テセントリク点滴静注1200 mg
（アテゾリズマブ（遺伝子組換え））

［非小細胞肺癌］

第2部　（モジュール2）：CTD の概要（サマリー）

2.7.4 臨床的安全性

中外製薬株式会社

略語一覧

略号	英名	和名
ALK	anaplastic lymphoma kinase	未分化リンパ腫キナーゼ
ATA	anti-therapeutic antibody	抗薬物抗体
CTCAE	common terminology criteria for adverse events	有害事象共通用語規準
DLT	dose limiting toxicity	用量制限毒性
ECOG PS	Eastern Cooperative Oncology Group performance status	—
EGFR	epidermal growth factor receptor	上皮増殖因子受容体
EML4	echinoderm microtubule associated protein-like 4	微小管会合蛋白4
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for human use	医薬品規制調和国際会議
IC スコア	—	腫瘍浸潤免疫細胞の PD-L1発現状況（又はその評価結果）
imAE	immune mediated adverse event	免疫介在性有害事象
KRAS	Kirsten rat sarcoma-2 viral oncogene homolog	カーステンラット肉腫ウイルス癌遺伝子ホモログ
MedDRA	medical dictionary for regulatory activities	ICH 国際医薬用語集
PD-1	programmed death-1	—
PD-L1	programmed death-ligand 1	—
QTcF	corrected QT according to Fridericia	Fridericia の補正式による QT 間隔
ΔQTcF	—	ベースラインからの QTcF の変化量
RECIST	response evaluation criteria in solid tumors	固形癌の治療効果判定のための規準
TC スコア	—	腫瘍細胞の PD-L1発現状況（又はその評価結果）

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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試験

テセントリク点滴静注1200 mg（以下，本剤）は，アテゾリズマブ（遺伝子組換え）（以下，アテゾリズマブ又は MPDL3280A）を有効成分として含有する点滴静脈内注射剤として開発されている。

本剤の安全性は，非小細胞肺癌患者を対象とした日本を含む国際共同第 III 相臨床試験である GO28915試験（OAK 試験），非小細胞肺癌患者を対象とした海外第 II 相臨床試験である GO28753試験（POPLAR 試験），programmed death-ligand 1（PD-L1）陽性非小細胞肺癌患者を対象とした日本を含む国際共同第 II 相臨床試験である GO28754試験（BIRCH 試験），PD-L1 陽性非小細胞肺癌患者を対象とした海外第 II 相臨床試験である GO28625試験（FIR 試験），固形癌患者又は造血器腫瘍患者を対象とした海外第 I 相臨床試験である PCD4989g 試験，及び固形癌患者を対象とした国内第 I 相臨床試験である JO28944試験の結果に基づき評価した。

OAK 試験及び POPLAR 試験の本剤群，並びに BIRCH 試験及び FIR 試験のいずれのコホートも，固定用量1200 mg の本剤を3週間に1回（1サイクル：21日）点滴静脈内投与した。PCD4989g 試験は，用量漸増ステージでは各コホートに規定された用量（0.01，0.03，0.1，0.3，1，3，10及び20 mg/kg）の本剤を，拡張ステージでは10，15，20 mg/kg 及び1200 mg/body の本剤を，3週間に1回点滴静脈内投与した。JO28944試験では，各コホートに規定された用量（10又は20 mg/kg）の本剤を3週間に1回点滴静脈内投与した。

OAK 試験（データカットオフ日：2016年7月7日），POPLAR 試験（データカットオフ日：2015年5月8日），BIRCH 試験（データカットオフ日：2015年5月28日），FIR 試験（データカットオフ日：2015年1月7日），PCD4989g 試験（データカットオフ日：2014年12月2日）及び JO28944試験（データカットオフ日：2014年11月15日）はいずれも主解析時の結果を記載した。

2.7.4.1.1.2 安全性の評価方法

(1) 有害事象の定義

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験，PCD4989g 試験及び JO28944試験のいずれにおいても，治験薬との因果関係の有無は問わない，治験薬が投与された被験者に生じたあらゆる好ましくない，意図しない兆候（臨床検査値の異常を含む），症状，疾病（ただし，原疾患の悪化を除く）を有害事象と定義した。

治験薬との因果関係は，OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験では「関連あり」，「関連なし」の2段階で判定し，JO28944試験では「関連なし」，「わずかにあり」，「可能性あり」，「多分あり」の4段階で判定した。いずれの治験においても「関連なし」以外に判定された有害事象を副作用（因果関係が否定できない有害事象）として取り扱った。

(2) 重篤な有害事象

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験，PCD4989g 試験及び JO28944試験のいずれにおいても，医薬品規制調和国際会議（ICH）E2ガイドラインに準じた重篤な有害事象が入手された。有害事象のうち下記の事項のいずれか1つ以上に該当する事象を重篤な有害事象と定義した。

- 致死的なもの（実際に死因となる，又は死に至る有害事象）
- 生命を脅かすもの（治験責任（分担）医師の判断により，直ちに死亡する危険があると考え

られる有害事象）
- 入院又は入院期間の延長を要するもの
- 永続的又は重大な障害・機能不全に至るもの（通常の生活機能を営む能力を著しく損なう有害事象）
- 治験薬に曝露された母親から生まれた新生児・乳児における先天異常・先天性欠損
- 治験責任（分担）医師により重要な医学的事象であると判断されるもの（例：被験者を危険に曝す，又は上記のいずれかの転帰を防ぐために内科的又は外科的な処置を必要とする事象）

(3) 有害事象の評価基準

OAK 試験，BIRCH 試験，POPLAR 試験，FIR 試験，PCD4989g 試験及び JO28944試験の有害事象の評価基準を表 2.7.4.1.1.2-1に示す。

表 2.7.4.1.1.2-1 有害事象の評価基準

試験	有害事象の重症度判定	有害事象の読替え用語集
OAK 試験	CTCAE v4.0	MedDRA Version 19.0
POPLAR 試験	CTCAE v4.0	MedDRA Version 18.0
BIRCH 試験	CTCAE v4.0	MedDRA Version 18.0
FIR 試験	CTCAE v4.0	MedDRA Version 18.0
PCD4989g 試験	CTCAE v4.0	MedDRA Version 18.0
JO28944試験	CTCAE v4.03	MedDRAJ Version 16.1

CTCAE：有害事象共通用語規準，MedDRA：ICH 国際医薬用語集

(4) 有害事象の収集

OAK 試験，BIRCH 試験，POPLAR 試験，FIR 試験，PCD4989g 試験及び JO28944試験の有害事象の収集範囲を表 2.7.4.1.1.2-2に示す。

表 2.7.4.1.1.2-2 有害事象の収集範囲

	期間	対象
OAK 試験	同意取得後，治験薬投与開始前	治験実施計画書に規定された処置に起因する重篤な有害事象（例：生検などの侵襲的処置に関連する重篤な有害事象）
	治験薬投与開始後，治験薬最終投与日から30日間，又は次の抗悪性腫瘍療法開始のいずれかに該当するまで	すべての有害事象及び重篤な有害事象（治験薬との因果関係にかかわらない）
	以降	治験薬投与又は治験手順と「関連あり」と考えられる死亡，重篤な有害事象及びその他の有害事象
POPLAR 試験	同意取得後，治験薬投与開始前	治験実施計画書に規定された処置に起因する重篤な有害事象（例：生検などの侵襲的処置に関連する重篤な有害事象）
	治験薬投与開始後，治験薬最終投与日から90日間又は次の抗悪性腫瘍療法開始のいずれかに該当するまで	すべての有害事象及び重篤な有害事象（治験薬との因果関係にかかわらない）
	以降	治験薬投与又は治験手順と「関連あり」と考えられる死亡，重篤な有害事象及びその他の有害事象
BIRCH 試験	同意取得後，治験薬投与開始前	治験実施計画書に規定された処置に起因する重篤な有害事象（例：生検などの侵襲的処置に関連する重篤な有害事象）

	治験薬投与開始後，治験薬最終投与日から30日間又は次の抗悪性腫瘍療法開始のいずれかに該当するまで	すべての有害事象及び重篤な有害事象（治験薬との因果関係にかかわらない）
	以降	治験薬投与又は治験手順と「関連あり」と考えられる死亡及び重篤な有害事象及びその他の有害事象
FIR 試験	同意取得後，治験薬投与開始前	治験実施計画書に規定された処置に起因する重篤な有害事象（例：生検などの侵襲的処置に関連する重篤な有害事象）
	治験薬投与開始後，治験薬最終投与日から90日間又は次の抗悪性腫瘍療法開始のいずれかに該当するまで	すべての有害事象及び重篤な有害事象（治験薬との因果関係にかかわらない）
	以降	治験薬投与又は治験手順と「関連あり」と考えられる死亡，重篤な有害事象及びその他の有害事象
PCD4989g 試験	同意取得後，治験薬投与開始前	治験実施計画書に規定された処置に起因する重篤な有害事象（例：生検などの侵襲的処置に関連する重篤な有害事象）
	治験薬投与開始後，治験薬最終投与日から90日間又は試験中止／終了，若しくは次の抗悪性腫瘍療法開始のいずれかに該当するまで	すべての有害事象及び重篤な有害事象（治験薬との因果関係にかかわらない）
	以降	治験薬投与と「関連あり」と考えられる死亡及び重篤な有害事象
JO28944試験	治験薬投与開始後から治験期間終了（治験薬最終投与後30日*）まで	すべての有害事象
	以降	治験薬との因果関係が否定できない重篤な有害事象

*:ただし，治験薬最終投与後30日以内に他治療に移行する場合は他治療開始前日まで，転院や被験者都合等の理由により来院が困難になった場合は最終来院日までを治験期間とする

(5) 有害事象の集計

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験では，治験薬との因果関係が否定できない重篤な有害事象，adverse events of special interest（5.3.5.1-1 Page 9256参照）及び免疫介在性有害事象（imAE）以外の有害事象については，治験薬投与開始後から治験薬最終投与後30日，次の抗悪性腫瘍療法開始又はデータカットオフ日のいずれかに該当するまでの期間に発現した事象を集計対象とした。なお，治験薬との因果関係が否定できない重篤な有害事象，adverse events of special interest 及び imAE については，治験薬投与開始後からデータカットオフ日までに発現したすべての事象を集計対象とした。

JO28944試験では，治験薬投与開始後から治験期間終了までに発現したすべての有害事象を集計した。

2.7.4.1.1.3 本剤の投与，休薬及び中止基準

(1) OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験の投与と休薬

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験では，被験者が休薬を要する有害事象を発現した場合，本剤の投与を一時休薬することが可能であった。各治験の許容された休薬期間を表 2.7.4.1.1.3-1に示す。いずれの治験も，休薬期間が許容日数を超えた場合には，本剤の投与を中止した。ただし，OAK 試験では，許容された休薬期間を超えた場合であっても，治験責任（分担）医師が本剤投与により被験者に臨床的有益性があると判断した場合は，Medical Monitor の許可により投与を再開できるとした。いずれの治験も，有害事象の治療に用いたステロイド薬の漸減を必要とする被験者の場合，本剤の休薬許容日数に関わら

ず，ステロイド薬による治療を終了又はプレドニゾン10 mg/日（又は相当量）以下となるまで本剤の休薬が可能であった。有害事象以外（外科的処置など）を理由とする休薬は，Medical Monitor の承認を得て許可されることがあるとし，許容される休薬期間の長さは治験責任（分担）医師と Medical Monitor の合意によって決められることとした。また，いずれの治験も本剤の減量は認めなかった。

表 2.7.4.1.1.3-1 許容された休薬期間

OAK 試験	POPLAR 試験	BIRCH 試験	FIR 試験	PCD4989g 試験
105日[*1]	105日[*2]	105日[*3]	105日[*2]	84日[*4]

*1: 治験実施計画書第2版までは42日
*2: 治験実施計画書第3版までは42日
*3: 治験実施計画書第2版までは42日
*4: 治験実施計画書第2版までは21日，治験実施計画書第5版までは42日

(2) JO28944試験の投与と休薬

JO28944試験では，サイクル開始基準を設定した。サイクル2以降は，次投与開始予定日を1日目として，22日目までに本剤を投与できなかった場合は，本剤の投与を中止することとした。また，体重変動以外を理由とする本剤の投与量変更を認めなかった。

(3) OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験の中止基準

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験では，以下の基準に該当する場合治験治療を中止することとした。

- 治験治療と関連する忍容不能な毒性が認められた。
- 治験薬投与を継続すると被験者の安全を脅かす可能性がある医学的状態が発生した。
- 他の抗悪性腫瘍療法に切り替えた。
- 妊娠が認められた。
- 画像データ，生検結果及び臨床状態の総合的評価を通じ，病勢進行に起因する症状悪化が発現したと治験責任（分担）医師が判断した（POPLAR 試験，BIRCH 試験及び FIR 試験）。
- 用量制限毒性（DLT）が発現した（PCD4989g 試験のみ）。

一次治療の被験者を対象とした BIRCH 試験及び FIR 試験のコホート1並びに，OAK 試験及び POPLAR 試験のドセタキセル群の被験者は，「固形癌の治療効果判定のための規準」（RECIST）v1.1に基づく病勢進行がみられた場合，治験治療を中止することとした。PCD4989g 試験の非小細胞肺癌コホートを含む固形癌の被験者は，RECIST v1.1及び免疫関連反応基準の両方で病勢進行とされた場合，治験治療を中止することとした。

二次治療又は三次治療以降の被験者を対象とした OAK 試験及び POPLAR 試験の本剤群，並びに BIRCH 試験及び FIR 試験のコホート2及びコホート3，並びに PCD4989g 試験の非小細胞肺癌コホートの被験者は，RECIST v1.1による病勢進行と評価された場合でも，以下の基準をすべて満たす場合には治験治療を継続してもよいとした。

- 明らかな病勢進行を示す症状・徴候（たとえば高カルシウム血症の発症／悪化などの，臨床検査値上の悪化を含む）がない。
- Eastern Cooperative Oncology Group Performance Status（ECOG PS）の悪化がない。
- 治験実施計画書で容認される医学的介入では管理不能な，重要な解剖学的部位における腫瘍の増殖（例：軟膜・髄膜病変）がない。
- 承認された既存の療法も選択可能な被験者は，最初に進行の所見を認めた時点で，そうした治療オプションを保留して治験治療を継続することを書面により同意していること。
- 治験責任（分担）医師により臨床的有用性があると判断された場合。

(4) JO28944試験の中止基準

JO28944試験では，以下の基準に該当する場合治験治療を中止することとした。

- 被験者が中止を希望した場合。
- 明らかな病勢の進行が確認された場合（RECIST 基準による病勢進行と評価された場合でも，臨床上明らかな病勢の進行が認められず，治験責任医師又は治験分担医師が投与の継続が被験者の利益になると判断した場合，治験薬の投与を継続することができる）。
- DLT 評価期間内に，DLT の定義に該当する毒性が発現した場合。
- 治験薬の次投与開始予定日を1日目として，22日目までに投与できなかった場合。
- 治験の継続が困難であると判断される有害事象が発現した場合。
- 選択基準違反，又は除外基準に抵触することが判明した場合。
- 被験者の妊娠が判明した場合。
- その他，治験責任医師又は治験分担医師が投与の継続を不適当と認めた場合。

2.7.4.1.2 全般的な曝露状況

本項以降に，OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験，PCD4989g 試験及び JO28944試験の成績を示す。PCD4989g 試験の非小細胞肺癌コホートの成績は M5.3.3.2-1に示した。

(1) 安全性解析対象例数

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験，PCD4989g 試験及び JO28944試験の安全性解析対象例数を表 2.7.4.1.2-1に示す。いずれの治験も，少なくとも1回治験薬を投与された被験者を安全性解析対象集団とした。

表 2.7.4.1.2-1 各治験の安全性解析対象例数

試験名	ドセタキセル群	本剤群	安全性解析対象例数
OAK 試験	578	609	1187
POPLAR 試験	135	142	277
BIRCH 試験	–	659	659
FIR 試験	–	137	137
PCD4989g 試験	–	481	481
JO28944試験	–	6	6

［5.3.5.1-1 Table 13，5.3.5.1-2 Table 16，5.3.5.2-1 Table 13，5.3.5.2-2 Table 9，5.3.3.2-1 Table 17及び5.3.3.2-2 Table 15.1-2を改変］

(2) 曝露状況の要約

1) 本剤の曝露状況

本剤1200 mg/body を3週間に1回（1サイクル：21日）投与した OAK 試験，POPLAR 試験，BIRCH 試験及び FIR 試験の曝露状況を表 2.7.4.1.2-2に，本剤0.01，0.03，0.1，0.3，1，3，10，15，20 mg/kg 及び1200 mg/body を3週間に1回投与した PCD4989g 試験の曝露状況を表 2.7.4.1.2-3に，本剤10又は20 mg/kg を3週間に1回投与した JO28944試験の曝露状況を表 2.7.4.1.2-4に示す。

表 2.7.4.1.2-2　曝露状況の要約（OAK 試験，BIRCH 試験，POPLAR 試験及び FIR 試験）

試験名	OAK 試験		POPLAR 試験		BIRCH 試験				FIR 試験			
群	ドセタキセル群	本剤群	ドセタキセル群	本剤群	コホート1	コホート2	コホート3	全体	コホート1	コホート2	コホート3	全体
例数	578	609	135	142	139	267	253	659	31	93	13	137
投与期間（月）												
平均値（SD）	3.0 (3.3)	6.2 (6.7)	3.1 (3.5)	6.2 (5.7)	5.3 (3.8)	4.8 (3.7)	4.8 (3.6)	4.9 (3.7)	5.0 (3.5)	4.8 (5.1)	3.9 (3.0)	4.8 (4.6)
中央値	2.1	3.4	2.1	3.7	4.9	4.1	4.1	4.2	4.3	2.5	3.5	2.9
範囲	0－23	0－26	0－17	0－19	0 - 14	0 - 15	0 - 14	0－15	0－11	0－19	1－10	0－19
投与期間（月）[*1]												
3カ月未満	351 (60.7%)	294 (48.3%)	82 (60.7%)	59 (41.5%)	51 (36.7%)	108 (40.4%)	102 (40.3%)	261 (39.6%)	11 (35.5%)	53 (57.0%)	6 (46.2%)	70 (51.1%)
3～6カ月	162 (28.0%)	113 (18.6%)	32 (23.7%)	26 (18.3%)	25 (18.0%)	50 (18.7%)	50 (19.8%)	125 (19.0%)	7 (22.6%)	10 (10.8%)	4 (30.8%)	21 (15.3%)
6～12カ月	51 (8.8%)	77 (12.6%)	16 (11.9%)	27 (19.0%)	57 (41.0%)	99 (37.1%)	96 (37.9%)	252 (38.2%)	13 (41.9%)	17 (18.3%)	3 (23.1%)	33 (24.1%)
12カ月以上	14 (2.4%)	125 (20.5%)	5 (3.7%)	30 (21.1%)	6 (4.3%)	10 (3.7%)	5 (2.0%)	21 (3.2%)	0	13 (14.0%)	0	13 (9.5%)
投与回数												
平均値（SD）	5.1 (4.4)	9.6 (9.5)	5.3 (4.8)	9.6 (8.0)	8.4 (5.3)	7.7 (5.1)	7.6 (5.1)	7.8 (5.2)	8.0 (4.7)	7.7 (7.3)	6.5 (4.2)	7.6 (6.5)
中央値	4.0	6.0	4.0	6.0	8.0	7.0	6.0	7.0	7.0	4.0	6.0	5.0
範囲	1－30	1－38	1－26	1－28	1 - 21	1 - 21	1 - 21	1－21	1－15	1－26	2－16	1－26
累積投与量（mg）												
平均値（SD）	641.8 (527.3)	11504.9 (11356.9)	702.7 (623.4)	11543.8 (9611.5)	－	－	－	－	－	－	－	－
中央値	514.9	7200.0	545.0	7200.0	－	－	－	－	－	－	－	－
範囲	1－3800	1200－45600	106－3879	1200－33600	－	－	－	－	－	－	－	－
Dose Intensity[*2]（%）												
平均値（SD）	96.0 (9.6)	96.0 (5.9)	96.3 (4.6)	96.1 (5.2)	98.7 (7.0)	98.3 (6.7)	97.9 (7.2)	98.2 (6.9)	97.9 (10.5)	95.6 (6.9)	96.0 (5.6)	96.1 (7.8)
中央値	97.7	97.7	97.7	97.7	100.0	100.0	100.0	100.0	98.8	97.7	98.4	97.8
範囲	50－286	44－108	65－100	68－102	33 - 100	50 - 100	50 - 100	33－100	80－147	60－109	80－100	60－147

*1: 投与期間 = 最終投与日 － 初回投与日 ＋1日
*2: 累積投与量（mg）/予定投与量（mg）× 100
［5.3.5.1-1 Table 55，5.3.5.1-2 Table 63，5.3.5.2-1 Table 54及び5.3.5.2-2 Table 33を改変］

表 2.7.4.1.2-3　曝露状況の要約（PCD4989g 試験）

Study Drug Exposure (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

	atezolizumab Total (N=481)	atezolizumab <=1 mg/kg q3w IV (N=9)	atezolizumab 3 mg/kg q3w IV (N=3)	atezolizumab 10 mg/kg q3w IV (N=36)	atezolizumab 15 mg/kg q3w IV (N=236)	atezolizumab 20 mg/kg q3w IV (N=146)	atezolizumab 1200 mg q3w IV (N=51)
Treatment duration (months)							
n	481	9	3	36	236	146	51
Mean (SD)	6.06 (6.98)	4.50 (6.95)	19.57 (16.41)	11.50 (10.95)	5.49 (5.59)	7.11 (7.34)	1.29 (0.99)
Median	3.45	2.07	21.46	9.48	3.42	4.62	1.34
Min - Max	0.0 - 35.0	0.7 - 21.9	2.3 - 35.0	0.0 - 32.4	0.0 - 29.7	0.0 - 32.6	0.0 - 4.1
Treatment duration (months)							
n	481	9	3	36	236	146	51
0 to <3	229 (47.6%)	6 (66.7%)	1 (33.3%)	10 (27.8%)	112 (47.5%)	53 (36.3%)	47 (92.2%)
>=3 to 6	76 (15.8%)	1 (11.1%)	0	4 (11.1%)	38 (16.1%)	29 (19.9%)	4 (7.8%)
>=6 to 12	122 (25.4%)	1 (11.1%)	0	13 (36.1%)	60 (25.4%)	48 (32.9%)	0
>=12	54 (11.2%)	1 (11.1%)	2 (66.7%)	9 (25.0%)	26 (11.0%)	16 (11.0%)	0
Dose intensity (%)							
n	481	9	3	36	236	146	51
Mean (SD)	100.1 (2.1)	100.8 (2.5)	113.1 (12.3)	99.9 (1.2)	100.1 (1.9)	99.9 (1.7)	100.0 (0.0)
Median	100.0	100.1	114.9	100.0	100.0	100.0	100.0
Min - Max	89 - 124	99 - 107	100 - 124	94 - 102	89 - 112	90 - 108	100 - 100
Number of doses							
n	481	9	3	36	236	146	51
Mean (SD)	8.5 (7.4)	7.3 (9.8)	26.0 (19.7)	12.6 (8.3)	8.2 (6.5)	9.8 (7.8)	2.8 (1.4)
Median	6.0	4.0	32.0	14.5	6.0	7.0	3.0
Min - Max	1 - 42	2 - 32	4 - 42	1 - 34	1 - 23	1 - 37	1 - 7
Total cumulative dose (mg)							
n	481	9	3	36	236	146	51
Mean (SD)	10885.9 (10363.5)	3583.2 (8866.5)	34037.4 (28606.6)	12676.4 (10693.8)	9589.3 (8164.0)	15142.0 (12135.5)	3364.7 (1663.1)
Median	6480.0	93.2	48188.7	12250.4	6142.5	11279.0	3600.0
Min - Max	1 - 57256	1 - 26838	1113 - 52810	794 - 43452	660 - 34917	1080 - 57256	1200 - 8400

Treatment duration is the date of the last dose of study medication minus the date of the first dose plus one day. Dose intensity is total amount of actual dose as reported by site divided by total amount of planned dose, which is calculated as planned dose * derived baseline weight * number of visits.
Extraction date: 15May2015 Datacut date: 02Dec2014

Adaptation from output t_ex_GO27831_SE
［5.3.5.3-1 t_ex_GO27831_SE を改変］

表 2.7.4.1.2-4 曝露状況の要約（JO28944試験）

Extent of Exposure to Trial Drug
Protocol(s): JO28944
Analysis: Safety Population

Variable Statistics	MPDL3280A 10 mg/kg (N=3)	MPDL3280A 20 mg/kg (N=3)
Treatment Duration (weeks)		
n	3	3
Mean	42.70	41.70
Median	53.90	56.10
Std Dev	25.89	25.64
Min-Max	13.1-61.1	12.1-56.9
Total Cumulative Dose (mg)		
n	3	3
Mean	7639.0	20424.7
Median	8920.0	26028.0
Std Dev	5241.3	14130.4
Min-Max	1876-12121	4352-30894
Number of Administration		
4	1 (33.3%)	1 (33.3%)
17	1 (33.3%)	0 (0.0%)
18	0 (0.0%)	1 (33.3%)
19	0 (0.0%)	1 (33.3%)
20	1 (33.3%)	0 (0.0%)
Relative Dose Intensity (%)		
n	3	3
Mean	94.70	98.43
Median	94.70	98.80
Std Dev	3.40	2.07
Min-Max	91.3-98.1	96.2-100.3

Adaptation from output mtsum_sp
［5.3.3.2-2 Table 15.3-1を改変］

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

(1) OAK 試験，POPLAR 試験，BIRCH 試験及び FIR 試験

OAK 試験，POPLAR 試験，BIRCH 試験，FIR 試験の人口統計学的特性及びその他の特性を表 2.7.4.1.3-1に示す。

OAK 試験及び POPLAR 試験の人口統計学的特性及びその他の特性では，安全性評価に影響を及ぼすような群間の差は認められなかった。

(2) PCD4989g 試験

全体集団の481例では，性別は男性が278例（57.8%），女性が203例（42.2%），年齢は中央値（範囲）が62.0（21～89）歳であった。30例以上登録された悪性腫瘍の種類は，多い順に尿路上皮癌が92例，非小細胞肺癌が88例，腎細胞癌が70例，トリプルネガティブ乳癌が54例，悪性黒色腫が45例であった。ECOG PS は0が215例（44.8%），1が263例（54.8%），2が2例（0.4%）であった。体重（範囲）は1 mg/kg 以下のコホートで49.9～90.7 kg，3 mg/kg コホートで72.6～114.3 kg，10 mg/kg コホートで55.8～149.2 kg，15 mg/kg コホートで42.0～149.0 kg，20 mg/kg コホートで36.5～168.0 kg，1200 mg コホートで45.6～124.0 kg であった（5.3.5.3-1 t_dm_all_GO27831_IT 参照）。

(3) JO28944試験

性別は男性が3例，女性が3例で，年齢は中央値（範囲）が51.0（41～69）歳であった。悪性腫瘍の種類は，肺癌が3例，その他が3例（膵癌，悪性黒色腫及び胸腺癌が各1例）であった。ECOG PS は0が2例，1が4例であった（5.3.3.2-2 11-2項参照）。体重（範囲）は10 mg/kg コホートで44.6～71.3 kg，20 mg/kg コホートで54.4～81.3 kg であった（5.3.3.2-2 表 11.2-1参照）。

表 2.7.4.1.3-1　人口統計学的特性及びその他の特性（OAK 試験，POPLAR 試験，BIRCH 試験及び FIR 試験）

	OAK 試験		POPLAR 試験		BIRCH 試験				FIR 試験			
	ドセタキセル群	本剤群	ドセタキセル群	本剤群	コホート1	コホート2	コホート3	全体	コホート1	コホート2	コホート3	全体
例数	612	613	143	144	139	267	253	659	31	93	13	137
年齢												
中央値	64.0	63.0	62.0	62.0	67.0	63.0	64.0	64.0	68.0	65.0	65.0	66.0
範囲	34 – 85	25 – 84	36 – 84	42 – 82	35 - 88	28 - 83	38 - 84	28 – 88	42 – 85	44 – 85	52 – 74	42 – 85
65歳未満	326 (53.3%)	335 (54.6%)	87 (60.8%)	87 (60.4%)	55 (39.6%)	142 (53.2%)	134 (53.0%)	331 (50.2%)	10 (32.3%)	45 (48.4%)	5 (38.5%)	60 (43.8%)
65歳以上	286 (46.7%)	278 (45.4%)	56 (39.2%)	57 (39.6%)	84 (60.4%)	125 (46.8%)	119 (47.0%)	328 (49.8%)	21 (67.7%)	48 (51.6%)	8 (61.5%)	77 (56.2%)
性別												
男性	379 (61.9%)	378 (61.7%)	76 (53.1%)	93 (64.6%)	71 (51.1%)	164 (61.4%)	153 (60.5%)	388 (58.9%)	14 (45.2%)	59 (63.4%)	6 (46.2%)	79 (57.7%)
女性	233 (38.1%)	235 (38.3%)	67 (46.9%)	51 (35.4%)	68 (48.9%)	103 (38.6%)	100 (39.5%)	271 (41.1%)	17 (54.8%)	34 (36.6%)	7 (53.8%)	58 (42.3%)
人種												
白人	432 (70.6%)	438 (71.5%)	116 (81.1%)	110 (76.4%)	121 (87.1%)	228 (85.4%)	200 (79.1%)	549 (83.3%)	27 (87.1%)	82 (88.2%)	13 (100.0%)	122 (89.1%)
アジア人	125 (20.4%)	124 (20.2%)	13 (9.1%)	23 (16.0%)	12 (8.6%)	27 (10.1%)	39 (15.4%)	78 (11.8%)	1 (3.2%)	5 (5.4%)	0	6 (4.4%)
黒人	16 (2.6%)	11 (1.8%)	4 (2.8%)	3 (2.1%)	2 (1.4%)	2 (0.7%)	6 (2.4%)	10 (1.5%)	3 (9.7%)	5 (5.4%)	0	8 (5.8%)
アメリカ先住民	2 (0.3%)	1 (0.2%)	1 (0.7%)	0	0	0	1 (0.4%)	1 (0.2%)	–	–	–	–
ハワイ先住民	2 (0.3%)	3 (0.5%)	0	2 (1.4%)	0	0	1 (0.4%)	1 (0.2%)	–	–	–	–
その他	12 (2.0%)	11 (1.8%)	4 (2.8%)	4 (2.8%)	0	3 (1.1%)	1 (0.4%)	4 (0.6%)	0	1 (1.1%)	0	1 (0.7%)
複数	1 (0.2%)	2 (0.3%)	–	–	1 (0.7%)	2 (0.7%)	2 (0.8%)	5 (0.8%)	–	–	–	–
不明	22 (3.6%)	23 (3.8%)	5 (3.5%)	2 (1.4%)	3 (2.2%)	5 (1.9%)	3 (1.2%)	11 (1.7%)	–	–	–	–
ベースライン時の ECOG PS			142	142					31	92	13	136
0	234 (38.2%)	221 (36.1%)	45 (31.7%)	46 (32.4%)	57 (41.0%)	95 (35.6%)	78 (30.8%)	230 (34.9%)	11 (35.5%)	24 (26.1%)	6 (46.2%)	41 (30.1%)
1	378 (61.8%)	392 (63.9%)	97 (68.3%)	96 (67.6%)	79 (56.8%)	169 (63.3%)	173 (68.4%)	421 (63.9%)	20 (64.5%)	68 (73.9%)	7 (53.8%)	95 (69.9%)
2	–	–	–	–	3 (2.2%)	3 (1.1%)	2 (0.8%)	8 (1.2%)	–			
喫煙歴												
なし	96 (15.7%)	112 (18.3%)	29 (20.3%)	27 (18.8%)	22 (15.8%)	47 (17.6%)	44 (17.4%)	113 (17.1%)	3 (9.7%)	15 (16.1%)	1 (7.7%)	19 (13.9%)
現在喫煙	107 (17.5%)	83 (13.5%)	21 (14.7%)	25 (17.4%)	16 (11.5%)	28 (10.5%)	26 (10.3%)	70 (10.6%)	3 (9.7%)	13 (14.0%)	2 (15.4%)	18 (13.1%)
過去にあり	409 (66.8%)	418 (68.2%)	93 (65.0%)	92 (63.9%)	101 (72.7%)	192 (71.9%)	183 (72.3%)	476 (72.2%)	25 (80.6%)	65 (69.9%)	10 (76.9%)	100 (73.0%)
組織型												
非扁平上皮癌	452 (73.9%)	452 (73.7%)	95 (66.4%)	95 (66.0%)	106 (76.3%)	185 (69.3%)	183 (72.3%)	474 (71.9%)	20 (64.5%)	67 (72.0%)	12 (92.3%)	99 (72.3%)
扁平上皮癌	160 (26.1%)	161 (26.3%)	48 (33.6%)	49 (34.0%)	33 (23.7%)	82 (30.7%)	70 (27.7%)	185 (28.1%)	11 (35.5%)	26 (28.0%)	1 (7.7%)	38 (27.7%)

	OAK 試験		POPLAR 試験		BIRCH 試験				FIR 試験			
	ドセタキセル群	本剤群	ドセタキセル群	本剤群	コホート1	コホート2	コホート3	全体	コホート1	コホート2	コホート3	全体
脳転移巣												
あり	66 (10.8%)	52 (8.5%)	15 (10.5%)	8 (5.6%)	0	1 (0.4%)	1 (0.4%)	2 (0.3%)	0	1 (1.1%)	9 (69.2%)	10 (7.3%)
なし	546 (89.2%)	561 (91.5%)	128 (89.5%)	136 (94.4%)	139 (100.0%)	266 (99.6%)	252 (99.6%)	657 (99.7%)	31 (100.0%)	92 (98.9%)	4 (30.8%)	127 (92.7%)
前治療数												
0	–	–	–	–	–	–	–	–	31 (100.0%)	1 (1.1%)	0	32 (23.4%)
1	465 (76.0%)	464 (75.7%)	96 (67.1%)	93 (64.6%)	–	–	–	–	0	48 (51.6%)	4 (30.8%)	52 (38.0%)
2	147 (24.0%)	149 (24.3%)	47 (32.9%)	51 (35.4%)	–	–	–	–	0	27 (29.0%)	7 (53.8%)	34 (24.8%)
3以上	–	–	–	–	–	–	–	–	0	17 (18.3%)	2 (15.4%)	19 (13.9%)
PD-L1 発現状況												
TC3又は IC3	85 (13.9%)	89 (14.5%)	23 (16.1%)	24 (16.7%)	65 (46.8%)	122 (45.7%)	115 (45.5%)	302 (45.8%)	7 (22.6%)	38 (40.9%)	8 (61.5%)	53 (38.7%)
相補的集団	523 (85.5%)	517 (84.3%)	120 (83.9%)	120 (83.3%)	74 (53.2%)	145 (54.3%)	137 (54.2%)	356 (54.0%)	24 (77.4%)	53 (57.0%)	5 (38.5%)	82 (59.9%)
不明	4 (0.7%)	7 (1.1%)	–	–	0	0	1 (0.4%)	1 (0.2%)	0	2 (2.2%)	0	2 (1.5%)
TC3 又は IC2/3	–	–	–	–	123 (88.5%)	247 (92.5%)	236 (93.3%)	606 (92.0%)	28 (90.3%)	78 (83.9%)	12 (92.3%)	118 (86.1%)
相補的集団	–	–	–	–	16 (11.5%)	20 (7.5%)	17 (6.7%)	53 (8.0%)	3 (9.7%)	13 (14.0%)	1 (7.7%)	17 (12.4%)
不明	–	–	–	–	–	–	–	–	0	2 (2.2%)	0	2 (1.5%)
TC2/3 又は IC2/3	182 (29.7%)	168 (27.4%)	55 (38.5%)	50 (34.7%)	–	–	–	–	–	–	–	–
相補的集団	425 (69.4%)	437 (71.3%)	88 (61.5%)	94 (65.3%)	–	–	–	–	–	–	–	–
不明	5 (0.8%)	8 (1.3%)	–	–								
TC1/2/3 又は IC1/2/3	337 (55.1%)	347 (56.6%)	102 (71.3%)	93 (64.6%)	–	–	–	–	–	–	–	–
TC0及び IC0	271 (44.3%)	260 (42.4%)	41 (28.7%)	51 (35.4%)	–	–	–	–	–	–	–	–
不明	4 (0.7%)	6 (1.0%)	–	–								

	OAK 試験		POPLAR 試験		BIRCH 試験				FIR 試験			
	ドセタキセル群	本剤群	ドセタキセル群	本剤群	コホート1	コホート2	コホート3	全体	コホート1	コホート2	コホート3	全体
EGFR 遺伝子変異												
n	612	613	83	83	73	130	124	327	13	51	7	71
陽性	53 (8.7%)	60 (9.8%)	8 (9.6%)	10 (12.0%)	10 (13.7%)	15 (11.5%)	14 (11.3%)	39 (11.9%)	0	5 (9.8%)	3 (42.9%)	8 (11.3%)
陰性	463 (75.7%)	455 (74.2%)	75 (90.4%)	72 (86.7%)	63 (86.3%)	115 (88.5%)	109 (87.9%)	287 (87.8%)	13 (100.0%)	44 (86.3%)	4 (57.1%)	61 (85.9%)
T790M	–	–	0	1 (1.2%)	0	0	1 (0.8%)	1 (0.3%)	0	2 (3.9%)	0	2 (2.8%)
不明	96 (15.7%)	98 (16.0%)	–	–	–	–	–	–	–	–	–	–
KRAS 遺伝子変異												
n	612	613	30	42	40	62	75	177	6	44	2	52
陽性	48 (7.8%)	42 (6.9%)	13 (43.3%)	14 (33.3%)	14 (35.0%)	21 (33.9%)	24 (32.0%)	59 (33.3%)	2 (33.3%)	15 (34.1%)	1 (50.0%)	18 (34.6%)
陰性	139 (22.7%)	149 (24.3%)	17 (56.7%)	28 (66.7%)	26 (65.0%)	41 (66.1%)	51 (68.0%)	118 (66.7%)	4 (66.7%)	29 (65.9%)	1 (50.0%)	34 (65.4%)
不明	425 (69.4%)	422 (68.8%)	–	–	–	–	–	–	–	–	–	–
EML4−ALK 融合遺伝子転座												
n	612	613	58	61	81	155	153	389	20	65	10	95
あり	1 (0.2%)	4 (0.7%)	3 (5.2%)	0	3 (3.7%)	2 (1.3%)	4 (2.6%)	9 (2.3%)	0	1 (1.5%)	0	1 (1.1%)
なし	289 (47.2%)	315 (51.4%)	55 (94.8%)	61 (100.0%)	76 (93.8%)	148 (95.5%)	143 (93.5%)	367 (94.3%)	20 (100.0%)	64 (98.5%)	10 (100.0%)	94 (98.9%)
不明	322 (52.6%)	294 (48.0%)	–	–	2 (2.5%)	5 (3.2%)	6 (3.9%)	13 (3.3%)	–	–	–	–

– : not applicable
TC スコア: 腫瘍細胞の PD-L1発現状況（又はその評価結果），IC スコア: 腫瘍浸潤免疫細胞の PD-L1発現状況（又はその評価結果）
上皮増殖因子受容体（EGFR）
カーステンラット肉腫ウイルス癌遺伝子ホモログ（KRAS）
微小管会合蛋白4（EML4）
未分化リンパ腫キナーゼ（ALK）
［5.3.5.1-1 t_dmt01_IT1225，t_lhis_IT1225，t_dmt01_pdl1_IT1225，5.3.5.1-2 Table 18，Table 19，Table 20，5.3.5.2-1 Table 15，t_lhis_SE，5.3.5.2-2 Table 11及び Table 13を改変］

2.7.4.2 有害事象

2.7.4.2.1 有害事象の解析

2.7.4.2.1.1 比較的よくみられる有害事象

(1) OAK 試験

1) 全 Grade の有害事象

いずれかの群で発現率が10%以上の有害事象の要約を表 2.7.4.2.1.1-1に示す。

2) Grade 3以上の有害事象

いずれかの群で発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.2.1.1-2に示す。

表 2.7.4.2.1.1-1 発現率10%以上の有害事象の要約（OAK 試験）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
Total number of patients with at least one adverse event	573 (94.1%)	390 (64.0%)	555 (96.0%)	496 (85.8%)
疲労	163 (26.8%)	87 (14.3%)	205 (35.5%)	177 (30.6%)
食欲減退	143 (23.5%)	52 (8.5%)	136 (23.5%)	116 (20.1%)
咳嗽	141 (23.2%)	23 (3.8%)	105 (18.2%)	13 (2.2%)
呼吸困難	118 (19.4%)	19 (3.1%)	112 (19.4%)	15 (2.6%)
無力症	116 (19.0%)	51 (8.4%)	114 (19.7%)	96 (16.6%)
悪心	108 (17.7%)	53 (8.7%)	131 (22.7%)	112 (19.4%)
発熱	108 (17.7%)	49 (8.0%)	76 (13.1%)	40 (6.9%)
便秘	107 (17.6%)	28 (4.6%)	82 (14.2%)	46 (8.0%)
下痢	94 (15.4%)	47 (7.7%)	141 (24.4%)	109 (18.9%)
嘔吐	74 (12.2%)	23 (3.8%)	62 (10.7%)	50 (8.7%)
関節痛	73 (12.0%)	28 (4.6%)	58 (10.0%)	41 (7.1%)
貧血	70 (11.5%)	24 (3.9%)	136 (23.5%)	114 (19.7%)
背部痛	67 (11.0%)	9 (1.5%)	42 (7.3%)	7 (1.2%)
筋骨格痛	64 (10.5%)	10 (1.6%)	25 (4.3%)	10 (1.7%)
末梢性浮腫	54 (8.9%)	15 (2.5%)	82 (14.2%)	57 (9.9%)
筋肉痛	39 (6.4%)	21 (3.4%)	91 (15.7%)	81 (14.0%)
末梢性ニューロパチー	24 (3.9%)	6 (1.0%)	65 (11.2%)	58 (10.0%)
口内炎	19 (3.1%)	13 (2.1%)	63 (10.9%)	59 (10.2%)
味覚異常	18 (3.0%)	11 (1.8%)	58 (10.0%)	56 (9.7%)
好中球減少症	10 (1.6%)	7 (1.1%)	90 (15.6%)	85 (14.7%)
脱毛症	3 (0.5%)	3 (0.5%)	202 (34.9%)	198 (34.3%)
発熱性好中球減少症	1 (0.2%)	0	62 (10.7%)	61 (10.6%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_p10_GO28915_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。

［5.3.5.1-3 ae_rae_p10_GO28915_SE を再掲］

表 2.7.4.2.1.1-2 発現率10%以上の有害事象の重症度別の要約（OAK 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) Any Grade No. (%)	Atezolizumab (Actual) (N=609) >= Grade3 No. (%)	Docetaxel (Actual) (N=578) Any Grade No. (%)	Docetaxel (Actual) (N=578) >= Grade3 No. (%)
Total number of patients with at least one adverse event	573 (94.1%)	237 (38.9%)	555 (96.0%)	324 (56.1%)
疲労	163 (26.8%)	17 (2.8%)	205 (35.5%)	23 (4.0%)
食欲減退	143 (23.5%)	2 (0.3%)	136 (23.5%)	9 (1.6%)
咳嗽	141 (23.2%)	2 (0.3%)	105 (18.2%)	1 (0.2%)
呼吸困難	118 (19.4%)	16 (2.6%)	112 (19.4%)	15 (2.6%)
無力症	116 (19.0%)	8 (1.3%)	114 (19.7%)	13 (2.2%)
悪心	108 (17.7%)	4 (0.7%)	131 (22.7%)	2 (0.3%)
発熱	108 (17.7%)	1 (0.2%)	76 (13.1%)	1 (0.2%)
便秘	107 (17.6%)	2 (0.3%)	82 (14.2%)	1 (0.2%)
下痢	94 (15.4%)	4 (0.7%)	141 (24.4%)	11 (1.9%)
嘔吐	74 (12.2%)	2 (0.3%)	62 (10.7%)	4 (0.7%)
関節痛	73 (12.0%)	3 (0.5%)	58 (10.0%)	1 (0.2%)
貧血	70 (11.5%)	14 (2.3%)	136 (23.5%)	33 (5.7%)
背部痛	67 (11.0%)	7 (1.1%)	42 (7.3%)	4 (0.7%)
筋骨格痛	64 (10.5%)	4 (0.7%)	25 (4.3%)	1 (0.2%)
末梢性浮腫	54 (8.9%)	1 (0.2%)	82 (14.2%)	3 (0.5%)
筋肉痛	39 (6.4%)	1 (0.2%)	91 (15.7%)	4 (0.7%)
末梢性ニューロパチー	24 (3.9%)	0	65 (11.2%)	7 (1.2%)
口内炎	19 (3.1%)	1 (0.2%)	63 (10.9%)	11 (1.9%)
味覚異常	18 (3.0%)	0	58 (10.0%)	0
好中球減少症	10 (1.6%)	3 (0.5%)	90 (15.6%)	75 (13.0%)
脱毛症	3 (0.5%)	0	202 (34.9%)	1 (0.2%)
発熱性好中球減少症	1 (0.2%)	1 (0.2%)	62 (10.7%)	62 (10.7%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_g3_p10_GO28915_SE.out
07DEC2016 17:04 Page 1 of 1

［5.3.5.1-3 ae_g3_p10_GO28915_SE を再掲］

(2) POPLAR 試験

1) 全 Grade の有害事象

いずれかの群で発現率が10%以上の有害事象の要約を表 2.7.4.2.1.1-3に示す。

2) Grade 3以上の有害事象

いずれかの群で発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.2.1.1-4に示す。

表 2.7.4.2.1.1-3 発現率10%以上の有害事象の要約（POPLAR 試験）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

MedDRA Preferred Term	atezolizumab 1200 mg q3w IV (N=142) AE No. (%)	atezolizumab 1200 mg q3w IV (N=142) Related AE No. (%)	Docetaxel (N=135) AE No. (%)	Docetaxel (N=135) Related AE No. (%)
Total number of patients with at least one adverse event	136 (95.8%)	95 (66.9%)	130 (96.3%)	119 (88.1%)
疲労	55 (38.7%)	29 (20.4%)	54 (40.0%)	47 (34.8%)
食欲減退	49 (34.5%)	25 (17.6%)	28 (20.7%)	21 (15.6%)
咳嗽	38 (26.8%)	1 (0.7%)	33 (24.4%)	5 (3.7%)
呼吸困難	38 (26.8%)	7 (4.9%)	27 (20.0%)	4 (3.0%)
悪心	31 (21.8%)	17 (12.0%)	45 (33.3%)	37 (27.4%)
便秘	29 (20.4%)	7 (4.9%)	32 (23.7%)	16 (11.9%)
下痢	24 (16.9%)	10 (7.0%)	38 (28.1%)	30 (22.2%)
発熱	24 (16.9%)	10 (7.0%)	16 (11.9%)	8 (5.9%)
貧血	23 (16.2%)	8 (5.6%)	26 (19.3%)	22 (16.3%)
関節痛	22 (15.5%)	6 (4.2%)	12 (8.9%)	7 (5.2%)
不眠症	19 (13.4%)	4 (2.8%)	11 (8.1%)	0
筋骨格痛	19 (13.4%)	2 (1.4%)	7 (5.2%)	1 (0.7%)
嘔吐	18 (12.7%)	8 (5.6%)	18 (13.3%)	16 (11.9%)
背部痛	16 (11.3%)	1 (0.7%)	11 (8.1%)	3 (2.2%)
発疹	15 (10.6%)	10 (7.0%)	16 (11.9%)	13 (9.6%)
肺炎	15 (10.6%)	3 (2.1%)	4 (3.0%)	3 (2.2%)
無力症	14 (9.9%)	9 (6.3%)	22 (16.3%)	18 (13.3%)
筋肉痛	8 (5.6%)	4 (2.8%)	18 (13.3%)	13 (9.6%)
脱毛症	3 (2.1%)	2 (1.4%)	52 (38.5%)	51 (37.8%)
好中球減少症	2 (1.4%)	1 (0.7%)	17 (12.6%)	15 (11.1%)
末梢性ニューロパチー	2 (1.4%)	1 (0.7%)	16 (11.9%)	15 (11.1%)

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_p10_GO28753_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。

［5.3.5.3-1 ae_rae_p10_GO28753_SE を再掲］

表 2.7.4.2.1.1-4 発現率10%以上の有害事象の重症度別の要約（POPLAR 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

	atezolizumab 1200 mg q3w IV (N=142)		Docetaxel (N=135)	
MedDRA Preferred Term	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	136 (95.8%)	63 (44.4%)	130 (96.3%)	76 (56.3%)
疲労	55 (38.7%)	3 (2.1%)	54 (40.0%)	10 (7.4%)
食欲減退	49 (34.5%)	2 (1.4%)	28 (20.7%)	0
咳嗽	38 (26.8%)	0	33 (24.4%)	0
呼吸困難	38 (26.8%)	10 (7.0%)	27 (20.0%)	2 (1.5%)
悪心	31 (21.8%)	1 (0.7%)	45 (33.3%)	0
便秘	29 (20.4%)	0	32 (23.7%)	1 (0.7%)
下痢	24 (16.9%)	1 (0.7%)	38 (28.1%)	4 (3.0%)
発熱	24 (16.9%)	0	16 (11.9%)	0
貧血	23 (16.2%)	4 (2.8%)	26 (19.3%)	5 (3.7%)
関節痛	22 (15.5%)	3 (2.1%)	12 (8.9%)	2 (1.5%)
不眠症	19 (13.4%)	0	11 (8.1%)	2 (1.5%)
筋骨格痛	19 (13.4%)	2 (1.4%)	7 (5.2%)	2 (1.5%)
嘔吐	18 (12.7%)	0	18 (13.3%)	0
背部痛	16 (11.3%)	1 (0.7%)	11 (8.1%)	1 (0.7%)
発疹	15 (10.6%)	2 (1.4%)	16 (11.9%)	1 (0.7%)
肺炎	15 (10.6%)	9 (6.3%)	4 (3.0%)	2 (1.5%)
無力症	14 (9.9%)	1 (0.7%)	22 (16.3%)	3 (2.2%)
筋肉痛	8 (5.6%)	1 (0.7%)	18 (13.3%)	3 (2.2%)
脱毛症	3 (2.1%)	0	52 (38.5%)	1 (0.7%)
好中球減少症	2 (1.4%)	0	17 (12.6%)	15 (11.1%)
末梢性ニューロパチー	2 (1.4%)	0	16 (11.9%)	1 (0.7%)

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_g3_p10_GO28753_SE.out
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［5.3.5.3-1 ae_g3_p10_GO28753_SE を再掲］

(3) BIRCH 試験

1) 全 Grade の有害事象

いずれかのコホートで発現率が10%以上の有害事象の要約を表 2.7.4.2.1.1-5に示す。

2) Grade 3以上の有害事象

いずれかのコホートで発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.2.1.1-6に示す。

表 2.7.4.2.1.1-5　発現率10%以上の有害事象の要約（BIRCH 試験）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
Total number of patients with at least one adverse event	617 (93.6%)	422 (64.0%)	127 (91.4%)	79 (56.8%)	246 (92.1%)	169 (63.3%)	244 (96.4%)	174 (68.8%)
疲労	203 (30.8%)	117 (17.8%)	45 (32.4%)	22 (15.8%)	74 (27.7%)	49 (18.4%)	84 (33.2%)	46 (18.2%)
食欲減退	148 (22.5%)	53 (8.0%)	32 (23.0%)	13 (9.4%)	47 (17.6%)	16 (6.0%)	69 (27.3%)	24 (9.5%)
咳嗽	144 (21.9%)	17 (2.6%)	33 (23.7%)	4 (2.9%)	45 (16.9%)	4 (1.5%)	66 (26.1%)	9 (3.6%)
呼吸困難	143 (21.7%)	24 (3.6%)	36 (25.9%)	5 (3.6%)	42 (15.7%)	9 (3.4%)	65 (25.7%)	10 (4.0%)
悪心	141 (21.4%)	68 (10.3%)	26 (18.7%)	12 (8.6%)	61 (22.8%)	27 (10.1%)	54 (21.3%)	29 (11.5%)
下痢	112 (17.0%)	64 (9.7%)	24 (17.3%)	10 (7.2%)	50 (18.7%)	29 (10.9%)	38 (15.0%)	25 (9.9%)
発熱	107 (16.2%)	52 (7.9%)	18 (12.9%)	9 (6.5%)	45 (16.9%)	19 (7.1%)	44 (17.4%)	24 (9.5%)
便秘	93 (14.1%)	25 (3.8%)	18 (12.9%)	6 (4.3%)	36 (13.5%)	7 (2.6%)	39 (15.4%)	12 (4.7%)
嘔吐	86 (13.1%)	26 (3.9%)	16 (11.5%)	3 (2.2%)	35 (13.1%)	9 (3.4%)	35 (13.8%)	14 (5.5%)
そう痒症	76 (11.5%)	60 (9.1%)	16 (11.5%)	10 (7.2%)	31 (11.6%)	25 (9.4%)	29 (11.5%)	25 (9.9%)
関節痛	75 (11.4%)	35 (5.3%)	14 (10.1%)	7 (5.0%)	30 (11.2%)	13 (4.9%)	31 (12.3%)	15 (5.9%)
無力症	71 (10.8%)	44 (6.7%)	13 (9.4%)	8 (5.8%)	24 (9.0%)	13 (4.9%)	34 (13.4%)	23 (9.1%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_p10_GO28754_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
背部痛	69 (10.5%)	12 (1.8%)	16 (11.5%)	1 (0.7%)	24 (9.0%)	6 (2.2%)	29 (11.5%)	5 (2.0%)
発疹	60 (9.1%)	43 (6.5%)	12 (8.6%)	6 (4.3%)	27 (10.1%)	21 (7.9%)	21 (8.3%)	16 (6.3%)
頭痛	59 (9.0%)	22 (3.3%)	12 (8.6%)	6 (4.3%)	19 (7.1%)	7 (2.6%)	28 (11.1%)	9 (3.6%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_p10_GO28754_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_p10_GO28754_SE を再掲］

表 2.7.4.2.1.1-6　発現率10%以上の有害事象の重症度別の要約（BIRCH 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659)		atezolizumab Cohort 1 (N=139)		atezolizumab Cohort 2 (N=267)		atezolizumab Cohort 3 (N=253)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	617 (93.6%)	271 (41.1%)	127 (91.4%)	58 (41.7%)	246 (92.1%)	108 (40.4%)	244 (96.4%)	105 (41.5%)
疲労	203 (30.8%)	15 (2.3%)	45 (32.4%)	3 (2.2%)	74 (27.7%)	7 (2.6%)	84 (33.2%)	5 (2.0%)
食欲減退	148 (22.5%)	6 (0.9%)	32 (23.0%)	0	47 (17.6%)	3 (1.1%)	69 (27.3%)	3 (1.2%)
咳嗽	144 (21.9%)	5 (0.8%)	33 (23.7%)	0	45 (16.9%)	3 (1.1%)	66 (26.1%)	2 (0.8%)
呼吸困難	143 (21.7%)	28 (4.2%)	36 (25.9%)	5 (3.6%)	42 (15.7%)	9 (3.4%)	65 (25.7%)	14 (5.5%)
悪心	141 (21.4%)	10 (1.5%)	26 (18.7%)	3 (2.2%)	61 (22.8%)	4 (1.5%)	54 (21.3%)	3 (1.2%)
下痢	112 (17.0%)	5 (0.8%)	24 (17.3%)	1 (0.7%)	50 (18.7%)	2 (0.7%)	38 (15.0%)	2 (0.8%)
発熱	107 (16.2%)	5 (0.8%)	18 (12.9%)	0	45 (16.9%)	3 (1.1%)	44 (17.4%)	2 (0.8%)
便秘	93 (14.1%)	2 (0.3%)	18 (12.9%)	0	36 (13.5%)	1 (0.4%)	39 (15.4%)	1 (0.4%)
嘔吐	86 (13.1%)	8 (1.2%)	16 (11.5%)	1 (0.7%)	35 (13.1%)	4 (1.5%)	35 (13.8%)	3 (1.2%)
そう痒症	76 (11.5%)	0	16 (11.5%)	0	31 (11.6%)	0	29 (11.5%)	0
関節痛	75 (11.4%)	4 (0.6%)	14 (10.1%)	1 (0.7%)	30 (11.2%)	3 (1.1%)	31 (12.3%)	0
無力症	71 (10.8%)	9 (1.4%)	13 (9.4%)	2 (1.4%)	24 (9.0%)	3 (1.1%)	34 (13.4%)	4 (1.6%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_g3_p10_GO28754_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) Any Grade No. (%)	atezolizumab Total (N=659) >= Grade3 No. (%)	atezolizumab Cohort 1 (N=139) Any Grade No. (%)	atezolizumab Cohort 1 (N=139) >= Grade3 No. (%)	atezolizumab Cohort 2 (N=267) Any Grade No. (%)	atezolizumab Cohort 2 (N=267) >= Grade3 No. (%)	atezolizumab Cohort 3 (N=253) Any Grade No. (%)	atezolizumab Cohort 3 (N=253) >= Grade3 No. (%)
背部痛	69 (10.5%)	10 (1.5%)	16 (11.5%)	3 (2.2%)	24 (9.0%)	2 (0.7%)	29 (11.5%)	5 (2.0%)
発疹	60 (9.1%)	2 (0.3%)	12 (8.6%)	0	27 (10.1%)	0	21 (8.3%)	2 (0.8%)
頭痛	59 (9.0%)	2 (0.3%)	12 (8.6%)	0	19 (7.1%)	1 (0.4%)	28 (11.1%)	1 (0.4%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_g3_p10_GO28754_SE.out
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［5.3.5.3-1 ae_g3_p10_GO28754_SE を再掲］

(4) FIR 試験

1) 全 Grade の有害事象

いずれかのコホートで発現率が10%以上の有害事象の要約を表 2.7.4.2.1.1-7に示す。

2) Grade 3以上の有害事象

いずれかのコホートで発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.2.1.1-8に示す。

表 2.7.4.2.1.1-7 発現率10%以上の有害事象の要約（FIR 試験）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
Total number of patients with at least one adverse event	136 (99.3%)	93 (67.9%)	31 (100.0%)	23 (74.2%)	92 (98.9%)	61 (65.6%)	13 (100.0%)	9 (69.2%)
疲労	56 (40.9%)	35 (25.5%)	15 (48.4%)	6 (19.4%)	36 (38.7%)	25 (26.9%)	5 (38.5%)	4 (30.8%)
呼吸困難	38 (27.7%)	3 (2.2%)	8 (25.8%)	2 (6.5%)	28 (30.1%)	1 (1.1%)	2 (15.4%)	0
咳嗽	37 (27.0%)	5 (3.6%)	4 (12.9%)	1 (3.2%)	31 (33.3%)	4 (4.3%)	2 (15.4%)	0
悪心	36 (26.3%)	20 (14.6%)	9 (29.0%)	8 (25.8%)	23 (24.7%)	11 (11.8%)	4 (30.8%)	1 (7.7%)
下痢	28 (20.4%)	12 (8.8%)	8 (25.8%)	3 (9.7%)	16 (17.2%)	5 (5.4%)	4 (30.8%)	4 (30.8%)
食欲減退	28 (20.4%)	19 (13.9%)	6 (19.4%)	5 (16.1%)	20 (21.5%)	12 (12.9%)	2 (15.4%)	2 (15.4%)
便秘	26 (19.0%)	3 (2.2%)	8 (25.8%)	2 (6.5%)	14 (15.1%)	1 (1.1%)	4 (30.8%)	0
関節痛	26 (19.0%)	8 (5.8%)	6 (19.4%)	2 (6.5%)	18 (19.4%)	5 (5.4%)	2 (15.4%)	1 (7.7%)
背部痛	26 (19.0%)	1 (0.7%)	5 (16.1%)	0	19 (20.4%)	1 (1.1%)	2 (15.4%)	0
発熱	25 (18.2%)	10 (7.3%)	6 (19.4%)	4 (12.9%)	17 (18.3%)	5 (5.4%)	2 (15.4%)	1 (7.7%)
貧血	24 (17.5%)	7 (5.1%)	6 (19.4%)	3 (9.7%)	17 (18.3%)	4 (4.3%)	1 (7.7%)	0
嘔吐	20 (14.6%)	8 (5.8%)	4 (12.9%)	1 (3.2%)	13 (14.0%)	7 (7.5%)	3 (23.1%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_p10_GO28625_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
低カリウム血症	18 (13.1%)	4 (2.9%)	2 (6.5%)	0	12 (12.9%)	4 (4.3%)	4 (30.8%)	0
上気道感染	17 (12.4%)	1 (0.7%)	4 (12.9%)	1 (3.2%)	13 (14.0%)	0	0	0
体重減少	15 (10.9%)	3 (2.2%)	6 (19.4%)	1 (3.2%)	8 (8.6%)	1 (1.1%)	1 (7.7%)	1 (7.7%)
肺炎	14 (10.2%)	0	3 (9.7%)	0	11 (11.8%)	0	0	0
頭痛	13 (9.5%)	3 (2.2%)	2 (6.5%)	1 (3.2%)	8 (8.6%)	0	3 (23.1%)	2 (15.4%)
喀血	12 (8.8%)	0	5 (16.1%)	0	6 (6.5%)	0	1 (7.7%)	0
そう痒症	12 (8.8%)	9 (6.6%)	4 (12.9%)	4 (12.9%)	7 (7.5%)	4 (4.3%)	1 (7.7%)	1 (7.7%)
末梢性浮腫	12 (8.8%)	3 (2.2%)	3 (9.7%)	0	7 (7.5%)	2 (2.2%)	2 (15.4%)	1 (7.7%)
胸痛	12 (8.8%)	1 (0.7%)	1 (3.2%)	0	9 (9.7%)	1 (1.1%)	2 (15.4%)	0
疼痛	11 (8.0%)	1 (0.7%)	5 (16.1%)	0	4 (4.3%)	0	2 (15.4%)	1 (7.7%)
皮膚乾燥	11 (8.0%)	5 (3.6%)	1 (3.2%)	1 (3.2%)	10 (10.8%)	4 (4.3%)	0	0
湿性咳嗽	11 (8.0%)	2 (1.5%)	1 (3.2%)	0	10 (10.8%)	2 (2.2%)	0	0
低ナトリウム血症	11 (8.0%)	1 (0.7%)	1 (3.2%)	0	10 (10.8%)	1 (1.1%)	0	0
不安	11 (8.0%)	0	0	0	9 (9.7%)	0	2 (15.4%)	0
尿路感染	7 (5.1%)	0	3 (9.7%)	0	2 (2.2%)	0	2 (15.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_p10_GO28625_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
アスパラギン酸アミノトランスフェラーゼ増加	6 (4.4%)	6 (4.4%)	2 (6.5%)	2 (6.5%)	2 (2.2%)	2 (2.2%)	2 (15.4%)	2 (15.4%)
アラニンアミノトランスフェラーゼ増加	6 (4.4%)	6 (4.4%)	2 (6.5%)	2 (6.5%)	2 (2.2%)	2 (2.2%)	2 (15.4%)	2 (15.4%)
腫瘍疼痛	6 (4.4%)	2 (1.5%)	0	0	4 (4.3%)	1 (1.1%)	2 (15.4%)	1 (7.7%)
骨痛	5 (3.6%)	2 (1.5%)	0	0	3 (3.2%)	1 (1.1%)	2 (15.4%)	1 (7.7%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_p10_GO28625_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_p10_GO28625_SE を再掲］

