号

該当なし

(12) 投与期間

DVd 及び DVTd レジメンでは，最大 18 サイクル（1 サイクルは 21 日間）又は被験者が移植の適応となるまで（該当する場合）とした。DVMP レジメンでは，最大 9 サイクル（1 サイクルは 42 日間）とした。DPd レジメンでは，投与サイクルは 28 日間とし，疾患進行まで投与を継続することとした。

(13) 評価基準

有効性は治験依頼者が国際骨髄腫作業部会（IMWG）のガイドラインに従い評価した。治療効果の評価には，1）独立データ安全性モニタリング委員会（IDSMB）による評価，2）バリデートされたコンピュータ・アルゴリズムによる評価，及び 3）治験担当医師による評価を用いた。その他の有効性評価には，血清／尿中 M 蛋白又は遊離軽鎖の減少，骨髄検査，CR，stringent complete response（sCR），CR の持続期間及び疾患進行の評価，全骨格検査による溶骨性病変の評価，髄外性形質細胞腫の記録が含まれた。安全性評価には，有害事象，臨床検査値，バイタルサイン，心電図（ECG）及び ECOG performance status が含まれた。薬物動態及び免疫原性の評価用に静脈血検体を採取した。潜在的バイオマーカー及びゲノム薬理の分析用に血液検体及び骨髄穿刺液も採取した。

(14) 統計手法

本治験は，本剤と様々な治療レジメンを併用した場合の予備的データを収集するためにデザインされた。したがって，被験者数は仮説検定に基づいた設定はしなかった。

安全性は，有害事象，臨床検査値，バイタルサイン及び ECG の結果を要約した。臨床的に注目すべき有害事象として，infusion related reaction（IRR），感染症／寄生虫症，好中球減少症等を要約した。有効性の主要評価項目は ORR とし，各治療効果カテゴリーの被験者数及び割合を両側正確 95%信頼区間とともに示した。副次評価項目の time-to-event 評価項目は Kaplan-Meier 法を用いて推定した。

解析に用いた対象集団は，安全性解析対象集団（DVd，DVMP，DVTd 又は DPd 投与被験者），DPd 奏効評価対象集団，薬物動態評価対象集団及び免疫反応評価対象集団とした。

2.7.6.8.1.2 結果

本項では，DPd 群（再発又は難治性の MM 患者を登録）の被験者背景，有効性及び安全性の結果，ボルテゾミブ併用群（DVd 群，DVMP 群及び DVTd 群：MM と初めて診断された被験者を登録）の被験者背景及び安全性の結果，DPd 群（103 例）とボルテゾミブ併用群（30 例）での薬物動態，免疫原性及びバイオマーカーの結果を示す。

(1) DPd 群

1) 対象集団

DPd 群の 103 例中，男性は 55%，女性は 45%であった。被験者の多く（77%）が白人で，年齢の中央値は 64 歳（範囲：35～86 歳），体重の中央値は 78.50 kg であった。ほとんど（88%）の被験者のベースライン ECOG performance status スコアは 0 又は 1 であった。IgG 型骨髄腫が 61%,

IgA 型骨髄腫が 17%，IgD 型骨髄腫が 2%であり，軽鎖病のみが認められた被験者は 19%であった。MM の初回診断からの期間の中央値は 5.1 年であった。治験実施医療機関で細胞遺伝学的データが得られた 87 例のうち 22 例（25%）にベースラインにおける高リスクの染色体異常が認められ，del17p が最も多かった（16 例，18%）。

すべての被験者に MM の前治療歴があった。すべての被験者が全身療法を受け，74%の被験者が自家造血幹細胞移植を受けていた。51%の被験者が 4 レジメン以上の前治療歴を有しており，前治療数の中央値は 4 レジメンであった。すべての被験者にレナリドミド，98%の被験者にボルテゾミブの前治療歴があった。71%の被験者が免疫調節薬とプロテアソーム阻害剤の両剤に対して治療抵抗性を示した。観察期間の中央値は 9.8 カ月であった。

投与期間の中央値は 6.0 カ月，本剤の投与回数の中央値は 14 回であった。完了サイクル数の中央値は 6 サイクル（範囲：1～18 サイクル）であった。57%の被験者が治験薬の投与を中止し，主な中止理由は疾患進行（33%），有害事象（14%）であった。有害事象により投与を中止した 14 例（14%）のうち，1 例は治験薬の最終投与から 30 日以降に発現した有害事象により投与を中止した。