表 2.7.4.2.1.1-8　発現率10%以上の有害事象の重症度別の要約（FIR 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137)		atezolizumab Cohort 1 (N=31)		atezolizumab Cohort 2 (N=93)		atezolizumab Cohort 3 (N=13)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	136 (99.3%)	71 (51.8%)	31 (100.0%)	15 (48.4%)	92 (98.9%)	49 (52.7%)	13 (100.0%)	7 (53.8%)
疲労	56 (40.9%)	2 (1.5%)	15 (48.4%)	0	36 (38.7%)	2 (2.2%)	5 (38.5%)	0
呼吸困難	38 (27.7%)	4 (2.9%)	8 (25.8%)	0	28 (30.1%)	4 (4.3%)	2 (15.4%)	0
咳嗽	37 (27.0%)	1 (0.7%)	4 (12.9%)	0	31 (33.3%)	1 (1.1%)	2 (15.4%)	0
悪心	36 (26.3%)	1 (0.7%)	9 (29.0%)	1 (3.2%)	23 (24.7%)	0	4 (30.8%)	0
下痢	28 (20.4%)	2 (1.5%)	8 (25.8%)	1 (3.2%)	16 (17.2%)	0	4 (30.8%)	1 (7.7%)
食欲減退	28 (20.4%)	0	6 (19.4%)	0	20 (21.5%)	0	2 (15.4%)	0
便秘	26 (19.0%)	1 (0.7%)	8 (25.8%)	0	14 (15.1%)	0	4 (30.8%)	1 (7.7%)
関節痛	26 (19.0%)	1 (0.7%)	6 (19.4%)	0	18 (19.4%)	1 (1.1%)	2 (15.4%)	0
背部痛	26 (19.0%)	4 (2.9%)	5 (16.1%)	0	19 (20.4%)	4 (4.3%)	2 (15.4%)	0
発熱	25 (18.2%)	0	6 (19.4%)	0	17 (18.3%)	0	2 (15.4%)	0
貧血	24 (17.5%)	5 (3.6%)	6 (19.4%)	1 (3.2%)	17 (18.3%)	4 (4.3%)	1 (7.7%)	0
嘔吐	20 (14.6%)	2 (1.5%)	4 (12.9%)	2 (6.5%)	13 (14.0%)	0	3 (23.1%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_g3_p10_GO28625_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137)		atezolizumab Cohort 1 (N=31)		atezolizumab Cohort 2 (N=93)		atezolizumab Cohort 3 (N=13)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
低カリウム血症	18 (13.1%)	5 (3.6%)	2 (6.5%)	1 (3.2%)	12 (12.9%)	2 (2.2%)	4 (30.8%)	2 (15.4%)
上気道感染	17 (12.4%)	2 (1.5%)	4 (12.9%)	2 (6.5%)	13 (14.0%)	0	0	0
体重減少	15 (10.9%)	0	6 (19.4%)	0	8 (8.6%)	0	1 (7.7%)	0
肺炎	14 (10.2%)	6 (4.4%)	3 (9.7%)	2 (6.5%)	11 (11.8%)	4 (4.3%)	0	0
頭痛	13 (9.5%)	0	2 (6.5%)	0	8 (8.6%)	0	3 (23.1%)	0
喀血	12 (8.8%)	1 (0.7%)	5 (16.1%)	0	6 (6.5%)	1 (1.1%)	1 (7.7%)	0
そう痒症	12 (8.8%)	0	4 (12.9%)	0	7 (7.5%)	0	1 (7.7%)	0
末梢性浮腫	12 (8.8%)	1 (0.7%)	3 (9.7%)	0	7 (7.5%)	0	2 (15.4%)	1 (7.7%)
胸痛	12 (8.8%)	2 (1.5%)	1 (3.2%)	0	9 (9.7%)	1 (1.1%)	2 (15.4%)	1 (7.7%)
疼痛	11 (8.0%)	2 (1.5%)	5 (16.1%)	0	4 (4.3%)	2 (2.2%)	2 (15.4%)	0
低ナトリウム血症	11 (8.0%)	6 (4.4%)	1 (3.2%)	1 (3.2%)	10 (10.8%)	5 (5.4%)	0	0
湿性咳嗽	11 (8.0%)	0	1 (3.2%)	0	10 (10.8%)	0	0	0
皮膚乾燥	11 (8.0%)	0	1 (3.2%)	0	10 (10.8%)	0	0	0
不安	11 (8.0%)	0	0	0	9 (9.7%)	0	2 (15.4%)	0
尿路感染	7 (5.1%)	0	3 (9.7%)	0	2 (2.2%)	0	2 (15.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) Any Grade No. (%)	atezolizumab Total (N=137) >= Grade3 No. (%)	atezolizumab Cohort 1 (N=31) Any Grade No. (%)	atezolizumab Cohort 1 (N=31) >= Grade3 No. (%)	atezolizumab Cohort 2 (N=93) Any Grade No. (%)	atezolizumab Cohort 2 (N=93) >= Grade3 No. (%)	atezolizumab Cohort 3 (N=13) Any Grade No. (%)	atezolizumab Cohort 3 (N=13) >= Grade3 No. (%)
アスパラギン酸アミノトランスフェラーゼ増加	6 (4.4%)	3 (2.2%)	2 (6.5%)	1 (3.2%)	2 (2.2%)	2 (2.2%)	2 (15.4%)	0
アラニンアミノトランスフェラーゼ増加	6 (4.4%)	3 (2.2%)	2 (6.5%)	1 (3.2%)	2 (2.2%)	2 (2.2%)	2 (15.4%)	0
腫瘍疼痛	6 (4.4%)	2 (1.5%)	0	0	4 (4.3%)	1 (1.1%)	2 (15.4%)	1 (7.7%)
骨痛	5 (3.6%)	1 (0.7%)	0	0	3 (3.2%)	0	2 (15.4%)	1 (7.7%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_g3_p10_GO28625_SE.out
09NOV2016 10:27

［5.3.5.3-1 ae_g3_p10_GO28625_SE を再掲］

(5) PCD4989g 試験

1) 全 Grade の有害事象

いずれかのコホートで発現率が10%以上の有害事象の要約を表 2.7.4.7.1-1に示す。

2) Grade 3以上の有害事象

いずれかのコホートで発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.7.1-2に示す。

(6) JO28944試験

1) 全 Grade の有害事象

いずれかのコホートで発現率が10%以上の有害事象の要約を表 2.7.4.2.1.1-9に示す。用量の違いにより有害事象の発現状況に特段の差異は認められなかった。

表 2.7.4.2.1.1-9 発現率10%以上の有害事象の要約（JO28944試験）

Adverse Events by Relation to Trial Treatment (JO28944)
Protocol(s):JO28944
Analysis:Safety Population

	atezolizumab Total N=6		atezolizumab 10 mg/kg q3w IV N=3		atezolizumab 20 mg/kg q3w IV N=3	
Adverse Event	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)
Total Number of patients with AE	6 (100.0)	6 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)
発疹	3 (50.0)	3 (50.0)	2 (66.7)	2 (66.7)	1 (33.3)	1 (33.3)
頭痛	2 (33.3)	2 (33.3)	2 (66.7)	2 (66.7)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (33.3)	2 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
アラニンアミノトランスフェラーゼ増加	2 (33.3)	2 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
血中アルカリホスファターゼ増加	2 (33.3)	2 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
下痢	2 (33.3)	1 (16.7)	1 (33.3)	1 (33.3)	1 (33.3)	0
ざ瘡様皮膚炎	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
そう痒症	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
インフルエンザ様疾患	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
悪心	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
筋肉痛	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
口腔咽頭不快感	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
紅斑	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
心電図ＱＴ延長	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
多形紅斑	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
疲労	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
嘔吐	1 (16.7)	1 (16.7)	1 (33.3)	1 (33.3)	0	0
歯痛	1 (16.7)	0	1 (33.3)	0	0	0
造影剤アレルギー	1 (16.7)	0	1 (33.3)	0	0	0
発熱	1 (16.7)	0	1 (33.3)	0	0	0
鼻咽頭炎	1 (16.7)	0	1 (33.3)	0	0	0
齲歯	1 (16.7)	0	1 (33.3)	0	0	0
リンパ球数減少	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
筋骨格痛	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
好中球数減少	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
白血球数減少	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
貧血	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
迷走神経障害	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
蕁麻疹	1 (16.7)	1 (16.7)	0	0	1 (33.3)	1 (33.3)
口腔咽頭痛	1 (16.7)	0	0	0	1 (33.3)	0
喉頭痛	1 (16.7)	0	0	0	1 (33.3)	0
挫傷	1 (16.7)	0	0	0	1 (33.3)	0
擦過傷	1 (16.7)	0	0	0	1 (33.3)	0
肺炎	1 (16.7)	0	0	0	1 (33.3)	0
不眠症	1 (16.7)	0	0	0	1 (33.3)	0

事象名:MedDRA ver. 16.1

Program : $PROD/cdt7446c/c28944b/ae_rae_p10_JO28944.sas
Output : $PROD/cdt7446c/c28944b/reports/ae_rae_p10_JO28944_sp.out
10NOV2016 19:17 Page 1 of 1

因果関係の判断基準：治験薬との因果関係は，「関連なし」，「わずかにあり」，「可能性あり」，「多分あり」の4段階で評価され，「関連なし」以外と判定された場合に，因果関係が否定できない事象として集計した。

［5.3.5.3-1 ae_rae_p10_JO28944_sp を再掲］

2) Grade 3以上の有害事象

Grade 3以上の有害事象の発現は認められなかった（5.3.3.2-2 Table15.3-7）。

2.7.4.2.1.2 死亡

(1) OAK 試験

治験期間中の死亡の内訳を表 2.7.4.2.1.2-1に示す。また，すべての死亡例の一覧を5.3.5.1-1 l_ael04_SE に示した。死亡に至った有害事象（Grade 5。発現日が治験薬投与開始日以降，最終投与日から30日まで又は治験実施計画書に記載されていない治療の開始前まで）の要約は表2.7.4.2.1.2-2に，個別症例の詳細は5.3.5.1-1 Narratives 1. Page 266に示した。

表 2.7.4.2.1.2-1 死亡の内訳（OAK 試験）

Death and the Cause of Death
All Safety Evaluable Patients
Protocol: GO28915 (Data Cut: 7JUL2016)

	Docetaxel (Actual) (N=578)	Atezolizumab (Actual) (N=609)	All Patients (N=1187)
All Deaths	402	383	785
<=30 days from last study drug administration	42 (10.4%)	62 (16.2%)	104 (13.2%)
Adverse Event	14 (33.3%)	10 (16.1%)	24 (23.1%)
Progressive Disease	28 (66.7%)	51 (82.3%)	79 (76.0%)
Other	0	1 (1.6%)	1 (1.0%)
>30 days from last study drug administration	360 (89.6%)	321 (83.8%)	681 (86.8%)
Adverse Event	10 (2.8%)	15 (4.7%)	25 (3.7%)
Progressive Disease	348 (96.7%)	306 (95.3%)	654 (96.0%)
Other	2 (0.6%)	0	2 (0.3%)

Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692h/s28915g/t_dd_cause.sas / Output:
/opt/BIOSTAT/prod/cdt7692h/s28915g/reports/t_dd_cause_SE.out
25SEP2016 1:33

［5.3.5.1-1 Table 61を再掲］

表 2.7.4.2.1.2-2 死亡に至った有害事象の要約（OAK 試験）

Adverse Events leading to Death by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
Total number of patients with at least one adverse event	10 (1.6%)	0	14 (2.4%)	1 (0.2%)
敗血症	2 (0.3%)	0	1 (0.2%)	0
突然死	1 (0.2%)	0	2 (0.3%)	0
肺炎	1 (0.2%)	0	2 (0.3%)	0
呼吸困難	1 (0.2%)	0	1 (0.2%)	0
肺出血	1 (0.2%)	0	1 (0.2%)	0
死亡	1 (0.2%)	0	0	0
心筋虚血	1 (0.2%)	0	0	0
腎不全	1 (0.2%)	0	0	0
敗血症性ショック	1 (0.2%)	0	0	0
気道感染	0	0	2 (0.3%)	1 (0.2%)
下部消化管出血	0	0	1 (0.2%)	0
呼吸窮迫	0	0	1 (0.2%)	0
自然気胸	0	0	1 (0.2%)	0
肺塞栓症	0	0	1 (0.2%)	0
喀血	0	0	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_dd_GO28915_SE.out
07DEC2016 17:09 Page 1 of 1

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.1-3 ae_rae_dd_GO28915_SE を再掲］

(2) POPLAR 試験

治験期間中の死亡の内訳を表 2.7.4.2.1.2-3に示す。また，すべての死亡例の一覧を5.3.5.1-2 l_ael04_SE_dc8May2015に示した。死亡に至った有害事象（Grade 5。発現日が治験薬投与開始日以降，最終投与日から30日まで又は治験実施計画書に記載されていない治療の開始前まで）の要約は表 2.7.4.2.1.2-4に，個別症例の詳細は5.3.5.1-2 Narratives 1 Page 248に示した。

表 2.7.4.2.1.2-3　死亡の内訳（POPLAR 試験）

Death and the Cause of Death
Safety-Evaluable Patients
Protocol: GO28753 (Data Cut: 8May2015)

Status	Docetaxel (N=135)	Atezolizumab (N=142)	All Patients (N=277)
Primary Cause of Death	92 (68.1%)	76 (53.5%)	168 (60.6%)
Adverse Event	4 (3.0%)	9 (6.3%)	13 (4.7%)
Progression of Disease	85 (63.0%)	66 (46.5%)	151 (54.5%)
Unknown	3 (2.2%)	1 (0.7%)	4 (1.4%)

Deaths due to Adverse Events included 9 patients (3 Docetaxel patients; 6 Atezolizumab patients) who died due to AE occurring =< 30 days from last dose or prior to initiation of non-protocol therapy and 4 patients (1 Docetaxel patient; 3 Atezolizumab patients) who died due to AE occurring > 30 days from last dose or after initiation of non-protocol therapy. In addition to these 13 patients summarized as Death due to Adverse events, the 4 patients summarized as Death due to Unknown cause were also reported as Grade 5 AEs per protocol convention, for 17 total Grade 5 AEs reports.

Unknown cause of death included 3 Docetaxel patients, 2 of which occurred =< 30 days from last dose of study treatment or prior to initiation of non-protocol therapy and are reported as Grade 5 adverse events of "DEATH." The remaining Docetaxel patient, and the one Atezolizumab patient died due to unknown cause > 30 days from last dose of study treatment or after initiation of non-protocol therapy and were reported as Grade 5 AEs per protocol convention.

Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692c/s28753j/t_deathsv1.sas
Output: /opt/BIOSTAT/prod/cdt7692c/s28753j/reports/t_deathsv1_SE_dc8May2015.out
20AUG2015 20:28

［5.3.5.1-2 Table 67を再掲］

表 2.7.4.2.1.2-4　死亡に至った有害事象の要約（POPLAR 試験）

Adverse Events leading to Death by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

MedDRA Preferred Term	atezolizumab 1200 mg q3w IV (N=142) AE No. (%)	atezolizumab 1200 mg q3w IV (N=142) Related AE No. (%)	Docetaxel (N=135) AE No. (%)	Docetaxel (N=135) Related AE No. (%)
Total number of patients with at least one adverse event	6 (4.2%)	1 (0.7%)	5 (3.7%)	3 (2.2%)
心不全	1 (0.7%)	1 (0.7%)	0	0
気胸	1 (0.7%)	0	0	0
塞栓症	1 (0.7%)	0	0	0
潰瘍性出血	1 (0.7%)	0	0	0
肺炎	1 (0.7%)	0	0	0
肺塞栓症	1 (0.7%)	0	0	0
死亡	0	0	2 (1.5%)	1 (0.7%)
敗血症	0	0	2 (1.5%)	1 (0.7%)
急性呼吸窮迫症候群	0	0	1 (0.7%)	1 (0.7%)

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_dd_GO28753_SE.out
17NOV2016 13:42
Page 1 of 1
因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dd_GO28753_SE を再掲］

(3)　BIRCH 試験

治験期間中の死亡の内訳を表 2.7.4.2.1.2-5に示す。また，すべての死亡例の一覧を5.3.5.2-1 l_dd_SE に示した。死亡に至った有害事象（Grade 5。発現日が治験薬投与開始日以降，最終投与日から30日まで又は治験実施計画書に記載されていない治療の開始前まで）の要約は表 2.7.4.2.1.2-6に，個別症例の詳細は5.3.5.2-1 NARRATIVES 1.1 Page 249に示した。

表 2.7.4.2.1.2-5　死亡の内訳（BIRCH 試験）

	Cohort 1 (N=139)	Cohort 2 (N=267)	Cohort 3 (N=253)	Cohort 2+3 (N=520)	All Patients (N=659)
All deaths					
n	36	87	100	187	223
<=30 days from last study drug administration	11 (7.9%)	23 (8.6%)	29 (11.5%)	52 (10.0%)	63 (9.6%)
>30 days from last study drug administration	25 (18.0%)	64 (24.0%)	71 (28.1%)	135 (26.0%)	160 (24.3%)
Disease Progression					
n	34	75	91	166	200
Disease Progression	34 (24.5%)	75 (28.1%)	91 (36.0%)	166 (31.9%)	200 (30.3%)
Other					
n	2	12	9	21	23
ACUTE CORONARY SYNDROME	0	0	1 (0.4%)	1 (0.2%)	1 (0.2%)
CARDIAC ARREST	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
CARDIOPULMONARY FAILURE	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
CEREBRAL INFARCTION	1 (0.7%)	0	0	0	1 (0.2%)
DEATH	0	0	1 (0.4%)	1 (0.2%)	1 (0.2%)
DEATH DUE TO UNKNOWN	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
GASTRIC PERFORATION	0	0	1 (0.4%)	1 (0.2%)	1 (0.2%)
HEPATIC FAILURE	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
INTERNAL HAEMORRHAGE	0	0	1 (0.4%)	1 (0.2%)	1 (0.2%)
JUGULAR VEIN THROMBOSIS	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
LUNG INFECTION	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
PNEUMONIA	0	1 (0.4%)	3 (1.2%)	4 (0.8%)	4 (0.6%)
PNEUMONIA ASPIRATION	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
PNEUMONITIS	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
RESPIRATORY DISTRESS	0	0	1 (0.4%)	1 (0.2%)	1 (0.2%)
RESPIRATORY FAILURE	1 (0.7%)	1 (0.4%)	0	1 (0.2%)	2 (0.3%)
SEPTIC SHOCK	0	1 (0.4%)	0	1 (0.2%)	1 (0.2%)
SUDDEN DEATH	0	1 (0.4%)	1 (0.4%)	2 (0.4%)	2 (0.3%)

Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692d/s28754e/t_dd_cause.sas / Output:
/opt/BIOSTAT/prod/cdt7692d/s28754e/reports/t_dd_cause_SE.out
28AUG2015 22:23

［5.3.5.2-1 Table 58を再掲］

表 2.7.4.2.1.2-6　死亡に至った有害事象の要約（BIRCH 試験）

Adverse Events leading to Death by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
Total number of patients with at least one adverse event	19 (2.9%)	1 (0.2%)	2 (1.4%)	0	10 (3.7%)	0	7 (2.8%)	1 (0.4%)
肺炎	3 (0.5%)	1 (0.2%)	0	0	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
突然死	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
呼吸不全	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
脳梗塞	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
肝不全	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
誤嚥性肺炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
心停止	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
心肺不全	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
脳血管発作	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
敗血症性ショック	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肺感染	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肺臓炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_dd_GO28754_SE.out
09NOV2016 10:39

Adverse Events leading to Death by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
急性冠動脈症候群	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
呼吸窮迫	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
死亡	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
内出血	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_dd_GO28754_SE.out
09NOV2016 10:39

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dd_GO28754_SE を再掲］

(4) FIR 試験

治験期間中の死亡の内訳を表 2.7.4.2.1.2-7に示す。また，すべての死亡例の一覧を5.3.5.2-2 l_dd_SE に示した。死亡に至った有害事象（Grade 5。発現日が治験薬投与開始日以降，最終投与日から30日まで又は治験実施計画書に記載されていない治療の開始前まで）の要約は表 2.7.4.2.1.2-8に，個別症例の詳細は5.3.5.2-2 Narratives 1 Page 155に示した。

表 2.7.4.2.1.2-7 死亡の内訳（FIR 試験）

Death and Cause of Death , Treated Patients
Protocol: GO28625

	Cohort 1 (N=31)	Cohort 2 (N=93)	Cohort 3 (N=13)	All Patients (N=137)
All deaths				
n	8	43	9	60
<=30 days from last study drug administration	2 (6.5%)	10 (10.8%)	2 (15.4%)	14 (10.2%)
>30 days from last study drug administration	6 (19.4%)	33 (35.5%)	7 (53.8%)	46 (33.6%)
Primary cause of death				
n	8	43	9	60
Adenocarcinoma	0	1 (1.1%)	0	1 (0.7%)
Cardiac Arrest	1 (3.2%)	0	0	1 (0.7%)
Cardiac Tamponade	1 (3.2%)	0	0	1 (0.7%)
Death Due to Euthanasia	0	1 (1.1%)	0	1 (0.7%)
Death Due to Progressive of Disease	3 (9.7%)	11 (11.8%)	4 (30.8%)	18 (13.1%)
Disseminated Intravascular Coagulation	0	1 (1.1%)	0	1 (0.7%)
Malignant Neoplasm Progression	0	2 (2.2%)	0	2 (1.5%)
Metastases to Meninges	0	0	1 (7.7%)	1 (0.7%)
Non-Small Cell Lung Cancer	3 (9.7%)	21 (22.6%)	4 (30.8%)	28 (20.4%)
Non-Small Cell Lung Cancer Metastatic	0	1 (1.1%)	0	1 (0.7%)
Non-Small Cell Lung Cancer Stage IV	0	1 (1.1%)	0	1 (0.7%)
Pericarditis Constrictive	0	1 (1.1%)	0	1 (0.7%)
Pneumonia	0	1 (1.1%)	0	1 (0.7%)
Respiratory Disorder	0	1 (1.1%)	0	1 (0.7%)
Squamous Cell Carcinoma	0	1 (1.1%)	0	1 (0.7%)

Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdpt7692/s28625i/t_dd_cause.sas / Output: /opt/BIOSTAT/prod/cdpt7692/s28625i/reports/t_dd_cause_SE.out
24AUG2015 20:30 Page 1 of 1

［5.3.5.2-2 t_dd_cause_SE を再掲］

表 2.7.4.2.1.2-8　死亡に至った有害事象の要約（FIR 試験）

Adverse Events leading to Death by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
Total number of patients with at least one adverse event	5 (3.6%)	1 (0.7%)	2 (6.5%)	0	3 (3.2%)	1 (1.1%)	0	0
心タンポナーデ	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
心停止	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
収縮性心膜炎	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
呼吸障害	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
播種性血管内凝固	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_dd_GO28625_SE.out
09NOV2016 10:29

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dd_GO28625_SE を再掲］

(5) PCD4989g 試験

治験期間中の死亡の内訳を表 2.7.4.2.1.2-9に示す。また，非小細胞肺癌コホートのすべての死亡例の一覧を5.3.3.2-1 l_dd_NSCLC_SE に示した。死亡に至った有害事象（Grade 5。発現日が治験薬投与開始日以降，最終投与日から30日まで又は治験実施計画書に記載されていない治療の開始前まで）の要約は表 2.7.4.2.1.2-10に，個別症例の詳細は5.3.3.2-1 Narratives 1.1.1 Page 7721に示した。

表 2.7.4.2.1.2-9　死亡の内訳（PCD4989g 試験）

Deaths by Cause of Death
Safety Evaluable Patients
Protocol: GO27831

	MPDL3280A <=1 mg/kg q3w IV (N=9)	MPDL3280A 3 mg/kg q3w IV (N=3)	MPDL3280A 10 mg/kg q3w IV (N=36)	MPDL3280A 15 mg/kg q3w IV (N=236)	MPDL3280A 20 mg/kg q3w IV (N=146)	MPDL3280A 1200 mg q3w IV (N=51)	All Patients (N=481)
All deaths							
<=30 days from last study drug administration	0	0	2 (5.6%)	23 (9.7%)	15 (10.3%)	6 (11.8%)	46 (9.6%)
>30 days from last study drug administration	4 (44.4%)	0	13 (36.1%)	88 (37.3%)	61 (41.8%)	1 (2.0%)	167 (34.7%)
Primary cause of death							
ACUTE RESPIRATORY FAILURE	0	0	0	1 (0.4%)	1 (0.7%)	0	2 (0.4%)
ALCOHOL ABUSE	0	0	0	1 (0.4%)	0	0	1 (0.2%)
BLADDER CANCER	0	0	0	1 (0.4%)	0	0	1 (0.2%)
BREAST CANCER METASTATIC	0	0	0	0	0	1 (2.0%)	1 (0.2%)
CARDIAC TAMPONADE	0	0	0	0	1 (0.7%)	0	1 (0.2%)
CARDIO-RESPIRATORY ARREST	0	0	0	0	1 (0.7%)	0	1 (0.2%)
DEATH	0	0	0	1 (0.4%)	0	1 (2.0%)	2 (0.4%)
DEATH DURING FOLLOW-UP	3 (33.3%)	0	9 (25.0%)	59 (25.0%)	50 (34.2%)	0	121 (25.2%)
DISEASE PROGRESSION	0	0	0	1 (0.4%)	0	0	1 (0.2%)
DYSPNOEA	0	0	0	0	0	1 (2.0%)	1 (0.2%)
FALL	0	0	0	1 (0.4%)	0	0	1 (0.2%)
HEPATIC HAEMATOMA	0	0	0	0	0	1 (2.0%)	1 (0.2%)
HYPONATRAEMIA	0	0	0	0	0	1 (2.0%)	1 (0.2%)
MALIGNANT NEOPLASM PROGRESSION	1 (11.1%)	0	5 (13.9%)	42 (17.8%)	21 (14.4%)	1 (2.0%)	70 (14.6%)
OBSTRUCTIVE AIRWAYS DISORDER	0	0	0	1 (0.4%)	0	0	1 (0.2%)
PNEUMONIA	0	0	1 (2.8%)	0	0	0	1 (0.2%)
PULMONARY HYPERTENSION	0	0	0	0	0	1 (2.0%)	1 (0.2%)
SEPSIS	0	0	0	1 (0.4%)	0	0	1 (0.2%)
SUDDEN DEATH	0	0	0	0	2 (1.4%)	0	2 (0.4%)
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME	0	0	0	1 (0.4%)	0	0	1 (0.2%)
UPPER GASTROINTESTINAL HAEMORRHAGE	0	0	0	1 (0.4%)	0	0	1 (0.2%)

Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692f/s27831o/t_dd_cause.sas / Output: /opt/BIOSTAT/prod/cdt7692f/s27831o/reports/t_dd_cause_SE.out
06JUN2015 1:52 Page 1 of 1

［5.3.3.2-1 t_dd_cause_SE を再掲］

表 2.7.4.2.1.2-10　死亡に至った有害事象の要約（PCD4989g 試験）

Adverse Events leading to Death by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
Total number of patients with at least one adverse event	17 (3.5%)	3 (0.6%)	0	0	0	0	1 (2.8%)	0
急性呼吸不全	2 (0.4%)	0	0	0	0	0	0	0
肺炎	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
アルコール乱用	1 (0.2%)	0	0	0	0	0	0	0
過量投与	1 (0.2%)	0	0	0	0	0	0	0
全身性炎症反応症候群	1 (0.2%)	0	0	0	0	0	0	0
転倒	1 (0.2%)	0	0	0	0	0	0	0
頭部損傷	1 (0.2%)	0	0	0	0	0	0	0
敗血症	1 (0.2%)	0	0	0	0	0	0	0
閉塞性気道障害	1 (0.2%)	0	0	0	0	0	0	0
心肺停止	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
心タンポナーデ	1 (0.2%)	0	0	0	0	0	0	0
突然死	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dd_GO27831_SE.out
09NOV2016 10:38

Adverse Events leading to Death by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
死亡	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
肺高血圧症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
肝血腫	1 (0.2%)	0	0	0	0	0	0	0
呼吸窮迫	1 (0.2%)	0	0	0	0	0	0	0
呼吸困難	1 (0.2%)	0	0	0	0	0	0	0
低ナトリウム血症	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dd_GO27831_SE.out
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Adverse Events leading to Death by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
Total number of patients with at least one adverse event	6 (2.5%)	0	4 (2.7%)	1 (0.7%)	6 (11.8%)	2 (3.9%)
急性呼吸不全	1 (0.4%)	0	1 (0.7%)	0	0	0
肺炎	0	0	0	0	0	0
アルコール乱用	1 (0.4%)	0	0	0	0	0
過量投与	1 (0.4%)	0	0	0	0	0
全身性炎症反応症候群	1 (0.4%)	0	0	0	0	0
転倒	1 (0.4%)	0	0	0	0	0
頭部損傷	1 (0.4%)	0	0	0	0	0
敗血症	1 (0.4%)	0	0	0	0	0
閉塞性気道障害	1 (0.4%)	0	0	0	0	0
心肺停止	0	0	1 (0.7%)	1 (0.7%)	0	0
心タンポナーデ	0	0	1 (0.7%)	0	0	0
突然死	0	0	1 (0.7%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dd_GO27831_SE.out
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Adverse Events leading to Death by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
死亡	0	0	0	0	1 (2.0%)	1 (2.0%)
肺高血圧症	0	0	0	0	1 (2.0%)	1 (2.0%)
肝血腫	0	0	0	0	1 (2.0%)	0
呼吸窮迫	0	0	0	0	1 (2.0%)	0
呼吸困難	0	0	0	0	1 (2.0%)	0
低ナトリウム血症	0	0	0	0	1 (2.0%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dd.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dd_GO27831_SE.out
09NOV2016 10:38

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dd_GO27831_SE を再掲］

(6) JO28944試験

本治験に参加した6例の被験者では，治験期間中（治験薬投与開始後～治験薬最終投与後30日まで）の死亡は認められなかった（5.3.3.2-2 Listing16.2-21）。

2.7.4.2.1.3 その他の重篤な有害事象

(1) OAK 試験

重篤な有害事象の要約を表 2.7.4.7.2-1に示す。また，重篤な有害事象発現例の一覧を5.3.5.1-1 l_ael03_SE に，治験薬との因果関係を否定できない重篤な有害事象を発現した個別症例の詳細は5.3.5.1-1 Narratives 5 Page 1072に示した。

重篤な有害事象は，本剤群で194/609例（31.9%），ドセタキセル群で181/578例（31.3%）に認められた。

(2) POPLAR 試験

重篤な有害事象の要約を表 2.7.4.7.2-2に示す。また，重篤な有害事象発現例の一覧を5.3.5.1-2 l_ael03_SE_dc8May2015に，治験薬との因果関係を否定できない重篤な有害事象を発現した個別症例の詳細は5.3.5.1-2 Narratives 5 Page 538に示した。

重篤な有害事象は，本剤群で50/142例（35.2%），ドセタキセル群で46/135例（34.1%）に認められた。

(3) BIRCH 試験

重篤な有害事象の要約を表 2.7.4.7.2-3に示す。また，重篤な有害事象発現例の一覧を5.3.5.3-1 l_sae_GO28754_SE に，本剤との因果関係を否定できない重篤な有害事象を発現した個別症例の詳細は5.3.5.2-1 Narratives 1.5 Page 725に示した。

重篤な有害事象は，コホート1で43/139例（30.9%），コホート2で96/267例（36.0%），コホート3で94/253例（37.2%），全体として233/659例（35.4%）に認められた。

(4) FIR 試験

重篤な有害事象の要約を表 2.7.4.7.2-4に示す。また，重篤な有害事象発現例の一覧を5.3.5.3-1 l_sae_GO28625_SE に，本剤との因果関係を否定できない重篤な有害事象を発現した個別症例の詳細は5.3.5.2-2 Narratives 5 Page 280に示した。

重篤な有害事象は，コホート1で16/31例（51.6%），コホート2で43/93例（46.2%），コホート3で6/13例（46.2%），全体として65/137例（47.4%）に認められた。

(5) PCD4989g 試験

重篤な有害事象の要約を表 2.7.4.7.2-5に示す。また，非小細胞肺癌コホートで発現した重篤な有害事象の一覧を5.3.3.2-1 l_ae_ser_NSCLC_SER_SE に，本剤との因果関係を否定できない重篤な有害事象を発現した個別症例の詳細を5.3.3.2-1 Narratives 1.5 Page 8412に示した。

重篤な有害事象は，1 mg/kg 以下のコホートで1/9例（11.1%），10 mg/kg コホートで15/36例（41.7%），15 mg/kg コホートで94/236例（39.8%），20 mg/kg コホートで56/146例（38.4%），1200 mg コホートで16/51例（31.4%），全体として182/481例（37.8%）に認められた。なお，3 mg/kg コホートの3例では，重篤な有害事象は認められなかった。

(6) JO28944試験

重篤な有害事象発現例の一覧を5.3.3.2-2 Listing16.2-19に，個別症例の詳細を2.7.6.2.2.1項に示す。

重篤な有害事象は，10 mg/kg コホートで1/3例，全体として1/6例に認められた。なお，20 mg/kg コホートの3例では，重篤な有害事象は認められなかった。

2.7.4.2.1.4 その他の重要な有害事象

2.7.4.2.1.4.1 治験薬の投与中止に至った有害事象

(1) OAK 試験

治験薬の投与中止に至った有害事象の要約を表 2.7.4.7.3-1に示す。

治験薬の投与中止に至った有害事象は，本剤群で46/609例（7.6%），ドセタキセル群で108/578例（18.7%）に認められた。

(2) POPLAR 試験

治験薬の投与中止に至った有害事象の要約を表 2.7.4.7.3-2に示す。

治験薬の投与中止に至った有害事象は，本剤群で11/142例（7.7%），ドセタキセル群で30/135例（22.2%）に認められた。

(3) BIRCH 試験

本剤の投与中止に至った有害事象の要約を表 2.7.4.7.3-3に示す。

本剤の投与中止に至った有害事象は，コホート1で8/139例（5.8%），コホート2で15/267例（5.6%），コホート3で11/253例（4.3%），全体として34/659例（5.2%）に認められた。

(4) FIR 試験

本剤の投与中止に至った有害事象の要約を表 2.7.4.7.3-4に示す。

本剤の投与中止に至った有害事象は，コホート1で2/31例（6.5%），コホート2で9/93例（9.7%），コホート3で2/13例（15.4%），全体として13/137例（9.5%）に認められた。

(5) PCD4989g 試験

本剤の投与中止に至った有害事象の要約を表 2.7.4.7.3-5に示す。

本剤の投与中止に至った有害事象は，10 mg/kg コホートで2/36例（5.6%），15 mg/kg コホートで20/236例（8.5%），20 mg/kg コホートで7/146例（4.8%），1200 mg コホートで3/51例（5.9%），全体として32/481例（6.7%）に認められた。なお，1 mg/kg 以下のコホートの9例及び3 mg/kg コホートの3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。

(6) JO28944試験

本治験に参加した6例の被験者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（5.3.3.2-2 Listing16.2-18）。

2.7.4.2.1.4.2 治験薬の投与量変更（休薬又は減量）に至った有害事象

(1) OAK 試験

治験薬の投与量変更に至った有害事象の要約を表 2.7.4.7.4-1に示す。

治験薬の投与量変更に至った有害事象は，本剤群で152/609例（25.0%），ドセタキセル群で210/578例（36.3%）に認められた。

(2) POPLAR 試験

治験薬の投与量変更に至った有害事象の要約を表 2.7.4.7.4-2に示す。

治験薬の投与量変更に至った有害事象は，本剤群で34/142例（23.9%），ドセタキセル群で44/135例（32.6%）に認められた。

(3) BIRCH 試験

本剤の休薬に至った有害事象の要約を表 2.7.4.7.4-3に示す。

本剤の休薬に至った有害事象は，コホート1で33/139例（23.7%），コホート2で66/267例（24.7%），コホート3で73/253例（28.9%），全体として172/659例（26.1%）に認められた。

(4) FIR 試験

本剤の休薬に至った有害事象の要約を表 2.7.4.7.4-4に示す。

本剤の休薬に至った有害事象は，コホート1で11/31例（35.5%），コホート2で19/93例（20.4%），コホート3で2/13例（15.4%），全体として32/137例（23.4%）に認められた。

(5) PCD4989g 試験

本剤の投与量変更に至った有害事象の要約を表 2.7.4.7.4-5に示す。

本剤の投与量変更に至った有害事象は，1 mg/kg 以下のコホートで2/9例（22.2%）3 mg/kg コホートで2/3例（66.7%），10 mg/kg コホートで12/36例（33.3%），15 mg/kg コホートで43/236例（18.2%），20 mg/kg コホートで28/146例（19.2%），1200 mg コホートで4/51例（7.8%），全体として91/481例（18.9%）に認められた。

(6) JO28944試験

本剤の休薬に至った有害事象の要約を表 2.7.4.7.4-6に示す。

本剤の休薬に至った有害事象は，10 mg/kg コホートで2/3例（66.7%），20 mg/kg コホートで1/3例（33.3%），全体として3/6例（50.0%）に認められた。

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

2.7.4.2.1.5.1 本剤の注目すべき有害事象

本剤により過度の免疫反応に起因すると考えられる様々な事象が認められることから，本剤の注目すべき有害事象として，以後に記載した事象群を用いて評価した。これらの事象群の評価は，OAK 試験の結果を中心に行った。

OAK 試験の安全性解析対象1187例の，本剤の注目すべき有害事象の要約を表 2.7.4.7.6-1に，Grade 5の本剤の注目すべき有害事象の要約を表 2.7.4.7.6-2に，重篤な有害事象として報告された本剤の注目すべき有害事象の要約を表 2.7.4.7.6-3に，治験薬の投与中止に至った本剤の注目すべき有害事象の要約を表 2.7.4.7.6-4に，治験薬の投与量変更に至った本剤の注目すべき有害事象の要約を表 2.7.4.7.6-5に示した。

(1) 肝炎

OAK 試験の安全性解析対象1187例の肝炎（事象群）の要約を表 2.7.4.2.1.5.1-1に，重篤な有害事象として報告された肝炎（事象群）の要約を表 2.7.4.2.1.5.1-2に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，肝炎（事象群）は本剤群の67例（11.0%），ドセタキセル群の22例（3.8%）に認められた。

Grade 5の肝炎（事象群）は両群で認められなかった。

重篤な有害事象として報告された肝炎（事象群）は本剤群の5例（0.8%）及びドセタキセル群の2例（0.3%）に認められた。

治験薬の投与中止に至った肝炎（事象群）は本剤群の5例（0.8%）及びドセタキセル群の1例（0.2%）に，治験薬の投与量変更に至った肝炎（事象群）は本剤群の10例（1.6%）及びドセタキセル群の2例（0.3%）に認められた。

表 2.7.4.2.1.5.1-1 肝炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肝炎			
- Overall -	- Any Grade -	67 (11.0%)	22 (3.8%)
	1	36 (5.9%)	15 (2.6%)
	2	13 (2.1%)	2 (0.3%)
	3	14 (2.3%)	4 (0.7%)
	4	4 (0.7%)	1 (0.2%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	38 (6.2%)	12 (2.1%)
	1	22 (3.6%)	9 (1.6%)
	2	11 (1.8%)	1 (0.2%)
	3	5 (0.8%)	2 (0.3%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	35 (5.7%)	14 (2.4%)
	1	22 (3.6%)	12 (2.1%)
	2	7 (1.1%)	0
	3	6 (1.0%)	2 (0.3%)
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	7 (1.1%)	2 (0.3%)
	1	3 (0.5%)	1 (0.2%)
	2	1 (0.2%)	0
	3	3 (0.5%)	1 (0.2%)
血中ビリルビン増加	- Any Grade -	7 (1.1%)	2 (0.3%)
	1	2 (0.3%)	0
	2	4 (0.7%)	0
	3	0	2 (0.3%)
	4	1 (0.2%)	0
肝機能異常	- Any Grade -	3 (0.5%)	2 (0.3%)
	1	2 (0.3%)	2 (0.3%)
	3	1 (0.2%)	0
腹水	- Any Grade -	3 (0.5%)	0
	2	3 (0.5%)	0
トランスアミナーゼ上昇	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
肝炎	- Any Grade -	2 (0.3%)	0
	4	2 (0.3%)	0
肝臓痛	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	0
	2	0	1 (0.2%)
肝酵素上昇	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肝細胞損傷	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肝障害	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肝病変	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
急性肝炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
急性肝不全	- Any Grade -	0	1 (0.2%)
	4	0	1 (0.2%)
高ビリルビン血症	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
脂肪肝	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
食道静脈瘤	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
食道静脈瘤出血	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
薬物性肝障害	- Any Grade -	1 (0.2%)	0
	4	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-2 重篤な有害事象として報告された肝炎（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肝炎			
- Overall -	- Any Grade -	5 (0.8%)	2 (0.3%)
	2	0	1 (0.2%)
	3	2 (0.3%)	0
	4	3 (0.5%)	1 (0.2%)
肝炎	- Any Grade -	2 (0.3%)	0
	4	2 (0.3%)	0
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
急性肝炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
急性肝不全	- Any Grade -	0	1 (0.2%)
	4	0	1 (0.2%)
食道静脈瘤出血	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
薬物性肝障害	- Any Grade -	1 (0.2%)	0
	4	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(2) 肺臓炎

OAK 試験の安全性解析対象1187例の肺臓炎（事象群）の要約を表 2.7.4.2.1.5.1-3に，重篤な有害事象として報告された肺臓炎（事象群）の要約を表 2.7.4.2.1.5.1-4に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，肺臓炎（事象群）は本剤群の14例（2.3%），ドセタキセル群の4例（0.7%）に認められた。

Grade 5の肺臓炎（事象群）は両群で認められなかった。

重篤な有害事象として報告された肺臓炎（事象群）は本剤群の7例（1.1%）及びドセタキセル群の1例（0.2%）に認められた。

治験薬の投与中止に至った肺臓炎（事象群）は本剤群の3例（0.5%）及びドセタキセル群の1例（0.2%）に，治験薬の投与量変更に至った肺臓炎（事象群）は本剤群の5例（0.8%）及びドセタキセル群の1例（0.2%）に認められた。

表 2.7.4.2.1.5.1-3 肺臓炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肺臓炎			
- Overall -	- Any Grade -	14 (2.3%)	4 (0.7%)
	1	2 (0.3%)	1 (0.2%)
	2	7 (1.1%)	1 (0.2%)
	3	5 (0.8%)	2 (0.3%)
肺臓炎	- Any Grade -	6 (1.0%)	4 (0.7%)
	1	0	1 (0.2%)
	2	2 (0.3%)	1 (0.2%)
	3	4 (0.7%)	2 (0.3%)
間質性肺疾患	- Any Grade -	3 (0.5%)	0
	1	1 (0.2%)	0
	2	2 (0.3%)	0
肺浸潤	- Any Grade -	2 (0.3%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
放射線性肺臓炎	- Any Grade -	2 (0.3%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0
細気管支炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-4 重篤な有害事象として報告された肺臓炎（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肺臓炎			
- Overall -	- Any Grade -	7 (1.1%)	1 (0.2%)
	2	3 (0.5%)	0
	3	4 (0.7%)	1 (0.2%)
肺臓炎	- Any Grade -	6 (1.0%)	1 (0.2%)
	2	2 (0.3%)	0
	3	4 (0.7%)	1 (0.2%)
間質性肺疾患	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(3) 大腸炎

OAK 試験の安全性解析対象1187例の大腸炎（事象群）の要約を表 2.7.4.2.1.5.1-5に，重篤な有害事象として報告された大腸炎（事象群）の要約を表 2.7.4.2.1.5.1-6に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，大腸炎（事象群）は本剤群の2例（0.3%），ドセタキセル群の2例（0.3%）に認められた。

Grade 5の大腸炎（事象群）は両群で認められなかった。

重篤な有害事象として報告された大腸炎（事象群）は本剤群の1例（0.2%）及びドセタキセル群の2例（0.3%）に認められた。

治験薬の投与中止に至った大腸炎（事象群）は両群で認められなかった。治験薬の投与量変更に至った大腸炎（事象群）は本剤群の1例（0.2%）及びドセタキセル群の2例（0.3%）に認められた。

表 2.7.4.2.1.5.1-5 大腸炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
大腸炎			
- Overall -	- Any Grade -	2 (0.3%)	2 (0.3%)
	2	2 (0.3%)	0
	3	0	2 (0.3%)
大腸炎	- Any Grade -	2 (0.3%)	2 (0.3%)
	2	2 (0.3%)	0
	3	0	2 (0.3%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-6 重篤な有害事象として報告された大腸炎（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
大腸炎			
- Overall -	- Any Grade -	1 (0.2%)	2 (0.3%)
	2	1 (0.2%)	0
	3	0	2 (0.3%)
大腸炎	- Any Grade -	1 (0.2%)	2 (0.3%)
	2	1 (0.2%)	0
	3	0	2 (0.3%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(4) 膵炎

OAK 試験の安全性解析対象1187例の膵炎（事象群）の要約を表 2.7.4.2.1.5.1-7に，重篤な有害事象として報告された膵炎（事象群）の要約を表 2.7.4.2.1.5.1-8に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，膵炎（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

Grade 5の膵炎（事象群）は両群で認められなかった。

重篤な有害事象として報告された膵炎（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

治験薬の投与中止に至った膵炎（事象群）は両群で認められなかった。治験薬の投与量変更に至った膵炎（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

表 2.7.4.2.1.5.1-7 膵炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
膵炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
膵炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-8 重篤な有害事象として報告された膵炎（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
膵炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
膵炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(5) 内分泌系

1) 糖尿病

OAK 試験の安全性解析対象1187例の糖尿病（事象群）の要約を表 2.7.4.2.1.5.1-9に，重篤な有害事象として報告された糖尿病（事象群）の要約を表 2.7.4.2.1.5.1-10に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，糖尿病（事象群）は本剤群の20例（3.3%）及びドセタキセル群の32例（5.5%）に認められた。

Grade 5の糖尿病（事象群）は認められなかった。

重篤な有害事象として報告された糖尿病（事象群）は本剤群の3例（0.5%）に認められ，ドセタキセル群では認められなかった。

治験薬の投与中止に至った糖尿病（事象群）は両群で認められなかった。治験薬の投与量変更に至った糖尿病（事象群）は本剤群の2例（0.3%）及びドセタキセル群の1例（0.2%）に認められた。

表 2.7.4.2.1.5.1-9 糖尿病（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
糖尿病			
- Overall -	- Any Grade -	20 (3.3%)	32 (5.5%)
	1	9 (1.5%)	13 (2.2%)
	2	4 (0.7%)	12 (2.1%)
	3	4 (0.7%)	7 (1.2%)
	4	3 (0.5%)	0
高血糖	- Any Grade -	18 (3.0%)	26 (4.5%)
	1	7 (1.1%)	11 (1.9%)
	2	4 (0.7%)	10 (1.7%)
	3	4 (0.7%)	5 (0.9%)
	4	3 (0.5%)	0
２型糖尿病	- Any Grade -	1 (0.2%)	1 (0.2%)
	2	0	1 (0.2%)
	3	1 (0.2%)	0
血中ブドウ糖増加	- Any Grade -	0	2 (0.3%)
	2	0	1 (0.2%)
	3	0	1 (0.2%)
糖尿病	- Any Grade -	0	2 (0.3%)
	1	0	1 (0.2%)
	3	0	1 (0.2%)
１型糖尿病	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
耐糖能障害	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
尿中ブドウ糖陽性	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-10 重篤な有害事象として報告された糖尿病（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
糖尿病			
- Overall -	- Any Grade -	3 (0.5%)	0
	3	1 (0.2%)	0
	4	2 (0.3%)	0
高血糖	- Any Grade -	3 (0.5%)	0
	3	1 (0.2%)	0
	4	2 (0.3%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

2) 甲状腺機能低下症

OAK 試験の安全性解析対象1187例の甲状腺機能低下症（事象群）の要約を表 2.7.4.2.1.5.1-11 に示す。なお，評価上，一部の事象（血中甲状腺刺激ホルモン増加等）は，甲状腺機能低下症（事象群）と，後述の甲状腺機能亢進症（事象群）の両方に含めて集計した。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，甲状腺機能低下症（事象群）は本剤群の27例（4.4%）及びドセタキセル群の2例（0.3%）に認められた。

Grade 5の甲状腺機能低下症（事象群），重篤な有害事象として報告された甲状腺機能低下症（事象群），治験薬の投与中止に至った甲状腺機能低下症（事象群）は両群で認められなかった。治験薬の投与量変更に至った甲状腺機能低下症（事象群）は本剤群の4例（0.7%）に認められ，ドセタキセル群では認められなかった。

表 2.7.4.2.1.5.1-11 甲状腺機能低下症（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
甲状腺機能低下症			
- Overall -	- Any Grade -	27 (4.4%)	2 (0.3%)
	1	10 (1.6%)	1 (0.2%)
	2	17 (2.8%)	1 (0.2%)
甲状腺機能低下症	- Any Grade -	18 (3.0%)	1 (0.2%)
	1	4 (0.7%)	0
	2	14 (2.3%)	1 (0.2%)
血中甲状腺刺激ホルモン増加	- Any Grade -	6 (1.0%)	1 (0.2%)
	1	5 (0.8%)	1 (0.2%)
	2	1 (0.2%)	0
血中甲状腺刺激ホルモン減少	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
甲状腺炎	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
甲状腺機能検査異常	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

3) 甲状腺機能亢進症

OAK 試験の安全性解析対象1187例の甲状腺機能亢進症（事象群）の要約を表 2.7.4.2.1.5.1-12 に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，甲状腺機能亢進症（事象群）は本剤群の17例（2.8%）及びドセタキセル群の1例（0.2%）に認められた。

Grade 5の甲状腺機能亢進症（事象群），重篤な有害事象として報告された甲状腺機能亢進症（事象群）及び治験薬の投与中止に至った甲状腺機能亢進症（事象群）は両群で認められなかった。治験薬の投与量変更に至った甲状腺機能亢進症（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

表 2.7.4.2.1.5.1-12 甲状腺機能亢進症（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
甲状腺機能亢進症			
- Overall -	- Any Grade -	17 (2.8%)	1 (0.2%)
	1	9 (1.5%)	1 (0.2%)
	2	8 (1.3%)	0
血中甲状腺刺激ホルモン増加	- Any Grade -	6 (1.0%)	1 (0.2%)
	1	5 (0.8%)	1 (0.2%)
	2	1 (0.2%)	0
甲状腺機能亢進症	- Any Grade -	7 (1.1%)	0
	1	3 (0.5%)	0
	2	4 (0.7%)	0
眼球突出症	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
血中甲状腺刺激ホルモン減少	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
甲状腺炎	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
甲状腺機能検査異常	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
内分泌性眼症	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

4) 副腎機能不全

OAK 試験の安全性解析対象1187例の副腎機能不全（事象群）の要約を表 2.7.4.2.1.5.1-13に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，副腎機能不全（事象群）は本剤群の3例（0.5%）に認められ，ドセタキセル群では認められなかった。

Grade 5の副腎機能不全（事象群），重篤な有害事象として報告された副腎機能不全（事象群），治験薬の投与中止に至った副腎機能不全（事象群）及び治験薬の投与量変更に至った副腎機能不全（事象群）は両群で認められなかった。

表 2.7.4.2.1.5.1-13 副腎機能不全（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
副腎機能不全			
- Overall -	- Any Grade -	3 (0.5%)	0
	1	1 (0.2%)	0
	2	2 (0.3%)	0
副腎機能不全	- Any Grade -	2 (0.3%)	0
	2	2 (0.3%)	0
原発性副腎機能不全	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

(6) 神経障害

1) ギラン・バレー症候群

OAK 試験の安全性解析対象1187例のギラン・バレー症候群（事象群）の要約を表 2.7.4.2.1.5.1-14に，重篤な有害事象として報告されたギラン・バレー症候群（事象群）の要約を表 2.7.4.2.1.5.1-15に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，ギラン・バレー症候群（事象群）は本剤群の4例（0.7%）に認められ，ドセタキセル群では認められなかった。

Grade 5のギラン・バレー症候群（事象群）は両群で認められなかった。

重篤な有害事象として報告されたギラン・バレー症候群（事象群）は本剤群の2例（0.3%）に認められ，ドセタキセル群では認められなかった。

治験薬の投与中止に至ったギラン・バレー症候群（事象群）は両群で認められなかった。治験薬の投与量変更に至ったギラン・バレー症候群（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

表 2.7.4.2.1.5.1-14 ギラン・バレー症候群（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
ギラン・バレー症候群			
- Overall -	- Any Grade -	4 (0.7%)	0
	2	1 (0.2%)	0
	3	3 (0.5%)	0
ギラン・バレー症候群	- Any Grade -	3 (0.5%)	0
	3	3 (0.5%)	0
脱髄性多発ニューロパチー	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-15 重篤な有害事象として報告されたギラン・バレー症候群（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
ギラン・バレー症候群			
- Overall -	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
ギラン・バレー症候群	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

2) 重症筋無力症

OAK 試験の安全性解析対象1187例では，重症筋無力症（事象群）は両群で認められなかった。

(7) 髄膜脳炎

OAK 試験の安全性解析対象1187例の髄膜脳炎（事象群）の要約を表 2.7.4.2.1.5.1-16に，重篤な有害事象として報告された髄膜脳炎（事象群）の要約を表 2.7.4.2.1.5.1-17に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，髄膜脳炎（事象群）は本剤群の5例（0.8%）に認められ，ドセタキセル群では認められなかった。

Grade 5の髄膜脳炎（事象群）は両群で認められなかった。

重篤な有害事象として報告された髄膜脳炎（事象群）及び治験薬の投与中止に至った髄膜脳炎（事象群）は本剤群の4例（0.7%）に認められ，ドセタキセル群では認められなかった。

治験薬の投与量変更に至った髄膜脳炎（事象群）は両群で認められなかった。

表 2.7.4.2.1.5.1-16 髄膜脳炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
髄膜脳炎			
- Overall -	- Any Grade -	5 (0.8%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0
	3	2 (0.3%)	0
	4	1 (0.2%)	0
髄膜炎	- Any Grade -	3 (0.5%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
	4	1 (0.2%)	0
脳炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
羞明	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-17 重篤な有害事象として報告された髄膜脳炎（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
髄膜脳炎			
- Overall -	- Any Grade -	4 (0.7%)	0
	2	1 (0.2%)	0
	3	2 (0.3%)	0
	4	1 (0.2%)	0
髄膜炎	- Any Grade -	3 (0.5%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
	4	1 (0.2%)	0
脳炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(8) ぶどう膜炎

OAK 試験の安全性解析対象1187例の髄膜脳炎（事象群）の要約を表 2.7.4.2.1.5.1-18に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，ぶどう膜炎（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

Grade 5のぶどう膜炎（事象群），重篤な有害事象として報告されたぶどう膜炎（事象群），治験薬の投与中止に至ったぶどう膜炎（事象群）及び治験薬の投与量変更に至ったぶどう膜炎（事象群）は両群で認められなかった。

表 2.7.4.2.1.5.1-18 ぶどう膜炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
ぶどう膜炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
ぶどう膜炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

(9) 腎炎

OAK 試験の安全性解析対象1187例の腎炎（事象群）の要約を表 2.7.4.2.1.5.1-19に，重篤な有害事象として報告された腎炎（事象群）の要約を表 2.7.4.2.1.5.1-20に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，腎炎（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

Grade 5の腎炎（事象群）は，両群で認められなかった。

重篤な有害事象として報告された腎炎（事象群）及び治験薬の投与中止に至った腎炎（事象群）は本剤群の1例（0.2%）に認められ，ドセタキセル群では認められなかった。

治験薬の投与量変更に至った腎炎（事象群）は両群で認められなかった。

表 2.7.4.2.1.5.1-19 腎炎（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
腎炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
ヘノッホ・シェーンライン紫斑病性腎炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-20 重篤な有害事象として報告された腎炎（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
腎炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
ヘノッホ・シェーンライン紫斑病性腎炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(10) 発疹

OAK 試験の安全性解析対象1187例の発疹（事象群）の要約を表 2.7.4.2.1.5.1-21に，重篤な有害事象として報告された発疹（事象群）の要約を表 2.7.4.2.1.5.1-22に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，発疹（事象群）は本剤群の177例（29.1%），ドセタキセル群の274例（47.4%）に認められた。

Grade 5の発疹（事象群）は両群で認められなかった。

重篤な有害事象として報告された発疹（事象群）は本剤群の5例（0.8%）に認められ，ドセタキセル群では認められなかった。

治験薬の投与中止に至った発疹（事象群）は本剤群の4例（0.7%）及びドセタキセル群の1例（0.2%）に，治験薬の投与量変更に至った発疹（事象群）は本剤群の10例（1.6%）及びドセタキセル群の8例（1.4%）に認められた。

表 2.7.4.2.1.5.1-21 発疹（事象群）の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
発疹			
- Overall -	- Any Grade -	177 (29.1%)	274 (47.4%)
	1	126 (20.7%)	143 (24.7%)
	2	39 (6.4%)	127 (22.0%)
	3	12 (2.0%)	4 (0.7%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_GO28915_SE
［5.3.5.1-3 aet04_aesi_GO28915_SE を改変］

表 2.7.4.2.1.5.1-22 重篤な有害事象として報告された発疹（事象群）の要約（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
発疹			
- Overall -	- Any Grade -	5 (0.8%)	0
	3	5 (0.8%)	0
そう痒症	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
水疱性皮膚炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
全身性そう痒症	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
発疹	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
類天疱瘡	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aet04_aesi_ser_GO28915_SE
［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を改変］

(11) 筋炎

OAK 試験の安全性解析対象1187例では，筋炎（事象群）は認められなかった。

(12) 本剤の注目すべき有害事象の初回発現時期

OAK 試験の安全性解析対象1187例に認められた本剤の注目すべき有害事象の初回発現までの期間の要約を表 2.7.4.2.1.5.1-23に示す。なお，各事象の値を含む初回発現までの期間の要約を表 2.7.4.7.7-1に，初回発現の時期ごとの要約を表 2.7.4.7.7-3に，本剤の注目すべき有害事象の発現から回復までの期間の要約を表 2.7.4.7.7-2に示した。

表 2.7.4.2.1.5.1-23 本剤の注目すべき有害事象の初回発現までの期間の要約（OAK 試験）

Time to First Onset of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
Infusion reaction	1	22.0	683	1	23.0	316
ぶどう膜炎	346	346.0	346	-	-	-
ギラン・バレー症候群	17	116.0	239	-	-	-
肝炎	1	22.0	638	6	21.5	188
甲状腺機能低下症	21	120.0	462	5	49.5	94
甲状腺機能亢進症	21	85.0	462	94	94.0	94
腎炎	400	400.0	400	-	-	-
髄膜脳炎	14	15.0	20	-	-	-
大腸炎	79	100.0	121	4	18.5	33
糖尿病	13	42.0	297	1	37.0	135
肺臓炎	6	96.0	526	5	20.0	43
発疹	1	44.0	517	1	19.0	297
副腎機能不全	96	174.0	407	-	-	-
胚・胎児毒性	10	26.5	43	7	34.0	57
膵炎	353	353.0	353	-	-	-

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output aefstsum_aesi_GO28915_SE
[5.3.5.1-3 aefstsum_aesi_GO28915_SE を改変]

2.7.4.2.1.5.2 imAE

本剤の作用機序から，imAE に注目し，解析を行った。imAE は他の明確な要因がなく全身性のステロイド投与を要した有害事象と定義し，症例報告書の併用療法及び有害事象ページから集計した。なお，全身性のステロイド投与を行った有害事象として集計された事象（Systemic Corticosteroid Dataset）の内，adverse events of special interest に該当する事象は，他の要因の有無に関わらず自動的に imAE の集計に含めた。