2) 有効性

主要評価項目：全奏効率（ORR）

IDSMB の評価（IMWG の治療効果判定規準を使用）に基づく ORR（PR 以上）は 59%であった。sCR 8%，CR 6%，very good partial response（VGPR）28%，PR 17%であった。臨床的有用率［sCR + CR + VGPR + PR + minimal response（MR）］は 62%であった。

副次評価項目

- IDSMB の評価に基づく奏効持続期間の中央値は 13.6 カ月であった。
- 初回奏効到達期間の中央値は 0.99 カ月，最良効果到達期間の中央値は 2.1 カ月，VGPR 以上到達期間の中央値は 1.9 カ月，CR 以上到達期間の中央値は 5.4 カ月であった。
- 無増悪生存期間（PFS）の中央値は 10.4 カ月，無増悪期間（TTP）の中央値は 10.9 カ月であった。
- クリニカルカットオフ時点で，全生存期間の中央値は未到達であり，12 カ月生存率の推定値は 72%であった。

3) 安全性

- DPd 群の全例で有害事象が認められた。発現割合が高かった（30%以上）有害事象は，好中球減少症（79%），貧血（52%），疲労（50%），血小板減少症（41%），下痢（38%），白血球減少症（37%），咳嗽（36%），便秘（33%），呼吸困難及び悪心（各 30%）であった。
- Grade 3 又は 4 の有害事象は 102 例（99%）で認められた。発現割合が高かった Grade 3 又は 4 の有害事象は，主に血液学的検査関連の事象であり，好中球減少症（77%），貧血

（27%），白血球減少症（24%），血小板減少症（17%），リンパ球減少症（14%），疲労（10%）及び肺炎（8%）であった。

- 投与期間中又は最終投与後 30 日以内に 7 例（7%）が死亡した。5 例は有害事象による死亡であり，このうち 2 例は感染症により死亡した。2 例は疾患進行による死亡であった。死亡に至った有害事象のうち治験薬と関連性があると判断されたものは，デキサメタゾンと関連性があった 1 件のみであった。治験担当医師が本剤又はポマリドミドと関連性があると判断した死亡は報告されなかった。
- 重篤な有害事象が 49%の被験者に認められた。重篤な有害事象の多くは 1 例又は 2 例で発現した。発現割合が高かった重篤な有害事象は，肺炎（7%），敗血症，発熱性好中球減少症及び転倒（各 4%）であった。
- 投与中止に至った有害事象が 13%の被験者に認められた。
- 本剤の投与調節（投与の延期又は休薬）に至った有害事象が 49%の被験者に認められた。発現割合が高かった事象は，好中球減少症（23%）及び血小板減少症（9%）であった。
- ポマリドミドの投与調節（投与の延期，休薬，減量後の増量又は減量）に至った有害事象が 73%の被験者に認められた。発現割合が高かった事象は，好中球減少症（48%），白血球減少症（8%），血小板減少症及び疲労（各 7%），貧血及び発熱性好中球減少症（各 5%）であった。
- IRR が 50%の被験者に認められた。Grade 3 の IRR が 4 例（4%）に認められたが，Grade 4 又は 5 の IRR は認められなかった。発現割合が高かった IRR は，悪寒（15%），咳嗽及び呼吸困難（各 11%），悪心（9%），鼻閉及び咽喉刺激感（各 7%）であった。1 例に本剤の投与中止に至った IRR（Grade 3 の低酸素症）が認められた。IRR は 1 件を除き，いずれも初回投与中に発現した。初回投与時における IRR 発現までの時間の中央値は 76 分であった。
- 好中球減少症が 79%の被験者に認められ，77%が Grade 3 又は 4 であった。1 例で重篤な好中球減少症が認められた。60%の被験者にサイクル遅延又は投与調節に至った好中球減少症が認められたが，好中球減少症のために投与を中止した被験者はいなかった。
- 器官別大分類の感染症及び寄生虫症に分類される有害事象が 70%の被験者に認められた。発現割合が高かった事象は，上気道感染（25%），副鼻腔炎（13%），肺炎（11%），気管支炎（10%），鼻咽頭炎（8%）及び尿路感染症（7%）であった。Grade 3 又は 4 の感染症／寄生虫症は 28%，Grade 5 の感染症／寄生虫症は 2%の被験者に認められた。5%の被験者が感染症のために投与を中止した。Grade 3 又は 4 の感染症／寄生虫症が認められた 29 例（28%）のうち，4 例（8%）のみが 6 カ月以降の発現であった。
- DPd 群で二次性悪性腫瘍が認められた被験者はいなかった。

(2) ボルテゾミブ併用群（DVd 群，DVMP 群及び DVTd 群）

1) 対象集団

本治験では，30 例がボルテゾミブと本剤の併用投与を受け，その内訳は DVd 群が 6 例，DVMP 群が 12 例，DVTd 群が 12 例であった。男性は 14 例（47%），女性は 16 例（53%）であり，2 例以外はいずれも白人，年齢の中央値は 67.5 歳，ほとんど（28 例，93%）の被験者でベースラインの ECOG performance status スコアは 0 又は 1 であった。

30 例中 13 例（43%）が治験実施計画書に従って治験薬の投与を完了し，17 例（57%）が治験薬の投与を中止した。観察期間の中央値は 19.1 カ月であった。

投与期間の中央値は 8.2 カ月，本剤の投与回数の中央値は 16 回であった。完了サイクル数の中央値は 9 サイクルであり，19 例（63%）が 7 サイクル以上を完了した。9 例（30%）（DVd 群 2 例，DVMP 群 2 例，DVTd 群 5 例）がサイクルを延期した。

2) 安全性

- ボルテゾミブ併用群の全例で有害事象が認められ，ほとんどの被験者（25 例，83%）に Grade 2 又は 3 の有害事象が認められた。DVd 群の 1 例（3%）に Grade 4 の有害事象（高血糖）が認められた。Grade 5 の有害事象が認められた被験者はいなかった。
- Grade 3 又は 4 の有害事象が 13 例（43%）に認められた。発現割合が高かった Grade 3 又は 4 の有害事象は，好中球減少症（6 例，20%），血小板減少症（4 例，13%），貧血（2 例，7%）であった。
- 治験期間中に 3 例が死亡した。3 例の死因は，疾患進行，大腸菌による敗血症性ショック，汎大腸炎が各 1 例であった。治験薬の最終投与後 30 日以内に死亡した被験者はいなかった。
- 重篤な有害事象が 4 例（13%）に認められ，うち 2 例の事象（肺炎，臨床検査干渉）は本剤と関連性があると判断された。投与中止に至った有害事象が 3 例に認められた。
- IRR が 10 例（33%）に発現したが，Grade 3 又は 4 の IRR は認められなかった。
- 好中球減少症が 13 例（43%）に認められ，Grade 3 又は 4 の好中球減少症が 6 例（20%）に認められた。好中球減少症のために治験薬の投与を中止した被験者はいなかった。
- 21 例（70%）に器官別大分類の感染症及び寄生虫症に分類される有害事象が認められた。発現割合が高かった事象は，上気道感染（9 例，30%），胃腸炎及び呼吸器感染（各 3 例，10%）であった。Grade 3 の感染症が 1 例に 2 件発現したが，その他の感染症／寄生虫症は軽度（Grade 1 又は 2）であった。
- 血液学的検査又は血液生化学検査パラメータ，バイタルサイン又は ECG に臨床的に重要な経時的変化は認められなかった。

(3) 薬物動態，免疫原性及びバイオマーカー（DPd 群及びボルテゾミブ併用群）

- Daratumumab のピーク濃度及びトラフ濃度は，4 つのレジメン（DPd，DVd，DVMP 及び DVTd）を投与された被験者で同様であった。
- ボルテゾミブ，サリドマイド及びポマリドミドの薬物動態パラメータは，文献で示されるデータと同様であった。被験者数は少なかったが，これらの結果から 4 つのレジメンで併用された薬剤と本剤に，臨床的に重要な相互作用は認められないことが示唆された。
- DVTd 群の 1 例で，本剤に対する抗体が後観察期に陽性となった。本剤と Pd 及びボルテゾミブ併用レジメンを併用しても免疫原性リスクは低いことが示された。
- 4 つの治療レジメンにおいて，本剤投与後に末梢血中及び骨髄中のナチュラルキラー（NK）細胞の減少が認められ，本剤単剤療法後に認められた結果と同様であった。これらの結果から，NK 細胞が CD38 を発現していること及び NK 細胞数が本剤の活性を反映するバイオマーカーであることが示された。

2.7.6.8.1.3　結論

本剤と Pd レジメンの併用による有効性が，レナリドミド及びボルテゾミブの両剤による前治療歴がある MM 患者に対して認められ，ORR は 59%であった。同様の対象患者に Pd レジメンを投与した過去の試験結果（ORR：約 30%，sCR or CR：1～3%，VGPR：0～5%，PFS：約 4 カ月）と比較すると，本剤を上乗せすることによって，より深い奏効及び PFS の延長が認められた。DPd レジメンは管理可能な安全性プロファイルを有しており，認められた有害事象は個々の薬剤で既知のものと同様であった。以上より，本治験の結果から，MM 患者の治療において，DPd レジメンは良好なリスクベネフィットプロファイルを有することが示された。