OAK 試験での imAE の発現状況の要約を5.3.5.1-1 Table 89に示す。

安全性解析対象1187例（本剤群609例，ドセタキセル群578例）中，imAE は本剤群の77例（12.6%），ドセタキセル群の55例（9.5%）に認められた。Grade 3の imAE は本剤群の31例（5.1%），ドセタキセル群の5例（0.9%）に，Grade 4の imAE は本剤群の7例（1.1%），ドセタキセル群の1例（0.2%）に認められた。Grade 5の imAE は両群で認められなかった。

imAE として集計された事象の内，本剤群の1%以上に認められた事象は，発疹［本剤群8例（1.3%），ドセタキセル群21例（3.6%）］，呼吸困難［本剤群7例（1.1%），ドセタキセル群1例（0.2%）］，肺臓炎［本剤群6例（1.0%），ドセタキセル群4例（0.7%）］及びアラニンアミノトランスフェラーゼ増加［本剤群6例（1.0%），ドセタキセル群5例（0.9%）］であった。ドセタキセル群の1%以上に認められた事象は，発疹（上記参照）及び末梢性ニューロパチー［本剤群0例，ドセタキセル群25例（4.3%）］であった。

2.7.4.2.1.6 PD-L1発現状況別の安全性の成績

腫瘍細胞の PD-L1発現状況（又はその評価結果）を TC スコア，腫瘍浸潤免疫細胞の PD-L1発現状況（又はその評価結果）を IC スコアと表記する。TC スコア及び IC スコアの内訳は表2.7.3.1.1-1に詳述した。

PD-L1の発現状況が安全性プロファイルに及ぼす影響の有無を考察するため，OAK 試験の本剤群の PD-L1発現状況別の安全性の成績を比較した（表 2.7.4.2.1.6-1）。

TC1/2/3又は IC1/2/3被験者集団と TC0及び IC0被験者集団の安全性成績は概ね同様であり，

OAK 試験の安全性解析対象集団の成績とも大きく異なるものではなかった。

表 2.7.4.2.1.6-1 PD-L1発現状況別の安全性成績（OAK 試験，本剤群）

項目	安全性解析対象集団	TC1/2/3又は IC1/2/3被験者集団	TC0及び IC0被験者集団
N	609	345	258
有害事象	573 (94.1%)	325 (94.2%)	242 (93.8%)
本剤との因果関係が否定できない有害事象	390 (64.0%)	226 (65.5%)	162 (62.8%)
Grade 5の有害事象	10 (1.6%)	3 (0.9%)	6 (2.3%)
Grade 3又は4の有害事象	227 (37.3%)	131 (38.0%)	94 (36.4%)
重篤な有害事象	194 (31.9%)	120 (34.8%)	71 (27.5%)
治験薬の中止に至った有害事象	46 (7.6%)	27 (7.8%)	18 (7.0%)
治験薬の投与量変更に至った有害事象	152 (25.0%)	103 (29.9%)	48 (18.6%)

［5.3.5.1-1 Table 54 (a)，t_aet01_SE_TC123IC123及び t_aet01_SE_TC0IC0を改変］

2.7.4.2.1.7 日本人の安全性成績（OAK 試験及び BIRCH 試験）

2.7.4.2.1.7.1 日本人の部分集団の成績

(1) OAK 試験

OAK 試験の日本人集団の10%以上に認められた有害事象の要約を表 2.7.4.2.1.7.1-1に，10%以上に認められた有害事象の重症度別の要約を表 2.7.4.2.1.7.1-2に，重篤な有害事象の要約を表 2.7.4.2.1.7.1-3に，治験薬の中止に至った有害事象の要約を表 2.7.4.2.1.7.1-4に，本剤の注目すべき有害事象の要約を表 2.7.4.7.6-6に示す。

なお，死亡に至った有害事象は認められなかった（5.3.5.1-3 ae_rae_dd_GO28915_SE_JAPAN 参照）。

表 2.7.4.2.1.7.1-1 発現率10%以上の有害事象（OAK 試験，日本人集団）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=56) AE No. (%)	Atezolizumab (Actual) (N=56) Related AE No. (%)	Docetaxel (Actual) (N=45) AE No. (%)	Docetaxel (Actual) (N=45) Related AE No. (%)
Total number of patients with at least one adverse event	52 (92.9%)	49 (87.5%)	45 (100.0%)	44 (97.8%)
発熱	20 (35.7%)	16 (28.6%)	11 (24.4%)	10 (22.2%)
鼻咽頭炎	11 (19.6%)	4 (7.1%)	6 (13.3%)	3 (6.7%)
発疹	9 (16.1%)	9 (16.1%)	13 (28.9%)	13 (28.9%)
食欲減退	8 (14.3%)	6 (10.7%)	26 (57.8%)	25 (55.6%)
便秘	8 (14.3%)	5 (8.9%)	15 (33.3%)	14 (31.1%)
下痢	8 (14.3%)	8 (14.3%)	11 (24.4%)	7 (15.6%)
頭痛	8 (14.3%)	7 (12.5%)	5 (11.1%)	4 (8.9%)
口内炎	7 (12.5%)	6 (10.7%)	20 (44.4%)	20 (44.4%)
疲労	7 (12.5%)	7 (12.5%)	9 (20.0%)	9 (20.0%)
不眠症	7 (12.5%)	1 (1.8%)	6 (13.3%)	2 (4.4%)
倦怠感	6 (10.7%)	6 (10.7%)	24 (53.3%)	24 (53.3%)
関節痛	6 (10.7%)	6 (10.7%)	14 (31.1%)	14 (31.1%)
悪心	5 (8.9%)	3 (5.4%)	19 (42.2%)	18 (40.0%)
そう痒症	5 (8.9%)	5 (8.9%)	5 (11.1%)	4 (8.9%)
白血球数減少	4 (7.1%)	4 (7.1%)	13 (28.9%)	13 (28.9%)
貧血	4 (7.1%)	4 (7.1%)	8 (17.8%)	8 (17.8%)
好中球減少症	3 (5.4%)	3 (5.4%)	16 (35.6%)	16 (35.6%)
白血球減少症	3 (5.4%)	3 (5.4%)	13 (28.9%)	13 (28.9%)
背部痛	3 (5.4%)	3 (5.4%)	6 (13.3%)	4 (8.9%)
好中球数減少	2 (3.6%)	1 (1.8%)	22 (48.9%)	22 (48.9%)
味覚異常	2 (3.6%)	1 (1.8%)	13 (28.9%)	13 (28.9%)
筋肉痛	2 (3.6%)	2 (3.6%)	9 (20.0%)	9 (20.0%)
末梢性浮腫	1 (1.8%)	1 (1.8%)	16 (35.6%)	16 (35.6%)
皮膚乾燥	1 (1.8%)	0	7 (15.6%)	4 (8.9%)
浮腫	1 (1.8%)	1 (1.8%)	5 (11.1%)	5 (11.1%)
脱毛症	0	0	28 (62.2%)	28 (62.2%)
発熱性好中球減少症	0	0	16 (35.6%)	16 (35.6%)
末梢性感覚ニューロパチー	0	0	14 (31.1%)	14 (31.1%)
爪変色	0	0	8 (17.8%)	8 (17.8%)
顔面浮腫	0	0	5 (11.1%)	5 (11.1%)
爪の障害	0	0	5 (11.1%)	5 (11.1%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_p10_GO28915_SE_JAPAN.out
07DEC2016 17:02 Page 1 of 1

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。

［5.3.5.1-3 ae_rae_p10_GO28915_SE_JAPAN を再掲］

表 2.7.4.2.1.7.1-2 重症度別の有害事象（発現率10%以上）（OAK 試験，日本人集団）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=56) Any Grade No. (%)	Atezolizumab (Actual) (N=56) >= Grade3 No. (%)	Docetaxel (Actual) (N=45) Any Grade No. (%)	Docetaxel (Actual) (N=45) >= Grade3 No. (%)
Total number of patients with at least one adverse event	52 (92.9%)	15 (26.8%)	45 (100.0%)	41 (91.1%)
発熱	20 (35.7%)	0	11 (24.4%)	0
鼻咽頭炎	11 (19.6%)	0	6 (13.3%)	0
発疹	9 (16.1%)	0	13 (28.9%)	0
食欲減退	8 (14.3%)	0	26 (57.8%)	3 (6.7%)
便秘	8 (14.3%)	0	15 (33.3%)	0
下痢	8 (14.3%)	0	11 (24.4%)	1 (2.2%)
頭痛	8 (14.3%)	0	5 (11.1%)	0
口内炎	7 (12.5%)	0	20 (44.4%)	2 (4.4%)
疲労	7 (12.5%)	2 (3.6%)	9 (20.0%)	0
不眠症	7 (12.5%)	0	6 (13.3%)	0
倦怠感	6 (10.7%)	0	24 (53.3%)	0
関節痛	6 (10.7%)	0	14 (31.1%)	0
悪心	5 (8.9%)	0	19 (42.2%)	0
そう痒症	5 (8.9%)	0	5 (11.1%)	0
白血球数減少	4 (7.1%)	0	13 (28.9%)	12 (26.7%)
貧血	4 (7.1%)	0	8 (17.8%)	1 (2.2%)
好中球減少症	3 (5.4%)	1 (1.8%)	16 (35.6%)	16 (35.6%)
白血球減少症	3 (5.4%)	0	13 (28.9%)	12 (26.7%)
背部痛	3 (5.4%)	0	6 (13.3%)	0
好中球数減少	2 (3.6%)	1 (1.8%)	22 (48.9%)	22 (48.9%)
味覚異常	2 (3.6%)	0	13 (28.9%)	0
筋肉痛	2 (3.6%)	0	9 (20.0%)	0
末梢性浮腫	1 (1.8%)	0	16 (35.6%)	0
皮膚乾燥	1 (1.8%)	0	7 (15.6%)	0
浮腫	1 (1.8%)	0	5 (11.1%)	0
脱毛症	0	0	28 (62.2%)	0
発熱性好中球減少症	0	0	16 (35.6%)	16 (35.6%)
末梢性感覚ニューロパチー	0	0	14 (31.1%)	0
爪変色	0	0	8 (17.8%)	0
顔面浮腫	0	0	5 (11.1%)	0
爪の障害	0	0	5 (11.1%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_g3_p10_GO28915_SE_JAPAN.out
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［5.3.5.1-3 ae_g3_p10_GO28915_SE_JAPAN を再掲］

表 2.7.4.2.1.7.1-3 重篤な有害事象（OAK 試験，日本人集団）

Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=56) AE No. (%)	Atezolizumab (Actual) (N=56) Related AE No. (%)	Docetaxel (Actual) (N=45) AE No. (%)	Docetaxel (Actual) (N=45) Related AE No. (%)
Total number of patients with at least one adverse event	11 (19.6%)	11 (19.6%)	9 (20.0%)	8 (17.8%)
髄膜炎	3 (5.4%)	3 (5.4%)	0	0
肺臓炎	2 (3.6%)	2 (3.6%)	1 (2.2%)	1 (2.2%)
肺炎	1 (1.8%)	0	2 (4.4%)	2 (4.4%)
発熱	1 (1.8%)	1 (1.8%)	1 (2.2%)	1 (2.2%)
ギラン・バレー症候群	1 (1.8%)	1 (1.8%)	0	0
ヘノッホ・シェーンライン紫斑病性腎炎	1 (1.8%)	1 (1.8%)	0	0
過敏症	1 (1.8%)	1 (1.8%)	0	0
間質性肺疾患	1 (1.8%)	1 (1.8%)	0	0
脳炎	1 (1.8%)	1 (1.8%)	0	0
細菌性肺炎	1 (1.8%)	0	0	0
発熱性好中球減少症	0	0	3 (6.7%)	3 (6.7%)
好中球数減少	0	0	1 (2.2%)	1 (2.2%)
気胸	0	0	1 (2.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE_JAPAN.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.1-3 ae_rae_ser_GO28915_SE_JAPAN を再掲］

表 2.7.4.2.1.7.1-4 治験薬の中止に至った有害事象（OAK 試験，日本人集団）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=56) AE No. (%)	Atezolizumab (Actual) (N=56) Related AE No. (%)	Docetaxel (Actual) (N=45) AE No. (%)	Docetaxel (Actual) (N=45) Related AE No. (%)
Total number of patients with at least one adverse event	10 (17.9%)	10 (17.9%)	3 (6.7%)	3 (6.7%)
髄膜炎	3 (5.4%)	3 (5.4%)	0	0
肺炎	1 (1.8%)	1 (1.8%)	1 (2.2%)	1 (2.2%)
ヘノッホ・シェーンライン紫斑病性腎炎	1 (1.8%)	1 (1.8%)	0	0
下垂体炎	1 (1.8%)	1 (1.8%)	0	0
過敏症	1 (1.8%)	1 (1.8%)	0	0
間質性肺疾患	1 (1.8%)	1 (1.8%)	0	0
脳炎	1 (1.8%)	1 (1.8%)	0	0
肺臓炎	1 (1.8%)	1 (1.8%)	0	0
好中球減少症	0	0	1 (2.2%)	1 (2.2%)
白血球減少症	0	0	1 (2.2%)	1 (2.2%)
末梢性感覚ニューロパチー	0	0	1 (2.2%)	1 (2.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_dis_GO28915_SE_JAPAN.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.1-3 ae_rae_dis_GO28915_SE_JAPAN を再掲］

(2) BIRCH 試験

BIRCH 試験の日本人集団の10%以上に認められた有害事象の要約を表 2.7.4.2.1.7.1-5に，10%以上に認められた有害事象の重症度別の要約を表 2.7.4.2.1.7.1-6に，重篤な有害事象の要約を表 2.7.4.2.1.7.1-7に示す。なお，死亡に至った有害事象は認められなかった（5.3.5.3-1 ae_rae_dd_GO28754_SE_JAPAN 参照）。

表 2.7.4.2.1.7.1-5　発現率10%以上の有害事象（BIRCH 試験，日本人集団）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Japanese Patients, Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=27) AE No. (%)	atezolizumab Total (N=27) Related AE No. (%)	atezolizumab Cohort 1 (N=3) AE No. (%)	atezolizumab Cohort 1 (N=3) Related AE No. (%)	atezolizumab Cohort 2 (N=12) AE No. (%)	atezolizumab Cohort 2 (N=12) Related AE No. (%)	atezolizumab Cohort 3 (N=12) AE No. (%)	atezolizumab Cohort 3 (N=12) Related AE No. (%)
Total number of patients with at least one adverse event	27 (100.0%)	23 (85.2%)	3 (100.0%)	3 (100.0%)	12 (100.0%)	10 (83.3%)	12 (100.0%)	10 (83.3%)
上気道感染	6 (22.2%)	1 (3.7%)	0	0	2 (16.7%)	0	4 (33.3%)	1 (8.3%)
そう痒症	5 (18.5%)	4 (14.8%)	0	0	2 (16.7%)	1 (8.3%)	3 (25.0%)	3 (25.0%)
食欲減退	5 (18.5%)	4 (14.8%)	0	0	1 (8.3%)	1 (8.3%)	4 (33.3%)	3 (25.0%)
発熱	5 (18.5%)	4 (14.8%)	0	0	1 (8.3%)	1 (8.3%)	4 (33.3%)	3 (25.0%)
倦怠感	4 (14.8%)	3 (11.1%)	2 (66.7%)	2 (66.7%)	1 (8.3%)	0	1 (8.3%)	1 (8.3%)
皮膚乾燥	4 (14.8%)	4 (14.8%)	0	0	3 (25.0%)	3 (25.0%)	1 (8.3%)	1 (8.3%)
下痢	3 (11.1%)	2 (7.4%)	1 (33.3%)	0	1 (8.3%)	1 (8.3%)	1 (8.3%)	1 (8.3%)
悪心	3 (11.1%)	0	0	0	2 (16.7%)	0	1 (8.3%)	0
斑状丘疹状皮疹	3 (11.1%)	3 (11.1%)	0	0	1 (8.3%)	1 (8.3%)	2 (16.7%)	2 (16.7%)
疲労	3 (11.1%)	3 (11.1%)	0	0	1 (8.3%)	1 (8.3%)	2 (16.7%)	2 (16.7%)
口内炎	2 (7.4%)	2 (7.4%)	1 (33.3%)	1 (33.3%)	1 (8.3%)	1 (8.3%)	0	0
甲状腺機能低下症	2 (7.4%)	2 (7.4%)	1 (33.3%)	1 (33.3%)	1 (8.3%)	1 (8.3%)	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_p10_GO28754_SE_JAPAN.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Japanese Patients, Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=27) AE No. (%)	atezolizumab Total (N=27) Related AE No. (%)	atezolizumab Cohort 1 (N=3) AE No. (%)	atezolizumab Cohort 1 (N=3) Related AE No. (%)	atezolizumab Cohort 2 (N=12) AE No. (%)	atezolizumab Cohort 2 (N=12) Related AE No. (%)	atezolizumab Cohort 3 (N=12) AE No. (%)	atezolizumab Cohort 3 (N=12) Related AE No. (%)
頭痛	2 (7.4%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	1 (8.3%)	0
嘔吐	2 (7.4%)	1 (3.7%)	1 (33.3%)	0	0	0	1 (8.3%)	1 (8.3%)
上腹部痛	2 (7.4%)	0	0	0	2 (16.7%)	0	0	0
便秘	2 (7.4%)	0	0	0	0	0	2 (16.7%)	0
インフルエンザ様疾患	1 (3.7%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	0	0
関節炎	1 (3.7%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	0	0
肺塞栓症	1 (3.7%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	0	0
リンパ節症	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
外耳炎	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
気管支肺炎	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
靱帯捻挫	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_p10_GO28754_SE_JAPAN.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_p10_GO28754_SE_JAPAN を再掲］

表 2.7.4.2.1.7.1-6　重症度別の有害事象（発現率10%以上）（BIRCH 試験，日本人集団）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28754:BIRCH)
Protocol: GO28754
Population: Japanese Patients, Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=27)		atezolizumab Cohort 1 (N=3)		atezolizumab Cohort 2 (N=12)		atezolizumab Cohort 3 (N=12)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	27 (100.0%)	8 (29.6%)	3 (100.0%)	2 (66.7%)	12 (100.0%)	2 (16.7%)	12 (100.0%)	4 (33.3%)
上気道感染	6 (22.2%)	0	0	0	2 (16.7%)	0	4 (33.3%)	0
そう痒症	5 (18.5%)	0	0	0	2 (16.7%)	0	3 (25.0%)	0
食欲減退	5 (18.5%)	0	0	0	1 (8.3%)	0	4 (33.3%)	0
発熱	5 (18.5%)	0	0	0	1 (8.3%)	0	4 (33.3%)	0
倦怠感	4 (14.8%)	0	2 (66.7%)	0	1 (8.3%)	0	1 (8.3%)	0
皮膚乾燥	4 (14.8%)	0	0	0	3 (25.0%)	0	1 (8.3%)	0
下痢	3 (11.1%)	0	1 (33.3%)	0	1 (8.3%)	0	1 (8.3%)	0
悪心	3 (11.1%)	0	0	0	2 (16.7%)	0	1 (8.3%)	0
疲労	3 (11.1%)	1 (3.7%)	0	0	1 (8.3%)	1 (8.3%)	2 (16.7%)	0
斑状丘疹状皮疹	3 (11.1%)	0	0	0	1 (8.3%)	0	2 (16.7%)	0
口内炎	2 (7.4%)	0	1 (33.3%)	0	1 (8.3%)	0	0	0
甲状腺機能低下症	2 (7.4%)	0	1 (33.3%)	0	1 (8.3%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_g3_p10_GO28754_SE_JAPAN.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28754:BIRCH)
Protocol: GO28754
Population: Japanese Patients, Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=27) Any Grade No. (%)	atezolizumab Total (N=27) >= Grade3 No. (%)	atezolizumab Cohort 1 (N=3) Any Grade No. (%)	atezolizumab Cohort 1 (N=3) >= Grade3 No. (%)	atezolizumab Cohort 2 (N=12) Any Grade No. (%)	atezolizumab Cohort 2 (N=12) >= Grade3 No. (%)	atezolizumab Cohort 3 (N=12) Any Grade No. (%)	atezolizumab Cohort 3 (N=12) >= Grade3 No. (%)
嘔吐	2 (7.4%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	1 (8.3%)	0
頭痛	2 (7.4%)	0	1 (33.3%)	0	0	0	1 (8.3%)	0
上腹部痛	2 (7.4%)	0	0	0	2 (16.7%)	0	0	0
便秘	2 (7.4%)	0	0	0	0	0	2 (16.7%)	0
気管支肺炎	1 (3.7%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	0	0
肺塞栓症	1 (3.7%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	0	0
インフルエンザ様疾患	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
リンパ節症	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
外耳炎	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
関節炎	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
靱帯捻挫	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_g3_p10_GO28754_SE_JAPAN.out
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［5.3.5.3-1 ae_g3_p10_GO28754_SE_JAPAN を再掲］

表 2.7.4.2.1.7.1-7　重篤な有害事象（BIRCH 試験，日本人集団）

Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Japanese Patients, Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=27)		atezolizumab Cohort 1 (N=3)		atezolizumab Cohort 2 (N=12)		atezolizumab Cohort 3 (N=12)	
	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)
Total number of patients with at least one adverse event	8 (29.6%)	6 (22.2%)	1 (33.3%)	1 (33.3%)	2 (16.7%)	1 (8.3%)	5 (41.7%)	4 (33.3%)
肺塞栓症	1 (3.7%)	1 (3.7%)	1 (33.3%)	1 (33.3%)	0	0	0	0
気管支肺炎	1 (3.7%)	0	1 (33.3%)	0	0	0	0	0
発熱	1 (3.7%)	1 (3.7%)	0	0	1 (8.3%)	1 (8.3%)	0	0
菌血症	1 (3.7%)	0	0	0	1 (8.3%)	0	0	0
下痢	1 (3.7%)	1 (3.7%)	0	0	0	0	1 (8.3%)	1 (8.3%)
大腸炎	1 (3.7%)	1 (3.7%)	0	0	0	0	1 (8.3%)	1 (8.3%)
尿路感染	1 (3.7%)	1 (3.7%)	0	0	0	0	1 (8.3%)	1 (8.3%)
肺臓炎	1 (3.7%)	1 (3.7%)	0	0	0	0	1 (8.3%)	1 (8.3%)
細菌性肺炎	1 (3.7%)	0	0	0	0	0	1 (8.3%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE_JAPAN.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_ser_GO28754_SE_JAPAN を再掲］

2.7.4.2.1.7.2 日本人集団と日本人以外の集団との比較

(1) OAK 試験

OAK 試験で日本人と外国人（日本人を除く全被験者）のいずれかの集団で全 Grade の発現率が10%以上であった有害事象を表 2.7.4.2.1.7.2-1に示す。

発現率10%以上の有害事象の重症度は，日本人及び外国人ともに大部分が Grade 1又は2の事象であった。

本剤群で外国人と比較して日本人で発現率が10%以上高かった有害事象は，発熱（日本人35.7%，外国人15.9%），鼻咽頭炎（日本人19.6%，外国人3.6%）及び口内炎（日本人12.5%，外国人2.2%）であった。Grade 3以上の事象の発現率は，日本人と外国人で差は認められなかった。

本剤群で認められた有害事象の種類，頻度及び重症度は日本人と外国人で大きく異なるものではなく，日本人患者に特有な安全性の懸念は確認されなかった。

ドセタキセル群で外国人と比較して日本人で発現率が10%以上高かった有害事象は，発熱，鼻咽頭炎，発疹，食欲減退，便秘，口内炎，関節痛，倦怠感，悪心，白血球数減少，好中球減少症，白血球減少症，味覚異常，好中球数減少，末梢性浮腫，皮膚乾燥，末梢性感覚ニューロパチー，脱毛症，顔面浮腫，発熱性好中球減少症及び爪変色であった。これらの事象の内，Grade 3以上の事象でも外国人と比較して日本人で発現率が10%以上高かったものは，白血球数減少（日本人26.7%，外国人1.7%），好中球数減少症（日本人35.6%，外国人11.1%），白血球減少症（日本人26.7%，外国人1.9%），好中球数減少（日本人48.9%，外国人5.6%）及び発熱性好中球減少症（日本人35.6%，外国人8.6%）であった。

表 2.7.4.2.1.7.2-1 発現率10%以上の有害事象の日本人と外国人の比較（OAK 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28915:OAK) (Japanese vs. non-Japanese)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab Japanese (N=56) Any Grade No. (%)	Atezolizumab Japanese (N=56) >= Grade3 No. (%)	Atezolizumab Non-Japanese (N=553) Any Grade No. (%)	Atezolizumab Non-Japanese (N=553) >= Grade3 No. (%)
Total number of patients with at least one adverse event	52 (92.9%)	15 (26.8%)	521 (94.2%)	222 (40.1%)
発熱	20 (35.7%)	0	88 (15.9%)	1 (0.2%)
鼻咽頭炎	11 (19.6%)	0	20 (3.6%)	0
発疹	9 (16.1%)	0	49 (8.9%)	2 (0.4%)
食欲減退	8 (14.3%)	0	135 (24.4%)	2 (0.4%)
便秘	8 (14.3%)	0	99 (17.9%)	2 (0.4%)
下痢	8 (14.3%)	0	86 (15.6%)	4 (0.7%)
頭痛	8 (14.3%)	0	49 (8.9%)	2 (0.4%)
疲労	7 (12.5%)	2 (3.6%)	156 (28.2%)	15 (2.7%)
不眠症	7 (12.5%)	0	42 (7.6%)	1 (0.2%)
口内炎	7 (12.5%)	0	12 (2.2%)	1 (0.2%)
関節痛	6 (10.7%)	0	67 (12.1%)	3 (0.5%)
倦怠感	6 (10.7%)	0	6 (1.1%)	0
悪心	5 (8.9%)	0	103 (18.6%)	4 (0.7%)
嘔吐	5 (8.9%)	0	69 (12.5%)	2 (0.4%)
そう痒症	5 (8.9%)	0	45 (8.1%)	3 (0.5%)
貧血	4 (7.1%)	0	66 (11.9%)	14 (2.5%)
白血球数減少	4 (7.1%)	0	1 (0.2%)	0
背部痛	3 (5.4%)	0	64 (11.6%)	7 (1.3%)
好中球減少症	3 (5.4%)	1 (1.8%)	7 (1.3%)	2 (0.4%)
白血球減少症	3 (5.4%)	0	1 (0.2%)	0
筋肉痛	2 (3.6%)	0	37 (6.7%)	1 (0.2%)
味覚異常	2 (3.6%)	0	16 (2.9%)	0
好中球数減少	2 (3.6%)	1 (1.8%)	0	0
咳嗽	1 (1.8%)	0	140 (25.3%)	2 (0.4%)
呼吸困難	1 (1.8%)	0	117 (21.2%)	16 (2.9%)
筋骨格痛	1 (1.8%)	0	63 (11.4%)	4 (0.7%)
末梢性浮腫	1 (1.8%)	0	53 (9.6%)	1 (0.2%)
皮膚乾燥	1 (1.8%)	0	26 (4.7%)	0
浮腫	1 (1.8%)	0	5 (0.9%)	0
無力症	0	0	116 (21.0%)	8 (1.4%)
末梢性ニューロパチー	0	0	24 (4.3%)	0
末梢性感覚ニューロパチー	0	0	6 (1.1%)	0
脱毛症	0	0	3 (0.5%)	0
顔面浮腫	0	0	3 (0.5%)	0
発熱性好中球減少症	0	0	1 (0.2%)	1 (0.2%)
爪変色	0	0	1 (0.2%)	0
爪の障害	0	0	0	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28915:OAK) (Japanese vs. non-Japanese)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Docetaxel Japanese (N=45) Any Grade No. (%)	Docetaxel Japanese (N=45) >= Grade3 No. (%)	Docetaxel Non-Japanese (N=533) Any Grade No. (%)	Docetaxel Non-Japanese (N=533) >= Grade3 No. (%)
Total number of patients with at least one adverse event	45 (100.0%)	41 (91.1%)	510 (95.7%)	283 (53.1%)
発熱	11 (24.4%)	0	65 (12.2%)	1 (0.2%)
鼻咽頭炎	6 (13.3%)	0	14 (2.6%)	0
発疹	13 (28.9%)	0	36 (6.8%)	0
食欲減退	26 (57.8%)	3 (6.7%)	110 (20.6%)	6 (1.1%)
便秘	15 (33.3%)	0	67 (12.6%)	1 (0.2%)
下痢	11 (24.4%)	1 (2.2%)	130 (24.4%)	10 (1.9%)
頭痛	5 (11.1%)	0	41 (7.7%)	1 (0.2%)
疲労	9 (20.0%)	0	196 (36.8%)	23 (4.3%)
不眠症	6 (13.3%)	0	36 (6.8%)	3 (0.6%)
口内炎	20 (44.4%)	2 (4.4%)	43 (8.1%)	9 (1.7%)
関節痛	14 (31.1%)	0	44 (8.3%)	1 (0.2%)
倦怠感	24 (53.3%)	0	5 (0.9%)	0
悪心	19 (42.2%)	0	112 (21.0%)	2 (0.4%)
嘔吐	4 (8.9%)	0	58 (10.9%)	4 (0.8%)
そう痒症	5 (11.1%)	0	13 (2.4%)	0
貧血	8 (17.8%)	1 (2.2%)	128 (24.0%)	32 (6.0%)
白血球数減少	13 (28.9%)	12 (26.7%)	16 (3.0%)	9 (1.7%)
背部痛	6 (13.3%)	0	36 (6.8%)	4 (0.8%)
好中球減少症	16 (35.6%)	16 (35.6%)	74 (13.9%)	59 (11.1%)
白血球減少症	13 (28.9%)	12 (26.7%)	12 (2.3%)	10 (1.9%)
筋肉痛	9 (20.0%)	0	82 (15.4%)	4 (0.8%)
味覚異常	13 (28.9%)	0	45 (8.4%)	0
好中球数減少	22 (48.9%)	22 (48.9%)	33 (6.2%)	30 (5.6%)
咳嗽	1 (2.2%)	0	104 (19.5%)	1 (0.2%)
呼吸困難	1 (2.2%)	0	111 (20.8%)	15 (2.8%)
筋骨格痛	0	0	25 (4.7%)	1 (0.2%)
末梢性浮腫	16 (35.6%)	0	66 (12.4%)	3 (0.6%)
皮膚乾燥	7 (15.6%)	0	27 (5.1%)	1 (0.2%)
浮腫	5 (11.1%)	0	9 (1.7%)	0
無力症	0	0	114 (21.4%)	13 (2.4%)
末梢性ニューロパチー	1 (2.2%)	0	64 (12.0%)	7 (1.3%)
末梢性感覚ニューロパチー	14 (31.1%)	0	29 (5.4%)	5 (0.9%)
脱毛症	28 (62.2%)	0	174 (32.6%)	1 (0.2%)
顔面浮腫	5 (11.1%)	0	6 (1.1%)	0
発熱性好中球減少症	16 (35.6%)	16 (35.6%)	46 (8.6%)	46 (8.6%)
爪変色	8 (17.8%)	0	18 (3.4%)	0
爪の障害	5 (11.1%)	0	25 (4.7%)	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.
Adaptation from output ae_g3_p10_jnj_GO28915_SE
［5.3.5.1-3 ae_g3_p10_jnj_GO28915_SE を改変］

(2) BIRCH 試験

BIRCH 試験で日本人と外国人（日本人を除く全被験者）のいずれかの集団で全 Grade の発現率が10%以上であった有害事象を表 2.7.4.2.1.7.2-2に示す。

発現率10%以上の有害事象の重症度は，日本人及び外国人ともに大部分が Grade 1又は2の事象であった。外国人と比較して日本人で発現率が10%以上高かった有害事象は，上気道感染（日本人22.2%，外国人5.1%），倦怠感（日本人14.8%，外国人3.3%），斑状丘疹状皮疹（日本人11.1%，外国人0.9%）であったが，Grade 3以上では差はみられなかった。なお，外国人と比較して日本人で発現率が20%以上高い事象は認められなかった。

日本人の検討例数が少ないため有害事象の発現率を直接比較することはできないが，認められた有害事象の種類，頻度及び重症度は日本人と外国人で大きく異なるものではなく，日本人

患者に特有な安全性の懸念は確認されなかった。

表 2.7.4.2.1.7.2-2 発現率10%以上の有害事象の日本人と外国人の比較（BIRCH 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO28754:BIRCH) (Japanese vs. non-Japanese)
Protocol: GO28754
Population: Treated Patients

	atezolizumab Total Japanese (N=27)		atezolizumab Total Non-Japanese (N=632)	
MedDRA Preferred Term	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	27 (100.0%)	8 (29.6%)	590 (93.4%)	263 (41.6%)
上気道感染	6 (22.2%)	0	32 (5.1%)	1 (0.2%)
食欲減退	5 (18.5%)	0	143 (22.6%)	6 (0.9%)
発熱	5 (18.5%)	0	102 (16.1%)	5 (0.8%)
そう痒症	5 (18.5%)	0	71 (11.2%)	0
皮膚乾燥	4 (14.8%)	0	36 (5.7%)	0
倦怠感	4 (14.8%)	0	21 (3.3%)	2 (0.3%)
疲労	3 (11.1%)	1 (3.7%)	200 (31.6%)	14 (2.2%)
悪心	3 (11.1%)	0	138 (21.8%)	10 (1.6%)
下痢	3 (11.1%)	0	109 (17.2%)	5 (0.8%)
斑状丘疹状皮疹	3 (11.1%)	0	6 (0.9%)	0
便秘	2 (7.4%)	0	91 (14.4%)	2 (0.3%)
嘔吐	2 (7.4%)	1 (3.7%)	84 (13.3%)	7 (1.1%)
頭痛	2 (7.4%)	0	57 (9.0%)	2 (0.3%)
甲状腺機能低下症	2 (7.4%)	0	22 (3.5%)	2 (0.3%)
上腹部痛	2 (7.4%)	0	18 (2.8%)	2 (0.3%)
口内炎	2 (7.4%)	0	17 (2.7%)	0
関節痛	1 (3.7%)	0	74 (11.7%)	4 (0.6%)
発疹	1 (3.7%)	1 (3.7%)	59 (9.3%)	1 (0.2%)
インフルエンザ様疾患	1 (3.7%)	0	41 (6.5%)	0
肺塞栓症	1 (3.7%)	1 (3.7%)	10 (1.6%)	8 (1.3%)
関節炎	1 (3.7%)	0	5 (0.8%)	0
リンパ節症	1 (3.7%)	0	4 (0.6%)	0
気管支肺炎	1 (3.7%)	1 (3.7%)	0	0
外耳炎	1 (3.7%)	0	0	0
靱帯捻挫	1 (3.7%)	0	0	0
咳嗽	0	0	144 (22.8%)	5 (0.8%)
呼吸困難	0	0	143 (22.6%)	28 (4.4%)
無力症	0	0	71 (11.2%)	9 (1.4%)
背部痛	0	0	69 (10.9%)	10 (1.6%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015
Adaptation from output ae_g3_p10_jnj_GO28754_SE
［5.3.5.3-1 ae_g3_p10_jnj_GO28754_SE を改変］

2.7.4.2.2 個別有害事象の文章による説明

死亡例及び重篤な有害事象の叙述は2.7.6.2.2項に記載した。

2.7.4.3 臨床検査値の評価

2.7.4.3.1 血液検査及び血液生化学検査

(1) OAK 試験

有害事象の内，器官別大分類の「臨床検査」に該当する事象を表 2.7.4.7.5-1に示す。また，ベースラインから1段階以上悪化して Grade 3又は Grade 4となった臨床検査値の要約を5.3.5.1-1 Table 93に示した。本剤群で Grade 3又は Grade 4となった臨床検査値は稀であり，多くは5%より少ない被験者で認められたものであった。本剤群の5%以上の被験者で Grade 3又は Grade 4となった臨床検査値は，リンパ球数低値（11.8%）及びナトリウム低値（5.8%）であった。

(2) POPLAR 試験

有害事象の内，器官別大分類の「臨床検査」に該当する事象を表 2.7.4.7.5-2に示す。また，ベースラインから1段階以上悪化して Grade 3又は Grade 4となった臨床検査値の要約を5.3.5.1-2 Table 81に示した。本剤群で Grade 3又は Grade 4となった臨床検査値は稀であり，多くは5%より少ない被験者で認められたものであった。本剤群の5%以上の被験者で Grade 3又は Grade 4となった臨床検査値は，ヘモグロビン低値（Grade 3：5.9%，Grade 4：0%）リンパ球数低値（Grade 3：6.9%，Grade 4：2.3%）及びナトリウム低値（Grade 3：9.6%，Grade 4：2.9%）であった。いずれも Grade 3への悪化が大部分であり，Grade 4への悪化はわずかであった。

(3) BIRCH 試験

有害事象の内，器官別大分類の「臨床検査」に該当する事象を表 2.7.4.7.5-3に示す。また，臨床検査値のシフトテーブルを5.3.5.2-1 t_lb_shift_HEM_SE，5.3.5.2-1 t_lb_shift_CHEM_SE に示した。Grade 3又は Grade 4となった臨床検査値は稀であり，多くは5%より少ない被験者で認められたものであった。全体集団の5%以上の被験者で Grade 3又は Grade 4となった臨床検査値は，リンパ球数低値（Grade 3：9.5%，Grade 4：1.6%）及びナトリウム低値（Grade 3：6.9%，Grade 4：0.6%）であった。いずれも Grade 3への悪化が大部分であり，Grade 4への悪化はわずかであった。

(4) FIR 試験

有害事象の内，器官別大分類の「臨床検査」に該当する事象を表 2.7.4.7.5-4に示す。また，ベースラインから1段階以上悪化して Grade 3又は Grade 4となった臨床検査値の要約を5.3.5.2-2 Table 41に示した。Grade 3又は Grade 4となった臨床検査値は稀であり，多くは5%より少ない被験者で認められたものであった。全体集団の5%以上の被験者で Grade 3又は Grade 4となった臨床検査値は，リンパ球数低値（Grade 3：8.6%，Grade 4：0%）及びナトリウム低値（Grade 3：6.2%，Grade 4：1.5%）であった。いずれも Grade 3への悪化が大部分であり，Grade 4への悪化はわずかであった。

(5) PCD4989g 試験

有害事象の内，器官別大分類の「臨床検査」に該当する事象を表 2.7.4.7.5-5に示す。器官別大分類が「臨床検査」で Grade 3以上の有害事象は稀であり，いずれも全体集団の5%より少ない被験者で認められたものであった。

(6) JO28944試験

有害事象の内，器官別大分類の「臨床検査」に該当する事象を表 2.7.4.7.5-6に示す。SOC が「臨床検査」で Grade 3以上の有害事象は認められなかった。

2.7.4.3.2 抗薬物抗体（ATA）

(1) ATA の発現状況

本剤の投与後に ATA 陽性を示した被験者は，OAK 試験の本剤群では172/565例（30.4%），POPLAR 試験の本剤群では73/135例（54.1%），BIRCH 試験では240/624例（38.5%），FIR 試験では66/129例（51.2%），PCD4989g 試験では139/439例（31.7%），JO28944試験では1/6例であった。（5.3.5.1-1 Table 94， 5.3.5.1-2 Table 84，5.3.5.2-1 Table 83，5.3.5.2-2 Table 45，5.3.3.2-1 t_ata1及び5.3.3.2-2 Table15.3-20参照）。

(2) ATA の発現と安全性の関連

OAK 試験では ATA 陰性例と ATA 陽性例に発現した有害事象及び adverse events of special interest を集計した。有害事象は ATA 陰性例の373/393例（94.9%），ATA 陽性例の164/172例（95.3%）に認められた。adverse events of special interest は，ATA 陰性例の123/393例（31.3%），ATA 陽性例の56/172例（32.6%）に認められた。ATA 陰性例と ATA 陽性例で発現した事象の種類及び重症度に特段の差異は認められなかった（5.3.5.1-1 Table 97 (a)及び Table 97 (b)参照）。

POPLAR 試験，BIRCH 試験，FIR 試験及び PCD4989g 試験（非小細胞肺癌コホート）でも ATA 陰性例と ATA 陽性例に発現した有害事象及び adverse events of special interest を集計したが，いずれの治験でも OAK 試験と同様，ATA 陰性例と ATA 陽性例で発現した事象の種類や頻度に特段の差異は認められなかった。（5.3.5.1-2 t_ae_aet04_byata_SE_MPDL_dc8May2015，t_ae_aet04_trtem_byata_SE_MPDL_aegrp01f_dc8May2015，5.3.5.2-1 t_ae_ata_ATA0_SE，t_ae_ata_ATA1_SE，t_aesi_ata_ATA0_SE，t_aesi_ata_ATA1_SE，5.3.5.2-2 t_ae_ATAN_SE，t_ae_ATAP_SE，t_ae_aesi_ATAN_SE，t_ae_aesi_ATAP_SE，5.3.3.2-1 Table 63及び t_ae_ctc_nowin_ata_NSCLC_IMMUNE_AEDPDFL_SE 参照）。

JO28944試験では，ATA 陽性を示した被験者で本剤の2回目投与以降に投与部位反応又は Infusion Reaction の発現は認められなかった（5.3.3.2-2 12.5.3項及び Listing16.2-18参照）。

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 バイタルサイン

(1) OAK 試験

いずれの投与群でも治験薬の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.5.1-1 t_vs_lbt01_SE 参照）。

(2) POPLAR 試験

いずれの投与群でも治験薬の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.5.1-2 t_vs_vst01_SE_dc8May2015参照）。

(3) BIRCH 試験

本剤の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.5.2-1 t_vs_cb_SE 参照）。

(4) FIR 試験

本剤の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.5.2-2 t_vs_cb_SE 参照）。

(5) PCD4989g 試験（非小細胞肺癌コホート）

本剤の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.3.2-1 t_vs_cb_NSCLC_SE 参照）。

(6) JO28944試験

本剤の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.3.2-2 Table15.3-13参照）。

2.7.4.4.2 心電図検査

(1) OAK 試験

ベースライン時の心電図検査では，異常（臨床的意義なし）が本剤群の224/605例（37.0%），ドセタキセル群の229/609例（37.6%）に認められ，臨床的意義のある異常が本剤群の3/605例（0.5%），ドセタキセル群の1/609例（0.2%）に認められた。

サイクル1，サイクル4とも，また，投与前，投与後とも，いずれの群でも臨床的意義のある異常は認められなかった（5.3.5.1-1 t_aeg_egt01_IT1225参照）。

(2) POPLAR 試験

ベースライン時の心電図検査では，異常（臨床的意義なし）が本剤群の68/143例（47.6%），ドセタキセル群の67/142例（47.2%）に認められ，臨床的意義のある異常がドセタキセル群の1/142例（0.7%）に認められた。

サイクル1の投与前及び投与後の心電図検査では，いずれの群でも臨床的意義のある異常は認められなかった。サイクル4の投与前及び投与後の心電図検査では，ドセタキセル群の1例で臨床的意義のある異常が認められた。（5.3.5.1-2 t_aeg_egt01_IT_dc8May2015参照）。

(3) BIRCH 試験

ベースライン時の心電図検査では，異常が265/644例（41.1%）に認められた。

サイクル1の投与前の心電図検査は85例でのみ実施され，コホート1の7例（58.3%），コホート2の14例（32.6%），コホート3の12例（40.0%）で異常が認められた（5.3.5.2-1 t_eg_cb_SE参照）。全体を通して，心電図検査異常に関連する臨床的に重要な事象の発現はみられなかった。

(4) FIR 試験

ベースライン時の心電図検査では，異常（臨床的意義なし）が76/132例（57.6%），臨床的意義のある異常が3/132例（2.3%）に認められた。

サイクル1の投与前及び投与後の心電図検査では，いずれも3例で臨床的意義のある異常が認められた。サイクル4の投与前の心電図検査では臨床的意義のある異常は認められず，投与後の心電図検査で1例に臨床的意義のある異常が認められた。（5.3.5.2-2 t_eg_ab_SE 参照）。

心電図パラメータのベースラインからの変化量は5.3.5.2-2 t_eg_cb_SE に示した。いずれのパラメータも本剤投与後に臨床的に重要な変動はみられなかった。

(5) PCD4989g 試験

非小細胞肺癌コホートの心電図検査に関する集計を5.3.3.2-1 t_eg_cb_NSCLC_SE に示した。

心電図の判定は417例を対象に実施され，Fridericia 補正法による QT 間隔（QTcF）及びベースラインからの QTcF の変化量（ΔQTcF）のカテゴリカル解析を行った。また，血清中アテゾリズマブ濃度と ΔQTcF の関連性を検討した結果，血清中アテゾリズマブと QT 間隔延長に明確な関連性はみられなかった（2.7.2.2.3.2項参照）。

(6) JO28944試験

心電図検査に関する集計を5.3.3.2-2 Table15.3-15～Table15.3-19に示した。

サイクル1 Day 1及びサイクル4 Day 1の投与前30分及び投与後30分及び最終観察時に心電図

検査を行った。10 mg/kg コホートで2例に QTcF で450 msec 以上の延長がみられたが，ΔQTcF が30 msec 以上の延長を示した被験者はみられなかった（2.7.2.2.3.1項参照）。

本剤投与後に心電図検査で認められた異常所見は3例8件であった。その内訳は，QT 延長が2例7件，I 度房室ブロックが1例1件であった（5.3.3.2-2 Listing16.2-25参照）。

2.7.4.5 特別な患者集団及び状況下における安全性

2.7.4.5.1 内因性要因

OAK 試験で発現した有害事象を年齢別（65歳未満 vs 65歳以上），性別，人種別に分析し，それぞれ表 2.7.4.5.1.1-1～表 2.7.4.5.1.3-1示した。

2.7.4.5.1.1 年齢別

年齢別（65歳未満 vs 65歳以上）の有害事象の概要を表 2.7.4.5.1.1-1に示す。年齢別の安全性成績に特段の差異は認められなかった。

表 2.7.4.5.1.1-1　年齢別の有害事象の概要（OAK 試験）

Safety Summary by Age
Protocol: GO28915
Population: All Safety Evaluable Patients

	Atezolizumab (Actual) (N=609)		Docetaxel (Actual) (N=578)		All Patients (N=1187)	
	< 65 (N=334)	>= 65 (N=275)	< 65 (N=312)	>= 65 (N=266)	< 65 (N=646)	>= 65 (N=541)
Total number of patients with at least one adverse event	317 (94.9%)	256 (93.1%)	298 (95.5%)	257 (96.6%)	615 (95.2%)	513 (94.8%)
Total number of events	2695	2530	3009	2896	5704	5426
Total number of patients with at least one						
Treatment-related AE	198 (59.3%)	192 (69.8%)	271 (86.9%)	225 (84.6%)	469 (72.6%)	417 (77.1%)
Grade 3-4 AE	118 (35.3%)	109 (39.6%)	156 (50.0%)	154 (57.9%)	274 (42.4%)	263 (48.6%)
Treatment-related Grade 3-4 AE	47 (14.1%)	43 (15.6%)	130 (41.7%)	117 (44.0%)	177 (27.4%)	160 (29.6%)
Grade 5 AE	6 (1.8%)	4 (1.5%)	7 (2.2%)	7 (2.6%)	13 (2.0%)	11 (2.0%)
Treatment-related Grade 5 AE	0	0	0	1 (0.4%)	0	1 (0.2%)
Serious Adverse Event	109 (32.6%)	85 (30.9%)	78 (25.0%)	103 (38.7%)	187 (28.9%)	188 (34.8%)
AE leading to withdrawal from treatment	26 (7.8%)	20 (7.3%)	53 (17.0%)	55 (20.7%)	79 (12.2%)	75 (13.9%)
AE leading to dose modification/interruption	84 (25.1%)	68 (24.7%)	105 (33.7%)	105 (39.5%)	189 (29.3%)	173 (32.0%)

Percentages are based on N in the column headings.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet01_age.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet01_age_GO28915_SE.out
07DEC2016 18:32

［5.3.5.1-3 aet01_age_GO28915_SE を再掲］

2.7.4.5.1.2　　性別

性別の有害事象の概要を表 2.7.4.5.1.2-1に示す。性別の安全性成績に特段の差異は認められなかった。

表 2.7.4.5.1.2-1　性別の有害事象の概要（OAK 試験）

Safety Summary by Sex
Protocol: GO28915
Population: All Safety Evaluable Patients

	Atezolizumab (Actual) (N=609)		Docetaxel (Actual) (N=578)		All Patients (N=1187)	
	Male (N=376)	Female (N=233)	Male (N=360)	Female (N=218)	Male (N=736)	Female (N=451)
Total number of patients with at least one adverse event	353 (93.9%)	220 (94.4%)	345 (95.8%)	210 (96.3%)	698 (94.8%)	430 (95.3%)
Total number of events	3088	2137	3591	2314	6679	4451
Total number of patients with at least one						
Treatment-related AE	240 (63.8%)	150 (64.4%)	311 (86.4%)	185 (84.9%)	551 (74.9%)	335 (74.3%)
Grade 3-4 AE	127 (33.8%)	100 (42.9%)	201 (55.8%)	109 (50.0%)	328 (44.6%)	209 (46.3%)
Treatment-related Grade 3-4 AE	54 (14.4%)	36 (15.5%)	157 (43.6%)	90 (41.3%)	211 (28.7%)	126 (27.9%)
Grade 5 AE	10 (2.7%)	0	11 (3.1%)	3 (1.4%)	21 (2.9%)	3 (0.7%)
Treatment-related Grade 5 AE	0	0	1 (0.3%)	0	1 (0.1%)	0
Serious Adverse Event	124 (33.0%)	70 (30.0%)	124 (34.4%)	57 (26.1%)	248 (33.7%)	127 (28.2%)
AE leading to withdrawal from treatment	32 (8.5%)	14 (6.0%)	71 (19.7%)	37 (17.0%)	103 (14.0%)	51 (11.3%)
AE leading to dose modification/interruption	93 (24.7%)	59 (25.3%)	127 (35.3%)	83 (38.1%)	220 (29.9%)	142 (31.5%)

Percentages are based on N in the column headings.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet01_sex.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet01_sex_GO28915_SE.out
07DEC2016 18:39

Page 1 of 1

［5.3.5.1-3 aet01_sex_GO28915_SE を再掲］

2.7.4.5.1.3　人種別

人種別の有害事象の概要を表 2.7.4.5.1.3-1に示す。人種別の安全性成績に特段の差異は認められなかった。

表 2.7.4.5.1.3-1　人種別の有害事象の概要（OAK 試験）

Safety Summary by Race
Protocol: GO28915
Population: All Safety Evaluable Patients

	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)			All Patients (N=1187)		
	Asian (N=124)	White (N=436)	Other (N=49)	Asian (N=119)	White (N=409)	Other (N=50)	Asian (N=243)	White (N=845)	Other (N=99)
Total number of patients with at least one adverse event	118 (95.2%)	407 (93.3%)	48 (98.0%)	119 (100.0%)	389 (95.1%)	47 (94.0%)	237 (97.5%)	796 (94.2%)	95 (96.0%)
Total number of events	908	3830	487	1652	3773	480	2560	7603	967
Total number of patients with at least one									
Treatment-related AE	88 (71.0%)	263 (60.3%)	39 (79.6%)	115 (96.6%)	336 (82.2%)	45 (90.0%)	203 (83.5%)	599 (70.9%)	84 (84.8%)
Grade 3-4 AE	40 (32.3%)	170 (39.0%)	17 (34.7%)	85 (71.4%)	205 (50.1%)	20 (40.0%)	125 (51.4%)	375 (44.4%)	37 (37.4%)
Treatment-related Grade 3-4 AE	19 (15.3%)	60 (13.8%)	11 (22.4%)	79 (66.4%)	152 (37.2%)	16 (32.0%)	98 (40.3%)	212 (25.1%)	27 (27.3%)
Grade 5 AE	0	7 (1.6%)	3 (6.1%)	2 (1.7%)	12 (2.9%)	0	2 (0.8%)	19 (2.2%)	3 (3.0%)
Treatment-related Grade 5 AE	0	0	0	0	1 (0.2%)	0	0	1 (0.1%)	0
Serious Adverse Event	32 (25.8%)	146 (33.5%)	16 (32.7%)	37 (31.1%)	132 (32.3%)	12 (24.0%)	69 (28.4%)	278 (32.9%)	28 (28.3%)
AE leading to withdrawal from treatment	12 (9.7%)	29 (6.7%)	5 (10.2%)	26 (21.8%)	71 (17.4%)	11 (22.0%)	38 (15.6%)	100 (11.8%)	16 (16.2%)
AE leading to dose modification/interruption	22 (17.7%)	116 (26.6%)	14 (28.6%)	71 (59.7%)	118 (28.9%)	21 (42.0%)	93 (38.3%)	234 (27.7%)	35 (35.4%)

Percentages are based on N in the column headings.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet01_race.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet01_race_GO28915_SE.out
07DEC2016 18:46

［5.3.5.1-3 aet01_race_GO28915_SE を再掲］

2.7.4.5.2 外因性要因

喫煙や飲酒等の外因性要因に関する部分集団解析は実施していない。

2.7.4.5.3 薬物相互作用

本剤と他の抗がん剤との薬物間相互作用の検討は，非小細胞肺癌患者を対象には検討されていない。また，薬物間相互作用試験は実施していない（2.7.2.3.9項参照）。

2.7.4.5.4 妊娠及び授乳時の使用

妊婦及び授乳中の女性を対象とした比較対照試験は実施されておらず，妊婦及び授乳中の女性に対する本剤の安全性は確立されていない。また，海外及び国内で実施されたいずれの治験でも妊婦及び授乳中の女性は被験者から除外したため，安全性の検討はできなかった。

いくつかの非臨床試験において PD-L1/programmed death-1（PD-1）経路が母体／胎児間の免疫寛容成立に必須であることが示されており，本剤投与による PD-L1/PD-1経路の阻害には，胚致死を含むヒト胎児発生に及ぼす安全性リスクの存在が示唆されている（2.4.4.4項参照）。以上のことから，妊婦又は妊娠している可能性のある婦人には投与することを推奨しないが，やむを得ず投与する場合には治療上の有益性が危険性を上回ると判断される場合にのみ投与することが必要である。また，妊娠する可能性のある女性患者には，本剤投与中及び本剤投与終了後5カ月間は適切な避妊法を用いるように指導することが必要である。

本剤の乳汁中排泄試験は実施していないが，免疫グロブリン G は乳汁中に移行することが知られている。本剤を授乳婦に投与する場合は，授乳を中止させることが必要である。

2.7.4.5.5 過量投与

OAK 試験，BIRCH 試験，POPLAR 試験及び FIR 試験では，治験実施計画書で本剤の用量を固定用量の1200 mg（15 mg/kg に相当）と規定しており，本剤の過量投与に関する情報は得られなかった。

なお，JO28944試験では，20 mg/kg コホートの2例で1200 mg を超える本剤が投与され（実投与量：1446 mg，1626 mg），PCD4989g 試験でも10 mg/kg コホート（体重：55.8～149.2 kg），15 mg/kg コホート（体重：42.0～149.0 kg），20 mg/kg コホート（体重：36.5～168.0 kg）で1200 mg を超える本剤が投与されたが，いずれの治験においても DLT に該当する事象は認められなかった。

2.7.4.5.6 薬物乱用

これまでに実施された臨床試験で，本剤に対する依存性は報告されていない。

2.7.4.5.7 離脱症状及び反跳現象

これまでに実施された臨床試験で，本剤の離脱症状及び反跳現象は報告されていない。

2.7.4.5.8 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

これまでに実施された臨床試験で，自動車運転及び機械操作に影響すると考えられる有害事象に関し，対照群と比較して本剤群で明らかに発現率が高い事象は認められていない。

2.7.4.6 市販後データ

2016年12月1日現在，本剤は米国等で承認され，市販されている。ただし，Periodic Benefit-Risk Evaluation Report 等集積評価について当局へ報告したものはない。

2.7.4.7　付録

2.7.4.7.1　発現率10%以上の有害事象（PCD4989g 試験）

(1)　発現率10%以上の有害事象の要約（PCD4989g 試験）

表 2.7.4.7.1-1　発現率10%以上の有害事象の要約（PCD4989g 試験）

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

	atezolizumab Total (N=481)		atezolizumab <=1 mg/kg q3w IV (N=9)		atezolizumab 3 mg/kg q3w IV (N=3)		atezolizumab 10 mg/kg q3w IV (N=36)	
MedDRA Preferred Term	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)
Total number of patients with at least one adverse event	466 (96.9%)	347 (72.1%)	9 (100.0%)	8 (88.9%)	3 (100.0%)	3 (100.0%)	35 (97.2%)	31 (86.1%)
疲労	180 (37.4%)	111 (23.1%)	7 (77.8%)	6 (66.7%)	3 (100.0%)	2 (66.7%)	16 (44.4%)	13 (36.1%)
悪心	126 (26.2%)	63 (13.1%)	7 (77.8%)	6 (66.7%)	2 (66.7%)	1 (33.3%)	9 (25.0%)	7 (19.4%)
食欲減退	125 (26.0%)	59 (12.3%)	3 (33.3%)	3 (33.3%)	1 (33.3%)	1 (33.3%)	9 (25.0%)	6 (16.7%)
発熱	107 (22.2%)	58 (12.1%)	4 (44.4%)	1 (11.1%)	3 (100.0%)	0	8 (22.2%)	6 (16.7%)
呼吸困難	103 (21.4%)	16 (3.3%)	4 (44.4%)	2 (22.2%)	1 (33.3%)	1 (33.3%)	12 (33.3%)	2 (5.6%)
咳嗽	103 (21.4%)	11 (2.3%)	3 (33.3%)	2 (22.2%)	3 (100.0%)	1 (33.3%)	10 (27.8%)	1 (2.8%)
下痢	102 (21.2%)	49 (10.2%)	5 (55.6%)	3 (33.3%)	0	0	16 (44.4%)	10 (27.8%)
便秘	102 (21.2%)	7 (1.5%)	2 (22.2%)	0	0	0	9 (25.0%)	1 (2.8%)
貧血	97 (20.2%)	24 (5.0%)	1 (11.1%)	0	0	0	7 (19.4%)	2 (5.6%)
嘔吐	90 (18.7%)	26 (5.4%)	0	0	1 (33.3%)	0	6 (16.7%)	2 (5.6%)
背部痛	80 (16.6%)	9 (1.9%)	1 (11.1%)	0	1 (33.3%)	1 (33.3%)	7 (19.4%)	0
無力症	80 (16.6%)	49 (10.2%)	1 (11.1%)	1 (11.1%)	0	0	2 (5.6%)	1 (2.8%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
09NOV2016 10:30

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
頭痛	79 (16.4%)	31 (6.4%)	3 (33.3%)	3 (33.3%)	1 (33.3%)	1 (33.3%)	13 (36.1%)	7 (19.4%)
関節痛	71 (14.8%)	33 (6.9%)	3 (33.3%)	1 (11.1%)	1 (33.3%)	0	9 (25.0%)	7 (19.4%)
発疹	71 (14.8%)	50 (10.4%)	1 (11.1%)	1 (11.1%)	2 (66.7%)	2 (66.7%)	8 (22.2%)	7 (19.4%)
そう痒症	64 (13.3%)	46 (9.6%)	2 (22.2%)	2 (22.2%)	1 (33.3%)	1 (33.3%)	9 (25.0%)	8 (22.2%)
腹痛	60 (12.5%)	12 (2.5%)	3 (33.3%)	2 (22.2%)	0	0	7 (19.4%)	1 (2.8%)
不眠症	60 (12.5%)	7 (1.5%)	2 (22.2%)	2 (22.2%)	1 (33.3%)	0	10 (27.8%)	2 (5.6%)
末梢性浮腫	57 (11.9%)	7 (1.5%)	1 (11.1%)	0	1 (33.3%)	0	8 (22.2%)	3 (8.3%)
悪寒	55 (11.4%)	31 (6.4%)	4 (44.4%)	3 (33.3%)	3 (100.0%)	1 (33.3%)	5 (13.9%)	4 (11.1%)
尿路感染	54 (11.2%)	2 (0.4%)	1 (11.1%)	0	0	0	4 (11.1%)	0
上気道感染	47 (9.8%)	6 (1.2%)	3 (33.3%)	2 (22.2%)	2 (66.7%)	0	6 (16.7%)	0
疼痛	44 (9.1%)	23 (4.8%)	4 (44.4%)	3 (33.3%)	1 (33.3%)	0	3 (8.3%)	2 (5.6%)
浮動性めまい	44 (9.1%)	11 (2.3%)	1 (11.1%)	1 (11.1%)	1 (33.3%)	0	7 (19.4%)	2 (5.6%)
不安	37 (7.7%)	0	2 (22.2%)	0	1 (33.3%)	0	6 (16.7%)	0
脱水	37 (7.7%)	8 (1.7%)	0	0	0	0	3 (8.3%)	0
四肢痛	36 (7.5%)	6 (1.2%)	2 (22.2%)	1 (11.1%)	0	0	3 (8.3%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
皮膚乾燥	36 (7.5%)	20 (4.2%)	1 (11.1%)	0	1 (33.3%)	1 (33.3%)	2 (5.6%)	2 (5.6%)
インフルエンザ様疾患	36 (7.5%)	29 (6.0%)	0	0	0	0	5 (13.9%)	5 (13.9%)
筋肉痛	35 (7.3%)	19 (4.0%)	2 (22.2%)	1 (11.1%)	0	0	2 (5.6%)	2 (5.6%)
上腹部痛	30 (6.2%)	5 (1.0%)	1 (11.1%)	1 (11.1%)	0	0	4 (11.1%)	2 (5.6%)
筋骨格痛	30 (6.2%)	2 (0.4%)	0	0	0	0	7 (19.4%)	1 (2.8%)
寝汗	29 (6.0%)	15 (3.1%)	2 (22.2%)	1 (11.1%)	3 (100.0%)	1 (33.3%)	3 (8.3%)	3 (8.3%)
口腔咽頭痛	29 (6.0%)	4 (0.8%)	1 (11.1%)	0	0	0	7 (19.4%)	2 (5.6%)
鼻閉	28 (5.8%)	3 (0.6%)	1 (11.1%)	1 (11.1%)	2 (66.7%)	0	3 (8.3%)	0
湿性咳嗽	27 (5.6%)	4 (0.8%)	1 (11.1%)	1 (11.1%)	0	0	4 (11.1%)	0
胸痛	24 (5.0%)	3 (0.6%)	1 (11.1%)	1 (11.1%)	1 (33.3%)	0	4 (11.1%)	1 (2.8%)
口内乾燥	22 (4.6%)	12 (2.5%)	1 (11.1%)	1 (11.1%)	0	0	1 (2.8%)	1 (2.8%)
嚥下障害	20 (4.2%)	1 (0.2%)	1 (11.1%)	0	0	0	0	0
高血糖	20 (4.2%)	2 (0.4%)	0	0	0	0	6 (16.7%)	0
甲状腺機能低下症	20 (4.2%)	16 (3.3%)	0	0	0	0	4 (11.1%)	4 (11.1%)
味覚異常	19 (4.0%)	12 (2.5%)	2 (22.2%)	2 (22.2%)	0	0	2 (5.6%)	2 (5.6%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
筋痙縮	19 (4.0%)	6 (1.2%)	1 (11.1%)	0	0	0	2 (5.6%)	2 (5.6%)
筋骨格系胸痛	18 (3.7%)	3 (0.6%)	1 (11.1%)	0	1 (33.3%)	0	3 (8.3%)	0
側腹部痛	18 (3.7%)	1 (0.2%)	1 (11.1%)	0	0	0	2 (5.6%)	0
低マグネシウム血症	18 (3.7%)	6 (1.2%)	1 (11.1%)	1 (11.1%)	0	0	1 (2.8%)	0
末梢性ニューロパチー	17 (3.5%)	4 (0.8%)	2 (22.2%)	2 (22.2%)	0	0	0	0
労作性呼吸困難	17 (3.5%)	1 (0.2%)	0	0	1 (33.3%)	0	4 (11.1%)	0
胃食道逆流性疾患	16 (3.3%)	2 (0.4%)	2 (22.2%)	1 (11.1%)	0	0	2 (5.6%)	1 (2.8%)
紅斑	16 (3.3%)	7 (1.5%)	0	0	1 (33.3%)	1 (33.3%)	2 (5.6%)	1 (2.8%)
頻尿	15 (3.1%)	1 (0.2%)	2 (22.2%)	0	0	0	4 (11.1%)	0
血尿	15 (3.1%)	3 (0.6%)	0	0	2 (66.7%)	0	3 (8.3%)	0
高血圧	14 (2.9%)	0	0	0	1 (33.3%)	0	1 (2.8%)	0
斑状丘疹状皮疹	14 (2.9%)	11 (2.3%)	0	0	0	0	4 (11.1%)	2 (5.6%)
錯感覚	13 (2.7%)	4 (0.8%)	0	0	0	0	4 (11.1%)	2 (5.6%)
多汗症	12 (2.5%)	8 (1.7%)	2 (22.2%)	2 (22.2%)	0	0	1 (2.8%)	0
上気道咳症候群	12 (2.5%)	2 (0.4%)	1 (11.1%)	0	0	0	4 (11.1%)	2 (5.6%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
消化不良	11 (2.3%)	3 (0.6%)	1 (11.1%)	1 (11.1%)	0	0	2 (5.6%)	1 (2.8%)
喘鳴	11 (2.3%)	3 (0.6%)	0	0	1 (33.3%)	0	3 (8.3%)	0
気管支炎	10 (2.1%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	1 (33.3%)	0	1 (2.8%)	0
ほてり	10 (2.1%)	3 (0.6%)	1 (11.1%)	1 (11.1%)	0	0	1 (2.8%)	0
口内炎	10 (2.1%)	8 (1.7%)	1 (11.1%)	1 (11.1%)	0	0	0	0
感覚鈍麻	9 (1.9%)	5 (1.0%)	1 (11.1%)	1 (11.1%)	0	0	2 (5.6%)	2 (5.6%)
胸部不快感	9 (1.9%)	2 (0.4%)	1 (11.1%)	1 (11.1%)	0	0	2 (5.6%)	1 (2.8%)
頻脈	9 (1.9%)	2 (0.4%)	1 (11.1%)	0	0	0	1 (2.8%)	1 (2.8%)
夜間頻尿	9 (1.9%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
歯痛	9 (1.9%)	0	0	0	1 (33.3%)	0	0	0
回転性めまい	8 (1.7%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	1 (2.8%)	0
副鼻腔うっ血	8 (1.7%)	0	0	0	0	0	4 (11.1%)	0
帯状疱疹	7 (1.5%)	4 (0.8%)	1 (11.1%)	0	1 (33.3%)	1 (33.3%)	0	0
心房細動	7 (1.5%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
非心臓性胸痛	7 (1.5%)	0	1 (11.1%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
蛋白尿	7 (1.5%)	0	0	0	1 (33.3%)	0	1 (2.8%)	0
動悸	6 (1.2%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
敗血症	6 (1.2%)	1 (0.2%)	1 (11.1%)	0	0	0	0	0
口腔内痛	6 (1.2%)	2 (0.4%)	1 (11.1%)	1 (11.1%)	0	0	0	0
腫瘍出血	6 (1.2%)	0	0	0	1 (33.3%)	0	0	0
リンパ節症	5 (1.0%)	1 (0.2%)	0	0	1 (33.3%)	0	0	0
体重増加	5 (1.0%)	0	0	0	1 (33.3%)	0	0	0
真菌感染	4 (0.8%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
脂漏性角化症	4 (0.8%)	0	1 (11.1%)	0	0	0	0	0
尋常性白斑	4 (0.8%)	4 (0.8%)	0	0	1 (33.3%)	1 (33.3%)	1 (2.8%)	1 (2.8%)
乳房痛	4 (0.8%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
肉離れ	4 (0.8%)	0	0	0	1 (33.3%)	0	0	0
高尿酸血症	4 (0.8%)	1 (0.2%)	0	0	1 (33.3%)	0	0	0
流涙増加	3 (0.6%)	2 (0.4%)	2 (22.2%)	2 (22.2%)	1 (33.3%)	0	0	0
眼そう痒症	3 (0.6%)	1 (0.2%)	2 (22.2%)	1 (11.1%)	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
耳感染	3 (0.6%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	1 (2.8%)	0
レッチング	3 (0.6%)	2 (0.4%)	1 (11.1%)	1 (11.1%)	0	0	0	0
食道炎	3 (0.6%)	1 (0.2%)	1 (11.1%)	0	0	0	0	0
限局性感染	3 (0.6%)	0	0	0	1 (33.3%)	0	1 (2.8%)	0
過角化	3 (0.6%)	1 (0.2%)	0	0	1 (33.3%)	0	0	0
腹部ヘルニア	3 (0.6%)	0	0	0	1 (33.3%)	0	0	0
口の感覚鈍麻	2 (0.4%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
日光角化症	2 (0.4%)	0	1 (11.1%)	0	0	0	0	0
ヘルニア痛	2 (0.4%)	0	1 (11.1%)	0	0	0	0	0
温度変化不耐症	2 (0.4%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
腫瘍の潰瘍形成	2 (0.4%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
深径覚の変化	1 (0.2%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
潰瘍性角膜炎	1 (0.2%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
睫毛眉毛脱落症	1 (0.2%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
出血時間延長	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
小水疱性皮疹	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
尿道閉塞	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
皮膚乳頭腫	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
表在性異物	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
膣粘膜水疱形成	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
乾癬様皮膚炎	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
耳閉	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
全身性皮疹	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
創合併症	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
体温上昇	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
股関節形成	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
腫瘍壊死	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
弛緩歯	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
軟骨症	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
乳房圧痛	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
Total number of patients with at least one adverse event	231 (97.9%)	172 (72.9%)	145 (99.3%)	108 (74.0%)	43 (84.3%)	25 (49.0%)
疲労	88 (37.3%)	51 (21.6%)	52 (35.6%)	33 (22.6%)	14 (27.5%)	6 (11.8%)
悪心	51 (21.6%)	23 (9.7%)	44 (30.1%)	18 (12.3%)	13 (25.5%)	8 (15.7%)
食欲減退	57 (24.2%)	26 (11.0%)	43 (29.5%)	15 (10.3%)	12 (23.5%)	8 (15.7%)
発熱	53 (22.5%)	30 (12.7%)	32 (21.9%)	16 (11.0%)	7 (13.7%)	5 (9.8%)
呼吸困難	31 (13.1%)	3 (1.3%)	45 (30.8%)	6 (4.1%)	10 (19.6%)	2 (3.9%)
咳嗽	51 (21.6%)	4 (1.7%)	31 (21.2%)	3 (2.1%)	5 (9.8%)	0
下痢	43 (18.2%)	21 (8.9%)	30 (20.5%)	11 (7.5%)	8 (15.7%)	4 (7.8%)
便秘	50 (21.2%)	0	35 (24.0%)	6 (4.1%)	6 (11.8%)	0
貧血	53 (22.5%)	11 (4.7%)	28 (19.2%)	8 (5.5%)	8 (15.7%)	3 (5.9%)
嘔吐	42 (17.8%)	10 (4.2%)	33 (22.6%)	11 (7.5%)	8 (15.7%)	3 (5.9%)
背部痛	41 (17.4%)	4 (1.7%)	29 (19.9%)	4 (2.7%)	1 (2.0%)	0
無力症	44 (18.6%)	25 (10.6%)	27 (18.5%)	16 (11.0%)	6 (11.8%)	6 (11.8%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
頭痛	31 (13.1%)	5 (2.1%)	25 (17.1%)	11 (7.5%)	6 (11.8%)	4 (7.8%)
関節痛	30 (12.7%)	17 (7.2%)	26 (17.8%)	8 (5.5%)	2 (3.9%)	0
発疹	33 (14.0%)	23 (9.7%)	25 (17.1%)	15 (10.3%)	2 (3.9%)	2 (3.9%)
そう痒症	31 (13.1%)	22 (9.3%)	16 (11.0%)	11 (7.5%)	5 (9.8%)	2 (3.9%)
腹痛	31 (13.1%)	5 (2.1%)	16 (11.0%)	3 (2.1%)	3 (5.9%)	1 (2.0%)
不眠症	25 (10.6%)	2 (0.8%)	20 (13.7%)	1 (0.7%)	2 (3.9%)	0
末梢性浮腫	24 (10.2%)	2 (0.8%)	17 (11.6%)	2 (1.4%)	6 (11.8%)	0
悪寒	24 (10.2%)	12 (5.1%)	17 (11.6%)	10 (6.8%)	2 (3.9%)	1 (2.0%)
尿路感染	31 (13.1%)	1 (0.4%)	15 (10.3%)	1 (0.7%)	3 (5.9%)	0
上気道感染	14 (5.9%)	1 (0.4%)	21 (14.4%)	3 (2.1%)	1 (2.0%)	0
疼痛	21 (8.9%)	9 (3.8%)	13 (8.9%)	7 (4.8%)	2 (3.9%)	2 (3.9%)
浮動性めまい	18 (7.6%)	5 (2.1%)	15 (10.3%)	2 (1.4%)	2 (3.9%)	1 (2.0%)
不安	15 (6.4%)	0	11 (7.5%)	0	2 (3.9%)	0
脱水	16 (6.8%)	3 (1.3%)	15 (10.3%)	4 (2.7%)	3 (5.9%)	1 (2.0%)
四肢痛	17 (7.2%)	2 (0.8%)	12 (8.2%)	3 (2.1%)	2 (3.9%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
皮膚乾燥	21 (8.9%)	11 (4.7%)	9 (6.2%)	6 (4.1%)	2 (3.9%)	0
インフルエンザ様疾患	12 (5.1%)	9 (3.8%)	17 (11.6%)	13 (8.9%)	2 (3.9%)	2 (3.9%)
筋肉痛	19 (8.1%)	9 (3.8%)	11 (7.5%)	7 (4.8%)	1 (2.0%)	0
上腹部痛	12 (5.1%)	1 (0.4%)	12 (8.2%)	1 (0.7%)	1 (2.0%)	0
筋骨格痛	7 (3.0%)	0	15 (10.3%)	1 (0.7%)	1 (2.0%)	0
寝汗	12 (5.1%)	4 (1.7%)	8 (5.5%)	5 (3.4%)	1 (2.0%)	1 (2.0%)
口腔咽頭痛	10 (4.2%)	0	11 (7.5%)	2 (1.4%)	0	0
鼻閉	11 (4.7%)	1 (0.4%)	11 (7.5%)	1 (0.7%)	0	0
湿性咳嗽	9 (3.8%)	1 (0.4%)	13 (8.9%)	2 (1.4%)	0	0
胸痛	6 (2.5%)	0	8 (5.5%)	1 (0.7%)	4 (7.8%)	0
口内乾燥	8 (3.4%)	4 (1.7%)	10 (6.8%)	5 (3.4%)	2 (3.9%)	1 (2.0%)
嚥下障害	13 (5.5%)	1 (0.4%)	6 (4.1%)	0	0	0
高血糖	8 (3.4%)	2 (0.8%)	6 (4.1%)	0	0	0
甲状腺機能低下症	9 (3.8%)	6 (2.5%)	7 (4.8%)	6 (4.1%)	0	0
味覚異常	9 (3.8%)	6 (2.5%)	6 (4.1%)	2 (1.4%)	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
筋痙縮	8 (3.4%)	3 (1.3%)	7 (4.8%)	1 (0.7%)	1 (2.0%)	0
筋骨格系胸痛	7 (3.0%)	2 (0.8%)	6 (4.1%)	1 (0.7%)	0	0
側腹部痛	8 (3.4%)	1 (0.4%)	7 (4.8%)	0	0	0
低マグネシウム血症	9 (3.8%)	3 (1.3%)	5 (3.4%)	1 (0.7%)	2 (3.9%)	1 (2.0%)
末梢性ニューロパチー	10 (4.2%)	1 (0.4%)	3 (2.1%)	1 (0.7%)	2 (3.9%)	0
労作性呼吸困難	6 (2.5%)	1 (0.4%)	3 (2.1%)	0	3 (5.9%)	0
胃食道逆流性疾患	4 (1.7%)	0	8 (5.5%)	0	0	0
紅斑	6 (2.5%)	3 (1.3%)	6 (4.1%)	1 (0.7%)	1 (2.0%)	1 (2.0%)
頻尿	6 (2.5%)	0	3 (2.1%)	1 (0.7%)	0	0
血尿	7 (3.0%)	2 (0.8%)	2 (1.4%)	1 (0.7%)	1 (2.0%)	0
高血圧	4 (1.7%)	0	5 (3.4%)	0	3 (5.9%)	0
斑状丘疹状皮疹	7 (3.0%)	6 (2.5%)	3 (2.1%)	3 (2.1%)	0	0
錯感覚	5 (2.1%)	2 (0.8%)	2 (1.4%)	0	2 (3.9%)	0
多汗症	3 (1.3%)	1 (0.4%)	4 (2.7%)	4 (2.7%)	2 (3.9%)	1 (2.0%)
上気道咳症候群	4 (1.7%)	0	3 (2.1%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
消化不良	5 (2.1%)	1 (0.4%)	3 (2.1%)	0	0	0
喘鳴	3 (1.3%)	1 (0.4%)	4 (2.7%)	2 (1.4%)	0	0
気管支炎	6 (2.5%)	0	1 (0.7%)	0	0	0
ほてり	4 (1.7%)	2 (0.8%)	4 (2.7%)	0	0	0
口内炎	6 (2.5%)	5 (2.1%)	3 (2.1%)	2 (1.4%)	0	0
感覚鈍麻	3 (1.3%)	1 (0.4%)	3 (2.1%)	1 (0.7%)	0	0
胸部不快感	3 (1.3%)	0	3 (2.1%)	0	0	0
頻脈	4 (1.7%)	1 (0.4%)	2 (1.4%)	0	1 (2.0%)	0
夜間頻尿	4 (1.7%)	0	2 (1.4%)	0	1 (2.0%)	0
歯痛	2 (0.8%)	0	5 (3.4%)	0	1 (2.0%)	0
回転性めまい	4 (1.7%)	0	2 (1.4%)	0	0	0
副鼻腔うっ血	3 (1.3%)	0	1 (0.7%)	0	0	0
帯状疱疹	4 (1.7%)	3 (1.3%)	1 (0.7%)	0	0	0
心房細動	3 (1.3%)	0	2 (1.4%)	0	0	0
非心臓性胸痛	1 (0.4%)	0	5 (3.4%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
蛋白尿	3 (1.3%)	0	2 (1.4%)	0	0	0
動悸	1 (0.4%)	0	3 (2.1%)	0	0	0
敗血症	5 (2.1%)	1 (0.4%)	0	0	0	0
口腔内痛	3 (1.3%)	1 (0.4%)	2 (1.4%)	0	0	0
腫瘍出血	4 (1.7%)	0	0	0	1 (2.0%)	0
リンパ節症	1 (0.4%)	0	3 (2.1%)	1 (0.7%)	0	0
体重増加	1 (0.4%)	0	3 (2.1%)	0	0	0
真菌感染	1 (0.4%)	0	1 (0.7%)	0	0	0
脂漏性角化症	3 (1.3%)	0	0	0	0	0
尋常性白斑	2 (0.8%)	2 (0.8%)	0	0	0	0
乳房痛	1 (0.4%)	0	2 (1.4%)	0	0	0
肉離れ	1 (0.4%)	0	1 (0.7%)	0	1 (2.0%)	0
高尿酸血症	0	0	3 (2.1%)	1 (0.7%)	0	0
流涙増加	0	0	0	0	0	0
眼そう痒症	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
耳感染	1 (0.4%)	0	0	0	0	0
レッチング	0	0	2 (1.4%)	1 (0.7%)	0	0
食道炎	0	0	2 (1.4%)	1 (0.7%)	0	0
限局性感染	1 (0.4%)	0	0	0	0	0
過角化	1 (0.4%)	1 (0.4%)	1 (0.7%)	0	0	0
腹部ヘルニア	0	0	1 (0.7%)	0	1 (2.0%)	0
口の感覚鈍麻	1 (0.4%)	0	0	0	0	0
日光角化症	1 (0.4%)	0	0	0	0	0
ヘルニア痛	0	0	1 (0.7%)	0	0	0
温度変化不耐症	1 (0.4%)	0	0	0	0	0
腫瘍の潰瘍形成	1 (0.4%)	0	0	0	0	0
深径覚の変化	0	0	0	0	0	0
潰瘍性角膜炎	0	0	0	0	0	0
睫毛眉毛脱落症	0	0	0	0	0	0
出血時間延長	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
小水疱性皮疹	0	0	0	0	0	0
尿道閉塞	0	0	0	0	0	0
皮膚乳頭腫	0	0	0	0	0	0
表在性異物	0	0	0	0	0	0
膣粘膜水疱形成	0	0	0	0	0	0
乾癬様皮膚炎	0	0	0	0	0	0
耳閉	0	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0
創合併症	0	0	0	0	0	0
体温上昇	0	0	0	0	0	0
股関節形成	0	0	0	0	0	0
腫瘍壊死	0	0	0	0	0	0
弛緩歯	0	0	0	0	0	0
軟骨症	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
乳房圧痛	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_p10_GO27831_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_p10_GO27831_SE を再掲］

(2) 発現率10%以上の有害事象の重症度別の要約（PCD4989g 試験）

表 2.7.4.7.1-2 発現率10%以上の有害事象の重症度別の要約（PCD4989g 試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481)		atezolizumab <=1 mg/kg q3w IV (N=9)		atezolizumab 3 mg/kg q3w IV (N=3)		atezolizumab 10 mg/kg q3w IV (N=36)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	466 (96.9%)	226 (47.0%)	9 (100.0%)	1 (11.1%)	3 (100.0%)	3 (100.0%)	35 (97.2%)	22 (61.1%)
疲労	180 (37.4%)	13 (2.7%)	7 (77.8%)	1 (11.1%)	3 (100.0%)	0	16 (44.4%)	1 (2.8%)
悪心	126 (26.2%)	5 (1.0%)	7 (77.8%)	0	2 (66.7%)	0	9 (25.0%)	0
食欲減退	125 (26.0%)	4 (0.8%)	3 (33.3%)	0	1 (33.3%)	0	9 (25.0%)	0
発熱	107 (22.2%)	2 (0.4%)	4 (44.4%)	0	3 (100.0%)	0	8 (22.2%)	1 (2.8%)
呼吸困難	103 (21.4%)	18 (3.7%)	4 (44.4%)	0	1 (33.3%)	0	12 (33.3%)	2 (5.6%)
咳嗽	103 (21.4%)	1 (0.2%)	3 (33.3%)	0	3 (100.0%)	0	10 (27.8%)	0
下痢	102 (21.2%)	1 (0.2%)	5 (55.6%)	0	0	0	16 (44.4%)	1 (2.8%)
便秘	102 (21.2%)	2 (0.4%)	2 (22.2%)	0	0	0	9 (25.0%)	0
貧血	97 (20.2%)	21 (4.4%)	1 (11.1%)	1 (11.1%)	0	0	7 (19.4%)	0
嘔吐	90 (18.7%)	3 (0.6%)	0	0	1 (33.3%)	0	6 (16.7%)	0
背部痛	80 (16.6%)	8 (1.7%)	1 (11.1%)	0	1 (33.3%)	0	7 (19.4%)	0
無力症	80 (16.6%)	8 (1.7%)	1 (11.1%)	0	0	0	2 (5.6%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
頭痛	79 (16.4%)	2 (0.4%)	3 (33.3%)	0	1 (33.3%)	0	13 (36.1%)	1 (2.8%)
関節痛	71 (14.8%)	1 (0.2%)	3 (33.3%)	0	1 (33.3%)	0	9 (25.0%)	1 (2.8%)
発疹	71 (14.8%)	0	1 (11.1%)	0	2 (66.7%)	0	8 (22.2%)	0
そう痒症	64 (13.3%)	0	2 (22.2%)	0	1 (33.3%)	0	9 (25.0%)	0
腹痛	60 (12.5%)	8 (1.7%)	3 (33.3%)	0	0	0	7 (19.4%)	0
不眠症	60 (12.5%)	1 (0.2%)	2 (22.2%)	0	1 (33.3%)	0	10 (27.8%)	0
末梢性浮腫	57 (11.9%)	0	1 (11.1%)	0	1 (33.3%)	0	8 (22.2%)	0
悪寒	55 (11.4%)	0	4 (44.4%)	0	3 (100.0%)	0	5 (13.9%)	0
尿路感染	54 (11.2%)	6 (1.2%)	1 (11.1%)	1 (11.1%)	0	0	4 (11.1%)	0
上気道感染	47 (9.8%)	0	3 (33.3%)	0	2 (66.7%)	0	6 (16.7%)	0
疼痛	44 (9.1%)	7 (1.5%)	4 (44.4%)	0	1 (33.3%)	0	3 (8.3%)	1 (2.8%)
浮動性めまい	44 (9.1%)	0	1 (11.1%)	0	1 (33.3%)	0	7 (19.4%)	0
不安	37 (7.7%)	0	2 (22.2%)	0	1 (33.3%)	0	6 (16.7%)	0
脱水	37 (7.7%)	9 (1.9%)	0	0	0	0	3 (8.3%)	0
四肢痛	36 (7.5%)	3 (0.6%)	2 (22.2%)	0	0	0	3 (8.3%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
皮膚乾燥	36 (7.5%)	0	1 (11.1%)	0	1 (33.3%)	0	2 (5.6%)	0
インフルエンザ様疾患	36 (7.5%)	1 (0.2%)	0	0	0	0	5 (13.9%)	0
筋肉痛	35 (7.3%)	0	2 (22.2%)	0	0	0	2 (5.6%)	0
上腹部痛	30 (6.2%)	2 (0.4%)	1 (11.1%)	0	0	0	4 (11.1%)	0
筋骨格痛	30 (6.2%)	1 (0.2%)	0	0	0	0	7 (19.4%)	0
寝汗	29 (6.0%)	0	2 (22.2%)	0	3 (100.0%)	0	3 (8.3%)	0
口腔咽頭痛	29 (6.0%)	0	1 (11.1%)	0	0	0	7 (19.4%)	0
鼻閉	28 (5.8%)	0	1 (11.1%)	0	2 (66.7%)	0	3 (8.3%)	0
湿性咳嗽	27 (5.6%)	0	1 (11.1%)	0	0	0	4 (11.1%)	0
胸痛	24 (5.0%)	1 (0.2%)	1 (11.1%)	0	1 (33.3%)	0	4 (11.1%)	0
口内乾燥	22 (4.6%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
嚥下障害	20 (4.2%)	5 (1.0%)	1 (11.1%)	0	0	0	0	0
高血糖	20 (4.2%)	7 (1.5%)	0	0	0	0	6 (16.7%)	1 (2.8%)
甲状腺機能低下症	20 (4.2%)	0	0	0	0	0	4 (11.1%)	0
味覚異常	19 (4.0%)	0	2 (22.2%)	0	0	0	2 (5.6%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
筋痙縮	19 (4.0%)	0	1 (11.1%)	0	0	0	2 (5.6%)	0
筋骨格系胸痛	18 (3.7%)	1 (0.2%)	1 (11.1%)	0	1 (33.3%)	0	3 (8.3%)	0
側腹部痛	18 (3.7%)	1 (0.2%)	1 (11.1%)	0	0	0	2 (5.6%)	1 (2.8%)
低マグネシウム血症	18 (3.7%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
末梢性ニューロパチー	17 (3.5%)	0	2 (22.2%)	0	0	0	0	0
労作性呼吸困難	17 (3.5%)	0	0	0	1 (33.3%)	0	4 (11.1%)	0
胃食道逆流性疾患	16 (3.3%)	0	2 (22.2%)	0	0	0	2 (5.6%)	0
紅斑	16 (3.3%)	0	0	0	1 (33.3%)	0	2 (5.6%)	0
頻尿	15 (3.1%)	0	2 (22.2%)	0	0	0	4 (11.1%)	0
血尿	15 (3.1%)	0	0	0	2 (66.7%)	0	3 (8.3%)	0
高血圧	14 (2.9%)	4 (0.8%)	0	0	1 (33.3%)	1 (33.3%)	1 (2.8%)	0
斑状丘疹状皮疹	14 (2.9%)	2 (0.4%)	0	0	0	0	4 (11.1%)	0
錯感覚	13 (2.7%)	0	0	0	0	0	4 (11.1%)	0
多汗症	12 (2.5%)	0	2 (22.2%)	0	0	0	1 (2.8%)	0
上気道咳症候群	12 (2.5%)	0	1 (11.1%)	0	0	0	4 (11.1%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
消化不良	11 (2.3%)	0	1 (11.1%)	0	0	0	2 (5.6%)	0
喘鳴	11 (2.3%)	1 (0.2%)	0	0	1 (33.3%)	0	3 (8.3%)	1 (2.8%)
気管支炎	10 (2.1%)	0	1 (11.1%)	0	1 (33.3%)	0	1 (2.8%)	0
ほてり	10 (2.1%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
口内炎	10 (2.1%)	0	1 (11.1%)	0	0	0	0	0
感覚鈍麻	9 (1.9%)	1 (0.2%)	1 (11.1%)	0	0	0	2 (5.6%)	0
胸部不快感	9 (1.9%)	0	1 (11.1%)	0	0	0	2 (5.6%)	0
頻脈	9 (1.9%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
夜間頻尿	9 (1.9%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
歯痛	9 (1.9%)	0	0	0	1 (33.3%)	0	0	0
回転性めまい	8 (1.7%)	0	0	0	1 (33.3%)	0	1 (2.8%)	0
副鼻腔うっ血	8 (1.7%)	0	0	0	0	0	4 (11.1%)	0
帯状疱疹	7 (1.5%)	0	1 (11.1%)	0	1 (33.3%)	0	0	0
心房細動	7 (1.5%)	3 (0.6%)	1 (11.1%)	0	0	0	1 (2.8%)	0
非心臓性胸痛	7 (1.5%)	0	1 (11.1%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
蛋白尿	7 (1.5%)	2 (0.4%)	0	0	1 (33.3%)	1 (33.3%)	1 (2.8%)	0
動悸	6 (1.2%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
敗血症	6 (1.2%)	4 (0.8%)	1 (11.1%)	0	0	0	0	0
口腔内痛	6 (1.2%)	0	1 (11.1%)	0	0	0	0	0
腫瘍出血	6 (1.2%)	0	0	0	1 (33.3%)	0	0	0
リンパ節症	5 (1.0%)	0	0	0	1 (33.3%)	0	0	0
体重増加	5 (1.0%)	0	0	0	1 (33.3%)	0	0	0
真菌感染	4 (0.8%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
脂漏性角化症	4 (0.8%)	0	1 (11.1%)	0	0	0	0	0
尋常性白斑	4 (0.8%)	0	0	0	1 (33.3%)	0	1 (2.8%)	0
乳房痛	4 (0.8%)	0	0	0	1 (33.3%)	0	0	0
肉離れ	4 (0.8%)	0	0	0	1 (33.3%)	0	0	0
高尿酸血症	4 (0.8%)	1 (0.2%)	0	0	1 (33.3%)	0	0	0
流涙増加	3 (0.6%)	0	2 (22.2%)	0	1 (33.3%)	0	0	0
眼そう痒症	3 (0.6%)	0	2 (22.2%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
耳感染	3 (0.6%)	0	1 (11.1%)	0	0	0	1 (2.8%)	0
レッチング	3 (0.6%)	0	1 (11.1%)	0	0	0	0	0
食道炎	3 (0.6%)	0	1 (11.1%)	0	0	0	0	0
限局性感染	3 (0.6%)	0	0	0	1 (33.3%)	0	1 (2.8%)	0
過角化	3 (0.6%)	0	0	0	1 (33.3%)	0	0	0
腹部ヘルニア	3 (0.6%)	0	0	0	1 (33.3%)	0	0	0
口の感覚鈍麻	2 (0.4%)	0	1 (11.1%)	0	0	0	0	0
日光角化症	2 (0.4%)	0	1 (11.1%)	0	0	0	0	0
ヘルニア痛	2 (0.4%)	0	1 (11.1%)	0	0	0	0	0
温度変化不耐症	2 (0.4%)	0	0	0	1 (33.3%)	0	0	0
腫瘍の潰瘍形成	2 (0.4%)	0	0	0	1 (33.3%)	0	0	0
出血時間延長	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
小水疱性皮疹	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
深径覚の変化	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
潰瘍性角膜炎	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
尿道閉塞	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
皮膚乳頭腫	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
表在性異物	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
睫毛眉毛脱落症	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
膣粘膜水疱形成	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
全身性皮疹	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
乾癬様皮膚炎	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
股関節形成	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
耳閉	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
腫瘍壊死	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
創合併症	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
体温上昇	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
弛緩歯	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
軟骨症	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) Any Grade No. (%)	atezolizumab Total (N=481) >= Grade3 No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Any Grade No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) >= Grade3 No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Any Grade No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) >= Grade3 No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Any Grade No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) >= Grade3 No. (%)
乳房圧痛	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
Total number of patients with at least one adverse event	231 (97.9%)	119 (50.4%)	145 (99.3%)	61 (41.8%)	43 (84.3%)	20 (39.2%)
疲労	88 (37.3%)	4 (1.7%)	52 (35.6%)	6 (4.1%)	14 (27.5%)	1 (2.0%)
悪心	51 (21.6%)	2 (0.8%)	44 (30.1%)	2 (1.4%)	13 (25.5%)	1 (2.0%)
食欲減退	57 (24.2%)	4 (1.7%)	43 (29.5%)	0	12 (23.5%)	0
発熱	53 (22.5%)	0	32 (21.9%)	0	7 (13.7%)	1 (2.0%)
呼吸困難	31 (13.1%)	4 (1.7%)	45 (30.8%)	9 (6.2%)	10 (19.6%)	3 (5.9%)
咳嗽	51 (21.6%)	1 (0.4%)	31 (21.2%)	0	5 (9.8%)	0
下痢	43 (18.2%)	0	30 (20.5%)	0	8 (15.7%)	0
便秘	50 (21.2%)	1 (0.4%)	35 (24.0%)	1 (0.7%)	6 (11.8%)	0
貧血	53 (22.5%)	10 (4.2%)	28 (19.2%)	7 (4.8%)	8 (15.7%)	3 (5.9%)
嘔吐	42 (17.8%)	1 (0.4%)	33 (22.6%)	1 (0.7%)	8 (15.7%)	1 (2.0%)
背部痛	41 (17.4%)	7 (3.0%)	29 (19.9%)	1 (0.7%)	1 (2.0%)	0
無力症	44 (18.6%)	3 (1.3%)	27 (18.5%)	5 (3.4%)	6 (11.8%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
頭痛	31 (13.1%)	1 (0.4%)	25 (17.1%)	0	6 (11.8%)	0
関節痛	30 (12.7%)	0	26 (17.8%)	0	2 (3.9%)	0
発疹	33 (14.0%)	0	25 (17.1%)	0	2 (3.9%)	0
そう痒症	31 (13.1%)	0	16 (11.0%)	0	5 (9.8%)	0
腹痛	31 (13.1%)	6 (2.5%)	16 (11.0%)	2 (1.4%)	3 (5.9%)	0
不眠症	25 (10.6%)	1 (0.4%)	20 (13.7%)	0	2 (3.9%)	0
末梢性浮腫	24 (10.2%)	0	17 (11.6%)	0	6 (11.8%)	0
悪寒	24 (10.2%)	0	17 (11.6%)	0	2 (3.9%)	0
尿路感染	31 (13.1%)	4 (1.7%)	15 (10.3%)	1 (0.7%)	3 (5.9%)	0
上気道感染	14 (5.9%)	0	21 (14.4%)	0	1 (2.0%)	0
疼痛	21 (8.9%)	4 (1.7%)	13 (8.9%)	2 (1.4%)	2 (3.9%)	0
浮動性めまい	18 (7.6%)	0	15 (10.3%)	0	2 (3.9%)	0
不安	15 (6.4%)	0	11 (7.5%)	0	2 (3.9%)	0
脱水	16 (6.8%)	4 (1.7%)	15 (10.3%)	5 (3.4%)	3 (5.9%)	0
四肢痛	17 (7.2%)	2 (0.8%)	12 (8.2%)	0	2 (3.9%)	1 (2.0%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
皮膚乾燥	21 (8.9%)	0	9 (6.2%)	0	2 (3.9%)	0
インフルエンザ様疾患	12 (5.1%)	1 (0.4%)	17 (11.6%)	0	2 (3.9%)	0
筋肉痛	19 (8.1%)	0	11 (7.5%)	0	1 (2.0%)	0
上腹部痛	12 (5.1%)	2 (0.8%)	12 (8.2%)	0	1 (2.0%)	0
筋骨格痛	7 (3.0%)	1 (0.4%)	15 (10.3%)	0	1 (2.0%)	0
寝汗	12 (5.1%)	0	8 (5.5%)	0	1 (2.0%)	0
口腔咽頭痛	10 (4.2%)	0	11 (7.5%)	0	0	0
鼻閉	11 (4.7%)	0	11 (7.5%)	0	0	0
湿性咳嗽	9 (3.8%)	0	13 (8.9%)	0	0	0
胸痛	6 (2.5%)	0	8 (5.5%)	0	4 (7.8%)	1 (2.0%)
口内乾燥	8 (3.4%)	0	10 (6.8%)	0	2 (3.9%)	0
嚥下障害	13 (5.5%)	5 (2.1%)	6 (4.1%)	0	0	0
高血糖	8 (3.4%)	4 (1.7%)	6 (4.1%)	2 (1.4%)	0	0
甲状腺機能低下症	9 (3.8%)	0	7 (4.8%)	0	0	0
味覚異常	9 (3.8%)	0	6 (4.1%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
筋痙縮	8 (3.4%)	0	7 (4.8%)	0	1 (2.0%)	0
筋骨格系胸痛	7 (3.0%)	1 (0.4%)	6 (4.1%)	0	0	0
側腹部痛	8 (3.4%)	0	7 (4.8%)	0	0	0
低マグネシウム血症	9 (3.8%)	0	5 (3.4%)	0	2 (3.9%)	0
末梢性ニューロパチー	10 (4.2%)	0	3 (2.1%)	0	2 (3.9%)	0
労作性呼吸困難	6 (2.5%)	0	3 (2.1%)	0	3 (5.9%)	0
胃食道逆流性疾患	4 (1.7%)	0	8 (5.5%)	0	0	0
紅斑	6 (2.5%)	0	6 (4.1%)	0	1 (2.0%)	0
頻尿	6 (2.5%)	0	3 (2.1%)	0	0	0
血尿	7 (3.0%)	0	2 (1.4%)	0	1 (2.0%)	0
高血圧	4 (1.7%)	0	5 (3.4%)	2 (1.4%)	3 (5.9%)	1 (2.0%)
斑状丘疹状皮疹	7 (3.0%)	1 (0.4%)	3 (2.1%)	1 (0.7%)	0	0
錯感覚	5 (2.1%)	0	2 (1.4%)	0	2 (3.9%)	0
多汗症	3 (1.3%)	0	4 (2.7%)	0	2 (3.9%)	0
上気道咳症候群	4 (1.7%)	0	3 (2.1%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
消化不良	5 (2.1%)	0	3 (2.1%)	0	0	0
喘鳴	3 (1.3%)	0	4 (2.7%)	0	0	0
気管支炎	6 (2.5%)	0	1 (0.7%)	0	0	0
ほてり	4 (1.7%)	0	4 (2.7%)	0	0	0
口内炎	6 (2.5%)	0	3 (2.1%)	0	0	0
感覚鈍麻	3 (1.3%)	0	3 (2.1%)	1 (0.7%)	0	0
胸部不快感	3 (1.3%)	0	3 (2.1%)	0	0	0
頻脈	4 (1.7%)	0	2 (1.4%)	0	1 (2.0%)	0
夜間頻尿	4 (1.7%)	0	2 (1.4%)	0	1 (2.0%)	0
歯痛	2 (0.8%)	0	5 (3.4%)	0	1 (2.0%)	0
回転性めまい	4 (1.7%)	0	2 (1.4%)	0	0	0
副鼻腔うっ血	3 (1.3%)	0	1 (0.7%)	0	0	0
帯状疱疹	4 (1.7%)	0	1 (0.7%)	0	0	0
心房細動	3 (1.3%)	2 (0.8%)	2 (1.4%)	1 (0.7%)	0	0
非心臓性胸痛	1 (0.4%)	0	5 (3.4%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
蛋白尿	3 (1.3%)	0	2 (1.4%)	1 (0.7%)	0	0
動悸	1 (0.4%)	0	3 (2.1%)	0	0	0
敗血症	5 (2.1%)	4 (1.7%)	0	0	0	0
口腔内痛	3 (1.3%)	0	2 (1.4%)	0	0	0
腫瘍出血	4 (1.7%)	0	0	0	1 (2.0%)	0
リンパ節症	1 (0.4%)	0	3 (2.1%)	0	0	0
体重増加	1 (0.4%)	0	3 (2.1%)	0	0	0
真菌感染	1 (0.4%)	0	1 (0.7%)	0	0	0
脂漏性角化症	3 (1.3%)	0	0	0	0	0
尋常性白斑	2 (0.8%)	0	0	0	0	0
乳房痛	1 (0.4%)	0	2 (1.4%)	0	0	0
肉離れ	1 (0.4%)	0	1 (0.7%)	0	1 (2.0%)	0
高尿酸血症	0	0	3 (2.1%)	1 (0.7%)	0	0
流涙増加	0	0	0	0	0	0
眼そう痒症	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
耳感染	1 (0.4%)	0	0	0	0	0
レッチング	0	0	2 (1.4%)	0	0	0
食道炎	0	0	2 (1.4%)	0	0	0
限局性感染	1 (0.4%)	0	0	0	0	0
過角化	1 (0.4%)	0	1 (0.7%)	0	0	0
腹部ヘルニア	0	0	1 (0.7%)	0	1 (2.0%)	0
口の感覚鈍麻	1 (0.4%)	0	0	0	0	0
日光角化症	1 (0.4%)	0	0	0	0	0
ヘルニア痛	0	0	1 (0.7%)	0	0	0
温度変化不耐症	1 (0.4%)	0	0	0	0	0
腫瘍の潰瘍形成	1 (0.4%)	0	0	0	0	0
出血時間延長	0	0	0	0	0	0
小水疱性皮疹	0	0	0	0	0	0
深径覚の変化	0	0	0	0	0	0
潰瘍性角膜炎	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
尿道閉塞	0	0	0	0	0	0
皮膚乳頭腫	0	0	0	0	0	0
表在性異物	0	0	0	0	0	0
睫毛眉毛脱落症	0	0	0	0	0	0
膣粘膜水疱形成	0	0	0	0	0	0
全身性皮疹	0	0	0	0	0	0
乾癬様皮膚炎	0	0	0	0	0	0
股関節形成	0	0	0	0	0	0
耳閉	0	0	0	0	0	0
腫瘍壊死	0	0	0	0	0	0
創合併症	0	0	0	0	0	0
体温上昇	0	0	0	0	0	0
弛緩歯	0	0	0	0	0	0
軟骨症	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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Adverse Events with an Incidence Rate at Least 10% by Intensity (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) Any Grade No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) >= Grade3 No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Any Grade No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) >= Grade3 No. (%)	atezolizumab 1200 mg q3w IV (N=51) Any Grade No. (%)	atezolizumab 1200 mg q3w IV (N=51) >= Grade3 No. (%)
乳房圧痛	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_g3_p10.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_g3_p10_GO27831_SE.out
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［5.3.5.3-1 ae_g3_p10_GO27831_SE を再掲］

2.7.4.7.2 重篤な有害事象

(1) 重篤な有害事象の要約（OAK 試験）

表 2.7.4.7.2-1 重篤な有害事象の要約（OAK 試験）

Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
Total number of patients with at least one adverse event	194 (31.9%)	59 (9.7%)	181 (31.3%)	102 (17.6%)
肺炎	20 (3.3%)	2 (0.3%)	31 (5.4%)	10 (1.7%)
呼吸困難	12 (2.0%)	1 (0.2%)	8 (1.4%)	1 (0.2%)
胸水	12 (2.0%)	1 (0.2%)	6 (1.0%)	3 (0.5%)
発熱	9 (1.5%)	3 (0.5%)	8 (1.4%)	5 (0.9%)
肺塞栓症	9 (1.5%)	0	2 (0.3%)	0
気道感染	8 (1.3%)	1 (0.2%)	4 (0.7%)	1 (0.2%)
貧血	5 (0.8%)	0	7 (1.2%)	4 (0.7%)
喀血	5 (0.8%)	0	5 (0.9%)	0
敗血症	5 (0.8%)	1 (0.2%)	2 (0.3%)	0
肺臓炎	5 (0.8%)	5 (0.8%)	1 (0.2%)	1 (0.2%)
心嚢液貯留	4 (0.7%)	1 (0.2%)	1 (0.2%)	0
骨痛	4 (0.7%)	0	0	0
疲労	3 (0.5%)	1 (0.2%)	4 (0.7%)	1 (0.2%)
下気道感染	3 (0.5%)	0	3 (0.5%)	2 (0.3%)
気胸	3 (0.5%)	1 (0.2%)	2 (0.3%)	0
低酸素症	3 (0.5%)	1 (0.2%)	2 (0.3%)	0
呼吸不全	3 (0.5%)	0	2 (0.3%)	1 (0.2%)
背部痛	3 (0.5%)	0	2 (0.3%)	0
上大静脈症候群	3 (0.5%)	1 (0.2%)	1 (0.2%)	0
低血圧	3 (0.5%)	0	1 (0.2%)	0
過敏症	3 (0.5%)	3 (0.5%)	0	0
髄膜炎	3 (0.5%)	3 (0.5%)	0	0
高血糖	3 (0.5%)	1 (0.2%)	0	0
股関節部骨折	3 (0.5%)	0	0	0
肺感染	2 (0.3%)	0	3 (0.5%)	3 (0.5%)
慢性閉塞性肺疾患	2 (0.3%)	0	3 (0.5%)	0
悪心	2 (0.3%)	1 (0.2%)	1 (0.2%)	0
全身健康状態低下	2 (0.3%)	0	1 (0.2%)	1 (0.2%)
胸痛	2 (0.3%)	0	1 (0.2%)	0
痙攣発作	2 (0.3%)	0	1 (0.2%)	0
ギラン・バレー症候群	2 (0.3%)	2 (0.3%)	0	0
肝炎	2 (0.3%)	2 (0.3%)	0	0
心タンポナーデ	2 (0.3%)	1 (0.2%)	0	0
末梢性浮腫	2 (0.3%)	1 (0.2%)	0	0
咽頭炎	2 (0.3%)	0	0	0
下腹部痛	2 (0.3%)	0	0	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
関節痛	2 (0.3%)	0	0	0
筋骨格系胸痛	2 (0.3%)	0	0	0
誤嚥性肺炎	2 (0.3%)	0	0	0
心筋梗塞	2 (0.3%)	0	0	0
脳血管発作	2 (0.3%)	0	0	0
肺敗血症	2 (0.3%)	0	0	0
下痢	1 (0.2%)	0	7 (1.2%)	6 (1.0%)
嘔吐	1 (0.2%)	0	5 (0.9%)	3 (0.5%)
腹痛	1 (0.2%)	0	4 (0.7%)	1 (0.2%)
脱水	1 (0.2%)	0	3 (0.5%)	3 (0.5%)
急性腎障害	1 (0.2%)	0	3 (0.5%)	2 (0.3%)
失神	1 (0.2%)	0	3 (0.5%)	2 (0.3%)
無力症	1 (0.2%)	0	3 (0.5%)	2 (0.3%)
心房細動	1 (0.2%)	0	3 (0.5%)	1 (0.2%)
大腸炎	1 (0.2%)	1 (0.2%)	2 (0.3%)	2 (0.3%)
錯乱状態	1 (0.2%)	1 (0.2%)	2 (0.3%)	0
上腕骨骨折	1 (0.2%)	0	2 (0.3%)	0
深部静脈血栓症	1 (0.2%)	0	2 (0.3%)	0
突然死	1 (0.2%)	0	2 (0.3%)	0
肺出血	1 (0.2%)	0	2 (0.3%)	0
上腹部痛	1 (0.2%)	1 (0.2%)	1 (0.2%)	0
低ナトリウム血症	1 (0.2%)	1 (0.2%)	1 (0.2%)	0
頻脈	1 (0.2%)	1 (0.2%)	1 (0.2%)	0
浮動性めまい	1 (0.2%)	1 (0.2%)	1 (0.2%)	0
筋骨格痛	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
敗血症性ショック	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
肺水腫	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
嚥下障害	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
インフルエンザ	1 (0.2%)	0	1 (0.2%)	0
亜イレウス	1 (0.2%)	0	1 (0.2%)	0
胃腸炎	1 (0.2%)	0	1 (0.2%)	0
医療機器関連感染	1 (0.2%)	0	1 (0.2%)	0
急性胆嚢炎	1 (0.2%)	0	1 (0.2%)	0
小腸閉塞	1 (0.2%)	0	1 (0.2%)	0
転倒	1 (0.2%)	0	1 (0.2%)	0
蜂巣炎	1 (0.2%)	0	1 (0.2%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.2%)	1 (0.2%)	0	0
アラニンアミノトランスフェラーゼ増加	1 (0.2%)	1 (0.2%)	0	0
インフルエンザ様疾患	1 (0.2%)	1 (0.2%)	0	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
ニューモシスチス・イロベチイ肺炎	1 (0.2%)	1 (0.2%)	0	0
ヘノッホ・シェーンライン紫斑病性腎炎	1 (0.2%)	1 (0.2%)	0	0
横紋筋融解症	1 (0.2%)	1 (0.2%)	0	0
咳嗽	1 (0.2%)	1 (0.2%)	0	0
感染性腸炎	1 (0.2%)	1 (0.2%)	0	0
間質性肺疾患	1 (0.2%)	1 (0.2%)	0	0
器質化肺炎	1 (0.2%)	1 (0.2%)	0	0
急性肝炎	1 (0.2%)	1 (0.2%)	0	0
急性呼吸窮迫症候群	1 (0.2%)	1 (0.2%)	0	0
胸膜瘻	1 (0.2%)	1 (0.2%)	0	0
限局性浮腫	1 (0.2%)	1 (0.2%)	0	0
誤嚥	1 (0.2%)	1 (0.2%)	0	0
細菌性上気道感染	1 (0.2%)	1 (0.2%)	0	0
耳下腺炎	1 (0.2%)	1 (0.2%)	0	0
全身性そう痒症	1 (0.2%)	1 (0.2%)	0	0
全身性炎症反応症候群	1 (0.2%)	1 (0.2%)	0	0
注入に伴う反応	1 (0.2%)	1 (0.2%)	0	0
腸閉塞	1 (0.2%)	1 (0.2%)	0	0
認知障害	1 (0.2%)	1 (0.2%)	0	0
脳炎	1 (0.2%)	1 (0.2%)	0	0
肺気腫	1 (0.2%)	1 (0.2%)	0	0
発作性頻脈	1 (0.2%)	1 (0.2%)	0	0
発疹	1 (0.2%)	1 (0.2%)	0	0
頻呼吸	1 (0.2%)	1 (0.2%)	0	0
網膜症	1 (0.2%)	1 (0.2%)	0	0
薬物性肝障害	1 (0.2%)	1 (0.2%)	0	0
類天疱瘡	1 (0.2%)	1 (0.2%)	0	0
扁桃炎	1 (0.2%)	1 (0.2%)	0	0
そう痒症	1 (0.2%)	0	0	0
びらん性胃炎	1 (0.2%)	0	0	0
クロストリジウム・ディフィシレ感染	1 (0.2%)	0	0	0
メレナ	1 (0.2%)	0	0	0
悪性新生物	1 (0.2%)	0	0	0
意識レベルの低下	1 (0.2%)	0	0	0
感染による慢性閉塞性気道疾患の増悪	1 (0.2%)	0	0	0
感染性胸水	1 (0.2%)	0	0	0
感染性皮膚潰瘍	1 (0.2%)	0	0	0
気管支痙攣	1 (0.2%)	0	0	0
偽膜性大腸炎	1 (0.2%)	0	0	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
急性呼吸不全	1 (0.2%)	0	0	0
胸部不快感	1 (0.2%)	0	0	0
胸膜痛	1 (0.2%)	0	0	0
頚部痛	1 (0.2%)	0	0	0
血栓症	1 (0.2%)	0	0	0
血尿	1 (0.2%)	0	0	0
高カルシウム血症	1 (0.2%)	0	0	0
腰椎骨折	1 (0.2%)	0	0	0
左室機能不全	1 (0.2%)	0	0	0
細菌性肺炎	1 (0.2%)	0	0	0
四肢痛	1 (0.2%)	0	0	0
死亡	1 (0.2%)	0	0	0
失語症	1 (0.2%)	0	0	0
食道閉塞症	1 (0.2%)	0	0	0
心筋虚血	1 (0.2%)	0	0	0
心膜炎	1 (0.2%)	0	0	0
神経痛	1 (0.2%)	0	0	0
腎不全	1 (0.2%)	0	0	0
成長障害	1 (0.2%)	0	0	0
脊椎圧迫骨折	1 (0.2%)	0	0	0
前立腺癌	1 (0.2%)	0	0	0
全身性強直性間代性発作	1 (0.2%)	0	0	0
大脳動脈塞栓症	1 (0.2%)	0	0	0
第３度熱傷	1 (0.2%)	0	0	0
胆汁うっ滞性黄疸	1 (0.2%)	0	0	0
尿路性敗血症	1 (0.2%)	0	0	0
熱性感染症	1 (0.2%)	0	0	0
脳症	1 (0.2%)	0	0	0
白質脳症	1 (0.2%)	0	0	0
不全片麻痺	1 (0.2%)	0	0	0
変色便	1 (0.2%)	0	0	0
便秘	1 (0.2%)	0	0	0
末梢性感覚ニューロパチー	1 (0.2%)	0	0	0
無気肺	1 (0.2%)	0	0	0
橈骨骨折	1 (0.2%)	0	0	0
膵炎	1 (0.2%)	0	0	0
発熱性好中球減少症	0	0	37 (6.4%)	36 (6.2%)
好中球数減少	0	0	5 (0.9%)	5 (0.9%)
感染	0	0	4 (0.7%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE.out
07DEC2016 17:13

Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
好中球減少症	0	0	3 (0.5%)	3 (0.5%)
好中球減少性敗血症	0	0	2 (0.3%)	2 (0.3%)
尿路感染	0	0	2 (0.3%)	2 (0.3%)
急性心筋梗塞	0	0	2 (0.3%)	1 (0.2%)
上室性頻脈	0	0	2 (0.3%)	1 (0.2%)
気管支炎	0	0	2 (0.3%)	0
憩室炎	0	0	2 (0.3%)	0
筋肉痛	0	0	1 (0.2%)	1 (0.2%)
口内炎	0	0	1 (0.2%)	1 (0.2%)
細菌性敗血症	0	0	1 (0.2%)	1 (0.2%)
十二指腸穿孔	0	0	1 (0.2%)	1 (0.2%)
消化管感染	0	0	1 (0.2%)	1 (0.2%)
上部消化管出血	0	0	1 (0.2%)	1 (0.2%)
食道静脈瘤出血	0	0	1 (0.2%)	1 (0.2%)
食欲減退	0	0	1 (0.2%)	1 (0.2%)
心停止	0	0	1 (0.2%)	1 (0.2%)
真菌性消化管感染	0	0	1 (0.2%)	1 (0.2%)
全身性浮腫	0	0	1 (0.2%)	1 (0.2%)
爪囲炎	0	0	1 (0.2%)	1 (0.2%)
白血球数減少	0	0	1 (0.2%)	1 (0.2%)
皮膚感染	0	0	1 (0.2%)	1 (0.2%)
腹部敗血症	0	0	1 (0.2%)	1 (0.2%)
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.2%)	0
ストレス心筋症	0	0	1 (0.2%)	0
下部消化管出血	0	0	1 (0.2%)	0
過量投与	0	0	1 (0.2%)	0
癌疼痛	0	0	1 (0.2%)	0
気管支閉塞	0	0	1 (0.2%)	0
急性肝不全	0	0	1 (0.2%)	0
急性腎前性腎不全	0	0	1 (0.2%)	0
狭心症	0	0	1 (0.2%)	0
胸膜感染	0	0	1 (0.2%)	0
結腸癌	0	0	1 (0.2%)	0
血腫	0	0	1 (0.2%)	0
血便排泄	0	0	1 (0.2%)	0
呼吸窮迫	0	0	1 (0.2%)	0
坐骨神経痛	0	0	1 (0.2%)	0
自然気胸	0	0	1 (0.2%)	0
処置後血尿	0	0	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE.out
07DEC2016 17:13

Serious Adverse Events by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
上肢骨折	0	0	1 (0.2%)	0
食道瘻	0	0	1 (0.2%)	0
心房粗動	0	0	1 (0.2%)	0
胆嚢炎	0	0	1 (0.2%)	0
虫垂炎	0	0	1 (0.2%)	0
低カリウム血症	0	0	1 (0.2%)	0
低血糖	0	0	1 (0.2%)	0
脳血栓症	0	0	1 (0.2%)	0
白血球増加症	0	0	1 (0.2%)	0
不整脈	0	0	1 (0.2%)	0
不明確な障害	0	0	1 (0.2%)	0
疼痛	0	0	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_ser_GO28915_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。

［5.3.5.1-3 ae_rae_ser_GO28915_SE を再掲］

(2) 重篤な有害事象の要約（POPLAR 試験）

表 2.7.4.7.2-2 重篤な有害事象の要約（POPLAR 試験）

Serious Adverse Events by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

	atezolizumab 1200 mg q3w IV (N=142)		Docetaxel (N=135)	
MedDRA Preferred Term	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)
Total number of patients with at least one adverse event	50 (35.2%)	12 (8.5%)	46 (34.1%)	23 (17.0%)
肺炎	8 (5.6%)	3 (2.1%)	3 (2.2%)	2 (1.5%)
呼吸困難	7 (4.9%)	0	1 (0.7%)	1 (0.7%)
胸水	4 (2.8%)	0	0	0
発熱	3 (2.1%)	3 (2.1%)	1 (0.7%)	1 (0.7%)
肺塞栓症	2 (1.4%)	0	6 (4.4%)	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.4%)	2 (1.4%)	0	0
発疹	2 (1.4%)	2 (1.4%)	0	0
低酸素症	2 (1.4%)	1 (0.7%)	0	0
気胸	2 (1.4%)	0	0	0
心タンポナーデ	2 (1.4%)	0	0	0
嚥下障害	2 (1.4%)	0	0	0
喀血	1 (0.7%)	0	3 (2.2%)	0
下痢	1 (0.7%)	1 (0.7%)	1 (0.7%)	0
急性腎不全	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
アラニンアミノトランスフェラーゼ増加	1 (0.7%)	1 (0.7%)	0	0
インフルエンザ様疾患	1 (0.7%)	1 (0.7%)	0	0
悪心	1 (0.7%)	1 (0.7%)	0	0
胸膜炎	1 (0.7%)	1 (0.7%)	0	0
心不全	1 (0.7%)	1 (0.7%)	0	0
静脈狭窄	1 (0.7%)	1 (0.7%)	0	0
大腸炎	1 (0.7%)	1 (0.7%)	0	0
肺臓炎	1 (0.7%)	1 (0.7%)	0	0
Ｈ１Ｎ１インフルエンザ	1 (0.7%)	0	0	0
リンパ節症	1 (0.7%)	0	0	0
医療機器位置異常	1 (0.7%)	0	0	0
咽頭炎	1 (0.7%)	0	0	0
下気道感染	1 (0.7%)	0	0	0
感染性胸水	1 (0.7%)	0	0	0
関節痛	1 (0.7%)	0	0	0
気管支炎	1 (0.7%)	0	0	0
気管閉塞	1 (0.7%)	0	0	0
気道感染	1 (0.7%)	0	0	0
筋肉痛	1 (0.7%)	0	0	0
血栓性痔核	1 (0.7%)	0	0	0
骨髄炎	1 (0.7%)	0	0	0
塞栓症	1 (0.7%)	0	0	0
細菌性気道感染	1 (0.7%)	0	0	0
錯乱状態	1 (0.7%)	0	0	0
小腸閉塞	1 (0.7%)	0	0	0
上大静脈症候群	1 (0.7%)	0	0	0
大腸穿孔	1 (0.7%)	0	0	0

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_ser_GO28753_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

MedDRA Preferred Term	atezolizumab 1200 mg q3w IV (N=142) AE No. (%)	atezolizumab 1200 mg q3w IV (N=142) Related AE No. (%)	Docetaxel (N=135) AE No. (%)	Docetaxel (N=135) Related AE No. (%)
大葉性肺炎	1 (0.7%)	0	0	0
潰瘍性出血	1 (0.7%)	0	0	0
肺感染	1 (0.7%)	0	0	0
変形性脊椎症	1 (0.7%)	0	0	0
蜂巣炎	1 (0.7%)	0	0	0
末梢性感覚ニューロパチー	1 (0.7%)	0	0	0
末梢性浮腫	1 (0.7%)	0	0	0
疼痛	1 (0.7%)	0	0	0
発熱性好中球減少症	0	0	7 (5.2%)	7 (5.2%)
敗血症	0	0	3 (2.2%)	2 (1.5%)
好中球減少症	0	0	2 (1.5%)	2 (1.5%)
死亡	0	0	2 (1.5%)	1 (0.7%)
慢性閉塞性肺疾患	0	0	2 (1.5%)	0
急性呼吸窮迫症候群	0	0	1 (0.7%)	1 (0.7%)
好中球数減少	0	0	1 (0.7%)	1 (0.7%)
錯感覚	0	0	1 (0.7%)	1 (0.7%)
腫瘍熱	0	0	1 (0.7%)	1 (0.7%)
脱水	0	0	1 (0.7%)	1 (0.7%)
疲労	0	0	1 (0.7%)	1 (0.7%)
貧血	0	0	1 (0.7%)	1 (0.7%)
便秘	0	0	1 (0.7%)	1 (0.7%)
無力症	0	0	1 (0.7%)	1 (0.7%)
２型糖尿病	0	0	1 (0.7%)	0
感覚鈍麻	0	0	1 (0.7%)	0
急性心筋梗塞	0	0	1 (0.7%)	0
高血糖	0	0	1 (0.7%)	0
上部消化管出血	0	0	1 (0.7%)	0
心嚢液貯留	0	0	1 (0.7%)	0
心房細動	0	0	1 (0.7%)	0
脊柱管狭窄症	0	0	1 (0.7%)	0
転移部痛	0	0	1 (0.7%)	0
洞性頻脈	0	0	1 (0.7%)	0
尿量減少	0	0	1 (0.7%)	0
背部痛	0	0	1 (0.7%)	0
腹痛	0	0	1 (0.7%)	0
放射線性肺臓炎	0	0	1 (0.7%)	0
末梢血管塞栓症	0	0	1 (0.7%)	0
末梢性虚血	0	0	1 (0.7%)	0
譫妄	0	0	1 (0.7%)	0

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_ser_GO28753_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。

［5.3.5.3-1 ae_rae_ser_GO28753_SE を再掲］

(3) 重篤な有害事象の要約（BIRCH 試験）

表 2.7.4.7.2-3 重篤な有害事象の要約（BIRCH 試験）

Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
Total number of patients with at least one adverse event	233 (35.4%)	60 (9.1%)	43 (30.9%)	11 (7.9%)	96 (36.0%)	27 (10.1%)	94 (37.2%)	22 (8.7%)
肺炎	22 (3.3%)	1 (0.2%)	3 (2.2%)	0	7 (2.6%)	0	12 (4.7%)	1 (0.4%)
呼吸困難	18 (2.7%)	1 (0.2%)	3 (2.2%)	0	4 (1.5%)	1 (0.4%)	11 (4.3%)	0
肺臓炎	15 (2.3%)	10 (1.5%)	2 (1.4%)	2 (1.4%)	8 (3.0%)	5 (1.9%)	5 (2.0%)	3 (1.2%)
発熱	15 (2.3%)	5 (0.8%)	0	0	8 (3.0%)	2 (0.7%)	7 (2.8%)	3 (1.2%)
嘔吐	7 (1.1%)	1 (0.2%)	0	0	4 (1.5%)	1 (0.4%)	3 (1.2%)	0
悪心	6 (0.9%)	4 (0.6%)	1 (0.7%)	1 (0.7%)	3 (1.1%)	2 (0.7%)	2 (0.8%)	1 (0.4%)
高カルシウム血症	6 (0.9%)	2 (0.3%)	0	0	5 (1.9%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
喀血	6 (0.9%)	0	0	0	2 (0.7%)	0	4 (1.6%)	0
肺塞栓症	5 (0.8%)	1 (0.2%)	2 (1.4%)	1 (0.7%)	2 (0.7%)	0	1 (0.4%)	0
下痢	5 (0.8%)	4 (0.6%)	2 (1.4%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.8%)	2 (0.8%)
胸水	5 (0.8%)	0	2 (1.4%)	0	1 (0.4%)	0	2 (0.8%)	0
背部痛	5 (0.8%)	0	2 (1.4%)	0	1 (0.4%)	0	2 (0.8%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
慢性閉塞性肺疾患	5 (0.8%)	0	1 (0.7%)	0	2 (0.7%)	0	2 (0.8%)	0
肺感染	4 (0.6%)	0	1 (0.7%)	0	3 (1.1%)	0	0	0
呼吸不全	4 (0.6%)	0	1 (0.7%)	0	2 (0.7%)	0	1 (0.4%)	0
尿路感染	4 (0.6%)	2 (0.3%)	1 (0.7%)	1 (0.7%)	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
無力症	4 (0.6%)	0	1 (0.7%)	0	1 (0.4%)	0	2 (0.8%)	0
胸痛	4 (0.6%)	0	0	0	2 (0.7%)	0	2 (0.8%)	0
脳血管発作	4 (0.6%)	0	0	0	1 (0.4%)	0	3 (1.2%)	0
気管支炎	3 (0.5%)	0	2 (1.4%)	0	1 (0.4%)	0	0	0
心タンポナーデ	3 (0.5%)	1 (0.2%)	1 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	0
大腸炎	3 (0.5%)	3 (0.5%)	1 (0.7%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
胆嚢炎	3 (0.5%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	2 (0.8%)	0
倦怠感	3 (0.5%)	1 (0.2%)	0	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
感染	3 (0.5%)	1 (0.2%)	0	0	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
誤嚥性肺炎	3 (0.5%)	1 (0.2%)	0	0	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
急性腎不全	3 (0.5%)	0	0	0	1 (0.4%)	0	2 (0.8%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
全身健康状態低下	3 (0.5%)	0	0	0	1 (0.4%)	0	2 (0.8%)	0
腹痛	3 (0.5%)	0	0	0	1 (0.4%)	0	2 (0.8%)	0
貧血	3 (0.5%)	2 (0.3%)	0	0	0	0	3 (1.2%)	2 (0.8%)
副腎機能不全	2 (0.3%)	1 (0.2%)	1 (0.7%)	0	1 (0.4%)	1 (0.4%)	0	0
深部静脈血栓症	2 (0.3%)	0	1 (0.7%)	0	1 (0.4%)	0	0	0
便秘	2 (0.3%)	0	1 (0.7%)	0	1 (0.4%)	0	0	0
上気道感染	2 (0.3%)	0	1 (0.7%)	0	0	0	1 (0.4%)	0
注入に伴う反応	2 (0.3%)	2 (0.3%)	0	0	2 (0.7%)	2 (0.7%)	0	0
低ナトリウム血症	2 (0.3%)	2 (0.3%)	0	0	2 (0.7%)	2 (0.7%)	0	0
失見当識	2 (0.3%)	1 (0.2%)	0	0	2 (0.7%)	1 (0.4%)	0	0
胃食道逆流性疾患	2 (0.3%)	0	0	0	2 (0.7%)	0	0	0
錯乱状態	2 (0.3%)	0	0	0	2 (0.7%)	0	0	0
吐血	2 (0.3%)	0	0	0	2 (0.7%)	0	0	0
病的骨折	2 (0.3%)	0	0	0	2 (0.7%)	0	0	0
筋力低下	2 (0.3%)	2 (0.3%)	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
甲状腺機能低下症	2 (0.3%)	2 (0.3%)	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
敗血症	2 (0.3%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	0
敗血症性ショック	2 (0.3%)	1 (0.2%)	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
下気道感染	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
咳嗽	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
急性冠動脈症候群	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
菌血症	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
心停止	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
脱水	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
突然死	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
肺出血	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
嚥下障害	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
疼痛	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
心房細動	2 (0.3%)	1 (0.2%)	0	0	0	0	2 (0.8%)	1 (0.4%)
呼吸窮迫	2 (0.3%)	0	0	0	0	0	2 (0.8%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
骨痛	2 (0.3%)	0	0	0	0	0	2 (0.8%)	0
間質性肺疾患	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
血小板減少症	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
対麻痺	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
くも膜下出血	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
インフルエンザ	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
ウイルス性上気道感染	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
クロストリジウム・ディフィシレ大腸炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
リンパ節炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
外傷性血胸	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
感染性胸水	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
気管支肺炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
急性心筋梗塞	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
骨髄炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
塞栓症	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
食道静脈瘤出血	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
心筋梗塞	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
脊髄症	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
大腿骨骨折	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
大葉性肺炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
第７脳神経麻痺	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
蓄膿	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
低血圧	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
低酸素症	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
脳炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
脳梗塞	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
脳出血	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
腹膜炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
末梢動脈閉塞性疾患	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
インフルエンザ様疾患	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
γ－グルタミルトランスフェラーゼ増加	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
肝酵素上昇	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
肝出血	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
血中乳酸脱水素酵素増加	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
構語障害	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
皮膚筋炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
頻脈	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
膵炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
アルコールの解毒	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
アレルギー性輸血反応	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
悪性胸水	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
悪性心嚢液貯留	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
胃炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
運動機能障害	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
冠動脈疾患	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
完全房室ブロック	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
感染性大腸炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肝腫大	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肝不全	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
気管狭窄	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
気管食道瘻	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
急性膵炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
虚血性脳卒中	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
頚静脈血栓症	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
血腫	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
喉頭出血	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
高熱	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
骨盤痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
失神寸前の状態	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
出血性胃潰瘍	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
小腸閉塞	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
消化管感染	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
上大静脈症候群	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
上腹部痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
食道穿孔	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
心肺不全	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
心房粗動	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
腎梗塞	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
腎盂腎炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
成長障害	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
精神状態変化	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
脊髄圧迫	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
多形性神経膠芽細胞腫	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
転倒	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
頭痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
熱性感染症	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肺膿瘍	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
皮下組織膿瘍	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
非心臓性胸痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
瘢痕ヘルニア	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
脾臓梗塞	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
膀胱癌	1 (0.2%)	0	0	0	1 (0.4%)	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 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
前庭神経炎	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
カテーテル留置部位感染	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
悪寒	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
一過性脳虚血発作	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
癌性リンパ管症	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
気管支出血	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
気管支閉塞	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
気胸	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
起立性低血圧	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
筋骨格系胸痛	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
傾眠	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
細菌性肺炎	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
死亡	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
腫瘍疼痛	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
食道狭窄	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
食欲減退	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
心不全	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
腎結石症	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
声帯麻痺	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
脊椎痛	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
椎間板圧迫	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
内出血	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Serious Adverse Events by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
肺水腫	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
疲労	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
腹水	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_ser_GO28754_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_ser_GO28754_SE を再掲］

(4) 重篤な有害事象の要約（FIR 試験）

表 2.7.4.7.2-4 重篤な有害事象の要約（FIR 試験）

Serious Adverse Events by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
Total number of patients with at least one adverse event	65 (47.4%)	14 (10.2%)	16 (51.6%)	2 (6.5%)	43 (46.2%)	11 (11.8%)	6 (46.2%)	1 (7.7%)
肺炎	7 (5.1%)	0	2 (6.5%)	0	5 (5.4%)	0	0	0
呼吸困難	6 (4.4%)	0	1 (3.2%)	0	5 (5.4%)	0	0	0
喀血	4 (2.9%)	0	2 (6.5%)	0	2 (2.2%)	0	0	0
背部痛	4 (2.9%)	0	1 (3.2%)	0	3 (3.2%)	0	0	0
下痢	3 (2.2%)	2 (1.5%)	2 (6.5%)	1 (3.2%)	1 (1.1%)	1 (1.1%)	0	0
胸痛	3 (2.2%)	0	0	0	1 (1.1%)	0	2 (15.4%)	0
上気道感染	2 (1.5%)	1 (0.7%)	2 (6.5%)	1 (3.2%)	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	2 (1.5%)	2 (1.5%)	1 (3.2%)	1 (3.2%)	1 (1.1%)	1 (1.1%)	0	0
アラニンアミノトランスフェラーゼ増加	2 (1.5%)	2 (1.5%)	1 (3.2%)	1 (3.2%)	1 (1.1%)	1 (1.1%)	0	0
胸水	2 (1.5%)	1 (0.7%)	1 (3.2%)	0	1 (1.1%)	1 (1.1%)	0	0
筋力低下	2 (1.5%)	1 (0.7%)	1 (3.2%)	0	1 (1.1%)	1 (1.1%)	0	0
心タンポナーデ	2 (1.5%)	1 (0.7%)	1 (3.2%)	0	1 (1.1%)	1 (1.1%)	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_ser_GO28625_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
心嚢液貯留	2 (1.5%)	0	1 (3.2%)	0	1 (1.1%)	0	0	0
深部静脈血栓症	2 (1.5%)	0	1 (3.2%)	0	1 (1.1%)	0	0	0
下気道感染	2 (1.5%)	0	0	0	2 (2.2%)	0	0	0
肺塞栓症	2 (1.5%)	0	0	0	2 (2.2%)	0	0	0
肺出血	2 (1.5%)	0	0	0	2 (2.2%)	0	0	0
疼痛	2 (1.5%)	0	0	0	2 (2.2%)	0	0	0
インフルエンザ	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
悪心	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
気管支炎	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
気管支狭窄	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
股関節部骨折	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
光視症	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
心筋梗塞	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
心停止	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
腎不全	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_ser_GO28625_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
脊椎圧迫骨折	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
腹痛	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
便秘	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
嘔吐	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
鼠径部膿瘍	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
ギラン・バレー症候群	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
下部消化管出血	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
急性甲状腺炎	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
甲状腺機能低下症	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
収縮性心膜炎	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
糖尿病	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
播種性帯状疱疹	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
肺高血圧症	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
肺臓炎	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
不全単麻痺	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_ser_GO28625_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
一過性黒内障	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
冠動脈疾患	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
関節痛	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
気管支閉塞	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
頚静脈血栓症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
頚部膿瘍	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
呼吸障害	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
高血圧	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
塞栓症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
錯乱状態	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
失神	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
心房粗動	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
神経系障害	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
声帯麻痺	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
脱水	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Serious Adverse Events by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
直腸出血	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
低カルシウム血症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
頭蓋内静脈洞血栓症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
播種性血管内凝固	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
敗血症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
肺水腫	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
副鼻腔炎	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
腹壁血腫	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
痙攣発作	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
発熱性好中球減少症	1 (0.7%)	1 (0.7%)	0	0	0	0	1 (7.7%)	1 (7.7%)
筋骨格痛	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0
骨痛	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0
精神状態変化	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0
転倒	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_ser_GO28625_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
発熱	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_ser_GO28625_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_ser_GO28625_SE を再掲］

(5) 重篤な有害事象の要約（PCD4989g 試験）

表 2.7.4.7.2-5 重篤な有害事象の要約（PCD4989g 試験）

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
Total number of patients with at least one adverse event	182 (37.8%)	40 (8.3%)	1 (11.1%)	0	0	0	15 (41.7%)	2 (5.6%)
呼吸困難	16 (3.3%)	4 (0.8%)	0	0	0	0	0	0
発熱	15 (3.1%)	8 (1.7%)	0	0	0	0	1 (2.8%)	0
腹痛	9 (1.9%)	1 (0.2%)	0	0	0	0	0	0
肺炎	8 (1.7%)	1 (0.2%)	0	0	0	0	2 (5.6%)	0
胸水	8 (1.7%)	0	0	0	0	0	1 (2.8%)	0
疲労	7 (1.5%)	2 (0.4%)	0	0	0	0	1 (2.8%)	1 (2.8%)
低酸素症	6 (1.2%)	3 (0.6%)	0	0	0	0	1 (2.8%)	0
尿路感染	6 (1.2%)	1 (0.2%)	0	0	0	0	0	0
背部痛	6 (1.2%)	0	0	0	0	0	0	0
疼痛	6 (1.2%)	1 (0.2%)	0	0	0	0	0	0
貧血	5 (1.0%)	0	1 (11.1%)	0	0	0	0	0
急性腎不全	5 (1.0%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
精神状態変化	4 (0.8%)	0	0	0	0	0	2 (5.6%)	0
肺塞栓症	4 (0.8%)	0	0	0	0	0	1 (2.8%)	0
小腸閉塞	4 (0.8%)	0	0	0	0	0	1 (2.8%)	0
敗血症	4 (0.8%)	0	0	0	0	0	0	0
脱水	4 (0.8%)	0	0	0	0	0	0	0
心房細動	4 (0.8%)	0	0	0	0	0	0	0
骨痛	4 (0.8%)	2 (0.4%)	0	0	0	0	0	0
気胸	4 (0.8%)	0	0	0	0	0	0	0
蜂巣炎	3 (0.6%)	0	0	0	0	0	1 (2.8%)	0
腎不全	3 (0.6%)	0	0	0	0	0	0	0
悪心	3 (0.6%)	1 (0.2%)	0	0	0	0	0	0
胃腸出血	3 (0.6%)	0	0	0	0	0	0	0
肺臓炎	3 (0.6%)	3 (0.6%)	0	0	0	0	0	0
倦怠感	2 (0.4%)	2 (0.4%)	0	0	0	0	1 (2.8%)	1 (2.8%)
肺感染	2 (0.4%)	0	0	0	0	0	1 (2.8%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
感染性関節炎	2 (0.4%)	0	0	0	0	0	1 (2.8%)	0
関節痛	2 (0.4%)	0	0	0	0	0	1 (2.8%)	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
咳嗽	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
下気道感染	2 (0.4%)	0	0	0	0	0	0	0
高カルシウム血症	2 (0.4%)	0	0	0	0	0	0	0
四肢痛	2 (0.4%)	0	0	0	0	0	0	0
上腹部痛	2 (0.4%)	0	0	0	0	0	0	0
中枢神経系転移	2 (0.4%)	0	0	0	0	0	0	0
尿閉	2 (0.4%)	0	0	0	0	0	0	0
脳血管発作	2 (0.4%)	0	0	0	0	0	0	0
心嚢液貯留	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
全身性炎症反応症候群	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
嘔吐	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
胃出血	2 (0.4%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
急性呼吸不全	2 (0.4%)	0	0	0	0	0	0	0
血腫	2 (0.4%)	0	0	0	0	0	0	0
高カリウム血症	2 (0.4%)	0	0	0	0	0	0	0
腫瘍疼痛	2 (0.4%)	0	0	0	0	0	0	0
上大静脈症候群	2 (0.4%)	0	0	0	0	0	0	0
成長障害	2 (0.4%)	0	0	0	0	0	0	0
脊髄圧迫	2 (0.4%)	0	0	0	0	0	0	0
転倒	2 (0.4%)	0	0	0	0	0	0	0
低ナトリウム血症	2 (0.4%)	0	0	0	0	0	0	0
心タンポナーデ	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
医療機器関連感染	2 (0.4%)	0	0	0	0	0	0	0
胆管閉塞	2 (0.4%)	0	0	0	0	0	0	0
病的骨折	2 (0.4%)	0	0	0	0	0	0	0
胸痛	2 (0.4%)	0	0	0	0	0	0	0
大腸炎	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (2.8%)	1 (2.8%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
インフルエンザ	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
ステント除去	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
悪性胸水	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
異型肺炎	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
気管支炎	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
肩回旋筋腱板症候群	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
誤嚥	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
自殺企図	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
蓄膿	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
敗血症性ショック	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
そう痒性皮疹	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
アラニンアミノトランスフェラーゼ増加	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
インフルエンザ性肺炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
インフルエンザ様疾患	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
下垂体炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
高熱	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
錯乱状態	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
自己免疫性肝炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
重症筋無力症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
全身健康状態低下	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
糖尿病	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
腹部膨満	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
そう痒症	1 (0.2%)	0	0	0	0	0	0	0
アルコール乱用	1 (0.2%)	0	0	0	0	0	0	0
過量投与	1 (0.2%)	0	0	0	0	0	0	0
筋骨格痛	1 (0.2%)	0	0	0	0	0	0	0
血中クレアチニン増加	1 (0.2%)	0	0	0	0	0	0	0
血中ビリルビン増加	1 (0.2%)	0	0	0	0	0	0	0
血尿	1 (0.2%)	0	0	0	0	0	0	0
限局性浮腫	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
呼吸停止	1 (0.2%)	0	0	0	0	0	0	0
女性生殖器瘻	1 (0.2%)	0	0	0	0	0	0	0
腎機能障害	1 (0.2%)	0	0	0	0	0	0	0
腎盂腎炎	1 (0.2%)	0	0	0	0	0	0	0
創傷感染	1 (0.2%)	0	0	0	0	0	0	0
創離開	1 (0.2%)	0	0	0	0	0	0	0
大腿骨頚部骨折	1 (0.2%)	0	0	0	0	0	0	0
大腿骨骨折	1 (0.2%)	0	0	0	0	0	0	0
大腸閉塞	1 (0.2%)	0	0	0	0	0	0	0
丹毒	1 (0.2%)	0	0	0	0	0	0	0
腸閉塞	1 (0.2%)	0	0	0	0	0	0	0
低血圧	1 (0.2%)	0	0	0	0	0	0	0
頭部損傷	1 (0.2%)	0	0	0	0	0	0	0
洞性頻脈	1 (0.2%)	0	0	0	0	0	0	0
尿管閉塞	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
尿路性敗血症	1 (0.2%)	0	0	0	0	0	0	0
尿路閉塞	1 (0.2%)	0	0	0	0	0	0	0
認知症	1 (0.2%)	0	0	0	0	0	0	0
脳症	1 (0.2%)	0	0	0	0	0	0	0
肺障害	1 (0.2%)	0	0	0	0	0	0	0
副腎機能不全	1 (0.2%)	0	0	0	0	0	0	0
腹水	1 (0.2%)	0	0	0	0	0	0	0
腹部癒着	1 (0.2%)	0	0	0	0	0	0	0
閉塞性気道障害	1 (0.2%)	0	0	0	0	0	0	0
嚥下障害	1 (0.2%)	0	0	0	0	0	0	0
運動失調	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
気管支閉塞	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
筋力低下	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
甲状腺機能低下症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
腫瘍崩壊症候群	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
心肺停止	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
末梢性浮腫	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
栄養障害	1 (0.2%)	0	0	0	0	0	0	0
気道感染	1 (0.2%)	0	0	0	0	0	0	0
骨溶解	1 (0.2%)	0	0	0	0	0	0	0
失神	1 (0.2%)	0	0	0	0	0	0	0
十二指腸潰瘍	1 (0.2%)	0	0	0	0	0	0	0
深部静脈血栓症	1 (0.2%)	0	0	0	0	0	0	0
水腎症	1 (0.2%)	0	0	0	0	0	0	0
胆管炎	1 (0.2%)	0	0	0	0	0	0	0
胆嚢炎	1 (0.2%)	0	0	0	0	0	0	0
胆嚢穿孔	1 (0.2%)	0	0	0	0	0	0	0
頭痛	1 (0.2%)	0	0	0	0	0	0	0
突然死	1 (0.2%)	0	0	0	0	0	0	0
非心臓性胸痛	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
頻脈	1 (0.2%)	0	0	0	0	0	0	0
便秘	1 (0.2%)	0	0	0	0	0	0	0
歩行障害	1 (0.2%)	0	0	0	0	0	0	0
無力症	1 (0.2%)	0	0	0	0	0	0	0
痙攣発作	1 (0.2%)	0	0	0	0	0	0	0
死亡	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
髄膜炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
肺高血圧症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
意識変容状態	1 (0.2%)	0	0	0	0	0	0	0
肝血腫	1 (0.2%)	0	0	0	0	0	0	0
頚部痛	1 (0.2%)	0	0	0	0	0	0	0
呼吸窮迫	1 (0.2%)	0	0	0	0	0	0	0
誤嚥性肺炎	1 (0.2%)	0	0	0	0	0	0	0
疾患進行	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
脊椎痛	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
Total number of patients with at least one adverse event	94 (39.8%)	20 (8.5%)	56 (38.4%)	14 (9.6%)	16 (31.4%)	4 (7.8%)
呼吸困難	4 (1.7%)	0	8 (5.5%)	3 (2.1%)	4 (7.8%)	1 (2.0%)
発熱	9 (3.8%)	6 (2.5%)	4 (2.7%)	2 (1.4%)	1 (2.0%)	0
腹痛	5 (2.1%)	0	4 (2.7%)	1 (0.7%)	0	0
肺炎	4 (1.7%)	1 (0.4%)	2 (1.4%)	0	0	0
胸水	1 (0.4%)	0	4 (2.7%)	0	2 (3.9%)	0
疲労	3 (1.3%)	0	3 (2.1%)	1 (0.7%)	0	0
低酸素症	3 (1.3%)	2 (0.8%)	2 (1.4%)	1 (0.7%)	0	0
尿路感染	5 (2.1%)	1 (0.4%)	1 (0.7%)	0	0	0
背部痛	5 (2.1%)	0	1 (0.7%)	0	0	0
疼痛	4 (1.7%)	0	2 (1.4%)	1 (0.7%)	0	0
貧血	2 (0.8%)	0	2 (1.4%)	0	0	0
急性腎不全	3 (1.3%)	0	1 (0.7%)	0	1 (2.0%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
精神状態変化	1 (0.4%)	0	0	0	1 (2.0%)	0
肺塞栓症	2 (0.8%)	0	1 (0.7%)	0	0	0
小腸閉塞	2 (0.8%)	0	0	0	1 (2.0%)	0
敗血症	4 (1.7%)	0	0	0	0	0
脱水	3 (1.3%)	0	1 (0.7%)	0	0	0
心房細動	2 (0.8%)	0	2 (1.4%)	0	0	0
骨痛	1 (0.4%)	0	3 (2.1%)	2 (1.4%)	0	0
気胸	1 (0.4%)	0	2 (1.4%)	0	1 (2.0%)	0
蜂巣炎	2 (0.8%)	0	0	0	0	0
腎不全	3 (1.3%)	0	0	0	0	0
悪心	2 (0.8%)	0	1 (0.7%)	1 (0.7%)	0	0
胃腸出血	2 (0.8%)	0	1 (0.7%)	0	0	0
肺臓炎	1 (0.4%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	1 (2.0%)	1 (2.0%)
倦怠感	1 (0.4%)	1 (0.4%)	0	0	0	0
肺感染	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
感染性関節炎	0	0	1 (0.7%)	0	0	0
関節痛	0	0	1 (0.7%)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8%)	1 (0.4%)	0	0	0	0
咳嗽	2 (0.8%)	1 (0.4%)	0	0	0	0
下気道感染	2 (0.8%)	0	0	0	0	0
高カルシウム血症	2 (0.8%)	0	0	0	0	0
四肢痛	2 (0.8%)	0	0	0	0	0
上腹部痛	2 (0.8%)	0	0	0	0	0
中枢神経系転移	2 (0.8%)	0	0	0	0	0
尿閉	2 (0.8%)	0	0	0	0	0
脳血管発作	2 (0.8%)	0	0	0	0	0
心嚢液貯留	1 (0.4%)	1 (0.4%)	1 (0.7%)	0	0	0
全身性炎症反応症候群	1 (0.4%)	0	1 (0.7%)	1 (0.7%)	0	0
嘔吐	1 (0.4%)	0	1 (0.7%)	1 (0.7%)	0	0
胃出血	1 (0.4%)	0	1 (0.7%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
急性呼吸不全	1 (0.4%)	0	1 (0.7%)	0	0	0
血腫	1 (0.4%)	0	1 (0.7%)	0	0	0
高カリウム血症	1 (0.4%)	0	1 (0.7%)	0	0	0
腫瘍疼痛	1 (0.4%)	0	1 (0.7%)	0	0	0
上大静脈症候群	1 (0.4%)	0	1 (0.7%)	0	0	0
成長障害	1 (0.4%)	0	1 (0.7%)	0	0	0
脊髄圧迫	1 (0.4%)	0	1 (0.7%)	0	0	0
転倒	1 (0.4%)	0	1 (0.7%)	0	0	0
低ナトリウム血症	1 (0.4%)	0	0	0	1 (2.0%)	0
心タンポナーデ	0	0	2 (1.4%)	1 (0.7%)	0	0
医療機器関連感染	0	0	2 (1.4%)	0	0	0
胆管閉塞	0	0	2 (1.4%)	0	0	0
病的骨折	0	0	2 (1.4%)	0	0	0
胸痛	0	0	1 (0.7%)	0	1 (2.0%)	0
大腸炎	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
インフルエンザ	0	0	0	0	0	0
ステント除去	0	0	0	0	0	0
悪性胸水	0	0	0	0	0	0
異型肺炎	0	0	0	0	0	0
気管支炎	0	0	0	0	0	0
肩回旋筋腱板症候群	0	0	0	0	0	0
誤嚥	0	0	0	0	0	0
自殺企図	0	0	0	0	0	0
蓄膿	0	0	0	0	0	0
敗血症性ショック	0	0	0	0	0	0
そう痒性皮疹	1 (0.4%)	1 (0.4%)	0	0	0	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%)	0	0	0	0
インフルエンザ性肺炎	1 (0.4%)	1 (0.4%)	0	0	0	0
インフルエンザ様疾患	1 (0.4%)	1 (0.4%)	0	0	0	0
下垂体炎	1 (0.4%)	1 (0.4%)	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
高熱	1 (0.4%)	1 (0.4%)	0	0	0	0
錯乱状態	1 (0.4%)	1 (0.4%)	0	0	0	0
自己免疫性肝炎	1 (0.4%)	1 (0.4%)	0	0	0	0
重症筋無力症	1 (0.4%)	1 (0.4%)	0	0	0	0
全身健康状態低下	1 (0.4%)	1 (0.4%)	0	0	0	0
糖尿病	1 (0.4%)	1 (0.4%)	0	0	0	0
腹部膨満	1 (0.4%)	1 (0.4%)	0	0	0	0
そう痒症	1 (0.4%)	0	0	0	0	0
アルコール乱用	1 (0.4%)	0	0	0	0	0
過量投与	1 (0.4%)	0	0	0	0	0
筋骨格痛	1 (0.4%)	0	0	0	0	0
血中クレアチニン増加	1 (0.4%)	0	0	0	0	0
血中ビリルビン増加	1 (0.4%)	0	0	0	0	0
血尿	1 (0.4%)	0	0	0	0	0
限局性浮腫	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
呼吸停止	1 (0.4%)	0	0	0	0	0
女性生殖器瘻	1 (0.4%)	0	0	0	0	0
腎機能障害	1 (0.4%)	0	0	0	0	0
腎盂腎炎	1 (0.4%)	0	0	0	0	0
創傷感染	1 (0.4%)	0	0	0	0	0
創離開	1 (0.4%)	0	0	0	0	0
大腿骨頚部骨折	1 (0.4%)	0	0	0	0	0
大腿骨骨折	1 (0.4%)	0	0	0	0	0
大腸閉塞	1 (0.4%)	0	0	0	0	0
丹毒	1 (0.4%)	0	0	0	0	0
腸閉塞	1 (0.4%)	0	0	0	0	0
低血圧	1 (0.4%)	0	0	0	0	0
頭部損傷	1 (0.4%)	0	0	0	0	0
洞性頻脈	1 (0.4%)	0	0	0	0	0
尿管閉塞	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
尿路性敗血症	1 (0.4%)	0	0	0	0	0
尿路閉塞	1 (0.4%)	0	0	0	0	0
認知症	1 (0.4%)	0	0	0	0	0
脳症	1 (0.4%)	0	0	0	0	0
肺障害	1 (0.4%)	0	0	0	0	0
副腎機能不全	1 (0.4%)	0	0	0	0	0
腹水	1 (0.4%)	0	0	0	0	0
腹部癒着	1 (0.4%)	0	0	0	0	0
閉塞性気道障害	1 (0.4%)	0	0	0	0	0
嚥下障害	1 (0.4%)	0	0	0	0	0
運動失調	0	0	1 (0.7%)	1 (0.7%)	0	0
気管支閉塞	0	0	1 (0.7%)	1 (0.7%)	0	0
筋力低下	0	0	1 (0.7%)	1 (0.7%)	0	0
甲状腺機能低下症	0	0	1 (0.7%)	1 (0.7%)	0	0
腫瘍崩壊症候群	0	0	1 (0.7%)	1 (0.7%)	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
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Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
心肺停止	0	0	1 (0.7%)	1 (0.7%)	0	0
末梢性浮腫	0	0	1 (0.7%)	1 (0.7%)	0	0
栄養障害	0	0	1 (0.7%)	0	0	0
気道感染	0	0	1 (0.7%)	0	0	0
骨溶解	0	0	1 (0.7%)	0	0	0
失神	0	0	1 (0.7%)	0	0	0
十二指腸潰瘍	0	0	1 (0.7%)	0	0	0
深部静脈血栓症	0	0	1 (0.7%)	0	0	0
水腎症	0	0	1 (0.7%)	0	0	0
胆管炎	0	0	1 (0.7%)	0	0	0
胆嚢炎	0	0	1 (0.7%)	0	0	0
胆嚢穿孔	0	0	1 (0.7%)	0	0	0
頭痛	0	0	1 (0.7%)	0	0	0
突然死	0	0	1 (0.7%)	0	0	0
非心臓性胸痛	0	0	1 (0.7%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
09NOV2016 10:43

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
頻脈	0	0	1 (0.7%)	0	0	0
便秘	0	0	1 (0.7%)	0	0	0
歩行障害	0	0	1 (0.7%)	0	0	0
無力症	0	0	1 (0.7%)	0	0	0
痙攣発作	0	0	1 (0.7%)	0	0	0
死亡	0	0	0	0	1 (2.0%)	1 (2.0%)
髄膜炎	0	0	0	0	1 (2.0%)	1 (2.0%)
肺高血圧症	0	0	0	0	1 (2.0%)	1 (2.0%)
意識変容状態	0	0	0	0	1 (2.0%)	0
肝血腫	0	0	0	0	1 (2.0%)	0
頚部痛	0	0	0	0	1 (2.0%)	0
呼吸窮迫	0	0	0	0	1 (2.0%)	0
誤嚥性肺炎	0	0	0	0	1 (2.0%)	0
疾患進行	0	0	0	0	1 (2.0%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
09NOV2016 10:43

Serious Adverse Events by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
脊椎痛	0	0	0	0	1 (2.0%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_ser.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_ser_GO27831_SE.out
09NOV2016 10:43

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_ser_GO27831_SE を再掲］

2.7.4.7.3 治験薬の投与中止に至った有害事象

(1) 治験薬の投与中止に至った有害事象の要約（OAK 試験）

表 2.7.4.7.3-1 治験薬の投与中止に至った有害事象の要約（OAK 試験）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
Total number of patients with at least one adverse event	46 (7.6%)	28 (4.6%)	108 (18.7%)	84 (14.5%)
肺炎	3 (0.5%)	2 (0.3%)	7 (1.2%)	5 (0.9%)
髄膜炎	3 (0.5%)	3 (0.5%)	0	0
胸水	2 (0.3%)	0	3 (0.5%)	2 (0.3%)
認知障害	2 (0.3%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
敗血症	2 (0.3%)	1 (0.2%)	1 (0.2%)	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.3%)	2 (0.3%)	0	0
過敏症	2 (0.3%)	2 (0.3%)	0	0
肝炎	2 (0.3%)	2 (0.3%)	0	0
水疱性皮膚炎	2 (0.3%)	2 (0.3%)	0	0
脳血管発作	2 (0.3%)	0	0	0
疲労	1 (0.2%)	0	15 (2.6%)	14 (2.4%)
呼吸困難	1 (0.2%)	0	6 (1.0%)	1 (0.2%)
突然死	1 (0.2%)	0	2 (0.3%)	0
肺出血	1 (0.2%)	0	2 (0.3%)	0
注入に伴う反応	1 (0.2%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
肺臓炎	1 (0.2%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
アラニンアミノトランスフェラーゼ増加	1 (0.2%)	1 (0.2%)	0	0
ヘノッホ・シェーンライン紫斑病性腎炎	1 (0.2%)	1 (0.2%)	0	0
下垂体炎	1 (0.2%)	1 (0.2%)	0	0
感染性腸炎	1 (0.2%)	1 (0.2%)	0	0
間質性肺疾患	1 (0.2%)	1 (0.2%)	0	0
視神経炎	1 (0.2%)	1 (0.2%)	0	0
全身性炎症反応症候群	1 (0.2%)	1 (0.2%)	0	0
脳炎	1 (0.2%)	1 (0.2%)	0	0
肺浸潤	1 (0.2%)	1 (0.2%)	0	0
網膜症	1 (0.2%)	1 (0.2%)	0	0
薬物性肝障害	1 (0.2%)	1 (0.2%)	0	0
類天疱瘡	1 (0.2%)	1 (0.2%)	0	0
気管支痙攣	1 (0.2%)	0	0	0
結腸癌	1 (0.2%)	0	0	0
骨痛	1 (0.2%)	0	0	0
死亡	1 (0.2%)	0	0	0
心筋虚血	1 (0.2%)	0	0	0
腎不全	1 (0.2%)	0	0	0
敗血症性ショック	1 (0.2%)	0	0	0
錯感覚	0	0	11 (1.9%)	11 (1.9%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_dis_GO28915_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
末梢性ニューロパチー	0	0	10 (1.7%)	10 (1.7%)
無力症	0	0	10 (1.7%)	10 (1.7%)
末梢性浮腫	0	0	6 (1.0%)	5 (0.9%)
末梢性感覚ニューロパチー	0	0	4 (0.7%)	4 (0.7%)
食欲減退	0	0	3 (0.5%)	3 (0.5%)
全身性浮腫	0	0	3 (0.5%)	3 (0.5%)
薬物過敏症	0	0	3 (0.5%)	3 (0.5%)
好中球減少症	0	0	2 (0.3%)	2 (0.3%)
発熱性好中球減少症	0	0	2 (0.3%)	2 (0.3%)
貧血	0	0	2 (0.3%)	2 (0.3%)
気道感染	0	0	2 (0.3%)	1 (0.2%)
アナフィラキシー反応	0	0	1 (0.2%)	1 (0.2%)
胃炎	0	0	1 (0.2%)	1 (0.2%)
眼刺激	0	0	1 (0.2%)	1 (0.2%)
呼吸不全	0	0	1 (0.2%)	1 (0.2%)
好中球減少性敗血症	0	0	1 (0.2%)	1 (0.2%)
上部消化管出血	0	0	1 (0.2%)	1 (0.2%)
食道静脈瘤出血	0	0	1 (0.2%)	1 (0.2%)
脱水	0	0	1 (0.2%)	1 (0.2%)
爪の障害	0	0	1 (0.2%)	1 (0.2%)
爪囲炎	0	0	1 (0.2%)	1 (0.2%)
低マグネシウム血症	0	0	1 (0.2%)	1 (0.2%)
低血圧	0	0	1 (0.2%)	1 (0.2%)
肺感染	0	0	1 (0.2%)	1 (0.2%)
肺水腫	0	0	1 (0.2%)	1 (0.2%)
白血球減少症	0	0	1 (0.2%)	1 (0.2%)
汎血球減少症	0	0	1 (0.2%)	1 (0.2%)
浮腫	0	0	1 (0.2%)	1 (0.2%)
腹痛	0	0	1 (0.2%)	1 (0.2%)
腹部敗血症	0	0	1 (0.2%)	1 (0.2%)
流涙増加	0	0	1 (0.2%)	1 (0.2%)
嚥下障害	0	0	1 (0.2%)	1 (0.2%)
下部消化管出血	0	0	1 (0.2%)	0
気管支炎	0	0	1 (0.2%)	0
急性心筋梗塞	0	0	1 (0.2%)	0
憩室炎	0	0	1 (0.2%)	0
限局性浮腫	0	0	1 (0.2%)	0
呼吸窮迫	0	0	1 (0.2%)	0
酸素飽和度低下	0	0	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_dis_GO28915_SE.out
07DEC2016 17:16

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
自然気胸	0	0	1 (0.2%)	0
小腸閉塞	0	0	1 (0.2%)	0
胆嚢炎	0	0	1 (0.2%)	0
虫垂炎	0	0	1 (0.2%)	0
尿閉	0	0	1 (0.2%)	0
肺塞栓症	0	0	1 (0.2%)	0
喀血	0	0	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_dis_GO28915_SE.out
07DEC2016 17:16 Page 3 of 3

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.1-3 ae_rae_dis_GO28915_SE を再掲］

(2) 治験薬の投与中止に至った有害事象の要約（POPLAR 試験）

表 2.7.4.7.3-2 治験薬の投与中止に至った有害事象の要約（POPLAR 試験）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

	atezolizumab 1200 mg q3w IV (N=142)		Docetaxel (N=135)	
MedDRA Preferred Term	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)
Total number of patients with at least one adverse event	11 (7.7%)	2 (1.4%)	30 (22.2%)	24 (17.8%)
呼吸困難	2 (1.4%)	0	0	0
肺炎	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7%)	1 (0.7%)	0	0
自己免疫性関節炎	1 (0.7%)	1 (0.7%)	0	0
ストレス	1 (0.7%)	0	0	0
気胸	1 (0.7%)	0	0	0
誤嚥性肺炎	1 (0.7%)	0	0	0
塞栓症	1 (0.7%)	0	0	0
大腸穿孔	1 (0.7%)	0	0	0
潰瘍性出血	1 (0.7%)	0	0	0
末梢性感覚ニューロパチー	0	0	4 (3.0%)	4 (3.0%)
疲労	0	0	4 (3.0%)	3 (2.2%)
敗血症	0	0	3 (2.2%)	2 (1.5%)
末梢性ニューロパチー	0	0	2 (1.5%)	2 (1.5%)
死亡	0	0	2 (1.5%)	1 (0.7%)
下痢	0	0	1 (0.7%)	1 (0.7%)
急性呼吸窮迫症候群	0	0	1 (0.7%)	1 (0.7%)
胸水	0	0	1 (0.7%)	1 (0.7%)
好中球減少症	0	0	1 (0.7%)	1 (0.7%)
錯感覚	0	0	1 (0.7%)	1 (0.7%)
脱水	0	0	1 (0.7%)	1 (0.7%)
爪肥厚	0	0	1 (0.7%)	1 (0.7%)
肺臓炎	0	0	1 (0.7%)	1 (0.7%)
発熱性好中球減少症	0	0	1 (0.7%)	1 (0.7%)
貧血	0	0	1 (0.7%)	1 (0.7%)
疼痛	0	0	1 (0.7%)	1 (0.7%)
急性心筋梗塞	0	0	1 (0.7%)	0
末梢血管塞栓症	0	0	1 (0.7%)	0
末梢性虚血	0	0	1 (0.7%)	0

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_dis_GO28753_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。

［5.3.5.3-1 ae_rae_dis_GO28753_SE を再掲］

(3) 本剤の投与中止に至った有害事象の要約（BIRCH 試験）

表 2.7.4.7.3-3 本剤の投与中止に至った有害事象の要約（BIRCH 試験）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
Total number of patients with at least one adverse event	34 (5.2%)	11 (1.7%)	8 (5.8%)	5 (3.6%)	15 (5.6%)	2 (0.7%)	11 (4.3%)	4 (1.6%)
肺臓炎	4 (0.6%)	2 (0.3%)	1 (0.7%)	1 (0.7%)	3 (1.1%)	1 (0.4%)	0	0
肺炎	3 (0.5%)	1 (0.2%)	0	0	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
血小板減少症	2 (0.3%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	1 (0.4%)	0
誤嚥性肺炎	2 (0.3%)	1 (0.2%)	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
敗血症性ショック	2 (0.3%)	1 (0.2%)	0	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
突然死	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
脳血管発作	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
間質性肺疾患	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
対麻痺	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
大腸炎	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
血中クレアチニン増加	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
呼吸不全	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_dis_GO28754_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
脳梗塞	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
注入に伴う反応	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
肝不全	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
気管食道瘻	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
高カルシウム血症	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
心停止	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
多形性神経膠芽細胞腫	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肺感染	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
筋力低下	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
上強膜炎	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
急性冠動脈症候群	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
呼吸窮迫	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
内出血	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
疲労	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_dis_GO28754_SE.out
09NOV2016 10:46

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dis_GO28754_SE を再掲］

(4) 本剤の投与中止に至った有害事象の要約（FIR 試験）

表 2.7.4.7.3-4 本剤の投与中止に至った有害事象の要約（FIR 試験）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
Total number of patients with at least one adverse event	13 (9.5%)	3 (2.2%)	2 (6.5%)	0	9 (9.7%)	3 (3.2%)	2 (15.4%)	0
体重減少	2 (1.5%)	0	1 (3.2%)	0	1 (1.1%)	0	0	0
呼吸困難	2 (1.5%)	0	0	0	2 (2.2%)	0	0	0
気管支狭窄	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
心嚢液貯留	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
嚥下障害	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
ギラン・バレー症候群	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
糖尿病	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
肺高血圧症	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
高カルシウム血症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
腫瘍疼痛	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
肺塞栓症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
貧血	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_dis_GO28625_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
喀血	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
精神状態変化	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0
全身健康状態低下	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_dis_GO28625_SE.out
09NOV2016 10:32

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dis_GO28625_SE を再掲］

(5) 本剤の投与中止に至った有害事象の要約（PCD4989g 試験）

表 2.7.4.7.3-5 本剤の投与中止に至った有害事象の要約（PCD4989g 試験）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
Total number of patients with at least one adverse event	32 (6.7%)	16 (3.3%)	0	0	0	0	2 (5.6%)	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
アラニンアミノトランスフェラーゼ増加	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
低酸素症	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
発熱	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
急性呼吸不全	2 (0.4%)	0	0	0	0	0	0	0
肺臓炎	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
自殺企図	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
蓄膿	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
リパーゼ増加	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
下垂体炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
倦怠感	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
自己免疫性肝炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dis_GO27831_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
脱水	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
注視麻痺	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
扁平苔癬	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
四肢痛	1 (0.2%)	0	0	0	0	0	0	0
上腹部痛	1 (0.2%)	0	0	0	0	0	0	0
腎不全	1 (0.2%)	0	0	0	0	0	0	0
全身健康状態低下	1 (0.2%)	0	0	0	0	0	0	0
全身性炎症反応症候群	1 (0.2%)	0	0	0	0	0	0	0
中枢神経系転移	1 (0.2%)	0	0	0	0	0	0	0
転倒	1 (0.2%)	0	0	0	0	0	0	0
頭部損傷	1 (0.2%)	0	0	0	0	0	0	0
認知症	1 (0.2%)	0	0	0	0	0	0	0
背部痛	1 (0.2%)	0	0	0	0	0	0	0
疼痛	1 (0.2%)	0	0	0	0	0	0	0
心肺停止	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dis_GO27831_SE.out
09NOV2016 10:47

Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
多汗症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
疲労	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
末梢性浮腫	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
無力症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
うつ病	1 (0.2%)	0	0	0	0	0	0	0
呼吸困難	1 (0.2%)	0	0	0	0	0	0	0
突然死	1 (0.2%)	0	0	0	0	0	0	0
腹痛	1 (0.2%)	0	0	0	0	0	0	0
肺高血圧症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
肝血腫	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dis_GO27831_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
Total number of patients with at least one adverse event	20 (8.5%)	10 (4.2%)	7 (4.8%)	4 (2.7%)	3 (5.9%)	2 (3.9%)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8%)	2 (0.8%)	0	0	0	0
アラニンアミノトランスフェラーゼ増加	2 (0.8%)	2 (0.8%)	0	0	0	0
低酸素症	1 (0.4%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
発熱	1 (0.4%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
急性呼吸不全	1 (0.4%)	0	1 (0.7%)	0	0	0
肺臓炎	1 (0.4%)	1 (0.4%)	0	0	1 (2.0%)	1 (2.0%)
自殺企図	0	0	0	0	0	0
蓄膿	0	0	0	0	0	0
リパーゼ増加	1 (0.4%)	1 (0.4%)	0	0	0	0
下垂体炎	1 (0.4%)	1 (0.4%)	0	0	0	0
倦怠感	1 (0.4%)	1 (0.4%)	0	0	0	0
自己免疫性肝炎	1 (0.4%)	1 (0.4%)	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dis_GO27831_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
脱水	1 (0.4%)	1 (0.4%)	0	0	0	0
注視麻痺	1 (0.4%)	1 (0.4%)	0	0	0	0
扁平苔癬	1 (0.4%)	1 (0.4%)	0	0	0	0
四肢痛	1 (0.4%)	0	0	0	0	0
上腹部痛	1 (0.4%)	0	0	0	0	0
腎不全	1 (0.4%)	0	0	0	0	0
全身健康状態低下	1 (0.4%)	0	0	0	0	0
全身性炎症反応症候群	1 (0.4%)	0	0	0	0	0
中枢神経系転移	1 (0.4%)	0	0	0	0	0
転倒	1 (0.4%)	0	0	0	0	0
頭部損傷	1 (0.4%)	0	0	0	0	0
認知症	1 (0.4%)	0	0	0	0	0
背部痛	1 (0.4%)	0	0	0	0	0
疼痛	1 (0.4%)	0	0	0	0	0
心肺停止	0	0	1 (0.7%)	1 (0.7%)	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dis_GO27831_SE.out
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Adverse Events Leading to Discontinuation of Trial Treatment by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
多汗症	0	0	1 (0.7%)	1 (0.7%)	0	0
疲労	0	0	1 (0.7%)	1 (0.7%)	0	0
末梢性浮腫	0	0	1 (0.7%)	1 (0.7%)	0	0
無力症	0	0	1 (0.7%)	1 (0.7%)	0	0
うつ病	0	0	1 (0.7%)	0	0	0
呼吸困難	0	0	1 (0.7%)	0	0	0
突然死	0	0	1 (0.7%)	0	0	0
腹痛	0	0	1 (0.7%)	0	0	0
肺高血圧症	0	0	0	0	1 (2.0%)	1 (2.0%)
肝血腫	0	0	0	0	1 (2.0%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_dis.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_dis_GO27831_SE.out
09NOV2016 10:47

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_dis_GO27831_SE を再掲］

2.7.4.7.4 治験薬の投与量変更に至った有害事象

(1) 治験薬の投与量変更に至った有害事象の要約（OAK 試験）

表 2.7.4.7.4-1 治験薬の投与量変更に至った有害事象の要約（OAK 試験）

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
Total number of patients with at least one adverse event	152 (25.0%)	66 (10.8%)	210 (36.3%)	167 (28.9%)
肺炎	13 (2.1%)	2 (0.3%)	10 (1.7%)	4 (0.7%)
呼吸困難	10 (1.6%)	3 (0.5%)	6 (1.0%)	2 (0.3%)
背部痛	8 (1.3%)	3 (0.5%)	0	0
疲労	7 (1.1%)	3 (0.5%)	18 (3.1%)	17 (2.9%)
気道感染	6 (1.0%)	0	8 (1.4%)	2 (0.3%)
発熱	6 (1.0%)	2 (0.3%)	6 (1.0%)	1 (0.2%)
無力症	5 (0.8%)	1 (0.2%)	12 (2.1%)	11 (1.9%)
下痢	5 (0.8%)	3 (0.5%)	11 (1.9%)	11 (1.9%)
注入に伴う反応	5 (0.8%)	5 (0.8%)	3 (0.5%)	3 (0.5%)
アスパラギン酸アミノトランスフェラーゼ増加	5 (0.8%)	1 (0.2%)	2 (0.3%)	0
アラニンアミノトランスフェラーゼ増加	5 (0.8%)	2 (0.3%)	1 (0.2%)	0
肺感染	4 (0.7%)	1 (0.2%)	4 (0.7%)	3 (0.5%)
喀血	4 (0.7%)	0	4 (0.7%)	0
そう痒症	4 (0.7%)	4 (0.7%)	0	0
甲状腺機能低下症	4 (0.7%)	4 (0.7%)	0	0
血小板減少症	3 (0.5%)	3 (0.5%)	1 (0.2%)	1 (0.2%)
発疹	3 (0.5%)	3 (0.5%)	1 (0.2%)	1 (0.2%)
上気道感染	3 (0.5%)	0	1 (0.2%)	0
四肢痛	3 (0.5%)	0	0	0
肺塞栓症	3 (0.5%)	0	0	0
貧血	2 (0.3%)	0	9 (1.6%)	8 (1.4%)
気管支炎	2 (0.3%)	0	3 (0.5%)	0
口内炎	2 (0.3%)	2 (0.3%)	2 (0.3%)	2 (0.3%)
潮紅	2 (0.3%)	2 (0.3%)	2 (0.3%)	2 (0.3%)
体重減少	2 (0.3%)	2 (0.3%)	2 (0.3%)	0
胸水	2 (0.3%)	1 (0.2%)	2 (0.3%)	1 (0.2%)
咳嗽	2 (0.3%)	1 (0.2%)	2 (0.3%)	0
血中ビリルビン増加	2 (0.3%)	1 (0.2%)	2 (0.3%)	0
肺臓炎	2 (0.3%)	2 (0.3%)	1 (0.2%)	1 (0.2%)
低酸素症	2 (0.3%)	1 (0.2%)	1 (0.2%)	0
咽頭炎	2 (0.3%)	0	1 (0.2%)	1 (0.2%)
筋骨格痛	2 (0.3%)	0	1 (0.2%)	1 (0.2%)
心房細動	2 (0.3%)	0	1 (0.2%)	0
トランスアミナーゼ上昇	2 (0.3%)	2 (0.3%)	0	0
γ－グルタミルトランスフェラーゼ増加	2 (0.3%)	2 (0.3%)	0	0
多形紅斑	2 (0.3%)	2 (0.3%)	0	0

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AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_mod_GO28915_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
斑状丘疹状皮疹	2 (0.3%)	2 (0.3%)	0	0
Ｃ－反応性蛋白増加	2 (0.3%)	1 (0.2%)	0	0
高血糖	2 (0.3%)	1 (0.2%)	0	0
肺浸潤	2 (0.3%)	1 (0.2%)	0	0
胃腸炎	2 (0.3%)	0	0	0
下気道感染	2 (0.3%)	0	0	0
心筋梗塞	2 (0.3%)	0	0	0
肺敗血症	2 (0.3%)	0	0	0
好中球減少症	1 (0.2%)	0	24 (4.2%)	24 (4.2%)
好中球数減少	1 (0.2%)	0	17 (2.9%)	17 (2.9%)
末梢性ニューロパチー	1 (0.2%)	0	7 (1.2%)	6 (1.0%)
末梢性浮腫	1 (0.2%)	1 (0.2%)	6 (1.0%)	6 (1.0%)
食欲減退	1 (0.2%)	1 (0.2%)	6 (1.0%)	5 (0.9%)
筋肉痛	1 (0.2%)	1 (0.2%)	4 (0.7%)	4 (0.7%)
過敏症	1 (0.2%)	1 (0.2%)	3 (0.5%)	3 (0.5%)
胸部不快感	1 (0.2%)	0	3 (0.5%)	3 (0.5%)
低血圧	1 (0.2%)	0	3 (0.5%)	0
倦怠感	1 (0.2%)	1 (0.2%)	2 (0.3%)	2 (0.3%)
大腸炎	1 (0.2%)	1 (0.2%)	2 (0.3%)	2 (0.3%)
粘膜の炎症	1 (0.2%)	1 (0.2%)	2 (0.3%)	2 (0.3%)
浮動性めまい	1 (0.2%)	1 (0.2%)	2 (0.3%)	2 (0.3%)
呼吸不全	1 (0.2%)	0	2 (0.3%)	1 (0.2%)
慢性閉塞性肺疾患	1 (0.2%)	0	2 (0.3%)	1 (0.2%)
インフルエンザ様疾患	1 (0.2%)	0	2 (0.3%)	0
関節痛	1 (0.2%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
血中アルカリホスファターゼ増加	1 (0.2%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
熱感	1 (0.2%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
感覚鈍麻	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
高血圧	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
心嚢液貯留	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
多汗症	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
脱水	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
低カリウム血症	1 (0.2%)	0	1 (0.2%)	1 (0.2%)
感染	1 (0.2%)	0	1 (0.2%)	0
気胸	1 (0.2%)	0	1 (0.2%)	0
錯乱状態	1 (0.2%)	0	1 (0.2%)	0
Ｃ－反応性蛋白	1 (0.2%)	1 (0.2%)	0	0
ほてり	1 (0.2%)	1 (0.2%)	0	0
ギラン・バレー症候群	1 (0.2%)	1 (0.2%)	0	0

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AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
悪寒	1 (0.2%)	1 (0.2%)	0	0
関節リウマチ	1 (0.2%)	1 (0.2%)	0	0
関節可動域低下	1 (0.2%)	1 (0.2%)	0	0
器質化肺炎	1 (0.2%)	1 (0.2%)	0	0
急性肝炎	1 (0.2%)	1 (0.2%)	0	0
胸膜瘻	1 (0.2%)	1 (0.2%)	0	0
憩室炎	1 (0.2%)	1 (0.2%)	0	0
血小板数減少	1 (0.2%)	1 (0.2%)	0	0
誤嚥	1 (0.2%)	1 (0.2%)	0	0
視神経炎	1 (0.2%)	1 (0.2%)	0	0
耳下腺炎	1 (0.2%)	1 (0.2%)	0	0
心タンポナーデ	1 (0.2%)	1 (0.2%)	0	0
帯状疱疹	1 (0.2%)	1 (0.2%)	0	0
腸閉塞	1 (0.2%)	1 (0.2%)	0	0
内分泌性眼症	1 (0.2%)	1 (0.2%)	0	0
膿疱性皮疹	1 (0.2%)	1 (0.2%)	0	0
肺気腫	1 (0.2%)	1 (0.2%)	0	0
発作性頻脈	1 (0.2%)	1 (0.2%)	0	0
皮脂欠乏性湿疹	1 (0.2%)	1 (0.2%)	0	0
皮膚炎	1 (0.2%)	1 (0.2%)	0	0
皮膚硬結	1 (0.2%)	1 (0.2%)	0	0
頻呼吸	1 (0.2%)	1 (0.2%)	0	0
放射線性肺臓炎	1 (0.2%)	1 (0.2%)	0	0
蜂巣炎	1 (0.2%)	1 (0.2%)	0	0
薬疹	1 (0.2%)	1 (0.2%)	0	0
扁桃炎	1 (0.2%)	1 (0.2%)	0	0
ＥＣＯＧパフォーマンスステータス悪化	1 (0.2%)	0	0	0
うつ病	1 (0.2%)	0	0	0
びらん性胃炎	1 (0.2%)	0	0	0
ウイルス感染	1 (0.2%)	0	0	0
クロストリジウム・ディフィシレ感染	1 (0.2%)	0	0	0
メレナ	1 (0.2%)	0	0	0
亜イレウス	1 (0.2%)	0	0	0
医療機器関連感染	1 (0.2%)	0	0	0
関節周囲炎	1 (0.2%)	0	0	0
癌疼痛	1 (0.2%)	0	0	0
急性胆嚢炎	1 (0.2%)	0	0	0
筋力低下	1 (0.2%)	0	0	0
筋痙縮	1 (0.2%)	0	0	0

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事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
血栓症	1 (0.2%)	0	0	0
血中クレアチニン増加	1 (0.2%)	0	0	0
股関節部骨折	1 (0.2%)	0	0	0
歯感染	1 (0.2%)	0	0	0
上大静脈症候群	1 (0.2%)	0	0	0
心電図ＱＴ延長	1 (0.2%)	0	0	0
深部静脈血栓症	1 (0.2%)	0	0	0
水疱性皮膚炎	1 (0.2%)	0	0	0
全身性浮腫	1 (0.2%)	0	0	0
大脳動脈塞栓症	1 (0.2%)	0	0	0
第３度熱傷	1 (0.2%)	0	0	0
胆汁うっ滞性黄疸	1 (0.2%)	0	0	0
蛋白尿	1 (0.2%)	0	0	0
中耳炎	1 (0.2%)	0	0	0
転倒	1 (0.2%)	0	0	0
軟部組織膿瘍	1 (0.2%)	0	0	0
粘膜乾燥	1 (0.2%)	0	0	0
粘膜感染	1 (0.2%)	0	0	0
脳症	1 (0.2%)	0	0	0
肺水腫	1 (0.2%)	0	0	0
皮膚真菌感染	1 (0.2%)	0	0	0
嘔吐	1 (0.2%)	0	0	0
膵炎	1 (0.2%)	0	0	0
鼠径ヘルニア	1 (0.2%)	0	0	0
発熱性好中球減少症	0	0	36 (6.2%)	35 (6.1%)
白血球減少症	0	0	7 (1.2%)	7 (1.2%)
末梢性感覚ニューロパチー	0	0	7 (1.2%)	7 (1.2%)
急性腎障害	0	0	3 (0.5%)	2 (0.3%)
尿路感染	0	0	3 (0.5%)	0
高血圧クリーゼ	0	0	2 (0.3%)	2 (0.3%)
白血球数減少	0	0	2 (0.3%)	2 (0.3%)
皮膚反応	0	0	2 (0.3%)	2 (0.3%)
浮腫	0	0	2 (0.3%)	2 (0.3%)
味覚異常	0	0	2 (0.3%)	2 (0.3%)
高カリウム血症	0	0	2 (0.3%)	1 (0.2%)
敗血症	0	0	2 (0.3%)	1 (0.2%)
胸膜感染	0	0	2 (0.3%)	0
白血球増加症	0	0	2 (0.3%)	0
イレウス	0	0	1 (0.2%)	1 (0.2%)

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事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
カンジダ感染	0	0	1 (0.2%)	1 (0.2%)
ヘモグロビン減少	0	0	1 (0.2%)	1 (0.2%)
悪心	0	0	1 (0.2%)	1 (0.2%)
医薬品副作用	0	0	1 (0.2%)	1 (0.2%)
回転性めまい	0	0	1 (0.2%)	1 (0.2%)
顔面浮腫	0	0	1 (0.2%)	1 (0.2%)
気管支痙攣	0	0	1 (0.2%)	1 (0.2%)
結膜炎	0	0	1 (0.2%)	1 (0.2%)
錯感覚	0	0	1 (0.2%)	1 (0.2%)
手掌・足底発赤知覚不全症候群	0	0	1 (0.2%)	1 (0.2%)
十二指腸穿孔	0	0	1 (0.2%)	1 (0.2%)
上室性頻脈	0	0	1 (0.2%)	1 (0.2%)
上腹部痛	0	0	1 (0.2%)	1 (0.2%)
腎不全	0	0	1 (0.2%)	1 (0.2%)
注入部位発疹	0	0	1 (0.2%)	1 (0.2%)
爪の障害	0	0	1 (0.2%)	1 (0.2%)
爪囲炎	0	0	1 (0.2%)	1 (0.2%)
爪感染	0	0	1 (0.2%)	1 (0.2%)
爪毒性	0	0	1 (0.2%)	1 (0.2%)
排尿困難	0	0	1 (0.2%)	1 (0.2%)
皮膚乾燥	0	0	1 (0.2%)	1 (0.2%)
腹部不快感	0	0	1 (0.2%)	1 (0.2%)
末梢性感覚運動ニューロパチー	0	0	1 (0.2%)	1 (0.2%)
流涙増加	0	0	1 (0.2%)	1 (0.2%)
インフルエンザ	0	0	1 (0.2%)	0
ウイルス性気道感染	0	0	1 (0.2%)	0
ストレス心筋症	0	0	1 (0.2%)	0
気管支閉塞	0	0	1 (0.2%)	0
胸痛	0	0	1 (0.2%)	0
胸膜痛	0	0	1 (0.2%)	0
結腸膿瘍	0	0	1 (0.2%)	0
高カルシウム血症	0	0	1 (0.2%)	0
歯周炎	0	0	1 (0.2%)	0
食道瘻	0	0	1 (0.2%)	0
脊椎圧迫骨折	0	0	1 (0.2%)	0
総蛋白減少	0	0	1 (0.2%)	0
大腸穿孔	0	0	1 (0.2%)	0
注入部位反応	0	0	1 (0.2%)	0
糖尿病	0	0	1 (0.2%)	0

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AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA Preferred Term	Atezolizumab (Actual) (N=609) AE No. (%)	Atezolizumab (Actual) (N=609) Related AE No. (%)	Docetaxel (Actual) (N=578) AE No. (%)	Docetaxel (Actual) (N=578) Related AE No. (%)
頭位性回転性めまい	0	0	1 (0.2%)	0
頭痛	0	0	1 (0.2%)	0
鼻咽頭炎	0	0	1 (0.2%)	0
膝蓋骨骨折	0	0	1 (0.2%)	0
副鼻腔炎	0	0	1 (0.2%)	0
腹部膿瘍	0	0	1 (0.2%)	0
無気肺	0	0	1 (0.2%)	0
労作性呼吸困難	0	0	1 (0.2%)	0
嗜眠	0	0	1 (0.2%)	0

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All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

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Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/ae_rae_mod_GO28915_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.1-3 ae_rae_mod_GO28915_SE を再掲］

(2) 治験薬の投与量変更に至った有害事象の要約（POPLAR 試験）

表 2.7.4.7.4-2 治験薬の投与量変更に至った有害事象の要約（POPLAR 試験）

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

MedDRA Preferred Term	atezolizumab 1200 mg q3w IV (N=142) AE No. (%)	atezolizumab 1200 mg q3w IV (N=142) Related AE No. (%)	Docetaxel (N=135) AE No. (%)	Docetaxel (N=135) Related AE No. (%)
Total number of patients with at least one adverse event	34 (23.9%)	15 (10.6%)	44 (32.6%)	32 (23.7%)
肺炎	3 (2.1%)	2 (1.4%)	0	0
呼吸困難	2 (1.4%)	2 (1.4%)	2 (1.5%)	1 (0.7%)
上気道感染	2 (1.4%)	0	2 (1.5%)	0
貧血	2 (1.4%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
アラニンアミノトランスフェラーゼ増加	2 (1.4%)	2 (1.4%)	0	0
甲状腺機能低下症	2 (1.4%)	2 (1.4%)	0	0
低酸素症	2 (1.4%)	2 (1.4%)	0	0
肺臓炎	2 (1.4%)	2 (1.4%)	0	0
疲労	1 (0.7%)	0	9 (6.7%)	9 (6.7%)
鼻咽頭炎	1 (0.7%)	0	2 (1.5%)	0
発疹	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
急性腎不全	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
胸水	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
注入に伴う反応	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
低血圧	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
無力症	1 (0.7%)	0	1 (0.7%)	1 (0.7%)
そう痒症	1 (0.7%)	1 (0.7%)	0	0
インフルエンザ様疾患	1 (0.7%)	1 (0.7%)	0	0
リンパ球数減少	1 (0.7%)	1 (0.7%)	0	0
血中アルカリホスファターゼ増加	1 (0.7%)	1 (0.7%)	0	0
血中ビリルビン増加	1 (0.7%)	1 (0.7%)	0	0
静脈狭窄	1 (0.7%)	1 (0.7%)	0	0
大腸炎	1 (0.7%)	1 (0.7%)	0	0
溶血	1 (0.7%)	1 (0.7%)	0	0
咽頭炎	1 (0.7%)	0	0	0
下気道感染	1 (0.7%)	0	0	0
肝機能検査異常	1 (0.7%)	0	0	0
気管支炎	1 (0.7%)	0	0	0
気道感染	1 (0.7%)	0	0	0
胸膜痛	1 (0.7%)	0	0	0
血中クレアチニン増加	1 (0.7%)	0	0	0
細菌性気道感染	1 (0.7%)	0	0	0
錯乱状態	1 (0.7%)	0	0	0
食道痛	1 (0.7%)	0	0	0
肺感染	1 (0.7%)	0	0	0
肺障害	1 (0.7%)	0	0	0
頻脈	1 (0.7%)	0	0	0
便秘	1 (0.7%)	0	0	0
喀血	1 (0.7%)	0	0	0
発熱性好中球減少症	0	0	5 (3.7%)	5 (3.7%)
末梢性感覚ニューロパチー	0	0	4 (3.0%)	3 (2.2%)

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_mod_GO28753_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

MedDRA Preferred Term	atezolizumab 1200 mg q3w IV (N=142) AE No. (%)	atezolizumab 1200 mg q3w IV (N=142) Related AE No. (%)	Docetaxel (N=135) AE No. (%)	Docetaxel (N=135) Related AE No. (%)
好中球減少症	0	0	3 (2.2%)	3 (2.2%)
好中球数減少	0	0	2 (1.5%)	2 (1.5%)
手掌・足底発赤知覚不全症候群	0	0	2 (1.5%)	2 (1.5%)
脱水	0	0	2 (1.5%)	2 (1.5%)
下痢	0	0	2 (1.5%)	1 (0.7%)
筋肉痛	0	0	2 (1.5%)	1 (0.7%)
発熱	0	0	2 (1.5%)	1 (0.7%)
帯状疱疹	0	0	2 (1.5%)	0
悪心	0	0	1 (0.7%)	1 (0.7%)
関節痛	0	0	1 (0.7%)	1 (0.7%)
錯感覚	0	0	1 (0.7%)	1 (0.7%)
食欲減退	0	0	1 (0.7%)	1 (0.7%)
腎不全	0	0	1 (0.7%)	1 (0.7%)
背部痛	0	0	1 (0.7%)	1 (0.7%)
腹水	0	0	1 (0.7%)	1 (0.7%)
末梢性ニューロパチー	0	0	1 (0.7%)	1 (0.7%)
嘔吐	0	0	1 (0.7%)	1 (0.7%)
疼痛	0	0	1 (0.7%)	1 (0.7%)
感覚鈍麻	0	0	1 (0.7%)	0
感染性皮膚嚢腫	0	0	1 (0.7%)	0
高血糖	0	0	1 (0.7%)	0
上部消化管出血	0	0	1 (0.7%)	0
神経因性膀胱	0	0	1 (0.7%)	0
蛋白尿	0	0	1 (0.7%)	0
洞性頻脈	0	0	1 (0.7%)	0
尿量減少	0	0	1 (0.7%)	0
尿路感染	0	0	1 (0.7%)	0
肺塞栓症	0	0	1 (0.7%)	0
末梢性虚血	0	0	1 (0.7%)	0

事象名：MedDRA ver. 18.0
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28753a/reports/ae_rae_mod_GO28753_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_mod_GO28753_SE を再掲］

(3) 本剤の休薬に至った有害事象の要約（BIRCH 試験）

表 2.7.4.7.4-3 本剤の休薬に至った有害事象の要約（BIRCH 試験）

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
Total number of patients with at least one adverse event	172 (26.1%)	83 (12.6%)	33 (23.7%)	12 (8.6%)	66 (24.7%)	35 (13.1%)	73 (28.9%)	36 (14.2%)
肺臓炎	18 (2.7%)	15 (2.3%)	1 (0.7%)	1 (0.7%)	8 (3.0%)	6 (2.2%)	9 (3.6%)	8 (3.2%)
呼吸困難	17 (2.6%)	6 (0.9%)	5 (3.6%)	2 (1.4%)	5 (1.9%)	3 (1.1%)	7 (2.8%)	1 (0.4%)
疲労	14 (2.1%)	9 (1.4%)	3 (2.2%)	2 (1.4%)	6 (2.2%)	4 (1.5%)	5 (2.0%)	3 (1.2%)
肺炎	9 (1.4%)	0	3 (2.2%)	0	2 (0.7%)	0	4 (1.6%)	0
下痢	7 (1.1%)	6 (0.9%)	2 (1.4%)	2 (1.4%)	4 (1.5%)	3 (1.1%)	1 (0.4%)	1 (0.4%)
注入に伴う反応	7 (1.1%)	7 (1.1%)	1 (0.7%)	1 (0.7%)	4 (1.5%)	4 (1.5%)	2 (0.8%)	2 (0.8%)
高カルシウム血症	5 (0.8%)	2 (0.3%)	0	0	4 (1.5%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
肺感染	4 (0.6%)	0	3 (2.2%)	0	1 (0.4%)	0	0	0
大腸炎	4 (0.6%)	4 (0.6%)	1 (0.7%)	1 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
背部痛	4 (0.6%)	1 (0.2%)	1 (0.7%)	0	2 (0.7%)	1 (0.4%)	1 (0.4%)	0
甲状腺機能低下症	4 (0.6%)	4 (0.6%)	1 (0.7%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	2 (0.8%)	2 (0.8%)
過敏症	4 (0.6%)	4 (0.6%)	0	0	2 (0.7%)	2 (0.7%)	2 (0.8%)	2 (0.8%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_mod_GO28754_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
関節痛	4 (0.6%)	2 (0.3%)	0	0	2 (0.7%)	1 (0.4%)	2 (0.8%)	1 (0.4%)
アスパラギン酸アミノトランスフェラーゼ増加	4 (0.6%)	3 (0.5%)	0	0	1 (0.4%)	1 (0.4%)	3 (1.2%)	2 (0.8%)
アラニンアミノトランスフェラーゼ増加	4 (0.6%)	3 (0.5%)	0	0	1 (0.4%)	1 (0.4%)	3 (1.2%)	2 (0.8%)
食欲減退	3 (0.5%)	2 (0.3%)	2 (1.4%)	2 (1.4%)	0	0	1 (0.4%)	0
低酸素症	3 (0.5%)	1 (0.2%)	1 (0.7%)	0	2 (0.7%)	1 (0.4%)	0	0
胸水	3 (0.5%)	1 (0.2%)	1 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
尿路感染	3 (0.5%)	1 (0.2%)	1 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	1 (0.4%)
鼻咽頭炎	3 (0.5%)	0	1 (0.7%)	0	1 (0.4%)	0	1 (0.4%)	0
無力症	3 (0.5%)	3 (0.5%)	1 (0.7%)	1 (0.7%)	0	0	2 (0.8%)	2 (0.8%)
慢性閉塞性肺疾患	3 (0.5%)	0	1 (0.7%)	0	0	0	2 (0.8%)	0
上気道感染	3 (0.5%)	0	0	0	3 (1.1%)	0	0	0
γ－グルタミルトランスフェラーゼ増加	3 (0.5%)	3 (0.5%)	0	0	2 (0.7%)	2 (0.7%)	1 (0.4%)	1 (0.4%)
発熱	3 (0.5%)	1 (0.2%)	0	0	1 (0.4%)	0	2 (0.8%)	1 (0.4%)
気管支炎	2 (0.3%)	0	2 (1.4%)	0	0	0	0	0
悪寒	2 (0.3%)	2 (0.3%)	1 (0.7%)	1 (0.7%)	1 (0.4%)	1 (0.4%)	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
倦怠感	2 (0.3%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	1 (0.4%)	0
インフルエンザ様疾患	2 (0.3%)	0	1 (0.7%)	0	0	0	1 (0.4%)	0
そう痒症	2 (0.3%)	2 (0.3%)	0	0	2 (0.7%)	2 (0.7%)	0	0
頻脈	2 (0.3%)	1 (0.2%)	0	0	2 (0.7%)	1 (0.4%)	0	0
病的骨折	2 (0.3%)	0	0	0	2 (0.7%)	0	0	0
筋肉痛	2 (0.3%)	2 (0.3%)	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
筋骨格系胸痛	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
喀血	2 (0.3%)	0	0	0	1 (0.4%)	0	1 (0.4%)	0
胸部コンピュータ断層撮影異常	2 (0.3%)	2 (0.3%)	0	0	0	0	2 (0.8%)	2 (0.8%)
血小板数減少	2 (0.3%)	1 (0.2%)	0	0	0	0	2 (0.8%)	1 (0.4%)
低ナトリウム血症	2 (0.3%)	1 (0.2%)	0	0	0	0	2 (0.8%)	1 (0.4%)
医薬品副作用	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
多汗症	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
脱毛症	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
胆嚢炎	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_mod_GO28754_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
肺浸潤	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
嗜眠	1 (0.2%)	1 (0.2%)	1 (0.7%)	1 (0.7%)	0	0	0	0
外傷性血胸	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
感染性胸水	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
気管支肺炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
胸痛	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
筋骨格痛	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
骨髄炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
塞栓症	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
心筋梗塞	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
腎不全	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
脊髄症	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
体重減少	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
大腿骨骨折	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
蓄膿	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
脳炎	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
発疹	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
末梢性ニューロパチー	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
末梢動脈閉塞性疾患	1 (0.2%)	0	1 (0.7%)	0	0	0	0	0
１型糖尿病	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
横紋筋融解症	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
肝酵素上昇	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
亀頭包皮炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
結膜炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
血中甲状腺刺激ホルモン増加	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
血中乳酸脱水素酵素増加	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
甲状腺機能亢進症	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
脊髄炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
苔癬様角化症	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
皮膚筋炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_mod_GO28754_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
副腎機能不全	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
膵炎	1 (0.2%)	1 (0.2%)	0	0	1 (0.4%)	1 (0.4%)	0	0
ウイルス性胃腸炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
ヘルペス後神経痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
悪性胸水	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
下気道感染	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
完全房室ブロック	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
感染性大腸炎	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
肝機能検査異常	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
気管狭窄	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
虚血性脳卒中	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
頚静脈血栓症	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
呼吸不全	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
喉頭出血	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
錯乱状態	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_mod_GO28754_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
失神寸前の状態	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
湿性咳嗽	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
腎結石症	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
尿路閉塞	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
非心臓性胸痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
貧血	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
腹痛	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
嘔吐	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
膀胱癌	1 (0.2%)	0	0	0	1 (0.4%)	0	0	0
アミラーゼ増加	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
乾癬	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
筋痙縮	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
血小板減少性紫斑病	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
血中クレアチンホスホキナーゼ増加	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
好中球減少症	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
四肢痛	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
心房細動	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
前庭神経炎	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
斑状皮疹	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
放射線性肺臓炎	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (0.4%)	1 (0.4%)
インフルエンザ	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
カテーテル留置部位感染	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
リンパ節感染	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
悪心	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
感染	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
肝機能異常	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
癌性リンパ管症	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
気管支閉塞	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
菌血症	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
血中アルカリホスファターゼ増加	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=659) AE No. (%)	atezolizumab Total (N=659) Related AE No. (%)	atezolizumab Cohort 1 (N=139) AE No. (%)	atezolizumab Cohort 1 (N=139) Related AE No. (%)	atezolizumab Cohort 2 (N=267) AE No. (%)	atezolizumab Cohort 2 (N=267) Related AE No. (%)	atezolizumab Cohort 3 (N=253) AE No. (%)	atezolizumab Cohort 3 (N=253) Related AE No. (%)
呼吸窮迫	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
股関節形成	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
誤嚥性肺炎	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
骨痛	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
細菌性肺炎	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
心停止	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
脳血管発作	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
白血球数減少	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
白血球増加症	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0
便秘	1 (0.2%)	0	0	0	0	0	1 (0.4%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28754a/reports/ae_rae_mod_GO28754_SE.out
09NOV2016 10:47

因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_mod_GO28754_SE を再掲］

(4) 本剤の休薬に至った有害事象の要約（FIR 試験）

表 2.7.4.7.4-4 本剤の休薬に至った有害事象の要約（FIR 試験）

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137)		atezolizumab Cohort 1 (N=31)		atezolizumab Cohort 2 (N=93)		atezolizumab Cohort 3 (N=13)	
	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)	AE No. (%)	Related AE No. (%)
Total number of patients with at least one adverse event	32 (23.4%)	11 (8.0%)	11 (35.5%)	4 (12.9%)	19 (20.4%)	6 (6.5%)	2 (15.4%)	1 (7.7%)
肺炎	4 (2.9%)	0	2 (6.5%)	0	2 (2.2%)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.5%)	2 (1.5%)	1 (3.2%)	1 (3.2%)	1 (1.1%)	1 (1.1%)	0	0
アラニンアミノトランスフェラーゼ増加	2 (1.5%)	2 (1.5%)	1 (3.2%)	1 (3.2%)	1 (1.1%)	1 (1.1%)	0	0
潮紅	2 (1.5%)	2 (1.5%)	1 (3.2%)	1 (3.2%)	1 (1.1%)	1 (1.1%)	0	0
呼吸困難	2 (1.5%)	0	1 (3.2%)	0	1 (1.1%)	0	0	0
上気道感染	2 (1.5%)	0	1 (3.2%)	0	1 (1.1%)	0	0	0
低血圧	2 (1.5%)	1 (0.7%)	0	0	2 (2.2%)	1 (1.1%)	0	0
肺塞栓症	2 (1.5%)	0	0	0	2 (2.2%)	0	0	0
血小板減少症	1 (0.7%)	1 (0.7%)	1 (3.2%)	1 (3.2%)	0	0	0	0
好中球減少症	1 (0.7%)	1 (0.7%)	1 (3.2%)	1 (3.2%)	0	0	0	0
水疱性皮膚炎	1 (0.7%)	1 (0.7%)	1 (3.2%)	1 (3.2%)	0	0	0	0
肺臓炎	1 (0.7%)	1 (0.7%)	1 (3.2%)	1 (3.2%)	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_mod_GO28625_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
斑状丘疹状皮疹	1 (0.7%)	1 (0.7%)	1 (3.2%)	1 (3.2%)	0	0	0	0
喘鳴	1 (0.7%)	1 (0.7%)	1 (3.2%)	1 (3.2%)	0	0	0	0
悪心	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
筋力低下	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
挫傷	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
手骨折	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
心筋梗塞	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
心房細動	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
深部静脈血栓症	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
脊椎圧迫骨折	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
体重減少	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
転倒	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
疲労	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
嘔吐	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0
靭帯捻挫	1 (0.7%)	0	1 (3.2%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
意識消失	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
咳嗽	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
胸痛	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
結膜炎	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
視力低下	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
播種性帯状疱疹	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
発熱	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
無力症	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
蕁麻疹	1 (0.7%)	1 (0.7%)	0	0	1 (1.1%)	1 (1.1%)	0	0
ヘリコバクター検査陽性	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
下気道感染	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
下痢	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
頚部膿瘍	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
好酸球性食道炎	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
錯乱状態	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_mod_GO28625_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA Preferred Term	atezolizumab Total (N=137) AE No. (%)	atezolizumab Total (N=137) Related AE No. (%)	atezolizumab Cohort 1 (N=31) AE No. (%)	atezolizumab Cohort 1 (N=31) Related AE No. (%)	atezolizumab Cohort 2 (N=93) AE No. (%)	atezolizumab Cohort 2 (N=93) Related AE No. (%)	atezolizumab Cohort 3 (N=13) AE No. (%)	atezolizumab Cohort 3 (N=13) Related AE No. (%)
心嚢液貯留	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
耐糖能障害	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
低カルシウム血症	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
軟部組織感染	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
背部痛	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
肺出血	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
肺水腫	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
貧血	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
複視	1 (0.7%)	0	0	0	1 (1.1%)	0	0	0
浮動性めまい	1 (0.7%)	1 (0.7%)	0	0	0	0	1 (7.7%)	1 (7.7%)
歩行障害	1 (0.7%)	1 (0.7%)	0	0	0	0	1 (7.7%)	1 (7.7%)
皮膚炎	1 (0.7%)	0	0	0	0	0	1 (7.7%)	0

事象名：MedDRA ver. 18.0
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28625a/reports/ae_rae_mod_GO28625_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_mod_GO28625_SE を再掲］

(5) 本剤の投与量変更に至った有害事象の要約（PCD4989g 試験）

表 2.7.4.7.4-5 本剤の投与量変更に至った有害事象の要約（PCD4989g 試験）

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
Total number of patients with at least one adverse event	91 (18.9%)	39 (8.1%)	2 (22.2%)	1 (11.1%)	2 (66.7%)	1 (33.3%)	12 (33.3%)	4 (11.1%)
呼吸困難	8 (1.7%)	5 (1.0%)	1 (11.1%)	1 (11.1%)	0	0	1 (2.8%)	0
発熱	5 (1.0%)	2 (0.4%)	1 (11.1%)	0	0	0	0	0
下痢	4 (0.8%)	2 (0.4%)	0	0	0	0	2 (5.6%)	1 (2.8%)
低酸素症	4 (0.8%)	2 (0.4%)	0	0	0	0	1 (2.8%)	0
アスパラギン酸アミノトランスフェラーゼ増加	4 (0.8%)	2 (0.4%)	0	0	0	0	0	0
肺炎	4 (0.8%)	1 (0.2%)	0	0	0	0	0	0
アラニンアミノトランスフェラーゼ増加	4 (0.8%)	3 (0.6%)	0	0	0	0	0	0
疲労	4 (0.8%)	1 (0.2%)	0	0	0	0	0	0
悪寒	3 (0.6%)	1 (0.2%)	2 (22.2%)	1 (11.1%)	0	0	0	0
上気道感染	3 (0.6%)	0	0	0	0	0	1 (2.8%)	0
血中アルカリホスファターゼ増加	3 (0.6%)	1 (0.2%)	0	0	0	0	0	0
気胸	3 (0.6%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
多汗症	2 (0.4%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
胸痛	2 (0.4%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
精神状態変化	2 (0.4%)	0	0	0	0	0	2 (5.6%)	0
自己免疫性肝炎	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
血中クレアチニン増加	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
脱水	2 (0.4%)	0	0	0	0	0	0	0
低ナトリウム血症	2 (0.4%)	0	0	0	0	0	0	0
低血圧	2 (0.4%)	0	0	0	0	0	0	0
肝機能検査異常	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
好中球減少症	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
心嚢液貯留	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
無力症	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
悪心	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
嘔吐	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
筋骨格痛	2 (0.4%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
錯乱状態	2 (0.4%)	0	0	0	0	0	0	0
貧血	2 (0.4%)	0	0	0	0	0	0	0
食欲減退	2 (0.4%)	1 (0.2%)	0	0	0	0	0	0
肺臓炎	2 (0.4%)	2 (0.4%)	0	0	0	0	0	0
感覚鈍麻	1 (0.2%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
胸部不快感	1 (0.2%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
口の感覚鈍麻	1 (0.2%)	1 (0.2%)	1 (11.1%)	1 (11.1%)	0	0	0	0
筋肉痛	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
食道炎	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
寝汗	1 (0.2%)	0	1 (11.1%)	0	0	0	0	0
腫瘍の潰瘍形成	1 (0.2%)	1 (0.2%)	0	0	1 (33.3%)	1 (33.3%)	0	0
蛋白尿	1 (0.2%)	0	0	0	1 (33.3%)	0	0	0
頭痛	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (2.8%)	1 (2.8%)
難聴	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (2.8%)	1 (2.8%)
皮膚真菌感染	1 (0.2%)	1 (0.2%)	0	0	0	0	1 (2.8%)	1 (2.8%)

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
側腹部痛	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
転倒	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
肺感染	1 (0.2%)	0	0	0	0	0	1 (2.8%)	0
そう痒性皮疹	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
咳嗽	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
胸部コンピュータ断層撮影異常	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
高ビリルビン血症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
重症筋無力症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
斑状丘疹状皮疹	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
腹部膨満	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
そう痒症	1 (0.2%)	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 (0.2%)	0	0	0	0	0	0	0
胃出血	1 (0.2%)	0	0	0	0	0	0	0
血液量減少症	1 (0.2%)	0	0	0	0	0	0	0
血腫	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
血中ビリルビン増加	1 (0.2%)	0	0	0	0	0	0	0
血尿	1 (0.2%)	0	0	0	0	0	0	0
口腔咽頭痛	1 (0.2%)	0	0	0	0	0	0	0
視野欠損	1 (0.2%)	0	0	0	0	0	0	0
上大静脈症候群	1 (0.2%)	0	0	0	0	0	0	0
深部静脈血栓症	1 (0.2%)	0	0	0	0	0	0	0
腎機能障害	1 (0.2%)	0	0	0	0	0	0	0
水腎症	1 (0.2%)	0	0	0	0	0	0	0
脊髄圧迫	1 (0.2%)	0	0	0	0	0	0	0
創離開	1 (0.2%)	0	0	0	0	0	0	0
帯状疱疹	1 (0.2%)	0	0	0	0	0	0	0
大腸閉塞	1 (0.2%)	0	0	0	0	0	0	0
洞性頻脈	1 (0.2%)	0	0	0	0	0	0	0
尿路性敗血症	1 (0.2%)	0	0	0	0	0	0	0
尿路閉塞	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
敗血症	1 (0.2%)	0	0	0	0	0	0	0
腹痛	1 (0.2%)	0	0	0	0	0	0	0
腹部膿瘍	1 (0.2%)	0	0	0	0	0	0	0
腹部癒着	1 (0.2%)	0	0	0	0	0	0	0
嚥下障害	1 (0.2%)	0	0	0	0	0	0	0
運動失調	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
甲状腺機能低下症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
甲状腺機能亢進症	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
骨痛	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
十二指腸潰瘍	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
全身性炎症反応症候群	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
体重減少	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
末梢性浮腫	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
疼痛	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
医療機器関連感染	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab Total (N=481) AE No. (%)	atezolizumab Total (N=481) Related AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) AE No. (%)	atezolizumab <=1 mg/kg q3w IV (N=9) Related AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) AE No. (%)	atezolizumab 3 mg/kg q3w IV (N=3) Related AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) AE No. (%)	atezolizumab 10 mg/kg q3w IV (N=36) Related AE No. (%)
胆管閉塞	1 (0.2%)	0	0	0	0	0	0	0
胆嚢炎	1 (0.2%)	0	0	0	0	0	0	0
動悸	1 (0.2%)	0	0	0	0	0	0	0
肺硬化	1 (0.2%)	0	0	0	0	0	0	0
肺塞栓症	1 (0.2%)	0	0	0	0	0	0	0
病的骨折	1 (0.2%)	0	0	0	0	0	0	0
歩行障害	1 (0.2%)	0	0	0	0	0	0	0
髄膜炎	1 (0.2%)	1 (0.2%)	0	0	0	0	0	0
急性腎不全	1 (0.2%)	0	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
Total number of patients with at least one adverse event	43 (18.2%)	17 (7.2%)	28 (19.2%)	14 (9.6%)	4 (7.8%)	2 (3.9%)
呼吸困難	3 (1.3%)	2 (0.8%)	3 (2.1%)	2 (1.4%)	0	0
発熱	3 (1.3%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
下痢	2 (0.8%)	1 (0.4%)	0	0	0	0
低酸素症	2 (0.8%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	3 (1.3%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
肺炎	3 (1.3%)	1 (0.4%)	1 (0.7%)	0	0	0
アラニンアミノトランスフェラーゼ増加	2 (0.8%)	1 (0.4%)	2 (1.4%)	2 (1.4%)	0	0
疲労	2 (0.8%)	0	1 (0.7%)	0	1 (2.0%)	1 (2.0%)
悪寒	1 (0.4%)	0	0	0	0	0
上気道感染	1 (0.4%)	0	1 (0.7%)	0	0	0
血中アルカリホスファターゼ増加	3 (1.3%)	1 (0.4%)	0	0	0	0
気胸	1 (0.4%)	0	2 (1.4%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
多汗症	1 (0.4%)	0	0	0	0	0
胸痛	0	0	1 (0.7%)	0	0	0
精神状態変化	0	0	0	0	0	0
自己免疫性肝炎	2 (0.8%)	2 (0.8%)	0	0	0	0
血中クレアチニン増加	2 (0.8%)	1 (0.4%)	0	0	0	0
脱水	2 (0.8%)	0	0	0	0	0
低ナトリウム血症	2 (0.8%)	0	0	0	0	0
低血圧	2 (0.8%)	0	0	0	0	0
肝機能検査異常	1 (0.4%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
好中球減少症	1 (0.4%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0	0
心嚢液貯留	1 (0.4%)	1 (0.4%)	1 (0.7%)	0	0	0
無力症	1 (0.4%)	1 (0.4%)	1 (0.7%)	0	0	0
悪心	1 (0.4%)	0	1 (0.7%)	1 (0.7%)	0	0
嘔吐	1 (0.4%)	0	1 (0.7%)	1 (0.7%)	0	0
筋骨格痛	1 (0.4%)	0	1 (0.7%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
錯乱状態	1 (0.4%)	0	1 (0.7%)	0	0	0
貧血	1 (0.4%)	0	1 (0.7%)	0	0	0
食欲減退	1 (0.4%)	1 (0.4%)	0	0	1 (2.0%)	0
肺臓炎	0	0	2 (1.4%)	2 (1.4%)	0	0
感覚鈍麻	0	0	0	0	0	0
胸部不快感	0	0	0	0	0	0
口の感覚鈍麻	0	0	0	0	0	0
筋肉痛	0	0	0	0	0	0
食道炎	0	0	0	0	0	0
寝汗	0	0	0	0	0	0
腫瘍の潰瘍形成	0	0	0	0	0	0
蛋白尿	0	0	0	0	0	0
頭痛	0	0	0	0	0	0
難聴	0	0	0	0	0	0
皮膚真菌感染	0	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
側腹部痛	0	0	0	0	0	0
転倒	0	0	0	0	0	0
肺感染	0	0	0	0	0	0
そう痒性皮疹	1 (0.4%)	1 (0.4%)	0	0	0	0
咳嗽	1 (0.4%)	1 (0.4%)	0	0	0	0
胸部コンピュータ断層撮影異常	1 (0.4%)	1 (0.4%)	0	0	0	0
高ビリルビン血症	1 (0.4%)	1 (0.4%)	0	0	0	0
重症筋無力症	1 (0.4%)	1 (0.4%)	0	0	0	0
斑状丘疹状皮疹	1 (0.4%)	1 (0.4%)	0	0	0	0
腹部膨満	1 (0.4%)	1 (0.4%)	0	0	0	0
そう痒症	1 (0.4%)	0	0	0	0	0
γ－グルタミルトランスフェラーゼ増加	1 (0.4%)	0	0	0	0	0
胃出血	1 (0.4%)	0	0	0	0	0
血液量減少症	1 (0.4%)	0	0	0	0	0
血腫	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
血中ビリルビン増加	1 (0.4%)	0	0	0	0	0
血尿	1 (0.4%)	0	0	0	0	0
口腔咽頭痛	1 (0.4%)	0	0	0	0	0
視野欠損	1 (0.4%)	0	0	0	0	0
上大静脈症候群	1 (0.4%)	0	0	0	0	0
深部静脈血栓症	1 (0.4%)	0	0	0	0	0
腎機能障害	1 (0.4%)	0	0	0	0	0
水腎症	1 (0.4%)	0	0	0	0	0
脊髄圧迫	1 (0.4%)	0	0	0	0	0
創離開	1 (0.4%)	0	0	0	0	0
帯状疱疹	1 (0.4%)	0	0	0	0	0
大腸閉塞	1 (0.4%)	0	0	0	0	0
洞性頻脈	1 (0.4%)	0	0	0	0	0
尿路性敗血症	1 (0.4%)	0	0	0	0	0
尿路閉塞	1 (0.4%)	0	0	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
敗血症	1 (0.4%)	0	0	0	0	0
腹痛	1 (0.4%)	0	0	0	0	0
腹部膿瘍	1 (0.4%)	0	0	0	0	0
腹部癒着	1 (0.4%)	0	0	0	0	0
嚥下障害	1 (0.4%)	0	0	0	0	0
運動失調	0	0	1 (0.7%)	1 (0.7%)	0	0
甲状腺機能低下症	0	0	1 (0.7%)	1 (0.7%)	0	0
甲状腺機能亢進症	0	0	1 (0.7%)	1 (0.7%)	0	0
骨痛	0	0	1 (0.7%)	1 (0.7%)	0	0
十二指腸潰瘍	0	0	1 (0.7%)	1 (0.7%)	0	0
全身性炎症反応症候群	0	0	1 (0.7%)	1 (0.7%)	0	0
体重減少	0	0	1 (0.7%)	1 (0.7%)	0	0
末梢性浮腫	0	0	1 (0.7%)	1 (0.7%)	0	0
疼痛	0	0	1 (0.7%)	1 (0.7%)	0	0
医療機器関連感染	0	0	1 (0.7%)	0	0	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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Adverse Events Leading to Dose Modification or Interruption by Relation to Trial Treatment (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA Preferred Term	atezolizumab 15 mg/kg q3w IV (N=236) AE No. (%)	atezolizumab 15 mg/kg q3w IV (N=236) Related AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) AE No. (%)	atezolizumab 20 mg/kg q3w IV (N=146) Related AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) AE No. (%)	atezolizumab 1200 mg q3w IV (N=51) Related AE No. (%)
胆管閉塞	0	0	1 (0.7%)	0	0	0
胆嚢炎	0	0	1 (0.7%)	0	0	0
動悸	0	0	1 (0.7%)	0	0	0
肺硬化	0	0	1 (0.7%)	0	0	0
肺塞栓症	0	0	1 (0.7%)	0	0	0
病的骨折	0	0	1 (0.7%)	0	0	0
歩行障害	0	0	1 (0.7%)	0	0	0
髄膜炎	0	0	0	0	1 (2.0%)	1 (2.0%)
急性腎不全	0	0	0	0	1 (2.0%)	0

事象名：MedDRA ver. 18.0
Extraction date: 15May2015 Datacut date: 02Dec2014

Program: /opt/BIOSTAT/prod/cdt7692j/ae_rae_mod.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j27831a/reports/ae_rae_mod_GO27831_SE.out
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因果関係の判断基準：治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された場合に，副作用として集計した。
［5.3.5.3-1 ae_rae_mod_GO27831_SE を再掲］

(6) 本剤の休薬に至った有害事象の要約（JO28944試験）

表 2.7.4.7.4-6 本剤の休薬に至った有害事象の要約（JO28944試験）

ae11mod_sp Adverse Events Leading to Dose Interruption
Protocol(s): JO28944
Analysis: AS SELECTED Center: ALL CENTERS
Safety Population

Body System/ Adverse Event	MPDL3280A 10 mg/kg N = 3 No. (%)	MPDL3280A 20 mg/kg N = 3 No. (%)	Total N = 6 No. (%)
ALL BODY SYSTEMS			
Total Pts with at Least one AE	2 (66.7)	1 (33.3)	3 (50.0)
Total Number of AEs	2	1	3
一般・全身障害および投与部位の状態			
Total Pts With at Least one AE	1 (33.3)	-	1 (16.7)
インフルエンザ様疾患	1 (33.3)	-	1 (16.7)
Total Number of AEs	1	-	1
感染症および寄生虫症			
Total Pts With at Least one AE	-	1 (33.3)	1 (16.7)
肺炎	-	1 (33.3)	1 (16.7)
Total Number of AEs	-	1	1
臨床検査			
Total Pts With at Least one AE	1 (33.3)	-	1 (16.7)
血中アルカリホスファターゼ増加	1 (33.3)	-	1 (16.7)
Total Number of AEs	1	-	1

Investigator text for Adverse Events encoded using MedDRA version 16.1.
Percentages are based on N.
Multiple occurrences of the same adverse event in one individual counted only once.
AE11 02FEB2015:13:20:36 (1 of 1)

［5.3.3.2-2 表 12.3.1.3-1を再掲］

2.7.4.7.5 器官別大分類が「臨床検査」の有害事象

(1) 器官別大分類が「臨床検査」の有害事象の要約（OAK 試験）

表 2.7.4.7.5-1 器官別大分類が「臨床検査」の有害事象の要約（OAK 試験）

Adverse Events by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

MedDRA System Organ Class MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)	All Patients (N=1187)
臨床検査				
- Overall -	- Any Grade -	159 (26.1%)	137 (23.7%)	296 (24.9%)
	1	88 (14.4%)	47 (8.1%)	135 (11.4%)
	2	48 (7.9%)	27 (4.7%)	75 (6.3%)
	3	22 (3.6%)	22 (3.8%)	44 (3.7%)
	4	1 (0.2%)	41 (7.1%)	42 (3.5%)
体重減少	- Any Grade -	55 (9.0%)	30 (5.2%)	85 (7.2%)
	1	38 (6.2%)	25 (4.3%)	63 (5.3%)
	2	17 (2.8%)	5 (0.9%)	22 (1.9%)
好中球数減少	- Any Grade -	2 (0.3%)	55 (9.5%)	57 (4.8%)
	2	1 (0.2%)	3 (0.5%)	4 (0.3%)
	3	1 (0.2%)	12 (2.1%)	13 (1.1%)
	4	0	40 (6.9%)	40 (3.4%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	38 (6.2%)	12 (2.1%)	50 (4.2%)
	1	22 (3.6%)	9 (1.6%)	31 (2.6%)
	2	11 (1.8%)	1 (0.2%)	12 (1.0%)
	3	5 (0.8%)	2 (0.3%)	7 (0.6%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	35 (5.7%)	14 (2.4%)	49 (4.1%)
	1	22 (3.6%)	12 (2.1%)	34 (2.9%)
	2	7 (1.1%)	0	7 (0.6%)
	3	6 (1.0%)	2 (0.3%)	8 (0.7%)
血中クレアチニン増加	- Any Grade -	23 (3.8%)	11 (1.9%)	34 (2.9%)
	1	17 (2.8%)	8 (1.4%)	25 (2.1%)
	2	5 (0.8%)	3 (0.5%)	8 (0.7%)
	3	1 (0.2%)	0	1 (<0.1%)
白血球数減少	- Any Grade -	5 (0.8%)	29 (5.0%)	34 (2.9%)
	1	4 (0.7%)	2 (0.3%)	6 (0.5%)
	2	1 (0.2%)	6 (1.0%)	7 (0.6%)
	3	0	14 (2.4%)	14 (1.2%)
	4	0	7 (1.2%)	7 (0.6%)
血小板数減少	- Any Grade -	10 (1.6%)	6 (1.0%)	16 (1.3%)
	1	7 (1.1%)	6 (1.0%)	13 (1.1%)
	2	3 (0.5%)	0	3 (0.3%)
血中アルカリホスファターゼ増加	- Any Grade -	12 (2.0%)	4 (0.7%)	16 (1.3%)
	1	7 (1.1%)	0	7 (0.6%)
	2	3 (0.5%)	4 (0.7%)	7 (0.6%)
	3	2 (0.3%)	0	2 (0.2%)
Ｃ－反応性蛋白増加	- Any Grade -	8 (1.3%)	3 (0.5%)	11 (0.9%)
	1	2 (0.3%)	1 (0.2%)	3 (0.3%)
	2	6 (1.0%)	2 (0.3%)	8 (0.7%)
血中乳酸脱水素酵素増加	- Any Grade -	6 (1.0%)	5 (0.9%)	11 (0.9%)
	1	5 (0.8%)	4 (0.7%)	9 (0.8%)
	2	1 (0.2%)	1 (0.2%)	2 (0.2%)
体重増加	- Any Grade -	5 (0.8%)	6 (1.0%)	11 (0.9%)
	1	2 (0.3%)	2 (0.3%)	4 (0.3%)
	2	2 (0.3%)	4 (0.7%)	6 (0.5%)
	3	1 (0.2%)	0	1 (<0.1%)
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	7 (1.1%)	2 (0.3%)	9 (0.8%)
	1	3 (0.5%)	1 (0.2%)	4 (0.3%)
	2	1 (0.2%)	0	1 (<0.1%)
	3	3 (0.5%)	1 (0.2%)	4 (0.3%)
血中ビリルビン増加	- Any Grade -	7 (1.1%)	2 (0.3%)	9 (0.8%)
	1	2 (0.3%)	0	2 (0.2%)
	2	4 (0.7%)	0	4 (0.3%)
	3	0	2 (0.3%)	2 (0.2%)
	4	1 (0.2%)	0	1 (<0.1%)
リンパ球数減少	- Any Grade -	5 (0.8%)	2 (0.3%)	7 (0.6%)
	2	1 (0.2%)	2 (0.3%)	3 (0.3%)
	3	4 (0.7%)	0	4 (0.3%)
血中甲状腺刺激ホルモン増加	- Any Grade -	6 (1.0%)	1 (0.2%)	7 (0.6%)
	1	5 (0.8%)	1 (0.2%)	6 (0.5%)
	2	1 (0.2%)	0	1 (<0.1%)
総蛋白減少	- Any Grade -	4 (0.7%)	3 (0.5%)	7 (0.6%)
	1	3 (0.5%)	2 (0.3%)	5 (0.4%)
	2	1 (0.2%)	1 (0.2%)	2 (0.2%)
ヘモグロビン減少	- Any Grade -	2 (0.3%)	2 (0.3%)	4 (0.3%)

	1	1 (0.2%)	0	1 (<0.1%)
	2	0	1 (0.2%)	1 (<0.1%)
	3	1 (0.2%)	1 (0.2%)	2 (0.2%)
好中球数増加	- Any Grade -	0	4 (0.7%)	4 (0.3%)
	1	0	4 (0.7%)	4 (0.3%)
ヘマトクリット減少	- Any Grade -	2 (0.3%)	1 (0.2%)	3 (0.3%)
	1	2 (0.3%)	1 (0.2%)	3 (0.3%)
血中鉄減少	- Any Grade -	3 (0.5%)	0	3 (0.3%)
	1	1 (0.2%)	0	1 (<0.1%)
	2	2 (0.3%)	0	2 (0.2%)
血中尿素増加	- Any Grade -	2 (0.3%)	1 (0.2%)	3 (0.3%)
	1	2 (0.3%)	1 (0.2%)	3 (0.3%)
呼吸音異常	- Any Grade -	1 (0.2%)	2 (0.3%)	3 (0.3%)
	1	1 (0.2%)	2 (0.3%)	3 (0.3%)
白血球数増加	- Any Grade -	1 (0.2%)	2 (0.3%)	3 (0.3%)
	1	1 (0.2%)	2 (0.3%)	3 (0.3%)
トランスアミナーゼ上昇	- Any Grade -	2 (0.3%)	0	2 (0.2%)
	3	2 (0.3%)	0	2 (0.2%)
トロポニンＩ増加	- Any Grade -	1 (0.2%)	1 (0.2%)	2 (0.2%)
	1	0	1 (0.2%)	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
血小板数増加	- Any Grade -	0	2 (0.3%)	2 (0.2%)
	1	0	2 (0.3%)	2 (0.2%)
血中アルカリホスファターゼ	- Any Grade -	2 (0.3%)	0	2 (0.2%)
	1	1 (0.2%)	0	1 (<0.1%)
	3	1 (0.2%)	0	1 (<0.1%)
血中アルブミン減少	- Any Grade -	2 (0.3%)	0	2 (0.2%)
	1	1 (0.2%)	0	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
血中カリウム増加	- Any Grade -	2 (0.3%)	0	2 (0.2%)
	1	2 (0.3%)	0	2 (0.2%)
血中ブドウ糖増加	- Any Grade -	0	2 (0.3%)	2 (0.2%)
	2	0	1 (0.2%)	1 (<0.1%)
	3	0	1 (0.2%)	1 (<0.1%)
血中マグネシウム減少	- Any Grade -	1 (0.2%)	1 (0.2%)	2 (0.2%)
	1	1 (0.2%)	1 (0.2%)	2 (0.2%)
国際標準比増加	- Any Grade -	0	2 (0.3%)	2 (0.2%)
	1	0	1 (0.2%)	1 (<0.1%)
	3	0	1 (0.2%)	1 (<0.1%)
心電図ＱＴ延長	- Any Grade -	2 (0.3%)	0	2 (0.2%)
	1	1 (0.2%)	0	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
尿中ブドウ糖	- Any Grade -	1 (0.2%)	1 (0.2%)	2 (0.2%)
	1	0	1 (0.2%)	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
Ｃ－反応性蛋白	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
ＥＣＯＧパフォーマンスステータス悪化	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
ＱＲＳ軸異常	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
アラニンアミノトランスフェラーゼ減少	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
肝酵素上昇	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
胸部コンピュータ断層撮影異常	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血清フェリチン増加	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
血中カリウム減少	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中クレアチン増加	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
血中クロール減少	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中コレステロール増加	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中ナトリウム減少	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中リン減少	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
血中リン増加	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中甲状腺刺激ホルモン減少	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
血中重炭酸塩減少	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中尿酸増加	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
血中尿素減少	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
甲状腺機能検査異常	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	2	1 (0.2%)	0	1 (<0.1%)
酸素飽和度低下	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	2	0	1 (0.2%)	1 (<0.1%)

心電図Ｔ波逆転	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
心拍数増加	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	2	0	1 (0.2%)	1 (<0.1%)
腎クレアチニン・クリアランス減少	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	2	0	1 (0.2%)	1 (<0.1%)
赤血球数減少	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
体温上昇	- Any Grade -	1 (0.2%)	0	1 (<0.1%)
	1	1 (0.2%)	0	1 (<0.1%)
単球数増加	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)
尿中ブドウ糖陽性	- Any Grade -	0	1 (0.2%)	1 (<0.1%)
	1	0	1 (0.2%)	1 (<0.1%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
AEs collected after first treatment dose and within 30 days from last treatment dose are included unless the AE occurred after the start of a non-protocol cancer therapy within the 30 day post-treatment period.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adaptation from output aet04_GO28915_SE
［5.3.5.1-3 aet04_GO28915_SE を改変］

(2) 器官別大分類が「臨床検査」の有害事象の要約（POPLAR 試験）

表 2.7.4.7.5-2 器官別大分類が「臨床検査」の有害事象の要約（POPLAR 試験）

Adverse Events by Intensity (CTCAE Grades 1-5) (GO28753:POPLAR)
Protocol: GO28753
Population: Safety-Evaluable Patients

MedDRA System Organ Class MedDRA Preferred Term	Grade	atezolizumab 1200 mg q3w IV (N=142)	Docetaxel (N=135)
臨床検査			
- Overall -	- Any Grade -	37 (26.1%)	29 (21.5%)
	1	21 (14.8%)	15 (11.1%)
	2	11 (7.7%)	7 (5.2%)
	3	5 (3.5%)	6 (4.4%)
	4	0	1 (0.7%)
体重減少	- Any Grade -	14 (9.9%)	9 (6.7%)
	1	9 (6.3%)	8 (5.9%)
	2	5 (3.5%)	1 (0.7%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	6 (4.2%)	1 (0.7%)
	1	1 (0.7%)	1 (0.7%)
	2	2 (1.4%)	0
	3	3 (2.1%)	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	6 (4.2%)	0
	2	3 (2.1%)	0
	3	3 (2.1%)	0
好中球数減少	- Any Grade -	1 (0.7%)	4 (3.0%)
	1	1 (0.7%)	0
	3	0	3 (2.2%)
	4	0	1 (0.7%)
血中アルカリホスファターゼ増加	- Any Grade -	4 (2.8%)	0
	1	1 (0.7%)	0
	2	2 (1.4%)	0
	3	1 (0.7%)	0
Ｃ－反応性蛋白増加	- Any Grade -	2 (1.4%)	1 (0.7%)
	1	1 (0.7%)	0
	2	1 (0.7%)	1 (0.7%)
ヘモグロビン減少	- Any Grade -	1 (0.7%)	2 (1.5%)
	2	0	2 (1.5%)
	3	1 (0.7%)	0
血中クレアチニン増加	- Any Grade -	3 (2.1%)	0
	1	2 (1.4%)	0
	2	1 (0.7%)	0
国際標準比増加	- Any Grade -	0	3 (2.2%)
	2	0	2 (1.5%)
	3	0	1 (0.7%)
体重増加	- Any Grade -	2 (1.4%)	1 (0.7%)
	1	2 (1.4%)	1 (0.7%)

白血球数減少	- Any Grade -	1 (0.7%)	2 (1.5%)
	1	1 (0.7%)	0
	3	0	2 (1.5%)
リンパ球数減少	- Any Grade -	2 (1.4%)	0
	2	1 (0.7%)	0
	3	1 (0.7%)	0
血中ビリルビン増加	- Any Grade -	1 (0.7%)	1 (0.7%)
	2	1 (0.7%)	1 (0.7%)
ステノトロフォモナス検査陽性	- Any Grade -	0	1 (0.7%)
	2	0	1 (0.7%)
フィブリンＤダイマー増加	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
プロカルシトニン増加	- Any Grade -	0	1 (0.7%)
	1	0	1 (0.7%)
リンパ球数増加	- Any Grade -	0	1 (0.7%)
	2	0	1 (0.7%)
活性化部分トロンボプラスチン時間延長	- Any Grade -	1 (0.7%)	0
	2	1 (0.7%)	0
肝機能検査異常	- Any Grade -	1 (0.7%)	0
	3	1 (0.7%)	0
血中アルブミン減少	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
血中クロール減少	- Any Grade -	0	1 (0.7%)
	1	0	1 (0.7%)
血中クロール増加	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
呼吸音異常	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
好酸球数増加	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
好中球数増加	- Any Grade -	0	1 (0.7%)
	1	0	1 (0.7%)
酸素飽和度低下	- Any Grade -	0	1 (0.7%)
	1	0	1 (0.7%)
糸球体濾過率減少	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
心雑音	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
心電図ＱＴ延長	- Any Grade -	1 (0.7%)	0
	1	1 (0.7%)	0
体温上昇	- Any Grade -	0	1 (0.7%)
	1	0	1 (0.7%)
尿量減少	- Any Grade -	0	1 (0.7%)
	1	0	1 (0.7%)

Percentages are based on N in the column headings.
事象名：MedDRA ver. 18.0
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Data Cut-off: 8 May 2015; SDTM Data Extracted: 16 Jul 2015.

Adaptation from output aet04_GO28753_SE
［5.3.5.3-1 aet04_GO28753_SE を改変］

(3) 器官別大分類が「臨床検査」の有害事象の要約（BIRCH 試験）

表 2.7.4.7.5-3 器官別大分類が「臨床検査」の有害事象の要約（BIRCH 試験）

Adverse Events by Intensity (CTCAE Grades 1-5) (GO28754:BIRCH)
Protocol: GO28754
Population: Treated Patients

MedDRA System Organ Class MedDRA Preferred Term	Grade	atezolizumab Total (N=659)	atezolizumab Cohort 1 (N=139)	atezolizumab Cohort 2 (N=267)	atezolizumab Cohort 3 (N=253)
臨床検査					
- Overall -	- Any Grade -	136 (20.6%)	20 (14.4%)	61 (22.8%)	55 (21.7%)
	1	69 (10.5%)	12 (8.6%)	32 (12.0%)	25 (9.9%)
	2	45 (6.8%)	6 (4.3%)	20 (7.5%)	19 (7.5%)
	3	22 (3.3%)	2 (1.4%)	9 (3.4%)	11 (4.3%)
体重減少	- Any Grade -	46 (7.0%)	6 (4.3%)	17 (6.4%)	23 (9.1%)
	1	32 (4.9%)	4 (2.9%)	13 (4.9%)	15 (5.9%)
	2	12 (1.8%)	2 (1.4%)	3 (1.1%)	7 (2.8%)
	3	2 (0.3%)	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	- Any Grade -	24 (3.6%)	2 (1.4%)	10 (3.7%)	12 (4.7%)
	1	14 (2.1%)	2 (1.4%)	4 (1.5%)	8 (3.2%)
	2	5 (0.8%)	0	3 (1.1%)	2 (0.8%)
	3	5 (0.8%)	0	3 (1.1%)	2 (0.8%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	21 (3.2%)	1 (0.7%)	9 (3.4%)	11 (4.3%)
	1	15 (2.3%)	1 (0.7%)	7 (2.6%)	7 (2.8%)
	2	4 (0.6%)	0	1 (0.4%)	3 (1.2%)
	3	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
血中クレアチニン増加	- Any Grade -	14 (2.1%)	3 (2.2%)	9 (3.4%)	2 (0.8%)
	1	13 (2.0%)	2 (1.4%)	9 (3.4%)	2 (0.8%)
	2	1 (0.2%)	1 (0.7%)	0	0
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	10 (1.5%)	1 (0.7%)	4 (1.5%)	5 (2.0%)
	1	1 (0.2%)	0	1 (0.4%)	0
	2	5 (0.8%)	0	2 (0.7%)	3 (1.2%)
	3	4 (0.6%)	1 (0.7%)	1 (0.4%)	2 (0.8%)
血中アルカリホスファターゼ増加	- Any Grade -	8 (1.2%)	2 (1.4%)	2 (0.7%)	4 (1.6%)
	1	5 (0.8%)	2 (1.4%)	1 (0.4%)	2 (0.8%)
	2	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	3	1 (0.2%)	0	0	1 (0.4%)
体重増加	- Any Grade -	8 (1.2%)	1 (0.7%)	5 (1.9%)	2 (0.8%)
	1	5 (0.8%)	1 (0.7%)	3 (1.1%)	1 (0.4%)
	2	3 (0.5%)	0	2 (0.7%)	1 (0.4%)
リンパ球数減少	- Any Grade -	6 (0.9%)	3 (2.2%)	1 (0.4%)	2 (0.8%)
	1	3 (0.5%)	2 (1.4%)	0	1 (0.4%)
	3	3 (0.5%)	1 (0.7%)	1 (0.4%)	1 (0.4%)
血小板数減少	- Any Grade -	5 (0.8%)	1 (0.7%)	2 (0.7%)	2 (0.8%)
	1	2 (0.3%)	1 (0.7%)	1 (0.4%)	0
	2	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	3	1 (0.2%)	0	0	1 (0.4%)
血中ビリルビン増加	- Any Grade -	5 (0.8%)	2 (1.4%)	2 (0.7%)	1 (0.4%)

	1	3 (0.5%)	1 (0.7%)	2 (0.7%)	0
	2	1 (0.2%)	1 (0.7%)	0	0
	3	1 (0.2%)	0	0	1 (0.4%)
血中リン減少	- Any Grade -	4 (0.6%)	0	2 (0.7%)	2 (0.8%)
	1	1 (0.2%)	0	1 (0.4%)	0
	2	3 (0.5%)	0	1 (0.4%)	2 (0.8%)
Ｃ－反応性蛋白増加	- Any Grade -	3 (0.5%)	1 (0.7%)	1 (0.4%)	1 (0.4%)
	1	1 (0.2%)	0	1 (0.4%)	0
	2	2 (0.3%)	1 (0.7%)	0	1 (0.4%)
肝機能検査異常	- Any Grade -	3 (0.5%)	0	3 (1.1%)	0
	1	2 (0.3%)	0	2 (0.7%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
白血球数減少	- Any Grade -	3 (0.5%)	0	2 (0.7%)	1 (0.4%)
	1	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
	3	1 (0.2%)	0	0	1 (0.4%)
トランスアミナーゼ上昇	- Any Grade -	2 (0.3%)	1 (0.7%)	1 (0.4%)	0
	2	2 (0.3%)	1 (0.7%)	1 (0.4%)	0
リパーゼ増加	- Any Grade -	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	2	1 (0.2%)	0	0	1 (0.4%)
	3	1 (0.2%)	0	1 (0.4%)	0
肝酵素上昇	- Any Grade -	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	2	1 (0.2%)	0	0	1 (0.4%)
	3	1 (0.2%)	0	1 (0.4%)	0
胸部コンピュータ断層撮影異常	- Any Grade -	2 (0.3%)	0	0	2 (0.8%)
	2	2 (0.3%)	0	0	2 (0.8%)
血小板数増加	- Any Grade -	2 (0.3%)	1 (0.7%)	1 (0.4%)	0
	2	2 (0.3%)	1 (0.7%)	1 (0.4%)	0
血中アルブミン減少	- Any Grade -	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	1	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
血中カルシウム減少	- Any Grade -	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	1	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
血中マグネシウム減少	- Any Grade -	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	1	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
血中甲状腺刺激ホルモン増加	- Any Grade -	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
	2	2 (0.3%)	0	1 (0.4%)	1 (0.4%)
心拍数不整	- Any Grade -	2 (0.3%)	0	2 (0.7%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
ＰＯ２低下	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
アミラーゼ増加	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	3	1 (0.2%)	0	0	1 (0.4%)
カテーテル培養陽性	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
ヘモグロビン減少	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	2	1 (0.2%)	0	0	1 (0.4%)
ヘモグロビン増加	- Any Grade -	1 (0.2%)	1 (0.7%)	0	0
	1	1 (0.2%)	1 (0.7%)	0	0
胃内ｐＨ低下	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
駆出率減少	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
血中カリウム	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
血中カリウム減少	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)

	1	1 (0.2%)	0	0	1 (0.4%)
血中クレアチンホスホキナーゼ増加	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	3	1 (0.2%)	0	0	1 (0.4%)
血中クロール減少	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	1	1 (0.2%)	0	0	1 (0.4%)
血中クロール増加	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	1	1 (0.2%)	0	0	1 (0.4%)
血中ナトリウム減少	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
血中ブドウ糖増加	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	2	1 (0.2%)	0	0	1 (0.4%)
血中乳酸脱水素酵素増加	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
血中尿酸増加	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
血中尿素増加	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	1	1 (0.2%)	0	0	1 (0.4%)
好中球数増加	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
糸球体濾過率減少	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
心拍出量低下	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
体温上昇	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0
二酸化炭素増加	- Any Grade -	1 (0.2%)	0	0	1 (0.4%)
	1	1 (0.2%)	0	0	1 (0.4%)
尿中蛋白陽性	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	2	1 (0.2%)	0	1 (0.4%)	0
白血球数増加	- Any Grade -	1 (0.2%)	0	1 (0.4%)	0
	1	1 (0.2%)	0	1 (0.4%)	0

Percentages are based on N in the column headings.
事象名：MedDRA ver. 18.0
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Clinical cut-off date: 28-MAY-2015; Final RAVE extraction date: 07-AUG-2015
Adaptation from output aet04_GO28754_SE
［5.3.5.3-1 aet04_GO28754_SE を改変］

(4) 器官別大分類が「臨床検査」の有害事象の要約（FIR 試験）

表 2.7.4.7.5-4 器官別大分類が「臨床検査」の有害事象の要約（FIR 試験）

Adverse Events by Intensity (CTCAE Grades 1-5) (GO28625:FIR)
Protocol: GO28625
Population: Treated Patients

MedDRA System Organ Class MedDRA Preferred Term	Grade	atezolizumab Total (N=137)	atezolizumab Cohort 1 (N=31)	atezolizumab Cohort 2 (N=93)	atezolizumab Cohort 3 (N=13)
臨床検査					
- Overall -	- Any Grade -	36 (26.3%)	10 (32.3%)	22 (23.7%)	4 (30.8%)
	1	16 (11.7%)	4 (12.9%)	12 (12.9%)	0
	2	13 (9.5%)	4 (12.9%)	6 (6.5%)	3 (23.1%)
	3	5 (3.6%)	2 (6.5%)	2 (2.2%)	1 (7.7%)
	4	2 (1.5%)	0	2 (2.2%)	0
体重減少	- Any Grade -	15 (10.9%)	6 (19.4%)	8 (8.6%)	1 (7.7%)
	1	9 (6.6%)	4 (12.9%)	5 (5.4%)	0
	2	6 (4.4%)	2 (6.5%)	3 (3.2%)	1 (7.7%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	6 (4.4%)	2 (6.5%)	2 (2.2%)	2 (15.4%)
	1	1 (0.7%)	1 (3.2%)	0	0
	2	2 (1.5%)	0	0	2 (15.4%)
	3	2 (1.5%)	1 (3.2%)	1 (1.1%)	0
	4	1 (0.7%)	0	1 (1.1%)	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	6 (4.4%)	2 (6.5%)	2 (2.2%)	2 (15.4%)
	1	1 (0.7%)	1 (3.2%)	0	0
	2	2 (1.5%)	0	0	2 (15.4%)
	3	1 (0.7%)	1 (3.2%)	0	0
	4	2 (1.5%)	0	2 (2.2%)	0
リンパ球数減少	- Any Grade -	4 (2.9%)	1 (3.2%)	3 (3.2%)	0
	1	1 (0.7%)	0	1 (1.1%)	0
	2	2 (1.5%)	1 (3.2%)	1 (1.1%)	0
	3	1 (0.7%)	0	1 (1.1%)	0
血中クレアチニン増加	- Any Grade -	4 (2.9%)	1 (3.2%)	2 (2.2%)	1 (7.7%)
	1	1 (0.7%)	0	1 (1.1%)	0
	2	3 (2.2%)	1 (3.2%)	1 (1.1%)	1 (7.7%)
体重増加	- Any Grade -	3 (2.2%)	1 (3.2%)	2 (2.2%)	0
	1	3 (2.2%)	1 (3.2%)	2 (2.2%)	0
ヘモグロビン減少	- Any Grade -	2 (1.5%)	1 (3.2%)	0	1 (7.7%)
	1	1 (0.7%)	1 (3.2%)	0	0
	3	1 (0.7%)	0	0	1 (7.7%)
血中アルカリホスファターゼ増加	- Any Grade -	2 (1.5%)	0	1 (1.1%)	1 (7.7%)
	1	1 (0.7%)	0	0	1 (7.7%)
	2	1 (0.7%)	0	1 (1.1%)	0
白血球数増加	- Any Grade -	2 (1.5%)	1 (3.2%)	1 (1.1%)	0
	1	1 (0.7%)	1 (3.2%)	0	0
	3	1 (0.7%)	0	1 (1.1%)	0
ヘリコバクター検査陽性	- Any Grade -	1 (0.7%)	0	1 (1.1%)	0
	2	1 (0.7%)	0	1 (1.1%)	0

活性化部分トロンボプラスチン時間延長	- Any Grade -	1 (0.7%)	0	1 (1.1%)	0
	1	1 (0.7%)	0	1 (1.1%)	0
血圧異常	- Any Grade -	1 (0.7%)	1 (3.2%)	0	0
	1	1 (0.7%)	1 (3.2%)	0	0
血中アルカリホスファターゼ	- Any Grade -	1 (0.7%)	1 (3.2%)	0	0
	3	1 (0.7%)	1 (3.2%)	0	0
血中甲状腺刺激ホルモン増加	- Any Grade -	1 (0.7%)	0	0	1 (7.7%)
	2	1 (0.7%)	0	0	1 (7.7%)
血中乳酸脱水素酵素増加	- Any Grade -	1 (0.7%)	0	1 (1.1%)	0
	1	1 (0.7%)	0	1 (1.1%)	0
国際標準比増加	- Any Grade -	1 (0.7%)	0	1 (1.1%)	0
	1	1 (0.7%)	0	1 (1.1%)	0
腎クレアチニン・クリアランス減少	- Any Grade -	1 (0.7%)	0	1 (1.1%)	0
	1	1 (0.7%)	0	1 (1.1%)	0

Percentages are based on N in the column headings.
事象名：MedDRA ver. 18.0
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Clinical cut-off date: 07-JAN-2015; Final RAVE extraction date: 20-MAY-2015
Adaptation from output aet04_GO28625_SE
［5.3.5.3-1 aet04_GO28625_SE を改変］

(5) 器官別大分類が「臨床検査」の有害事象の要約（PCD4989g 試験）

表 2.7.4.7.5-5 器官別大分類が「臨床検査」の有害事象の要約（PCD4989g 試験）

Adverse Events by Intensity (CTCAE Grades 1-5) (GO27831:PCD4989g)
Protocol: GO27831
Population: Safety Evaluable Patients

MedDRA System Organ Class MedDRA Preferred Term	Grade	atezolizumab Total (N=481)	atezolizumab <=1 mg/kg q3w IV (N=9)	atezolizumab 3 mg/kg q3w IV (N=3)	atezolizumab 10 mg/kg q3w IV (N=36)	atezolizumab 15 mg/kg q3w IV (N=236)	atezolizumab 20 mg/kg q3w IV (N=146)	atezolizumab 1200 mg q3w IV (N=51)
臨床検査								
- Overall -	- Any Grade -	129 (26.8%)	1 (11.1%)	2 (66.7%)	9 (25.0%)	68 (28.8%)	39 (26.7%)	10 (19.6%)
	1	58 (12.1%)	1 (11.1%)	2 (66.7%)	6 (16.7%)	26 (11.0%)	19 (13.0%)	4 (7.8%)
	2	39 (8.1%)	0	0	1 (2.8%)	23 (9.7%)	12 (8.2%)	3 (5.9%)
	3	26 (5.4%)	0	0	1 (2.8%)	16 (6.8%)	6 (4.1%)	3 (5.9%)
	4	6 (1.2%)	0	0	1 (2.8%)	3 (1.3%)	2 (1.4%)	0
体重減少	- Any Grade -	32 (6.7%)	0	0	2 (5.6%)	15 (6.4%)	12 (8.2%)	3 (5.9%)
	1	23 (4.8%)	0	0	2 (5.6%)	11 (4.7%)	8 (5.5%)	2 (3.9%)
	2	8 (1.7%)	0	0	0	3 (1.3%)	4 (2.7%)	1 (2.0%)
	3	1 (0.2%)	0	0	0	1 (0.4%)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	27 (5.6%)	0	0	0	16 (6.8%)	8 (5.5%)	3 (5.9%)
	1	12 (2.5%)	0	0	0	7 (3.0%)	3 (2.1%)	2 (3.9%)
	2	7 (1.5%)	0	0	0	3 (1.3%)	3 (2.1%)	1 (2.0%)
	3	7 (1.5%)	0	0	0	5 (2.1%)	2 (1.4%)	0
	4	1 (0.2%)	0	0	0	1 (0.4%)	0	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	25 (5.2%)	0	0	1 (2.8%)	13 (5.5%)	9 (6.2%)	2 (3.9%)
	1	14 (2.9%)	0	0	1 (2.8%)	6 (2.5%)	6 (4.1%)	1 (2.0%)
	2	4 (0.8%)	0	0	0	3 (1.3%)	0	1 (2.0%)
	3	5 (1.0%)	0	0	0	2 (0.8%)	3 (2.1%)	0
	4	2 (0.4%)	0	0	0	2 (0.8%)	0	0
血中クレアチニン増加	- Any Grade -	25 (5.2%)	0	0	0	22 (9.3%)	1 (0.7%)	2 (3.9%)
	1	12 (2.5%)	0	0	0	10 (4.2%)	1 (0.7%)	1 (2.0%)
	2	11 (2.3%)	0	0	0	11 (4.7%)	0	0
	3	2 (0.4%)	0	0	0	1 (0.4%)	0	1 (2.0%)
血中アルカリホスファターゼ増加	- Any Grade -	19 (4.0%)	0	0	0	15 (6.4%)	3 (2.1%)	1 (2.0%)
	1	8 (1.7%)	0	0	0	5 (2.1%)	3 (2.1%)	0
	2	8 (1.7%)	0	0	0	7 (3.0%)	0	1 (2.0%)
	3	3 (0.6%)	0	0	0	3 (1.3%)	0	0
血中ビリルビン増加	- Any Grade -	9 (1.9%)	0	0	1 (2.8%)	6 (2.5%)	2 (1.4%)	0
	1	3 (0.6%)	0	0	0	3 (1.3%)	0	0
	2	2 (0.4%)	0	0	1 (2.8%)	1 (0.4%)	0	0
	3	3 (0.6%)	0	0	0	2 (0.8%)	1 (0.7%)	0
	4	1 (0.2%)	0	0	0	0	1 (0.7%)	0
リンパ球数減少	- Any Grade -	7 (1.5%)	0	0	2 (5.6%)	3 (1.3%)	1 (0.7%)	1 (2.0%)
	1	2 (0.4%)	0	0	0	1 (0.4%)	0	1 (2.0%)
	2	2 (0.4%)	0	0	1 (2.8%)	0	1 (0.7%)	0
	3	2 (0.4%)	0	0	0	2 (0.8%)	0	0
	4	1 (0.2%)	0	0	1 (2.8%)	0	0	0

γ－グルタミルトランスフェラーゼ増加	- Any Grade -	6 (1.2%)	0	0	0	3 (1.3%)	1 (0.7%)	2 (3.9%)
	2	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	3	4 (0.8%)	0	0	0	1 (0.4%)	1 (0.7%)	2 (3.9%)
	4	1 (0.2%)	0	0	0	1 (0.4%)	0	0
血小板数減少	- Any Grade -	6 (1.2%)	0	0	2 (5.6%)	3 (1.3%)	1 (0.7%)	0
	1	4 (0.8%)	0	0	1 (2.8%)	3 (1.3%)	0	0
	2	1 (0.2%)	0	0	1 (2.8%)	0	0	0
	4	1 (0.2%)	0	0	0	0	1 (0.7%)	0
血中リン減少	- Any Grade -	6 (1.2%)	0	0	0	4 (1.7%)	2 (1.4%)	0
	1	2 (0.4%)	0	0	0	0	2 (1.4%)	0
	2	3 (0.6%)	0	0	0	3 (1.3%)	0	0
	3	1 (0.2%)	0	0	0	1 (0.4%)	0	0
白血球数減少	- Any Grade -	6 (1.2%)	0	0	1 (2.8%)	4 (1.7%)	0	1 (2.0%)
	1	5 (1.0%)	0	0	1 (2.8%)	3 (1.3%)	0	1 (2.0%)
	3	1 (0.2%)	0	0	0	1 (0.4%)	0	0
トランスアミナーゼ上昇	- Any Grade -	5 (1.0%)	0	0	0	3 (1.3%)	1 (0.7%)	1 (2.0%)
	1	3 (0.6%)	0	0	0	2 (0.8%)	0	1 (2.0%)
	2	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	3	1 (0.2%)	0	0	0	1 (0.4%)	0	0
体重増加	- Any Grade -	5 (1.0%)	0	1 (33.3%)	0	1 (0.4%)	3 (2.1%)	0
	1	2 (0.4%)	0	1 (33.3%)	0	1 (0.4%)	0	0
	2	3 (0.6%)	0	0	0	0	3 (2.1%)	0
国際標準比増加	- Any Grade -	4 (0.8%)	0	0	0	3 (1.3%)	1 (0.7%)	0
	2	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	3	3 (0.6%)	0	0	0	2 (0.8%)	1 (0.7%)	0
血中甲状腺刺激ホルモン増加	- Any Grade -	3 (0.6%)	0	0	0	0	3 (2.1%)	0
	1	2 (0.4%)	0	0	0	0	2 (1.4%)	0
	2	1 (0.2%)	0	0	0	0	1 (0.7%)	0
リパーゼ増加	- Any Grade -	2 (0.4%)	0	0	0	2 (0.8%)	0	0
	3	2 (0.4%)	0	0	0	2 (0.8%)	0	0
肝機能検査異常	- Any Grade -	2 (0.4%)	0	0	0	1 (0.4%)	1 (0.7%)	0
	2	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	3	1 (0.2%)	0	0	0	0	1 (0.7%)	0
血中アルブミン減少	- Any Grade -	2 (0.4%)	0	0	0	2 (0.8%)	0	0
	1	2 (0.4%)	0	0	0	2 (0.8%)	0	0
血中カルシウム減少	- Any Grade -	2 (0.4%)	0	0	0	2 (0.8%)	0	0
	1	2 (0.4%)	0	0	0	2 (0.8%)	0	0
血中カルシウム増加	- Any Grade -	2 (0.4%)	0	0	0	1 (0.4%)	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	3	1 (0.2%)	0	0	0	1 (0.4%)	0	0
血中クレアチンホスホキナーゼ増加	- Any Grade -	2 (0.4%)	0	0	0	2 (0.8%)	0	0
	2	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	3	1 (0.2%)	0	0	0	1 (0.4%)	0	0
血中乳酸脱水素酵素増加	- Any Grade -	2 (0.4%)	0	0	1 (2.8%)	1 (0.4%)	0	0
	1	2 (0.4%)	0	0	1 (2.8%)	1 (0.4%)	0	0
アミラーゼ増加	- Any Grade -	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	2	1 (0.2%)	0	0	0	1 (0.4%)	0	0
グリコヘモグロビン増加	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	2	1 (0.2%)	0	0	0	0	1 (0.7%)	0
サイロキシン減少	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	2	1 (0.2%)	0	0	0	0	1 (0.7%)	0
ハプトグロビン減少	- Any Grade -	1 (0.2%)	0	0	1 (2.8%)	0	0	0
	1	1 (0.2%)	0	0	1 (2.8%)	0	0	0
ヘマトクリット増加	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
ヘモグロビン減少	- Any Grade -	1 (0.2%)	0	0	0	1 (0.4%)	0	0

	2	1 (0.2%)	0	0	0	1 (0.4%)	0	0
ヘモグロビン増加	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
胸部コンピュータ断層撮影異常	- Any Grade -	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	1	1 (0.2%)	0	0	0	1 (0.4%)	0	0
血中クロール増加	- Any Grade -	1 (0.2%)	0	0	1 (2.8%)	0	0	0
	1	1 (0.2%)	0	0	1 (2.8%)	0	0	0
血中テストステロン減少	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
血中マグネシウム増加	- Any Grade -	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	1	1 (0.2%)	0	0	0	1 (0.4%)	0	0
血中甲状腺刺激ホルモン減少	- Any Grade -	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	1	1 (0.2%)	0	0	0	1 (0.4%)	0	0
血中尿酸増加	- Any Grade -	1 (0.2%)	0	0	1 (2.8%)	0	0	0
	1	1 (0.2%)	0	0	1 (2.8%)	0	0	0
血中尿素増加	- Any Grade -	1 (0.2%)	0	0	1 (2.8%)	0	0	0
	1	1 (0.2%)	0	0	1 (2.8%)	0	0	0
酸素飽和度低下	- Any Grade -	1 (0.2%)	0	0	0	1 (0.4%)	0	0
	1	1 (0.2%)	0	0	0	1 (0.4%)	0	0
出血時間延長	- Any Grade -	1 (0.2%)	1 (11.1%)	0	0	0	0	0
	1	1 (0.2%)	1 (11.1%)	0	0	0	0	0
心電図ＰＲ延長	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
体温上昇	- Any Grade -	1 (0.2%)	0	1 (33.3%)	0	0	0	0
	1	1 (0.2%)	0	1 (33.3%)	0	0	0	0
尿培養陽性	- Any Grade -	1 (0.2%)	0	0	1 (2.8%)	0	0	0
	3	1 (0.2%)	0	0	1 (2.8%)	0	0	0
白血球数増加	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
便潜血陽性	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0
喀痰異常	- Any Grade -	1 (0.2%)	0	0	0	0	1 (0.7%)	0
	1	1 (0.2%)	0	0	0	0	1 (0.7%)	0

Percentages are based on N in the column headings.
事象名：MedDRA ver. 18.0
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Extraction date: 15May2015 Datacut date: 02Dec2014

Adaptation from output aet04_GO27831_SE
［5.3.5.3-1 aet04_GO27831_SE を改変］

(6) 器官別大分類が「臨床検査」の有害事象の要約（JO28944試験）

表 2.7.4.7.5-6 器官別大分類が「臨床検査」の有害事象の要約（JO28944試験）

Body System/ Adverse Event	Total	CTC Grading				
		1	2	3	4	5
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
臨床検査						
Total Pts With at Least one AE	3 (50.0)	3 (50.0)	2 (33.3)	-	-	-
アスパラギン酸アミノトランスフェラーゼ増加	2 (33.3)	2 (33.3)	-	-	-	-
アラニンアミノトランスフェラーゼ増加	2 (33.3)	2 (33.3)	-	-	-	-
血中アルカリホスファターゼ増加	2 (33.3)	1 (16.7)	1 (16.7)	-	-	-
リンパ球数減少	1 (16.7)	-	1 (16.7)	-	-	-
好中球数減少	1 (16.7)	1 (16.7)	-	-	-	-
心電図ＱＴ延長	1 (16.7)	1 (16.7)	-	-	-	-
白血球数減少	1 (16.7)	-	1 (16.7)	-	-	-
Total Number of AEs	10	7	3	-	-	-

Investigator text for Adverse Events encoded using MedDRA version 16.1.
Percentages are based on N.
Only the most severe intensity is counted for multiple occurrences of the same adverse event in one individual.
Any difference between the total number and sum of AEs is due to missing investigators assessment of intensity.
Adaptation from output ae17_sp
［5.3.3.2-2 Table 15.3-5を改変］

2.7.4.7.6 本剤の注目すべき有害事象（OAK 試験）

表 2.7.4.7.6-1 本剤の注目すべき有害事象の要約（OAK 試験）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
- Any adverse events -	- Any Grade -	377 (61.9%)	390 (67.5%)
	1	171 (28.1%)	160 (27.7%)
	2	139 (22.8%)	191 (33.0%)
	3	55 (9.0%)	34 (5.9%)
	4	11 (1.8%)	4 (0.7%)
	5	1 (0.2%)	1 (0.2%)
Infusion reaction - Overall -	- Any Grade -	243 (39.9%)	223 (38.6%)
	1	138 (22.7%)	116 (20.1%)
	2	80 (13.1%)	85 (14.7%)
	3	21 (3.4%)	18 (3.1%)
	4	3 (0.5%)	3 (0.5%)
	5	1 (0.2%)	1 (0.2%)
呼吸困難	- Any Grade -	119 (19.5%)	113 (19.6%)
	1	53 (8.7%)	54 (9.3%)
	2	49 (8.0%)	44 (7.6%)
	3	15 (2.5%)	12 (2.1%)
	4	1 (0.2%)	2 (0.3%)
	5	1 (0.2%)	1 (0.2%)
発熱	- Any Grade -	109 (17.9%)	77 (13.3%)
	1	90 (14.8%)	65 (11.2%)
	2	17 (2.8%)	11 (1.9%)
	3	2 (0.3%)	0
	4	0	1 (0.2%)
低血圧	- Any Grade -	17 (2.8%)	23 (4.0%)
	1	6 (1.0%)	7 (1.2%)
	2	9 (1.5%)	13 (2.2%)
	3	1 (0.2%)	3 (0.5%)
	4	1 (0.2%)	0
悪寒	- Any Grade -	22 (3.6%)	9 (1.6%)
	1	18 (3.0%)	8 (1.4%)
	2	3 (0.5%)	1 (0.2%)
	3	1 (0.2%)	0
潮紅	- Any Grade -	6 (1.0%)	14 (2.4%)
	1	5 (0.8%)	9 (1.6%)
	2	0	5 (0.9%)
	3	1 (0.2%)	0
頻脈	- Any Grade -	11 (1.8%)	8 (1.4%)
	1	5 (0.8%)	5 (0.9%)
	2	5 (0.8%)	3 (0.5%)
	3	1 (0.2%)	0
過敏症	- Any Grade -	6 (1.0%)	11 (1.9%)
	1	2 (0.3%)	2 (0.3%)
	2	3 (0.5%)	9 (1.6%)
	4	1 (0.2%)	0
顔面浮腫	- Any Grade -	3 (0.5%)	11 (1.9%)
	1	3 (0.5%)	10 (1.7%)
	2	0	1 (0.2%)
注入に伴う反応	- Any Grade -	5 (0.8%)	6 (1.0%)
	1	1 (0.2%)	0
	2	3 (0.5%)	5 (0.9%)
	3	1 (0.2%)	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
喘鳴	- Any Grade -	6 (1.0%)	5 (0.9%)
	1	5 (0.8%)	4 (0.7%)
	2	1 (0.2%)	1 (0.2%)
蕁麻疹	- Any Grade -	5 (0.8%)	2 (0.3%)
	1	4 (0.7%)	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
薬物過敏症	- Any Grade -	3 (0.5%)	3 (0.5%)
	1	2 (0.3%)	0
	2	1 (0.2%)	1 (0.2%)
	3	0	2 (0.3%)
眼窩周囲浮腫	- Any Grade -	4 (0.7%)	1 (0.2%)
	1	4 (0.7%)	1 (0.2%)
眼球浮腫	- Any Grade -	2 (0.3%)	2 (0.3%)
	1	2 (0.3%)	2 (0.3%)
気管支痙攣	- Any Grade -	3 (0.5%)	1 (0.2%)
	1	1 (0.2%)	1 (0.2%)
	2	2 (0.3%)	0
顔面腫脹	- Any Grade -	1 (0.2%)	2 (0.3%)
	1	0	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
アナフィラキシー反応	- Any Grade -	0	2 (0.3%)
	2	0	1 (0.2%)
	3	0	1 (0.2%)
眼部腫脹	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	1 (0.2%)
眼瞼浮腫	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
血管浮腫	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
口唇腫脹	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
舌腫脹	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
舌浮腫	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
発疹			
- Overall -	- Any Grade -	177 (29.1%)	274 (47.4%)
	1	126 (20.7%)	143 (24.7%)
	2	39 (6.4%)	127 (22.0%)
	3	12 (2.0%)	4 (0.7%)
脱毛症	- Any Grade -	3 (0.5%)	202 (34.9%)
	1	2 (0.3%)	101 (17.5%)
	2	1 (0.2%)	100 (17.3%)
	3	0	1 (0.2%)
発疹	- Any Grade -	59 (9.7%)	49 (8.5%)
	1	47 (7.7%)	37 (6.4%)
	2	10 (1.6%)	12 (2.1%)
	3	2 (0.3%)	0
そう痒症	- Any Grade -	50 (8.2%)	18 (3.1%)
	1	39 (6.4%)	15 (2.6%)
	2	8 (1.3%)	3 (0.5%)
	3	3 (0.5%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
皮膚乾燥	- Any Grade -	27 (4.4%)	34 (5.9%)
	1	25 (4.1%)	32 (5.5%)
	2	2 (0.3%)	1 (0.2%)
	3	0	1 (0.2%)
爪の障害	- Any Grade -	0	30 (5.2%)
	1	0	25 (4.3%)
	2	0	4 (0.7%)
	3	0	1 (0.2%)
爪変色	- Any Grade -	1 (0.2%)	26 (4.5%)
	1	1 (0.2%)	25 (4.3%)
	2	0	1 (0.2%)
紅斑	- Any Grade -	13 (2.1%)	11 (1.9%)
	1	9 (1.5%)	9 (1.6%)
	2	4 (0.7%)	2 (0.3%)
寝汗	- Any Grade -	14 (2.3%)	4 (0.7%)
	1	12 (2.0%)	3 (0.5%)
	2	2 (0.3%)	1 (0.2%)
斑状丘疹状皮疹	- Any Grade -	9 (1.5%)	5 (0.9%)
	1	5 (0.8%)	4 (0.7%)
	2	3 (0.5%)	1 (0.2%)
	3	1 (0.2%)	0
爪甲脱落症	- Any Grade -	0	13 (2.2%)
	1	0	7 (1.2%)
	2	0	6 (1.0%)
湿疹	- Any Grade -	7 (1.1%)	3 (0.5%)
	1	6 (1.0%)	3 (0.5%)
	2	1 (0.2%)	0
ざ瘡様皮膚炎	- Any Grade -	5 (0.8%)	4 (0.7%)
	1	5 (0.8%)	4 (0.7%)
手掌・足底発赤知覚不全症候群	- Any Grade -	0	9 (1.6%)
	1	0	4 (0.7%)
	2	0	4 (0.7%)
	3	0	1 (0.2%)
多汗症	- Any Grade -	5 (0.8%)	3 (0.5%)
	1	4 (0.7%)	2 (0.3%)
	2	1 (0.2%)	1 (0.2%)
皮膚色素過剰	- Any Grade -	4 (0.7%)	4 (0.7%)
	1	4 (0.7%)	3 (0.5%)
	2	0	1 (0.2%)
爪毒性	- Any Grade -	0	7 (1.2%)
	1	0	4 (0.7%)
	2	0	3 (0.5%)
皮膚炎	- Any Grade -	4 (0.7%)	3 (0.5%)
	1	2 (0.3%)	1 (0.2%)
	2	2 (0.3%)	2 (0.3%)
蕁麻疹	- Any Grade -	5 (0.8%)	2 (0.3%)
	1	4 (0.7%)	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
そう痒性皮疹	- Any Grade -	4 (0.7%)	2 (0.3%)
	1	4 (0.7%)	2 (0.3%)
皮膚剥脱	- Any Grade -	2 (0.3%)	4 (0.7%)
	1	2 (0.3%)	3 (0.5%)
	2	0	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
乾癬	- Any Grade -	4 (0.7%)	1 (0.2%)
	1	2 (0.3%)	1 (0.2%)
	2	2 (0.3%)	0
爪線状隆起	- Any Grade -	2 (0.3%)	3 (0.5%)
	1	2 (0.3%)	3 (0.5%)
紅斑性皮疹	- Any Grade -	3 (0.5%)	1 (0.2%)
	1	2 (0.3%)	1 (0.2%)
	2	1 (0.2%)	0
全身性そう痒症	- Any Grade -	4 (0.7%)	0
	1	3 (0.5%)	0
	3	1 (0.2%)	0
爪甲離床症	- Any Grade -	1 (0.2%)	3 (0.5%)
	1	1 (0.2%)	3 (0.5%)
皮膚腫瘤	- Any Grade -	3 (0.5%)	1 (0.2%)
	1	3 (0.5%)	0
	2	0	1 (0.2%)
顔面腫脹	- Any Grade -	1 (0.2%)	2 (0.3%)
	1	0	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
水疱性皮膚炎	- Any Grade -	3 (0.5%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
爪ジストロフィー	- Any Grade -	1 (0.2%)	2 (0.3%)
	1	1 (0.2%)	1 (0.2%)
	2	0	1 (0.2%)
点状出血	- Any Grade -	2 (0.3%)	1 (0.2%)
	1	2 (0.3%)	1 (0.2%)
皮膚病変	- Any Grade -	2 (0.3%)	1 (0.2%)
	1	2 (0.3%)	1 (0.2%)
皮膚疼痛	- Any Grade -	2 (0.3%)	1 (0.2%)
	1	1 (0.2%)	1 (0.2%)
	3	1 (0.2%)	0
褥瘡性潰瘍	- Any Grade -	2 (0.3%)	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
	3	1 (0.2%)	0
ざ瘡	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	1 (0.2%)
接触性皮膚炎	- Any Grade -	0	2 (0.3%)
	1	0	2 (0.3%)
全身性皮疹	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	1 (0.2%)
多形紅斑	- Any Grade -	2 (0.3%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
爪痛	- Any Grade -	0	2 (0.3%)
	1	0	1 (0.2%)
	2	0	1 (0.2%)
爪破損	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	1 (0.2%)
皮膚硬結	- Any Grade -	2 (0.3%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
皮膚潰瘍	- Any Grade -	2 (0.3%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0
皮膚毒性	- Any Grade -	0	2 (0.3%)
	1	0	2 (0.3%)
皮膚嚢腫	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	0
	2	0	1 (0.2%)
皮膚反応	- Any Grade -	0	2 (0.3%)
	1	0	1 (0.2%)
	2	0	1 (0.2%)
嵌入爪	- Any Grade -	0	2 (0.3%)
	1	0	1 (0.2%)
	2	0	1 (0.2%)
うっ滞性皮膚炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
アトピー性皮膚炎	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
過角化	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
乾皮症	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
丘疹性皮疹	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
血管浮腫	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
光線角化症	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
紅色症	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
黒皮症	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
脂漏性皮膚炎	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
手掌紅斑	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
色素沈着障害	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
尋常性白斑	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
水疱	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
爪床出血	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
爪肥厚	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
頭部粃糠疹	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
斑	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
皮脂欠乏性湿疹	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
皮膚萎縮	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
皮膚亀裂	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
皮膚刺激	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
皮膚障害	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
皮膚色素減少	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
皮膚軟化	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
皮膚粘膜発疹	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
皮膚変色	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
薬疹	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
立毛	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
類天疱瘡	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
冷汗	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
扁平苔癬	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
痒疹	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
睫毛眉毛脱落症	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
肝炎			
- Overall -	- Any Grade -	67 (11.0%)	22 (3.8%)
	1	36 (5.9%)	15 (2.6%)
	2	13 (2.1%)	2 (0.3%)
	3	14 (2.3%)	4 (0.7%)
	4	4 (0.7%)	1 (0.2%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	38 (6.2%)	12 (2.1%)
	1	22 (3.6%)	9 (1.6%)
	2	11 (1.8%)	1 (0.2%)
	3	5 (0.8%)	2 (0.3%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	35 (5.7%)	14 (2.4%)
	1	22 (3.6%)	12 (2.1%)
	2	7 (1.1%)	0
	3	6 (1.0%)	2 (0.3%)
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	7 (1.1%)	2 (0.3%)
	1	3 (0.5%)	1 (0.2%)
	2	1 (0.2%)	0
	3	3 (0.5%)	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
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Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
血中ビリルビン増加	- Any Grade -	7 (1.1%)	2 (0.3%)
	1	2 (0.3%)	0
	2	4 (0.7%)	0
	3	0	2 (0.3%)
	4	1 (0.2%)	0
肝機能異常	- Any Grade -	3 (0.5%)	2 (0.3%)
	1	2 (0.3%)	2 (0.3%)
	3	1 (0.2%)	0
腹水	- Any Grade -	3 (0.5%)	0
	2	3 (0.5%)	0
トランスアミナーゼ上昇	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
肝炎	- Any Grade -	2 (0.3%)	0
	4	2 (0.3%)	0
肝臓痛	- Any Grade -	1 (0.2%)	1 (0.2%)
	1	1 (0.2%)	0
	2	0	1 (0.2%)
肝酵素上昇	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肝細胞損傷	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肝障害	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肝病変	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
急性肝炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
急性肝不全	- Any Grade -	0	1 (0.2%)
	4	0	1 (0.2%)
高ビリルビン血症	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
脂肪肝	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
食道静脈瘤	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
食道静脈瘤出血	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
薬物性肝障害	- Any Grade -	1 (0.2%)	0
	4	1 (0.2%)	0
糖尿病			
- Overall -	- Any Grade -	20 (3.3%)	32 (5.5%)
	1	9 (1.5%)	13 (2.2%)
	2	4 (0.7%)	12 (2.1%)
	3	4 (0.7%)	7 (1.2%)
	4	3 (0.5%)	0
高血糖	- Any Grade -	18 (3.0%)	26 (4.5%)
	1	7 (1.1%)	11 (1.9%)
	2	4 (0.7%)	10 (1.7%)
	3	4 (0.7%)	5 (0.9%)
	4	3 (0.5%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

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Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
２型糖尿病	- Any Grade -	1 (0.2%)	1 (0.2%)
	2	0	1 (0.2%)
	3	1 (0.2%)	0
血中ブドウ糖増加	- Any Grade -	0	2 (0.3%)
	2	0	1 (0.2%)
	3	0	1 (0.2%)
糖尿病	- Any Grade -	0	2 (0.3%)
	1	0	1 (0.2%)
	3	0	1 (0.2%)
１型糖尿病	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
耐糖能障害	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
尿中ブドウ糖陽性	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
甲状腺機能低下症			
- Overall -	- Any Grade -	27 (4.4%)	2 (0.3%)
	1	10 (1.6%)	1 (0.2%)
	2	17 (2.8%)	1 (0.2%)
甲状腺機能低下症	- Any Grade -	18 (3.0%)	1 (0.2%)
	1	4 (0.7%)	0
	2	14 (2.3%)	1 (0.2%)
血中甲状腺刺激ホルモン増加	- Any Grade -	6 (1.0%)	1 (0.2%)
	1	5 (0.8%)	1 (0.2%)
	2	1 (0.2%)	0
血中甲状腺刺激ホルモン減少	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
甲状腺炎	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
甲状腺機能検査異常	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
甲状腺機能亢進症			
- Overall -	- Any Grade -	17 (2.8%)	1 (0.2%)
	1	9 (1.5%)	1 (0.2%)
	2	8 (1.3%)	0
血中甲状腺刺激ホルモン増加	- Any Grade -	6 (1.0%)	1 (0.2%)
	1	5 (0.8%)	1 (0.2%)
	2	1 (0.2%)	0
甲状腺機能亢進症	- Any Grade -	7 (1.1%)	0
	1	3 (0.5%)	0
	2	4 (0.7%)	0
眼球突出症	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
血中甲状腺刺激ホルモン減少	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
甲状腺炎	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
甲状腺機能検査異常	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
内分泌性眼症	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

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To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肺臓炎			
- Overall -	- Any Grade -	14 (2.3%)	4 (0.7%)
	1	2 (0.3%)	1 (0.2%)
	2	7 (1.1%)	1 (0.2%)
	3	5 (0.8%)	2 (0.3%)
肺臓炎	- Any Grade -	6 (1.0%)	4 (0.7%)
	1	0	1 (0.2%)
	2	2 (0.3%)	1 (0.2%)
	3	4 (0.7%)	2 (0.3%)
間質性肺疾患	- Any Grade -	3 (0.5%)	0
	1	1 (0.2%)	0
	2	2 (0.3%)	0
肺浸潤	- Any Grade -	2 (0.3%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
放射線性肺臓炎	- Any Grade -	2 (0.3%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0
細気管支炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
髄膜脳炎			
- Overall -	- Any Grade -	5 (0.8%)	0
	1	1 (0.2%)	0
	2	1 (0.2%)	0
	3	2 (0.3%)	0
	4	1 (0.2%)	0
髄膜炎	- Any Grade -	3 (0.5%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
	4	1 (0.2%)	0
脳炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
羞明	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
胚・胎児毒性			
- Overall -	- Any Grade -	2 (0.3%)	3 (0.5%)
	1	0	1 (0.2%)
	2	1 (0.2%)	2 (0.3%)
	3	1 (0.2%)	0
成長障害	- Any Grade -	1 (0.2%)	2 (0.3%)
	1	0	1 (0.2%)
	2	0	1 (0.2%)
	3	1 (0.2%)	0
乳腺炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
表皮融解	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)

Percentages are based on N in the column headings.
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To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
ギラン・バレー症候群			
- Overall -	- Any Grade -	4 (0.7%)	0
	2	1 (0.2%)	0
	3	3 (0.5%)	0
ギラン・バレー症候群	- Any Grade -	3 (0.5%)	0
	3	3 (0.5%)	0
脱髄性多発ニューロパチー	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
大腸炎			
- Overall -	- Any Grade -	2 (0.3%)	2 (0.3%)
	2	2 (0.3%)	0
	3	0	2 (0.3%)
大腸炎	- Any Grade -	2 (0.3%)	2 (0.3%)
	2	2 (0.3%)	0
	3	0	2 (0.3%)
副腎機能不全			
- Overall -	- Any Grade -	3 (0.5%)	0
	1	1 (0.2%)	0
	2	2 (0.3%)	0
副腎機能不全	- Any Grade -	2 (0.3%)	0
	2	2 (0.3%)	0
原発性副腎機能不全	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
ぶどう膜炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
ぶどう膜炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
腎炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
ヘノッホ・シェーンライン紫斑病性腎炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
膵炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
膵炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE.out
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［5.3.5.1-3 aet04_aesi_GO28915_SE を再掲］

表 2.7.4.7.6-2 死亡に至った本剤の注目すべき有害事象（Grade 5）の要約（OAK 試験）

AESI leading to Death by Relation to Trial Treatment (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
- Any adverse events -	- Any Grade -	1 (0.2%)	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
Infusion reaction			
- Overall -	- Any Grade -	1 (0.2%)	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
呼吸困難	- Any Grade -	1 (0.2%)	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_dd.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_dd_GO28915_SE.out
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［5.3.5.1-3 aet04_aesi_dd_GO28915_SE を再掲］

表 2.7.4.7.6-3 重篤な有害事象として報告された本剤の注目すべき有害事象（OAK 試験）

Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
- Any adverse events -	- Any Grade -	57 (9.4%)	22 (3.8%)
	1	5 (0.8%)	4 (0.7%)
	2	15 (2.5%)	6 (1.0%)
	3	27 (4.4%)	9 (1.6%)
	4	9 (1.5%)	2 (0.3%)
	5	1 (0.2%)	1 (0.2%)
Infusion reaction			
- Overall -	- Any Grade -	31 (5.1%)	18 (3.1%)
	1	5 (0.8%)	4 (0.7%)
	2	10 (1.6%)	5 (0.9%)
	3	12 (2.0%)	7 (1.2%)
	4	3 (0.5%)	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
呼吸困難	- Any Grade -	13 (2.1%)	8 (1.4%)
	1	1 (0.2%)	0
	2	1 (0.2%)	0
	3	9 (1.5%)	6 (1.0%)
	4	1 (0.2%)	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
発熱	- Any Grade -	10 (1.6%)	8 (1.4%)
	1	4 (0.7%)	4 (0.7%)
	2	5 (0.8%)	4 (0.7%)
	3	1 (0.2%)	0
低血圧	- Any Grade -	3 (0.5%)	1 (0.2%)
	2	1 (0.2%)	0
	3	1 (0.2%)	1 (0.2%)
	4	1 (0.2%)	0
過敏症	- Any Grade -	3 (0.5%)	0
	2	2 (0.3%)	0
	4	1 (0.2%)	0
頻脈	- Any Grade -	1 (0.2%)	1 (0.2%)
	2	0	1 (0.2%)
	3	1 (0.2%)	0
気管支痙攣	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
注入に伴う反応	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
肺臓炎			
- Overall -	- Any Grade -	7 (1.1%)	1 (0.2%)
	2	3 (0.5%)	0
	3	4 (0.7%)	1 (0.2%)
肺臓炎	- Any Grade -	6 (1.0%)	1 (0.2%)
	2	2 (0.3%)	0
	3	4 (0.7%)	1 (0.2%)
間質性肺疾患	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_ser_GO28915_SE.out
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Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肝炎			
- Overall -	- Any Grade -	5 (0.8%)	2 (0.3%)
	2	0	1 (0.2%)
	3	2 (0.3%)	0
	4	3 (0.5%)	1 (0.2%)
肝炎	- Any Grade -	2 (0.3%)	0
	4	2 (0.3%)	0
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
急性肝炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
急性肝不全	- Any Grade -	0	1 (0.2%)
	4	0	1 (0.2%)
食道静脈瘤出血	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
薬物性肝障害	- Any Grade -	1 (0.2%)	0
	4	1 (0.2%)	0
発疹			
- Overall -	- Any Grade -	5 (0.8%)	0
	3	5 (0.8%)	0
そう痒症	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
水疱性皮膚炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
全身性そう痒症	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
発疹	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
類天疱瘡	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
髄膜脳炎			
- Overall -	- Any Grade -	4 (0.7%)	0
	2	1 (0.2%)	0
	3	2 (0.3%)	0
	4	1 (0.2%)	0
髄膜炎	- Any Grade -	3 (0.5%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
	4	1 (0.2%)	0
脳炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
大腸炎			
- Overall -	- Any Grade -	1 (0.2%)	2 (0.3%)
	2	1 (0.2%)	0
	3	0	2 (0.3%)
大腸炎	- Any Grade -	1 (0.2%)	2 (0.3%)
	2	1 (0.2%)	0
	3	0	2 (0.3%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_ser_GO28915_SE.out
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Serious AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
糖尿病			
- Overall -	- Any Grade -	3 (0.5%)	0
	3	1 (0.2%)	0
	4	2 (0.3%)	0
高血糖	- Any Grade -	3 (0.5%)	0
	3	1 (0.2%)	0
	4	2 (0.3%)	0
ギラン・バレー症候群			
- Overall -	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
ギラン・バレー症候群	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
腎炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
ヘノッホ・シェーンライン紫斑病性腎炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
胚・胎児毒性			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
成長障害	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
膵炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
膵炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_ser.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_ser_GO28915_SE.out
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［5.3.5.1-3 aet04_aesi_ser_GO28915_SE を再掲］

表 2.7.4.7.6-4 治験薬の投与中止に至った本剤の注目すべき有害事象の要約（OAK 試験）

AESI Leading to Discontinuation of Trial Treatment by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
- Any adverse events -	- Any Grade -	22 (3.6%)	14 (2.4%)
	1	0	1 (0.2%)
	2	7 (1.1%)	4 (0.7%)
	3	10 (1.6%)	7 (1.2%)
	4	4 (0.7%)	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
Infusion reaction			
- Overall -	- Any Grade -	5 (0.8%)	11 (1.9%)
	1	0	1 (0.2%)
	2	4 (0.7%)	1 (0.2%)
	3	0	7 (1.2%)
	4	0	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
呼吸困難	- Any Grade -	1 (0.2%)	6 (1.0%)
	1	0	1 (0.2%)
	3	0	3 (0.5%)
	4	0	1 (0.2%)
	5	1 (0.2%)	1 (0.2%)
薬物過敏症	- Any Grade -	0	3 (0.5%)
	2	0	1 (0.2%)
	3	0	2 (0.3%)
過敏症	- Any Grade -	2 (0.3%)	0
	2	2 (0.3%)	0
注入に伴う反応	- Any Grade -	1 (0.2%)	1 (0.2%)
	2	1 (0.2%)	0
	3	0	1 (0.2%)
アナフィラキシー反応	- Any Grade -	0	1 (0.2%)
	3	0	1 (0.2%)
気管支痙攣	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
低血圧	- Any Grade -	0	1 (0.2%)
	3	0	1 (0.2%)
肝炎			
- Overall -	- Any Grade -	5 (0.8%)	1 (0.2%)
	2	0	1 (0.2%)
	3	2 (0.3%)	0
	4	3 (0.5%)	0
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
肝炎	- Any Grade -	2 (0.3%)	0
	4	2 (0.3%)	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
食道静脈瘤出血	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
薬物性肝障害	- Any Grade -	1 (0.2%)	0
	4	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_dis_GO28915_SE.out
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AESI Leading to Discontinuation of Trial Treatment by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
発疹			
- Overall -	- Any Grade -	4 (0.7%)	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
	3	3 (0.5%)	0
水疱性皮膚炎	- Any Grade -	2 (0.3%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
多形紅斑	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
爪の障害	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
類天疱瘡	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
髄膜脳炎			
- Overall -	- Any Grade -	4 (0.7%)	0
	2	1 (0.2%)	0
	3	2 (0.3%)	0
	4	1 (0.2%)	0
髄膜炎	- Any Grade -	3 (0.5%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
	4	1 (0.2%)	0
脳炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
肺臓炎			
- Overall -	- Any Grade -	3 (0.5%)	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)
	3	2 (0.3%)	0
肺臓炎	- Any Grade -	1 (0.2%)	1 (0.2%)
	2	0	1 (0.2%)
	3	1 (0.2%)	0
間質性肺疾患	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
肺浸潤	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
腎炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
ヘノッホ・シェーンライン紫斑病性腎炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_dis.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_dis_GO28915_SE.out
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［5.3.5.1-3 aet04_aesi_dis_GO28915_SE を再掲］

表 2.7.4.7.6-5 治験薬の投与量変更に至った本剤の注目すべき有害事象の要約（OAK 試験）

AESI Leading to Dose Modification or Interruption by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
- Any adverse events -	- Any Grade -	56 (9.2%)	33 (5.7%)
	1	9 (1.5%)	7 (1.2%)
	2	25 (4.1%)	15 (2.6%)
	3	20 (3.3%)	11 (1.9%)
	4	2 (0.3%)	0
Infusion reaction			
- Overall -	- Any Grade -	23 (3.8%)	22 (3.8%)
	1	6 (1.0%)	7 (1.2%)
	2	9 (1.5%)	13 (2.2%)
	3	7 (1.1%)	2 (0.3%)
	4	1 (0.2%)	0
呼吸困難	- Any Grade -	10 (1.6%)	6 (1.0%)
	1	1 (0.2%)	3 (0.5%)
	2	4 (0.7%)	1 (0.2%)
	3	5 (0.8%)	2 (0.3%)
発熱	- Any Grade -	6 (1.0%)	6 (1.0%)
	1	3 (0.5%)	4 (0.7%)
	2	2 (0.3%)	2 (0.3%)
	3	1 (0.2%)	0
注入に伴う反応	- Any Grade -	5 (0.8%)	3 (0.5%)
	1	1 (0.2%)	0
	2	3 (0.5%)	3 (0.5%)
	3	1 (0.2%)	0
過敏症	- Any Grade -	1 (0.2%)	3 (0.5%)
	2	0	3 (0.5%)
	4	1 (0.2%)	0
潮紅	- Any Grade -	2 (0.3%)	2 (0.3%)
	1	1 (0.2%)	0
	2	0	2 (0.3%)
	3	1 (0.2%)	0
低血圧	- Any Grade -	1 (0.2%)	3 (0.5%)
	2	1 (0.2%)	3 (0.5%)
悪寒	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
顔面浮腫	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
気管支痙攣	- Any Grade -	0	1 (0.2%)
	1	0	1 (0.2%)
発疹			
- Overall -	- Any Grade -	10 (1.6%)	8 (1.4%)
	1	0	1 (0.2%)
	2	5 (0.8%)	4 (0.7%)
	3	5 (0.8%)	3 (0.5%)
そう痒症	- Any Grade -	4 (0.7%)	0
	2	2 (0.3%)	0
	3	2 (0.3%)	0
発疹	- Any Grade -	3 (0.5%)	1 (0.2%)
	2	2 (0.3%)	1 (0.2%)
	3	1 (0.2%)	0
多汗症	- Any Grade -	1 (0.2%)	1 (0.2%)
	2	1 (0.2%)	1 (0.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_mod_GO28915_SE.out
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AESI Leading to Dose Modification or Interruption by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
多形紅斑	- Any Grade -	2 (0.3%)	0
	2	2 (0.3%)	0
斑状丘疹状皮疹	- Any Grade -	2 (0.3%)	0
	2	1 (0.2%)	0
	3	1 (0.2%)	0
皮膚反応	- Any Grade -	0	2 (0.3%)
	1	0	1 (0.2%)
	2	0	1 (0.2%)
手掌・足底発赤知覚不全症候群	- Any Grade -	0	1 (0.2%)
	3	0	1 (0.2%)
水疱性皮膚炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
爪の障害	- Any Grade -	0	1 (0.2%)
	3	0	1 (0.2%)
爪毒性	- Any Grade -	0	1 (0.2%)
	2	0	1 (0.2%)
皮脂欠乏性湿疹	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
皮膚炎	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
皮膚乾燥	- Any Grade -	0	1 (0.2%)
	3	0	1 (0.2%)
皮膚硬結	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
薬疹	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
肝炎			
- Overall -	- Any Grade -	10 (1.6%)	2 (0.3%)
	1	2 (0.3%)	0
	2	2 (0.3%)	0
	3	6 (1.0%)	2 (0.3%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	5 (0.8%)	2 (0.3%)
	1	2 (0.3%)	0
	2	1 (0.2%)	1 (0.2%)
	3	2 (0.3%)	1 (0.2%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	5 (0.8%)	1 (0.2%)
	1	2 (0.3%)	0
	2	2 (0.3%)	0
	3	1 (0.2%)	1 (0.2%)
血中ビリルビン増加	- Any Grade -	2 (0.3%)	2 (0.3%)
	1	1 (0.2%)	0
	2	1 (0.2%)	0
	3	0	2 (0.3%)
トランスアミナーゼ上昇	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
γーグルタミルトランスフェラーゼ増加	- Any Grade -	2 (0.3%)	0
	3	2 (0.3%)	0
急性肝炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_mod_GO28915_SE.out
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AESI Leading to Dose Modification or Interruption by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
肺臓炎			
- Overall -	- Any Grade -	5 (0.8%)	1 (0.2%)
	1	1 (0.2%)	0
	2	4 (0.7%)	0
	3	0	1 (0.2%)
肺臓炎	- Any Grade -	2 (0.3%)	1 (0.2%)
	2	2 (0.3%)	0
	3	0	1 (0.2%)
肺浸潤	- Any Grade -	2 (0.3%)	0
	2	2 (0.3%)	0
放射線性肺臓炎	- Any Grade -	1 (0.2%)	0
	1	1 (0.2%)	0
甲状腺機能低下症			
- Overall -	- Any Grade -	4 (0.7%)	0
	2	4 (0.7%)	0
甲状腺機能低下症	- Any Grade -	4 (0.7%)	0
	2	4 (0.7%)	0
大腸炎			
- Overall -	- Any Grade -	1 (0.2%)	2 (0.3%)
	2	1 (0.2%)	0
	3	0	2 (0.3%)
大腸炎	- Any Grade -	1 (0.2%)	2 (0.3%)
	2	1 (0.2%)	0
	3	0	2 (0.3%)
糖尿病			
- Overall -	- Any Grade -	2 (0.3%)	1 (0.2%)
	3	1 (0.2%)	1 (0.2%)
	4	1 (0.2%)	0
高血糖	- Any Grade -	2 (0.3%)	0
	3	1 (0.2%)	0
	4	1 (0.2%)	0
糖尿病	- Any Grade -	0	1 (0.2%)
	3	0	1 (0.2%)
ギラン・バレー症候群			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
ギラン・バレー症候群	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0
甲状腺機能亢進症			
- Overall -	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
内分泌性眼症	- Any Grade -	1 (0.2%)	0
	2	1 (0.2%)	0
膵炎			
- Overall -	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_mod_GO28915_SE.out
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AESI Leading to Dose Modification or Interruption by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=609)	Docetaxel (Actual) (N=578)
膵炎	- Any Grade -	1 (0.2%)	0
	3	1 (0.2%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi_mod.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_mod_GO28915_SE.out
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［5.3.5.1-3 aet04_aesi_mod_GO28915_SE を再掲］

表 2.7.4.7.6-6 本剤の注目すべき有害事象の要約（OAK 試験，日本人集団）

AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=56)	Docetaxel (Actual) (N=45)
- Any adverse events -	- Any Grade -	46 (82.1%)	39 (86.7%)
	1	28 (50.0%)	15 (33.3%)
	2	10 (17.9%)	23 (51.1%)
	3	7 (12.5%)	1 (2.2%)
	4	1 (1.8%)	0
発疹			
- Overall -	- Any Grade -	25 (44.6%)	35 (77.8%)
	1	21 (37.5%)	15 (33.3%)
	2	2 (3.6%)	20 (44.4%)
	3	2 (3.6%)	0
脱毛症	- Any Grade -	0	28 (62.2%)
	1	0	9 (20.0%)
	2	0	19 (42.2%)
発疹	- Any Grade -	9 (16.1%)	13 (28.9%)
	1	9 (16.1%)	11 (24.4%)
	2	0	2 (4.4%)
そう痒症	- Any Grade -	5 (8.9%)	5 (11.1%)
	1	4 (7.1%)	3 (6.7%)
	2	1 (1.8%)	2 (4.4%)
爪変色	- Any Grade -	0	8 (17.8%)
	1	0	7 (15.6%)
	2	0	1 (2.2%)
皮膚乾燥	- Any Grade -	1 (1.8%)	7 (15.6%)
	1	1 (1.8%)	7 (15.6%)
爪の障害	- Any Grade -	0	5 (11.1%)
	1	0	5 (11.1%)
ざ瘡様皮膚炎	- Any Grade -	2 (3.6%)	1 (2.2%)
	1	2 (3.6%)	1 (2.2%)
湿疹	- Any Grade -	1 (1.8%)	2 (4.4%)
	1	1 (1.8%)	2 (4.4%)
斑状丘疹状皮疹	- Any Grade -	2 (3.6%)	1 (2.2%)
	1	2 (3.6%)	1 (2.2%)
紅斑	- Any Grade -	2 (3.6%)	0
	1	2 (3.6%)	0
手掌・足底発赤知覚不全症候群	- Any Grade -	0	2 (4.4%)
	1	0	2 (4.4%)
多形紅斑	- Any Grade -	2 (3.6%)	0
	2	1 (1.8%)	0
	3	1 (1.8%)	0
蕁麻疹	- Any Grade -	0	2 (4.4%)
	1	0	1 (2.2%)
	2	0	1 (2.2%)
ざ瘡	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
そう痒性皮疹	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
寝汗	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
接触性皮膚炎	- Any Grade -	0	1 (2.2%)
	1	0	1 (2.2%)
全身性皮疹	- Any Grade -	0	1 (2.2%)
	1	0	1 (2.2%)

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE_JAPAN.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=56)	Docetaxel (Actual) (N=45)
爪甲脱落症	- Any Grade -	0	1 (2.2%)
	2	0	1 (2.2%)
爪床出血	- Any Grade -	0	1 (2.2%)
	1	0	1 (2.2%)
皮脂欠乏性湿疹	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
皮膚萎縮	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
皮膚炎	- Any Grade -	0	1 (2.2%)
	1	0	1 (2.2%)
皮膚粘膜発疹	- Any Grade -	0	1 (2.2%)
	2	0	1 (2.2%)
Infusion reaction			
- Overall -	- Any Grade -	22 (39.3%)	20 (44.4%)
	1	19 (33.9%)	14 (31.1%)
	2	3 (5.4%)	6 (13.3%)
発熱	- Any Grade -	20 (35.7%)	11 (24.4%)
	1	18 (32.1%)	9 (20.0%)
	2	2 (3.6%)	2 (4.4%)
顔面浮腫	- Any Grade -	0	5 (11.1%)
	1	0	4 (8.9%)
	2	0	1 (2.2%)
過敏症	- Any Grade -	1 (1.8%)	1 (2.2%)
	2	1 (1.8%)	1 (2.2%)
呼吸困難	- Any Grade -	1 (1.8%)	1 (2.2%)
	1	1 (1.8%)	1 (2.2%)
潮紅	- Any Grade -	0	2 (4.4%)
	1	0	1 (2.2%)
	2	0	1 (2.2%)
蕁麻疹	- Any Grade -	0	2 (4.4%)
	1	0	1 (2.2%)
	2	0	1 (2.2%)
悪寒	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
眼窩周囲浮腫	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
舌浮腫	- Any Grade -	0	1 (2.2%)
	1	0	1 (2.2%)
低血圧	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
肝炎			
- Overall -	- Any Grade -	10 (17.9%)	5 (11.1%)
	1	7 (12.5%)	5 (11.1%)
	2	1 (1.8%)	0
	3	2 (3.6%)	0
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	4 (7.1%)	4 (8.9%)
	1	3 (5.4%)	4 (8.9%)
	2	1 (1.8%)	0
アラニンアミノトランスフェラーゼ増加	- Any Grade -	4 (7.1%)	4 (8.9%)
	1	3 (5.4%)	4 (8.9%)
	2	1 (1.8%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE_JAPAN.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=56)	Docetaxel (Actual) (N=45)
肝機能異常	- Any Grade -	2 (3.6%)	1 (2.2%)
	1	1 (1.8%)	1 (2.2%)
	3	1 (1.8%)	0
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
肝障害	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
血中ビリルビン増加	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
肺臓炎			
- Overall -	- Any Grade -	5 (8.9%)	1 (2.2%)
	1	1 (1.8%)	0
	2	3 (5.4%)	0
	3	1 (1.8%)	1 (2.2%)
肺臓炎	- Any Grade -	2 (3.6%)	1 (2.2%)
	2	1 (1.8%)	0
	3	1 (1.8%)	1 (2.2%)
放射線性肺臓炎	- Any Grade -	2 (3.6%)	0
	1	1 (1.8%)	0
	2	1 (1.8%)	0
間質性肺疾患	- Any Grade -	1 (1.8%)	0
	2	1 (1.8%)	0
甲状腺機能低下症			
- Overall -	- Any Grade -	3 (5.4%)	1 (2.2%)
	1	1 (1.8%)	1 (2.2%)
	2	2 (3.6%)	0
血中甲状腺刺激ホルモン増加	- Any Grade -	2 (3.6%)	1 (2.2%)
	1	1 (1.8%)	1 (2.2%)
	2	1 (1.8%)	0
甲状腺機能低下症	- Any Grade -	1 (1.8%)	0
	2	1 (1.8%)	0
髄膜脳炎			
- Overall -	- Any Grade -	4 (7.1%)	0
	2	1 (1.8%)	0
	3	2 (3.6%)	0
	4	1 (1.8%)	0
髄膜炎	- Any Grade -	3 (5.4%)	0
	2	1 (1.8%)	0
	3	1 (1.8%)	0
	4	1 (1.8%)	0
脳炎	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
甲状腺機能亢進症			
- Overall -	- Any Grade -	2 (3.6%)	1 (2.2%)
	1	1 (1.8%)	1 (2.2%)
	2	1 (1.8%)	0
血中甲状腺刺激ホルモン増加	- Any Grade -	2 (3.6%)	1 (2.2%)
	1	1 (1.8%)	1 (2.2%)
	2	1 (1.8%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE_JAPAN.out
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AESI by Intensity (CTCAE Grades 1-5) (GO28915:OAK)
Protocol: GO28915
Population: Japanese Patients, All Safety Evaluable Patients

AE of Special Interest Medical Concept MedDRA Preferred Term	Grade	Atezolizumab (Actual) (N=56)	Docetaxel (Actual) (N=45)
ギラン・バレー症候群			
- Overall -	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
ギラン・バレー症候群	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
腎炎			
- Overall -	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
ヘノッホ・シェーンライン紫斑病性腎炎	- Any Grade -	1 (1.8%)	0
	3	1 (1.8%)	0
糖尿病			
- Overall -	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0
耐糖能障害	- Any Grade -	1 (1.8%)	0
	1	1 (1.8%)	0

Percentages are based on N in the column headings.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the Overall row counts, a patient contributes only with the AE occurring with the highest grade within the group.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aet04_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aet04_aesi_GO28915_SE_JAPAN.out
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［5.3.5.1-3 aet04_aesi_GO28915_SE_JAPAN を再掲］

2.7.4.7.7 本剤の注目すべき有害事象の発現時期及び回復時期（OAK 試験）

表 2.7.4.7.7-1 本剤の注目すべき有害事象の初回発現までの期間の要約（OAK 試験）

Time to First Onset of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
Infusion reaction	1	22.0	683	1	23.0	316
アナフィラキシー反応	–	–	–	1	15.5	30
悪寒	1	25.0	539	2	8.5	119
過敏症	22	64.5	242	1	20.0	61
眼球浮腫	120	159.0	198	13	83.5	154
眼部腫脹	–	–	–	1	1.0	1
眼瞼浮腫	473	473.0	473	–	–	–
眼窩周囲浮腫	1	5.0	88	126	126.0	126
顔面腫脹	55	55.0	55	22	27.5	33
顔面浮腫	52	107.0	473	3	77.0	128
気管支痙攣	17	41.0	90	1	1.0	1
血管浮腫	153	153.0	153	–	–	–
呼吸困難	1	43.0	610	1	38.0	409
口唇腫脹	–	–	–	1	1.0	1
舌腫脹	–	–	–	1	1.0	1
舌浮腫	–	–	–	29	29.0	29
注入に伴う反応	21	22.0	43	1	22.5	27
潮紅	1	32.0	172	1	21.0	129
低血圧	1	28.0	459	6	47.0	152
発熱	1	14.0	683	1	29.0	453
頻脈	5	42.0	534	1	31.5	252
薬物過敏症	43	239.0	242	1	22.0	26
喘鳴	10	32.5	147	1	23.0	55
蕁麻疹	5	50.0	72	2	4.0	6
ぶどう膜炎	346	346.0	346	–	–	–
ぶどう膜炎	346	346.0	346	–	–	–
ギラン・バレー症候群	17	116.0	239	–	–	–
ギラン・バレー症候群	17	20.0	212	–	–	–
脱髄性多発ニューロパチー	239	239.0	239	–	–	–

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aefstsum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aefstsum_aesi_GO28915_SE.out
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Time to First Onset of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
肝炎	1	22.0	638	6	21.5	188
アスパラギン酸アミノトランスフェラーゼ増加	4	22.0	638	6	20.5	188
アラニンアミノトランスフェラーゼ増加	4	22.0	638	6	20.5	188
トランスアミナーゼ上昇	103	180.5	258	-	-	-
γ－グルタミルトランスフェラーゼ増加	22	105.0	428	22	64.5	107
肝炎	9	49.5	90	-	-	-
肝機能異常	11	101.0	292	9	58.5	108
肝酵素上昇	21	21.0	21	-	-	-
肝細胞損傷	20	20.0	20	-	-	-
肝障害	86	86.0	86	-	-	-
肝臓痛	64	64.0	64	8	8.0	8
肝病変	200	200.0	200	-	-	-
急性肝炎	8	8.0	8	-	-	-
急性肝不全	-	-	-	93	93.0	93
血中ビリルビン増加	1	68.0	258	22	53.0	84
高ビリルビン血症	20	20.0	20	-	-	-
脂肪肝	165	165.0	165	-	-	-
食道静脈瘤	-	-	-	13	13.0	13
食道静脈瘤出血	-	-	-	8	8.0	8
腹水	14	14.0	311	-	-	-
薬物性肝障害	82	82.0	82	-	-	-
甲状腺機能低下症	21	120.0	462	5	49.5	94
血中甲状腺刺激ホルモン減少	39	39.0	39	-	-	-
血中甲状腺刺激ホルモン増加	21	224.0	462	94	94.0	94
甲状腺炎	42	42.0	42	-	-	-
甲状腺機能検査異常	85	85.0	85	-	-	-
甲状腺機能低下症	22	123.5	435	5	5.0	5
甲状腺機能亢進症	21	85.0	462	94	94.0	94
眼球突出症	130	130.0	130	-	-	-
血中甲状腺刺激ホルモン減少	39	39.0	39	-	-	-
血中甲状腺刺激ホルモン増加	21	224.0	462	94	94.0	94
甲状腺炎	42	42.0	42	-	-	-
甲状腺機能検査異常	85	85.0	85	-	-	-
甲状腺機能亢進症	31	62.0	355	-	-	-
内分泌性眼症	277	277.0	277	-	-	-
腎炎	400	400.0	400	-	-	-
ヘノッホ・シェーンライン紫斑病性腎炎	400	400.0	400	-	-	-

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aefstsum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aefstsum_aesi_GO28915_SE.out
07DEC2016 17:30

Time to First Onset of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
髄膜脳炎	14	15.0	20	-	-	-
髄膜炎	15	15.0	16	-	-	-
脳炎	14	14.0	14	-	-	-
羞明	20	20.0	20	-	-	-
大腸炎	79	100.0	121	4	18.5	33
大腸炎	79	100.0	121	4	18.5	33
糖尿病	13	42.0	297	1	37.0	135
１型糖尿病	-	-	-	-	-	-
２型糖尿病	29	29.0	29	20	20.0	20
血中ブドウ糖増加	-	-	-	22	43.0	64
高血糖	13	41.5	297	1	37.0	135
耐糖能障害	42	42.0	42	-	-	-
糖尿病	-	-	-	66	82.0	98
尿中ブドウ糖陽性	-	-	-	21	21.0	21
肺臓炎	6	96.0	526	5	20.0	43
間質性肺疾患	111	126.0	128	-	-	-
細気管支炎	88	88.0	88	-	-	-
肺浸潤	65	84.5	104	-	-	-
肺臓炎	6	107.5	526	5	20.0	43
放射線性肺臓炎	8	11.5	15	-	-	-
発疹	1	44.0	517	1	19.0	297
うっ滞性皮膚炎	123	123.0	123	-	-	-
ざ瘡	14	14.0	14	23	23.0	23
ざ瘡様皮膚炎	5	62.0	139	8	19.5	28
そう痒症	2	58.0	496	1	24.0	105
そう痒性皮疹	8	17.5	85	14	18.0	22
アトピー性皮膚炎	-	-	-	1	1.0	1
過角化	-	-	-	49	49.0	49
乾皮症	331	331.0	331	-	-	-
乾癬	42	123.5	343	22	22.0	22
顔面腫脹	55	55.0	55	22	27.5	33
丘疹性皮疹	147	147.0	147	-	-	-
血管浮腫	153	153.0	153	-	-	-
光線角化症	-	-	-	180	180.0	180
紅色症	-	-	-	146	146.0	146
紅斑	4	112.0	495	1	22.0	47
紅斑性皮疹	23	184.0	345	219	219.0	219
黒皮症	-	-	-	14	14.0	14
脂漏性皮膚炎	-	-	-	44	44.0	44

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aefstsum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aefstsum_aesi_GO28915_SE.out
07DEC2016 17:30

Time to First Onset of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
湿疹	7	198.0	479	5	5.0	21
手掌・足底発赤知覚不全症候群	–	–	–	2	43.0	92
手掌紅斑	–	–	–	43	43.0	43
色素沈着障害	–	–	–	195	195.0	195
寝汗	2	18.0	262	21	75.5	104
尋常性白斑	107	107.0	107	–	–	–
水疱	76	76.0	76	–	–	–
水疱性皮膚炎	59	204.0	472	–	–	–
接触性皮膚炎	–	–	–	11	15.0	19
全身性そう痒症	15	40.0	418	–	–	–
全身性皮疹	85	85.0	85	7	7.0	7
多汗症	13	42.5	155	1	32.0	65
多形紅斑	10	59.0	108	–	–	–
脱毛症	1	41.0	44	1	18.0	170
爪の障害	–	–	–	40	86.5	276
爪ジストロフィー	421	421.0	421	106	135.5	165
爪甲脱落症	–	–	–	3	148.0	297
爪甲離床症	182	182.0	182	85	87.0	150
爪床出血	–	–	–	59	59.0	59
爪線状隆起	212	302.5	393	8	13.0	64
爪痛	–	–	–	61	74.0	87
爪毒性	–	–	–	24	112.0	127
爪破損	166	166.0	166	184	184.0	184
爪肥厚	142	142.0	142	–	–	–
爪変色	434	434.0	434	1	70.5	167
点状出血	15	203.5	392	39	39.0	39
頭部粃糠疹	247	247.0	247	–	–	–
発疹	2	62.0	354	1	22.5	297
斑	–	–	–	–	–	–
斑状丘疹状皮疹	6	82.0	517	5	7.0	118
皮脂欠乏性湿疹	28	28.0	28	–	–	–
皮膚萎縮	85	85.0	85	–	–	–
皮膚炎	8	79.5	430	31	92.0	105
皮膚乾燥	4	64.0	302	3	29.0	411
皮膚亀裂	–	–	–	21	21.0	21
皮膚硬結	328	385.5	443	–	–	–
皮膚刺激	–	–	–	28	28.0	28
皮膚腫瘤	21	43.0	400	39	39.0	39
皮膚障害	129	129.0	129	–	–	–
皮膚色素過剰	22	49.0	106	29	50.0	105
皮膚色素減少	–	–	–	22	22.0	22
皮膚潰瘍	17	17.0	17	–	–	–
皮膚毒性	–	–	–	21	64.5	108

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aefstsum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aefstsum_aesi_GO28915_SE.out
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Time to First Onset of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
皮膚軟化	–	–	–	5	5.0	5
皮膚粘膜発疹	–	–	–	113	113.0	113
皮膚嚢腫	700	700.0	700	78	78.0	78
皮膚剥脱	155	330.0	505	19	34.0	62
皮膚反応	–	–	–	52	74.5	97
皮膚病変	196	263.5	331	44	44.0	44
皮膚変色	233	233.0	233	–	–	–
皮膚疼痛	530	575.0	620	15	15.0	15
薬疹	141	141.0	141	–	–	–
立毛	1	1.0	1	–	–	–
類天疱瘡	347	347.0	347	–	–	–
冷汗	547	547.0	547	–	–	–
嵌入爪	–	–	–	2	63.0	124
扁平苔癬	122	122.0	122	–	–	–
痒疹	213	213.0	213	–	–	–
睫毛眉毛脱落症	–	–	–	177	177.0	177
蕁麻疹	5	50.0	72	2	4.0	6
褥瘡性潰瘍	20	143.5	267	56	56.0	56
副腎機能不全	96	174.0	407	–	–	–
原発性副腎機能不全	174	174.0	174	–	–	–
副腎機能不全	96	251.5	407	–	–	–
胚・胎児毒性	10	26.5	43	7	34.0	57
成長障害	10	10.0	10	7	20.5	34
乳腺炎	43	43.0	43	–	–	–
表皮融解	–	–	–	57	57.0	57
膵炎	353	353.0	353	–	–	–
膵炎	353	353.0	353	–	–	–

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aefstsum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aefstsum_aesi_GO28915_SE.out
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［5.3.5.1-3 aefstsum_aesi_GO28915_SE を再掲］

表 2.7.4.7.7-2 本剤の注目すべき有害事象の発現から回復までの期間の要約（OAK 試験）

Time from Frist Onset to Resolution of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
Infusion reaction	1	5.5	412	1	5.0	219
アナフィラキシー反応	-	-	-	1	1.0	1
悪寒	1	5.0	191	1	7.0	23
過敏症	1	1.5	49	1	1.5	32
眼球浮腫	9	36.0	63	1	1.0	1
眼部腫脹	-	-	-	8	8.0	8
眼瞼浮腫	-	-	-	-	-	-
眼窩周囲浮腫	5	29.0	105	-	-	-
顔面腫脹	-	-	-	4	7.0	10
顔面浮腫	26	65.0	104	8	36.5	105
気管支痙攣	17	17.0	17	1	1.0	1
血管浮腫	6	6.0	6	-	-	-
呼吸困難	1	21.0	235	1	10.0	219
口唇腫脹	-	-	-	8	8.0	8
舌腫脹	-	-	-	8	8.0	8
舌浮腫	-	-	-	47	47.0	47
注入に伴う反応	1	1.0	2	1	1.0	22
潮紅	1	1.0	41	1	4.0	203
低血圧	1	2.0	21	1	3.0	22
発熱	1	4.0	168	1	3.0	65
頻脈	1	2.0	55	1	14.5	22
薬物過敏症	1	5.5	10	1	1.0	15
喘鳴	1	26.0	42	-	-	-
蕁麻疹	2	15.5	412	9	9.5	10
ぶどう膜炎	41	41.0	41	-	-	-
ぶどう膜炎	41	41.0	41	-	-	-
ギラン・バレー症候群	19	131.5	244	-	-	-
ギラン・バレー症候群	19	131.5	244	-	-	-
脱髄性多発ニューロパチー	-	-	-	-	-	-

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aedursum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aedursum_aesi_GO28915_SE.out
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Time from Frist Onset to Resolution of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
肝炎	1	22.0	391	3	16.0	71
アスパラギン酸アミノトランスフェラーゼ増加	1	22.0	391	3	8.5	52
アラニンアミノトランスフェラーゼ増加	1	22.0	64	3	13.0	52
トランスアミナーゼ上昇	6	7.0	8	-	-	-
γ－グルタミルトランスフェラーゼ増加	22	22.0	66	71	71.0	71
肝炎	9	13.0	17	-	-	-
肝機能異常	22	22.0	22	21	21.5	22
肝酵素上昇	-	-	-	-	-	-
肝細胞損傷	30	30.0	30	-	-	-
肝障害	8	8.0	8	-	-	-
肝臓痛	29	29.0	29	-	-	-
肝病変	-	-	-	-	-	-
急性肝炎	56	56.0	56	-	-	-
急性肝不全	-	-	-	-	-	-
血中ビリルビン増加	1	6.5	43	14	33.0	52
高ビリルビン血症	61	61.0	61	-	-	-
脂肪肝	-	-	-	-	-	-
食道静脈瘤	-	-	-	14	14.0	14
食道静脈瘤出血	-	-	-	6	6.0	6
腹水	-	-	-	-	-	-
薬物性肝障害	107	107.0	107	-	-	-
甲状腺機能低下症	20	77.0	345	-	-	-
血中甲状腺刺激ホルモン減少	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	20	65.0	118	-	-	-
甲状腺炎	345	345.0	345	-	-	-
甲状腺機能検査異常	-	-	-	-	-	-
甲状腺機能低下症	22	77.0	137	-	-	-
甲状腺機能亢進症	38	88.5	345	-	-	-
眼球突出症	-	-	-	-	-	-
血中甲状腺刺激ホルモン減少	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	20	65.0	118	-	-	-
甲状腺炎	345	345.0	345	-	-	-
甲状腺機能検査異常	-	-	-	-	-	-
甲状腺機能亢進症	42	46.5	51	-	-	-
内分泌性眼症	207	207.0	207	-	-	-
腎炎	-	-	-	-	-	-
ヘノッホ・シェーンライン紫斑病性腎炎	-	-	-	-	-	-

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aedursum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aedursum_aesi_GO28915_SE.out
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Time from Frist Onset to Resolution of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
髄膜脳炎	14	22.0	102	-	-	-
髄膜炎	14	22.0	102	-	-	-
脳炎	-	-	-	-	-	-
羞明	22	22.0	22	-	-	-
大腸炎	21	24.5	28	4	6.5	9
大腸炎	21	24.5	28	4	6.5	9
糖尿病	1	22.0	99	1	21.0	64
１型糖尿病	-	-	-	-	-	-
２型糖尿病	-	-	-	-	-	-
血中ブドウ糖増加	-	-	-	9	15.5	22
高血糖	1	22.0	99	1	21.0	43
耐糖能障害	43	43.0	43	-	-	-
糖尿病	-	-	-	7	7.0	7
尿中ブドウ糖陽性	-	-	-	64	64.0	64
肺臓炎	3	14.0	70	5	31.0	67
間質性肺疾患	-	-	-	-	-	-
細気管支炎	29	29.0	29	-	-	-
肺浸潤	14	15.5	17	-	-	-
肺臓炎	3	8.5	70	5	31.0	67
放射線性肺臓炎	-	-	-	-	-	-
発疹	1	24.0	518	1	23.0	408
うっ滞性皮膚炎	-	-	-	-	-	-
ざ瘡	-	-	-	-	-	-
ざ瘡様皮膚炎	4	15.5	222	8	35.0	143
そう痒症	2	25.0	179	1	27.0	246
そう痒性皮疹	5	22.0	81	8	8.0	8
アトピー性皮膚炎	-	-	-	-	-	-
過角化	-	-	-	-	-	-
乾皮症	-	-	-	-	-	-
乾癬	71	71.0	71	-	-	-
顔面腫脹	-	-	-	4	7.0	10
丘疹性皮疹	44	44.0	44	-	-	-
血管浮腫	6	6.0	6	-	-	-
光線角化症	-	-	-	95	95.0	95
紅色症	-	-	-	5	5.0	5
紅斑	1	20.0	93	1	18.0	120
紅斑性皮疹	43	43.0	43	22	22.0	22
黒皮症	-	-	-	56	56.0	56
脂漏性皮膚炎	-	-	-	41	41.0	41

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aedursum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aedursum_aesi_GO28915_SE.out
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Time from Frist Onset to Resolution of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
湿疹	14	21.0	134	7	12.5	18
手掌・足底発赤知覚不全症候群	–	–	–	9	13.0	93
手掌紅斑	–	–	–	–	–	–
色素沈着障害	–	–	–	–	–	–
寝汗	1	39.0	106	22	62.0	111
尋常性白斑	–	–	–	–	–	–
水疱	27	27.0	27	–	–	–
水疱性皮膚炎	8	28.0	184	–	–	–
接触性皮膚炎	–	–	–	4	10.5	17
全身性そう痒症	35	54.0	63	–	–	–
全身性皮疹	–	–	–	10	10.0	10
多汗症	4	4.0	4	1	1.5	2
多形紅斑	30	30.0	30	–	–	–
脱毛症	335	335.0	335	2	63.5	488
爪の障害	–	–	–	14	93.5	418
爪ジストロフィー	–	–	–	153	153.0	153
爪甲脱落症	–	–	–	1	43.5	313
爪甲離床症	21	21.0	21	21	32.0	43
爪床出血	–	–	–	15	15.0	15
爪線状隆起	155	207.5	260	207	207.0	207
爪痛	–	–	–	29	29.0	29
爪毒性	–	–	–	9	78.0	192
爪破損	–	–	–	–	–	–
爪肥厚	127	127.0	127	–	–	–
爪変色	–	–	–	11	135.0	636
点状出血	20	20.5	21	–	–	–
頭部粃糠疹	26	26.0	26	–	–	–
発疹	1	22.0	163	1	16.0	87
斑	–	–	–	–	–	–
斑状丘疹状皮疹	3	22.0	142	2	16.0	17
皮脂欠乏性湿疹	518	518.0	518	–	–	–
皮膚萎縮	–	–	–	–	–	–
皮膚炎	6	6.0	8	28	55.5	83
皮膚乾燥	5	31.0	361	13	22.0	275
皮膚亀裂	–	–	–	–	–	–
皮膚硬結	10	10.0	10	–	–	–
皮膚刺激	–	–	–	6	6.0	6
皮膚腫瘤	22	23.0	24	–	–	–
皮膚障害	28	28.0	28	–	–	–
皮膚色素過剰	127	127.0	127	–	–	–
皮膚色素減少	–	–	–	–	–	–
皮膚潰瘍	–	–	–	–	–	–
皮膚毒性	–	–	–	21	21.0	21

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aedursum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aedursum_aesi_GO28915_SE.out
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Time from Frist Onset to Resolution of AESI (Day) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Atezolizumab (Actual) (N=609)			Docetaxel (Actual) (N=578)		
	Min	Median	Max	Min	Median	Max
皮膚軟化	–	–	–	–	–	–
皮膚粘膜発疹	–	–	–	11	11.0	11
皮膚嚢腫	–	–	–	–	–	–
皮膚剥脱	15	15.0	15	135	135.0	135
皮膚反応	–	–	–	24	27.5	31
皮膚病変	5	22.0	39	42	42.0	42
皮膚変色	–	–	–	–	–	–
皮膚疼痛	4	4.0	4	18	18.0	18
薬疹	16	16.0	16	–	–	–
立毛	1	1.0	1	–	–	–
類天疱瘡	–	–	–	–	–	–
冷汗	–	–	–	–	–	–
嵌入爪	–	–	–	–	–	–
扁平苔癬	367	367.0	367	–	–	–
痒疹	35	35.0	35	–	–	–
睫毛眉毛脱落症	–	–	–	199	199.0	199
蕁麻疹	2	15.5	412	9	9.5	10
褥瘡性潰瘍	–	–	–	–	–	–
副腎機能不全	510	510.0	510	–	–	–
原発性副腎機能不全	–	–	–	–	–	–
副腎機能不全	510	510.0	510	–	–	–
胚・胎児毒性	8	8.0	8	3	10.0	30
成長障害	–	–	–	3	6.5	10
乳腺炎	8	8.0	8	–	–	–
表皮融解	–	–	–	30	30.0	30
膵炎	27	27.0	27	–	–	–
膵炎	27	27.0	27	–	–	–

AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aedursum_aesi.sas
Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aedursum_aesi_GO28915_SE.out
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［5.3.5.1-3 aedursum_aesi_GO28915_SE を再掲］

表 2.7.4.7.7-3　本剤の注目すべき有害事象の初回発現までの期間の時期別の要約（OAK 試験）

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) ; N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
No. of Pts treated in each period	609	609	584	552	529	493	469	444	419	389
ALL AE of Special Interest Medical Concept										
Total Pts with at least one AE	377(61.9)	215(35.3)	46(7.9)	29(5.3)	26(4.9)	19(3.9)	9(1.9)	7(1.6)	4(1.0)	4(1.0)
Infusion reaction										
Total Pts with at least one AE	243(39.9)	136(22.3)	27(4.6)	21(3.8)	15(2.8)	9(1.8)	6(1.3)	3(0.7)	5(1.2)	6(1.5)
呼吸困難	119(19.5)	46(7.6)	18(3.1)	13(2.4)	13(2.5)	6(1.2)	5(1.1)	1(0.2)	4(1.0)	3(0.8)
発熱	109(17.9)	79(13.0)	8(1.4)	5(0.9)	3(0.6)	1(0.2)	1(0.2)	2(0.5)	1(0.2)	-
悪寒	22(3.6)	12(2.0)	3(0.5)	2(0.4)	1(0.2)	1(0.2)	-	-	-	2(0.5)
低血圧	17(2.8)	10(1.6)	1(0.2)	2(0.4)	2(0.4)	-	1(0.2)	-	-	-
頻脈	11(1.8)	3(0.5)	3(0.5)	1(0.2)	1(0.2)	-	-	-	-	1(0.3)
過敏症	6(1.0)	1(0.2)	-	3(0.5)	-	-	1(0.2)	-	-	1(0.3)
潮紅	6(1.0)	3(0.5)	2(0.3)	-	-	-	-	1(0.2)	-	-
喘鳴	6(1.0)	3(0.5)	1(0.2)	1(0.2)	-	-	1(0.2)	-	-	-
注入に伴う反応	5(0.8)	3(0.5)	2(0.3)	-	-	-	-	-	-	-
蕁麻疹	5(0.8)	2(0.3)	1(0.2)	2(0.4)	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
Infusion reaction										
眼窩周囲浮腫	4(0.7)	3(0.5)	-	-	1(0.2)	-	-	-	-	-
顔面浮腫	3(0.5)	-	1(0.2)	-	1(0.2)	-	-	-	-	-
気管支痙攣	3(0.5)	1(0.2)	1(0.2)	-	1(0.2)	-	-	-	-	-
薬物過敏症	3(0.5)	-	1(0.2)	-	-	-	-	-	-	2(0.5)
眼球浮腫	2(0.3)	-	-	-	-	1(0.2)	-	-	1(0.2)	-
眼部腫脹	1(0.2)	-	-	-	-	-	-	-	-	-
眼瞼浮腫	1(0.2)	-	-	-	-	-	-	-	-	-
顔面腫脹	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
血管浮腫	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
発疹										
Total Pts with at least one AE	177(29.1)	71(11.7)	25(4.3)	15(2.7)	17(3.2)	8(1.6)	7(1.5)	4(0.9)	4(1.0)	4(1.0)
発疹	59(9.7)	19(3.1)	10(1.7)	3(0.5)	7(1.3)	2(0.4)	3(0.6)	1(0.2)	2(0.5)	3(0.8)
そう痒症	50(8.2)	17(2.8)	6(1.0)	8(1.4)	4(0.8)	3(0.6)	-	2(0.5)	2(0.5)	1(0.3)
皮膚乾燥	27(4.4)	7(1.1)	6(1.0)	2(0.4)	3(0.6)	1(0.2)	4(0.9)	1(0.2)	-	1(0.3)
寝汗	14(2.3)	9(1.5)	3(0.5)	1(0.2)	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Any Period No. (%)	Period 0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
発疹										
紅斑	13(2.1)	4(0.7)	1(0.2)	1(0.2)	1(0.2)	1(0.2)	-	1(0.2)	-	1(0.3)
斑状丘疹状皮疹	9(1.5)	3(0.5)	-	1(0.2)	1(0.2)	-	-	-	-	-
湿疹	7(1.1)	1(0.2)	-	-	1(0.2)	-	1(0.2)	-	1(0.2)	-
ざ瘡様皮膚炎	5(0.8)	1(0.2)	1(0.2)	2(0.4)	-	1(0.2)	-	-	-	-
多汗症	5(0.8)	2(0.3)	-	1(0.2)	-	-	1(0.2)	-	-	-
蕁麻疹	5(0.8)	2(0.3)	1(0.2)	2(0.4)	-	-	-	-	-	-
そう痒性皮疹	4(0.7)	3(0.5)	-	-	1(0.2)	-	-	-	-	-
乾癬	4(0.7)	-	2(0.3)	-	-	-	-	-	1(0.2)	-
全身性そう痒症	4(0.7)	1(0.2)	2(0.3)	-	-	-	-	-	-	-
皮膚炎	4(0.7)	2(0.3)	-	-	-	1(0.2)	-	-	-	-
皮膚色素過剰	4(0.7)	1(0.2)	1(0.2)	-	1(0.2)	-	-	-	-	-
紅斑性皮疹	3(0.5)	1(0.2)	-	-	-	-	-	-	-	-
水疱性皮膚炎	3(0.5)	-	-	1(0.2)	-	-	-	-	1(0.2)	-
脱毛症	3(0.5)	1(0.2)	2(0.3)	-	-	-	-	-	-	-
皮膚腫瘤	3(0.5)	1(0.2)	1(0.2)	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
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発疹										
多形紅斑	2(0.3)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
爪線状隆起	2(0.3)	-	-	-	-	-	-	-	1(0.2)	-
点状出血	2(0.3)	1(0.2)	-	-	-	-	-	-	-	-
皮膚硬結	2(0.3)	-	-	-	-	-	-	-	-	-
皮膚潰瘍	2(0.3)	1(0.2)	-	-	-	-	-	-	-	-
皮膚剥脱	2(0.3)	-	-	-	-	-	1(0.2)	-	-	-
皮膚病変	2(0.3)	-	-	-	-	-	-	1(0.2)	-	-
皮膚疼痛	2(0.3)	-	-	-	-	-	-	-	-	-
褥瘡性潰瘍	2(0.3)	1(0.2)	-	-	-	-	-	-	-	-
うっ滞性皮膚炎	1(0.2)	-	-	-	-	1(0.2)	-	-	-	-
ざ瘡	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
乾皮症	1(0.2)	-	-	-	-	-	-	-	-	-
顔面腫脹	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
丘疹性皮疹	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
血管浮腫	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
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発疹										
尋常性白斑	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
水疱	1(0.2)	-	-	1(0.2)	-	-	-	-	-	-
全身性皮疹	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
爪ジストロフィー	1(0.2)	-	-	-	-	-	-	-	-	-
爪甲離床症	1(0.2)	-	-	-	-	-	-	1(0.2)	-	-
爪破損	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
爪肥厚	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
爪変色	1(0.2)	-	-	-	-	-	-	-	-	-
頭部粃糠疹	1(0.2)	-	-	-	-	-	-	-	-	1(0.3)
斑	1(0.2)	-	-	-	-	-	-	-	-	-
皮脂欠乏性湿疹	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
皮膚萎縮	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
皮膚障害	1(0.2)	-	-	-	-	1(0.2)	-	-	-	-
皮膚嚢腫	1(0.2)	-	-	-	-	-	-	-	-	-
皮膚変色	1(0.2)	-	-	-	-	-	-	-	-	1(0.3)

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	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
発疹										
薬疹	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
立毛	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
類天疱瘡	1(0.2)	-	-	-	-	-	-	-	-	-
冷汗	1(0.2)	-	-	-	-	-	-	-	-	-
扁平苔癬	1(0.2)	-	-	-	-	1(0.2)	-	-	-	-
痒疹	1(0.2)	-	-	-	-	-	-	-	1(0.2)	-
肝炎										
Total Pts with at least one AE	67(11.0)	37(6.1)	2(0.3)	5(0.9)	6(1.1)	5(1.0)	2(0.4)	1(0.2)	2(0.5)	1(0.3)
アスパラギン酸アミノトランスフェラーゼ増加	38(6.2)	24(3.9)	2(0.3)	1(0.2)	-	3(0.6)	-	1(0.2)	1(0.2)	1(0.3)
アラニンアミノトランスフェラーゼ増加	35(5.7)	20(3.3)	2(0.3)	3(0.5)	-	4(0.8)	-	1(0.2)	1(0.2)	-
γ－グルタミルトランスフェラーゼ増加	7(1.1)	1(0.2)	-	-	3(0.6)	-	1(0.2)	-	-	-
血中ビリルビン増加	7(1.1)	2(0.3)	1(0.2)	1(0.2)	-	1(0.2)	-	-	-	1(0.3)
肝機能異常	3(0.5)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
腹水	3(0.5)	2(0.3)	-	-	-	-	-	-	-	-

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事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
肝炎										
トランスアミナーゼ上昇	2(0.3)	-	-	-	1(0.2)	-	-	-	-	-
肝炎	2(0.3)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
肝酵素上昇	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
肝細胞損傷	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
肝障害	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
肝臓痛	1(0.2)	-	-	1(0.2)	-	-	-	-	-	-
肝病変	1(0.2)	-	-	-	-	-	-	-	1(0.2)	-
急性肝炎	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
高ビリルビン血症	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
脂肪肝	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
薬物性肝障害	1(0.2)	-	-	1(0.2)	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
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Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period								
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
甲状腺機能低下症										
Total Pts with at least one AE	27(4.4)	2(0.3)	4(0.7)	1(0.2)	6(1.1)	3(0.6)	1(0.2)	3(0.7)	-	-
甲状腺機能低下症	18(3.0)	1(0.2)	2(0.3)	1(0.2)	4(0.8)	3(0.6)	1(0.2)	2(0.5)	-	-
血中甲状腺刺激ホルモン増加	6(1.0)	1(0.2)	-	-	1(0.2)	-	-	1(0.2)	-	-
血中甲状腺刺激ホルモン減少	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
甲状腺炎	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
甲状腺機能検査異常	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
糖尿病										
Total Pts with at least one AE	20(3.3)	8(1.3)	3(0.5)	2(0.4)	2(0.4)	1(0.2)	1(0.2)	1(0.2)	-	-
高血糖	18(3.0)	8(1.3)	2(0.3)	2(0.4)	2(0.4)	1(0.2)	1(0.2)	1(0.2)	-	-
１型糖尿病	1(0.2)	-	-	-	-	-	-	-	-	-
２型糖尿病	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
耐糖能障害	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-

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事象名 : MedDRA ver. 19.0
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
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Atezolizumab (Actual) : N = 609

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甲状腺機能亢進症										
Total Pts with at least one AE	17(2.8)	1(0.2)	5(0.9)	2(0.4)	2(0.4)	1(0.2)	-	1(0.2)	1(0.2)	-
甲状腺機能亢進症	7(1.1)	-	3(0.5)	2(0.4)	-	-	-	-	1(0.2)	-
血中甲状腺刺激ホルモン増加	6(1.0)	1(0.2)	-	-	1(0.2)	-	-	1(0.2)	-	-
眼球突出症	1(0.2)	-	-	-	-	1(0.2)	-	-	-	-
血中甲状腺刺激ホルモン減少	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
甲状腺炎	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
甲状腺機能検査異常	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
内分泌性眼症	1(0.2)	-	-	-	-	-	-	-	-	-

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事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
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肺臓炎										
Total Pts with at least one AE	14(2.3)	4(0.7)	1(0.2)	1(0.2)	3(0.6)	2(0.4)	-	1(0.2)	-	-
肺臓炎	6(1.0)	2(0.3)	1(0.2)	-	-	-	-	1(0.2)	-	-
間質性肺疾患	3(0.5)	-	-	-	1(0.2)	2(0.4)	-	-	-	-
肺浸潤	2(0.3)	-	-	1(0.2)	1(0.2)	-	-	-	-	-
放射線性肺臓炎	2(0.3)	2(0.3)	-	-	-	-	-	-	-	-
細気管支炎	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
髄膜脳炎										
Total Pts with at least one AE	5(0.8)	5(0.8)	-	-	-	-	-	-	-	-
髄膜炎	3(0.5)	3(0.5)	-	-	-	-	-	-	-	-
脳炎	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
羞明	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-

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Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
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	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
ギラン・バレー症候群										
Total Pts with at least one AE	4(0.7)	2(0.3)	-	-	-	-	-	-	1(0.2)	1(0.3)
ギラン・バレー症候群	3(0.5)	2(0.3)	-	-	-	-	-	-	1(0.2)	-
脱髄性多発ニューロパチー	1(0.2)	-	-	-	-	-	-	-	-	1(0.3)
副腎機能不全										
Total Pts with at least one AE	3(0.5)	-	-	-	1(0.2)	-	-	1(0.2)	-	-
副腎機能不全	2(0.3)	-	-	-	1(0.2)	-	-	-	-	-
原発性副腎機能不全	1(0.2)	-	-	-	-	-	-	1(0.2)	-	-
大腸炎										
Total Pts with at least one AE	2(0.3)	-	-	1(0.2)	-	1(0.2)	-	-	-	-
大腸炎	2(0.3)	-	-	1(0.2)	-	1(0.2)	-	-	-	-
胚・胎児毒性										
Total Pts with at least one AE	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-
成長障害	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
乳腺炎	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) ; N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period								
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
ぶどう膜炎										
Total Pts with at least one AE	1(0.2)	-	-	-	-	-	-	-	-	-
ぶどう膜炎	1(0.2)	-	-	-	-	-	-	-	-	-
腎炎										
Total Pts with at least one AE	1(0.2)	-	-	-	-	-	-	-	-	-
ヘノッホ・シェーンライン紫斑病性腎炎	1(0.2)	-	-	-	-	-	-	-	-	-
膵炎										
Total Pts with at least one AE	1(0.2)	-	-	-	-	-	-	-	-	-
膵炎	1(0.2)	-	-	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
No. of Pts treated in each period	578	578	558	530	495	464	430	393	361	335
ALL AE of Special Interest Medical Concept										
Total Pts with at least one AE	390(67.5)	292(50.5)	45(8.1)	19(3.6)	15(3.0)	9(1.9)	5(1.2)	-	-	-
発疹										
Total Pts with at least one AE	274(47.4)	205(35.5)	26(4.7)	8(1.5)	17(3.4)	8(1.7)	2(0.5)	-	1(0.3)	-
脱毛症	202(34.9)	162(28.0)	23(4.1)	4(0.8)	4(0.8)	2(0.4)	1(0.2)	1(0.3)	-	-
発疹	49(8.5)	32(5.5)	6(1.1)	4(0.8)	2(0.4)	-	1(0.2)	1(0.3)	1(0.3)	-
皮膚乾燥	34(5.9)	16(2.8)	5(0.9)	2(0.4)	5(1.0)	1(0.2)	2(0.5)	-	-	-
爪の障害	30(5.2)	-	7(1.3)	6(1.1)	5(1.0)	7(1.5)	4(0.9)	-	-	-
爪変色	26(4.5)	3(0.5)	5(0.9)	6(1.1)	7(1.4)	2(0.4)	3(0.7)	-	-	-
そう痒症	18(3.1)	11(1.9)	2(0.4)	3(0.6)	2(0.4)	-	-	-	-	-
爪甲脱落症	13(2.2)	2(0.3)	1(0.2)	-	2(0.4)	1(0.2)	3(0.7)	1(0.3)	-	1(0.3)
紅斑	11(1.9)	7(1.2)	4(0.7)	-	-	-	-	-	-	-
手掌・足底発赤知覚不全症候群	9(1.6)	3(0.5)	4(0.7)	1(0.2)	1(0.2)	-	-	-	-	-
爪毒性	7(1.2)	1(0.2)	-	-	3(0.6)	3(0.6)	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
発疹										
斑状丘疹状皮疹	5(0.9)	3(0.5)	1(0.2)	-	-	1(0.2)	-	-	-	-
ざ瘡様皮膚炎	4(0.7)	4(0.7)	-	-	-	-	-	-	-	-
寝汗	4(0.7)	1(0.2)	-	1(0.2)	2(0.4)	-	-	-	-	-
皮膚色素過剰	4(0.7)	-	2(0.4)	1(0.2)	1(0.2)	-	-	-	-	-
皮膚剥脱	4(0.7)	1(0.2)	1(0.2)	1(0.2)	-	-	-	-	-	-
湿疹	3(0.5)	3(0.5)	-	-	-	-	-	-	-	-
多汗症	3(0.5)	1(0.2)	1(0.2)	1(0.2)	-	-	-	-	-	-
爪甲離床症	3(0.5)	-	-	-	2(0.4)	-	1(0.2)	-	-	-
爪線状隆起	3(0.5)	2(0.3)	-	1(0.2)	-	-	-	-	-	-
皮膚炎	3(0.5)	-	1(0.2)	-	2(0.4)	-	-	-	-	-
そう痒性皮疹	2(0.3)	2(0.3)	-	-	-	-	-	-	-	-
顔面腫脹	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-
接触性皮膚炎	2(0.3)	2(0.3)	-	-	-	-	-	-	-	-
爪ジストロフィー	2(0.3)	-	-	-	1(0.2)	-	1(0.2)	-	-	-
爪痛	2(0.3)	-	-	1(0.2)	1(0.2)	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
発疹										
皮膚毒性	2(0.3)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
皮膚反応	2(0.3)	-	1(0.2)	-	1(0.2)	-	-	-	-	-
嵌入爪	2(0.3)	1(0.2)	-	-	-	1(0.2)	-	-	-	-
蕁麻疹	2(0.3)	2(0.3)	-	-	-	-	-	-	-	-
ざ瘡	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
アトピー性皮膚炎	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
過角化	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
乾癬	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
光線角化症	1(0.2)	-	-	-	-	-	-	1(0.3)	-	-
紅色症	1(0.2)	-	-	-	-	-	1(0.2)	-	-	-
紅斑性皮疹	1(0.2)	-	-	-	-	-	-	-	1(0.3)	-
黒皮症	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
脂漏性皮膚炎	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
手掌紅斑	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
色素沈着障害	1(0.2)	-	-	-	-	-	-	1(0.3)	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
発疹										
全身性皮疹	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
爪床出血	1(0.2)	-	-	1(0.2)	-	-	-	-	-	-
爪破損	1(0.2)	-	-	-	-	-	-	1(0.3)	-	-
点状出血	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
皮膚亀裂	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
皮膚刺激	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
皮膚腫瘤	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
皮膚色素減少	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
皮膚軟化	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
皮膚粘膜発疹	1(0.2)	-	-	-	-	1(0.2)	-	-	-	-
皮膚嚢腫	1(0.2)	-	-	1(0.2)	-	-	-	-	-	-
皮膚病変	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
皮膚疼痛	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
睫毛眉毛脱落症	1(0.2)	-	-	-	-	-	-	1(0.3)	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
発疹										
褥瘡性潰瘍	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-
Infusion reaction										
Total Pts with at least one AE	223(38.6)	119(20.6)	44(7.9)	26(4.9)	10(2.0)	8(1.7)	7(1.6)	1(0.3)	2(0.6)	2(0.6)
呼吸困難	113(19.6)	44(7.6)	26(4.7)	17(3.2)	9(1.8)	5(1.1)	6(1.4)	2(0.5)	-	-
発熱	77(13.3)	37(6.4)	20(3.6)	10(1.9)	4(0.8)	-	-	-	3(0.8)	1(0.3)
低血圧	23(4.0)	8(1.4)	6(1.1)	4(0.8)	1(0.2)	2(0.4)	2(0.5)	-	-	-
潮紅	14(2.4)	9(1.6)	1(0.2)	1(0.2)	2(0.4)	1(0.2)	-	-	-	-
過敏症	11(1.9)	9(1.6)	1(0.2)	1(0.2)	-	-	-	-	-	-
顔面浮腫	11(1.9)	2(0.3)	1(0.2)	4(0.8)	2(0.4)	2(0.4)	-	-	-	-
悪寒	9(1.6)	7(1.2)	-	-	-	1(0.2)	-	-	-	-
頻脈	8(1.4)	4(0.7)	2(0.4)	1(0.2)	-	-	-	-	-	1(0.3)
注入に伴う反応	6(1.0)	6(1.0)	-	-	-	-	-	-	-	-
喘鳴	5(0.9)	3(0.5)	2(0.4)	-	-	-	-	-	-	-
薬物過敏症	3(0.5)	3(0.5)	-	-	-	-	-	-	-	-
アナフィラキシー反応	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
Infusion reaction										
眼球浮腫	2(0.3)	1(0.2)	-	-	-	-	1(0.2)	-	-	-
顔面腫脹	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-
蕁麻疹	2(0.3)	2(0.3)	-	-	-	-	-	-	-	-
眼部腫脹	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
眼窩周囲浮腫	1(0.2)	-	-	-	-	1(0.2)	-	-	-	-
気管支痙攣	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
口唇腫脹	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
舌腫脹	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
舌浮腫	1(0.2)	-	1(0.2)	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period								
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
糖尿病										
Total Pts with at least one AE	32(5.5)	15(2.6)	4(0.7)	6(1.1)	4(0.8)	3(0.6)	-	-	-	-
高血糖	26(4.5)	12(2.1)	4(0.7)	4(0.8)	3(0.6)	3(0.6)	-	-	-	-
血中ブドウ糖増加	2(0.3)	1(0.2)	-	1(0.2)	-	-	-	-	-	-
糖尿病	2(0.3)	-	-	1(0.2)	1(0.2)	-	-	-	-	-
２型糖尿病	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
尿中ブドウ糖陽性	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period								
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
肝炎										
Total Pts with at least one AE	22(3.8)	13(2.2)	-	2(0.4)	3(0.6)	1(0.2)	2(0.5)	1(0.3)	-	-
アラニンアミノトランスフェラーゼ増加	14(2.4)	9(1.6)	-	1(0.2)	-	1(0.2)	2(0.5)	1(0.3)	-	-
アスパラギン酸アミノトランスフェラーゼ増加	12(2.1)	8(1.4)	-	1(0.2)	-	-	2(0.5)	1(0.3)	-	-
γ－グルタミルトランスフェラーゼ増加	2(0.3)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
肝機能異常	2(0.3)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
血中ビリルビン増加	2(0.3)	1(0.2)	-	1(0.2)	-	-	-	-	-	-
肝臓痛	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
急性肝不全	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
食道静脈瘤	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
食道静脈瘤出血	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
肺臓炎										
Total Pts with at least one AE	4(0.7)	3(0.5)	1(0.2)	-	-	-	-	-	-	-
肺臓炎	4(0.7)	3(0.5)	1(0.2)	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period								
	Any Period No. (%)	0 <- 4w No. (%)	4 <- 8w No. (%)	8 <- 12w No. (%)	12 <- 16w No. (%)	16 <- 20w No. (%)	20 <- 24w No. (%)	24 <- 28w No. (%)	28 <- 32w No. (%)	32 <- 36w No. (%)
胚・胎児毒性										
Total Pts with at least one AE	3(0.5)	1(0.2)	1(0.2)	1(0.2)	-	-	-	-	-	-
成長障害	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-
表皮融解	1(0.2)	-	-	1(0.2)	-	-	-	-	-	-
甲状腺機能低下症										
Total Pts with at least one AE	2(0.3)	1(0.2)	-	-	1(0.2)	-	-	-	-	-
血中甲状腺刺激ホルモン増加	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
甲状腺機能低下症	1(0.2)	1(0.2)	-	-	-	-	-	-	-	-
大腸炎										
Total Pts with at least one AE	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-
大腸炎	2(0.3)	1(0.2)	1(0.2)	-	-	-	-	-	-	-
甲状腺機能亢進症										
Total Pts with at least one AE	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-
血中甲状腺刺激ホルモン増加	1(0.2)	-	-	-	1(0.2)	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
No. of Pts treated in each period	363	350	327	311	303	290	276	254	212	179
ALL AE of Special Interest Medical Concept										
Total Pts with at least one AE	3(0.8)	1(0.3)	1(0.3)	4(1.3)	3(1.0)	1(0.3)	1(0.4)	-	-	-
Infusion reaction										
Total Pts with at least one AE	1(0.3)	1(0.3)	1(0.3)	1(0.3)	3(1.0)	-	-	3(1.2)	-	-
呼吸困難	-	1(0.3)	1(0.3)	-	3(1.0)	-	-	1(0.4)	-	-
発熱	1(0.3)	2(0.6)	-	2(0.6)	-	-	-	1(0.4)	-	-
悪寒	-	-	-	-	-	-	-	-	-	-
低血圧	-	-	-	-	-	-	-	1(0.4)	-	-
頻脈	1(0.3)	-	-	-	-	-	-	-	-	-
過敏症	-	-	-	-	-	-	-	-	-	-
潮紅	-	-	-	-	-	-	-	-	-	-
喘鳴	-	-	-	-	-	-	-	-	-	-
注入に伴う反応	-	-	-	-	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-	-	-	-	-

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Infusion reaction										
眼窩周囲浮腫	-	-	-	-	-	-	-	-	-	-
顔面浮腫	-	-	-	-	-	-	-	1(0.4)	-	-
気管支痙攣	-	-	-	-	-	-	-	-	-	-
薬物過敏症	-	-	-	-	-	-	-	-	-	-
眼球浮腫	-	-	-	-	-	-	-	-	-	-
眼部腫脹	-	-	-	-	-	-	-	-	-	-
眼瞼浮腫	-	-	-	-	-	-	-	1(0.4)	-	-
顔面腫脹	-	-	-	-	-	-	-	-	-	-
血管浮腫	-	-	-	-	-	-	-	-	-	-
発疹										
Total Pts with at least one AE	5(1.4)	4(1.1)	1(0.3)	3(1.0)	1(0.3)	3(1.0)	2(0.7)	-	-	1(0.6)
発疹	2(0.6)	3(0.9)	1(0.3)	3(1.0)	-	-	-	-	-	-
そう痒症	-	2(0.6)	1(0.3)	-	-	-	-	-	1(0.5)	-
皮膚乾燥	1(0.3)	1(0.3)	-	-	-	-	-	-	-	-
寝汗	1(0.3)	-	-	-	-	-	-	-	-	-

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発疹										
紅斑	-	1(0.3)	-	1(0.3)	-	-	-	-	1(0.5)	-
斑状丘疹状皮疹	-	-	-	-	-	1(0.3)	1(0.4)	-	-	1(0.6)
湿疹	1(0.3)	-	-	-	-	-	-	1(0.4)	1(0.5)	-
ざ瘡様皮膚炎	-	-	-	-	-	-	-	-	-	-
多汗症	-	-	-	-	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-	-	-	-	-
そう痒性皮疹	-	-	-	-	-	-	-	-	-	-
乾癬	-	-	-	1(0.3)	-	-	-	-	-	-
全身性そう痒症	-	-	-	-	-	1(0.3)	-	-	-	-
皮膚炎	-	-	-	-	-	-	1(0.4)	-	-	-
皮膚色素過剰	-	-	-	-	-	-	-	-	-	-
紅斑性皮疹	-	-	-	1(0.3)	-	-	-	-	-	-
水疱性皮膚炎	-	-	-	-	-	-	-	1(0.4)	-	-
脱毛症	-	-	-	-	-	-	-	-	-	-
皮膚腫瘤	-	-	-	-	-	1(0.3)	-	-	-	-

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発疹										
多形紅斑	-	-	-	-	-	-	-	-	-	-
爪線状隆起	-	-	-	-	-	1(0.3)	-	-	-	-
点状出血	-	-	-	-	1(0.3)	-	-	-	-	-
皮膚硬結	-	-	1(0.3)	-	-	-	1(0.4)	-	-	-
皮膚潰瘍	-	-	-	-	-	-	-	-	-	-
皮膚剥脱	-	-	-	-	-	-	-	-	-	1(0.6)
皮膚病変	-	-	1(0.3)	-	-	-	-	-	-	-
皮膚疼痛	-	-	-	-	-	-	-	-	-	1(0.6)
褥瘡性潰瘍	1(0.3)	-	-	-	-	-	-	-	-	-
うっ滞性皮膚炎	-	-	-	-	-	-	-	-	-	-
ざ瘡	-	-	-	-	-	-	-	-	-	-
乾皮症	-	-	1(0.3)	-	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-	-	-	-	-
丘疹性皮疹	-	-	-	-	-	-	-	-	-	-
血管浮腫	-	-	-	-	-	-	-	-	-	-

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発疹										
尋常性白斑	-	-	-	-	-	-	-	-	-	-
水疱	-	-	-	-	-	-	-	-	-	-
全身性皮疹	-	-	-	-	-	-	-	-	-	-
爪ジストロフィー	-	-	-	-	-	-	1(0.4)	-	-	-
爪甲離床症	-	-	-	-	-	-	-	-	-	-
爪破損	-	-	-	-	-	-	-	-	-	-
爪肥厚	-	-	-	-	-	-	-	-	-	-
爪変色	-	-	-	-	-	-	1(0.4)	-	-	-
頭部粃糠疹	-	-	-	-	-	-	-	-	-	-
斑	-	-	-	-	-	-	-	-	-	-
皮脂欠乏性湿疹	-	-	-	-	-	-	-	-	-	-
皮膚萎縮	-	-	-	-	-	-	-	-	-	-
皮膚障害	-	-	-	-	-	-	-	-	-	-
皮膚嚢腫	-	-	-	-	-	-	-	-	-	-
皮膚変色	-	-	-	-	-	-	-	-	-	-

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発疹										
薬疹	-	-	-	-	-	-	-	-	-	-
立毛	-	-	-	-	-	-	-	-	-	-
類天疱瘡	-	-	-	1(0.3)	-	-	-	-	-	-
冷汗	-	-	-	-	-	-	-	-	-	-
扁平苔癬	-	-	-	-	-	-	-	-	-	-
痒疹	-	-	-	-	-	-	-	-	-	-
肝炎										
Total Pts with at least one AE	2(0.6)	1(0.3)	1(0.3)	-	-	1(0.3)	-	-	-	-
アスパラギン酸アミノトランスフェラーゼ増加	1(0.3)	-	1(0.3)	-	-	1(0.3)	1(0.4)	-	-	-
アラニンアミノトランスフェラーゼ増加	-	-	-	1(0.3)	-	1(0.3)	1(0.4)	-	-	-
γ－グルタミルトランスフェラーゼ増加	1(0.3)	-	-	-	-	-	1(0.4)	-	-	-
血中ビリルビン増加	1(0.3)	-	-	-	-	-	-	-	-	-
肝機能異常	-	1(0.3)	-	-	-	-	-	-	-	-
腹水	-	-	1(0.3)	-	-	-	-	-	-	-

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肝炎										
トランスアミナーゼ上昇	1(0.3)	-	-	-	-	-	-	-	-	-
肝炎	-	-	-	-	-	-	-	-	-	-
肝酵素上昇	-	-	-	-	-	-	-	-	-	-
肝細胞損傷	-	-	-	-	-	-	-	-	-	-
肝障害	-	-	-	-	-	-	-	-	-	-
肝臓痛	-	-	-	-	-	-	-	-	-	-
肝病変	-	-	-	-	-	-	-	-	-	-
急性肝炎	-	-	-	-	-	-	-	-	-	-
高ビリルビン血症	-	-	-	-	-	-	-	-	-	-
脂肪肝	-	-	-	-	-	-	-	-	-	-
薬物性肝障害	-	-	-	-	-	-	-	-	-	-

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甲状腺機能低下症										
Total Pts with at least one AE	1(0.3)	1(0.3)	1(0.3)	-	-	2(0.7)	1(0.4)	1(0.4)	-	-
甲状腺機能低下症	-	-	1(0.3)	-	-	2(0.7)	1(0.4)	-	-	-
血中甲状腺刺激ホルモン増加	1(0.3)	1(0.3)	-	-	-	-	-	1(0.4)	-	-
血中甲状腺刺激ホルモン減少	-	-	-	-	-	-	-	-	-	-
甲状腺炎	-	-	-	-	-	-	-	-	-	-
甲状腺機能検査異常	-	-	-	-	-	-	-	-	-	-
糖尿病										
Total Pts with at least one AE	-	1(0.3)	-	-	-	-	-	-	-	-
高血糖	-	1(0.3)	-	-	-	-	-	-	-	-
１型糖尿病	-	-	-	-	-	-	-	-	-	-
２型糖尿病	-	-	-	-	-	-	-	-	-	-
耐糖能障害	-	-	-	-	-	-	-	-	-	-

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甲状腺機能亢進症										
Total Pts with at least one AE	2(0.6)	-	-	1(0.3)	-	-	-	1(0.4)	-	-
甲状腺機能亢進症	-	-	-	1(0.3)	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	1(0.3)	1(0.3)	-	-	-	-	-	1(0.4)	-	-
眼球突出症	-	-	-	-	-	-	-	-	-	-
血中甲状腺刺激ホルモン減少	-	-	-	-	-	-	-	-	-	-
甲状腺炎	-	-	-	-	-	-	-	-	-	-
甲状腺機能検査異常	-	-	-	-	-	-	-	-	-	-
内分泌性眼症	1(0.3)	-	-	-	-	-	-	-	-	-

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肺臓炎										
Total Pts with at least one AE	-	-	-	1(0.3)	-	-	-	-	-	1(0.6)
肺臓炎	-	-	-	1(0.3)	-	-	-	-	-	1(0.6)
間質性肺疾患	-	-	-	-	-	-	-	-	-	-
肺浸潤	-	-	-	-	-	-	-	-	-	-
放射線性肺臓炎	-	-	-	-	-	-	-	-	-	-
細気管支炎	-	-	-	-	-	-	-	-	-	-
髄膜脳炎										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
髄膜炎	-	-	-	-	-	-	-	-	-	-
脳炎	-	-	-	-	-	-	-	-	-	-
羞明	-	-	-	-	-	-	-	-	-	-

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ギラン・バレー症候群										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
ギラン・バレー症候群	-	-	-	-	-	-	-	-	-	-
脱髄性多発ニューロパチー	-	-	-	-	-	-	-	-	-	-
副腎機能不全										
Total Pts with at least one AE	-	-	-	-	-	1(0.3)	-	-	-	-
副腎機能不全	-	-	-	-	-	1(0.3)	-	-	-	-
原発性副腎機能不全	-	-	-	-	-	-	-	-	-	-
大腸炎										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
大腸炎	-	-	-	-	-	-	-	-	-	-
胚・胎児毒性										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
成長障害	-	-	-	-	-	-	-	-	-	-
乳腺炎	-	-	-	-	-	-	-	-	-	-

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ぶどう膜炎										
Total Pts with at least one AE	-	-	-	1(0.3)	-	-	-	-	-	-
ぶどう膜炎	-	-	-	1(0.3)	-	-	-	-	-	-
腎炎										
Total Pts with at least one AE	-	-	-	-	-	1(0.3)	-	-	-	-
ヘノッホ・シェーンライン紫斑病性腎炎	-	-	-	-	-	1(0.3)	-	-	-	-
膵炎										
Total Pts with at least one AE	-	-	-	1(0.3)	-	-	-	-	-	-
膵炎	-	-	-	1(0.3)	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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事象名 : MedDRA ver. 19.0
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
No. of Pts treated in each period	308	284	266	250	227	211	197	178	150	121
ALL AE of Special Interest Medical Concept										
Total Pts with at least one AE	1(0.3)	-	-	-	-	-	-	-	-	-
発疹										
Total Pts with at least one AE	1(0.3)	1(0.4)	-	-	-	-	-	-	-	-
脱毛症	-	-	-	-	-	-	-	-	-	-
発疹	-	1(0.4)	-	-	-	-	-	-	-	-
皮膚乾燥	-	1(0.4)	-	-	-	1(0.5)	-	-	-	-
爪の障害	1(0.3)	-	-	-	-	-	-	-	-	-
爪変色	-	-	-	-	-	-	-	-	-	-
そう痒症	-	-	-	-	-	-	-	-	-	-
爪甲脱落症	1(0.3)	1(0.4)	-	-	-	-	-	-	-	-
紅斑	-	-	-	-	-	-	-	-	-	-
手掌・足底発赤知覚不全症候群	-	-	-	-	-	-	-	-	-	-
爪毒性	-	-	-	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period									
	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
発疹										
斑状丘疹状皮疹	-	-	-	-	-	-	-	-	-	-
ざ瘡様皮膚炎	-	-	-	-	-	-	-	-	-	-
寝汗	-	-	-	-	-	-	-	-	-	-
皮膚色素過剰	-	-	-	-	-	-	-	-	-	-
皮膚剥脱	-	-	-	-	-	-	-	-	-	-
湿疹	-	-	-	-	-	-	-	-	-	-
多汗症	-	-	-	-	-	-	-	-	-	-
爪甲離床症	-	-	-	-	-	-	-	-	-	-
爪線状隆起	-	-	-	-	-	-	-	-	-	-
皮膚炎	-	-	-	-	-	-	-	-	-	-
そう痒性皮疹	-	-	-	-	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-	-	-	-	-
接触性皮膚炎	-	-	-	-	-	-	-	-	-	-
爪ジストロフィー	-	-	-	-	-	-	-	-	-	-
爪痛	-	-	-	-	-	-	-	-	-	-

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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
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Docetaxel (Actual) ; N = 578

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発疹										
皮膚毒性	-	-	-	-	-	-	-	-	-	-
皮膚反応	-	-	-	-	-	-	-	-	-	-
嵌入爪	-	-	-	-	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-	-	-	-	-
ざ瘡	-	-	-	-	-	-	-	-	-	-
アトピー性皮膚炎	-	-	-	-	-	-	-	-	-	-
過角化	-	-	-	-	-	-	-	-	-	-
乾癬	-	-	-	-	-	-	-	-	-	-
光線角化症	-	-	-	-	-	-	-	-	-	-
紅色症	-	-	-	-	-	-	-	-	-	-
紅斑性皮疹	-	-	-	-	-	-	-	-	-	-
黒皮症	-	-	-	-	-	-	-	-	-	-
脂漏性皮膚炎	-	-	-	-	-	-	-	-	-	-
手掌紅斑	-	-	-	-	-	-	-	-	-	-
色素沈着障害	-	-	-	-	-	-	-	-	-	-

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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

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発疹										
全身性皮疹	-	-	-	-	-	-	-	-	-	-
爪床出血	-	-	-	-	-	-	-	-	-	-
爪破損	-	-	-	-	-	-	-	-	-	-
点状出血	-	-	-	-	-	-	-	-	-	-
皮膚亀裂	-	-	-	-	-	-	-	-	-	-
皮膚刺激	-	-	-	-	-	-	-	-	-	-
皮膚腫瘤	-	-	-	-	-	-	-	-	-	-
皮膚色素減少	-	-	-	-	-	-	-	-	-	-
皮膚軟化	-	-	-	-	-	-	-	-	-	-
皮膚粘膜発疹	-	-	-	-	-	-	-	-	-	-
皮膚嚢腫	-	-	-	-	-	-	-	-	-	-
皮膚病変	-	-	-	-	-	-	-	-	-	-
皮膚疼痛	-	-	-	-	-	-	-	-	-	-
睫毛眉毛脱落症	-	-	-	-	-	-	-	-	-	-

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Adverse Events by Time Period (First Onset) (GO28915:OAK)
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Docetaxel (Actual) ; N = 578

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	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
発疹										
褥瘡性潰瘍	-	-	-	-	-	-	-	-	-	-
Infusion reaction										
Total Pts with at least one AE	-	-	1(0.4)	-	-	-	-	-	-	-
呼吸困難	-	-	1(0.4)	-	-	1(0.5)	-	-	-	-
発熱	-	-	-	-	-	-	-	1(0.6)	-	-
低血圧	-	-	-	-	-	-	-	-	-	-
潮紅	-	-	-	-	-	-	-	-	-	-
過敏症	-	-	-	-	-	-	-	-	-	-
顔面浮腫	-	-	-	-	-	-	-	-	-	-
悪寒	-	-	-	-	-	-	-	-	-	-
頻脈	-	-	-	-	-	-	-	-	-	-
注入に伴う反応	-	-	-	-	-	-	-	-	-	-
喘鳴	-	-	-	-	-	-	-	-	-	-
薬物過敏症	-	-	-	-	-	-	-	-	-	-
アナフィラキシー反応	-	-	-	-	-	-	-	-	-	-

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Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
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Infusion reaction										
眼球浮腫	-	-	-	-	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-	-	-	-	-
眼部腫脹	-	-	-	-	-	-	-	-	-	-
眼窩周囲浮腫	-	-	-	-	-	-	-	-	-	-
気管支痙攣	-	-	-	-	-	-	-	-	-	-
口唇腫脹	-	-	-	-	-	-	-	-	-	-
舌腫脹	-	-	-	-	-	-	-	-	-	-
舌浮腫	-	-	-	-	-	-	-	-	-	-

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	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
糖尿病										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
高血糖	-	-	-	-	-	-	-	-	-	-
血中ブドウ糖増加	-	-	-	-	-	-	-	-	-	-
糖尿病	-	-	-	-	-	-	-	-	-	-
２型糖尿病	-	-	-	-	-	-	-	-	-	-
尿中ブドウ糖陽性	-	-	-	-	-	-	-	-	-	-

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Adverse Events by Time Period (First Onset) (GO28915:OAK)
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Docetaxel (Actual) ; N = 578

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	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
肝炎										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
アラニンアミノトランスフェラーゼ増加	-	-	-	-	-	-	-	-	-	-
アスパラギン酸アミノトランスフェラーゼ増加	-	-	-	-	-	-	-	-	-	-
γ－グルタミルトランスフェラーゼ増加	-	-	-	-	-	-	-	-	-	-
肝機能異常	-	-	-	-	-	-	-	-	-	-
血中ビリルビン増加	-	-	-	-	-	-	-	-	-	-
肝臓痛	-	-	-	-	-	-	-	-	-	-
急性肝不全	-	-	-	-	-	-	-	-	-	-
食道静脈瘤	-	-	-	-	-	-	-	-	-	-
食道静脈瘤出血	-	-	-	-	-	-	-	-	-	-
肺臓炎										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
肺臓炎	-	-	-	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

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	36 <- 40w No. (%)	40 <- 44w No. (%)	44 <- 48w No. (%)	48 <- 52w No. (%)	52 <- 56w No. (%)	56 <- 60w No. (%)	60 <- 64w No. (%)	64 <- 68w No. (%)	68 <- 72w No. (%)	72 <- 76w No. (%)
胚・胎児毒性										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
成長障害	-	-	-	-	-	-	-	-	-	-
表皮融解	-	-	-	-	-	-	-	-	-	-
甲状腺機能低下症										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	-	-	-	-	-	-	-	-	-	-
甲状腺機能低下症	-	-	-	-	-	-	-	-	-	-
大腸炎										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
大腸炎	-	-	-	-	-	-	-	-	-	-
甲状腺機能亢進症										
Total Pts with at least one AE	-	-	-	-	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	-	-	-	-	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period 76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
No. of Pts treated in each period	166	157	133	102	72	50
ALL AE of Special Interest Medical Concept						
Total Pts with at least one AE	-	-	-	1(1.0)	-	-
Infusion reaction						
Total Pts with at least one AE	1(0.6)	1(0.6)	-	-	-	1(2.0)
呼吸困難	-	1(0.6)	1(0.8)	-	-	-
発熱	1(0.6)	1(0.6)	-	-	-	1(2.0)
悪寒	1(0.6)	-	-	-	-	-
低血圧	-	-	-	-	-	-
頻脈	1(0.6)	-	-	-	-	-
過敏症	-	-	-	-	-	-
潮紅	-	-	-	-	-	-
喘鳴	-	-	-	-	-	-
注入に伴う反応	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
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Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
Infusion reaction						
眼窩周囲浮腫	-	-	-	-	-	-
顔面浮腫	-	-	-	-	-	-
気管支痙攣	-	-	-	-	-	-
薬物過敏症	-	-	-	-	-	-
眼球浮腫	-	-	-	-	-	-
眼部腫脹	-	-	-	-	-	-
眼瞼浮腫	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-
血管浮腫	-	-	-	-	-	-
発疹						
Total Pts with at least one AE	-	-	-	-	-	-
発疹	-	-	-	-	-	-
そう痒症	-	-	-	-	-	-
皮膚乾燥	-	-	-	-	-	-
寝汗	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
紅斑	-	-	-	-	-	-
斑状丘疹状皮疹	-	-	-	-	-	-
湿疹	-	-	-	-	-	-
ざ瘡様皮膚炎	-	-	-	-	-	-
多汗症	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-
そう痒性皮疹	-	-	-	-	-	-
乾癬	-	-	-	-	-	-
全身性そう痒症	-	-	-	-	-	-
皮膚炎	-	-	-	-	-	-
皮膚色素過剰	-	-	-	-	-	-
紅斑性皮疹	-	-	-	-	-	-
水疱性皮膚炎	-	-	-	-	-	-
脱毛症	-	-	-	-	-	-
皮膚腫瘤	-	-	-	-	-	-

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Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period 76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
多形紅斑	-	-	-	-	-	-
爪線状隆起	-	-	-	-	-	-
点状出血	-	-	-	-	-	-
皮膚硬結	-	-	-	-	-	-
皮膚潰瘍	-	-	-	-	-	-
皮膚剥脱	-	-	-	-	-	-
皮膚病変	-	-	-	-	-	-
皮膚疼痛	-	-	-	1(1.0)	-	-
褥瘡性潰瘍	-	-	-	-	-	-
うっ滞性皮膚炎	-	-	-	-	-	-
ざ瘡	-	-	-	-	-	-
乾皮症	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-
丘疹性皮疹	-	-	-	-	-	-
血管浮腫	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period 76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
尋常性白斑	-	-	-	-	-	-
水疱	-	-	-	-	-	-
全身性皮疹	-	-	-	-	-	-
爪ジストロフィー	-	-	-	-	-	-
爪甲離床症	-	-	-	-	-	-
爪破損	-	-	-	-	-	-
爪肥厚	-	-	-	-	-	-
爪変色	-	-	-	-	-	-
頭部粃糠疹	-	-	-	-	-	-
斑	-	-	-	-	-	-
皮脂欠乏性湿疹	-	-	-	-	-	-
皮膚萎縮	-	-	-	-	-	-
皮膚障害	-	-	-	-	-	-
皮膚嚢腫	-	-	-	-	-	1(2.0)
皮膚変色	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
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	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
薬疹	-	-	-	-	-	-
立毛	-	-	-	-	-	-
類天疱瘡	-	-	-	-	-	-
冷汗	1(0.6)	-	-	-	-	-
扁平苔癬	-	-	-	-	-	-
痒疹	-	-	-	-	-	-
肝炎						
Total Pts with at least one AE	-	-	-	1(1.0)	-	-
アスパラギン酸アミノトランスフェラーゼ増加	-	-	-	1(1.0)	-	-
アラニンアミノトランスフェラーゼ増加	-	-	-	1(1.0)	-	-
γ－グルタミルトランスフェラーゼ増加	-	-	-	-	-	-
血中ビリルビン増加	-	-	-	-	-	-
肝機能異常	-	-	-	-	-	-
腹水	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aepn_aesi.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aepn_aesi_GO28915_SE.out
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
肝炎						
トランスアミナーゼ上昇	-	-	-	-	-	-
肝炎	-	-	-	-	-	-
肝酵素上昇	-	-	-	-	-	-
肝細胞損傷	-	-	-	-	-	-
肝障害	-	-	-	-	-	-
肝臓痛	-	-	-	-	-	-
肝病変	-	-	-	-	-	-
急性肝炎	-	-	-	-	-	-
高ビリルビン血症	-	-	-	-	-	-
脂肪肝	-	-	-	-	-	-
薬物性肝障害	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
甲状腺機能低下症						
Total Pts with at least one AE	-	-	-	-	-	-
甲状腺機能低下症	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	-	-	-	-	-	-
血中甲状腺刺激ホルモン減少	-	-	-	-	-	-
甲状腺炎	-	-	-	-	-	-
甲状腺機能検査異常	-	-	-	-	-	-
糖尿病						
Total Pts with at least one AE	-	-	-	-	-	-
高血糖	-	-	-	-	-	-
１型糖尿病	-	-	-	-	-	-
２型糖尿病	-	-	-	-	-	-
耐糖能障害	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aepn_aesi.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aepn_aesi_GO28915_SE.out
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Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
甲状腺機能亢進症						
Total Pts with at least one AE	-	-	-	-	-	-
甲状腺機能亢進症	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	-	-	-	-	-	-
眼球突出症	-	-	-	-	-	-
血中甲状腺刺激ホルモン減少	-	-	-	-	-	-
甲状腺炎	-	-	-	-	-	-
甲状腺機能検査異常	-	-	-	-	-	-
内分泌性眼症	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
肺臓炎						
Total Pts with at least one AE	-	-	-	-	-	-
肺臓炎	-	-	-	-	-	-
間質性肺疾患	-	-	-	-	-	-
肺浸潤	-	-	-	-	-	-
放射線性肺臓炎	-	-	-	-	-	-
細気管支炎	-	-	-	-	-	-
髄膜脳炎						
Total Pts with at least one AE	-	-	-	-	-	-
髄膜炎	-	-	-	-	-	-
脳炎	-	-	-	-	-	-
羞明	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
ギラン・バレー症候群						
Total Pts with at least one AE	-	-	-	-	-	-
ギラン・バレー症候群	-	-	-	-	-	-
脱髄性多発ニューロパチー	-	-	-	-	-	-
副腎機能不全						
Total Pts with at least one AE	-	-	-	-	-	-
副腎機能不全	-	-	-	-	-	-
原発性副腎機能不全	-	-	-	-	-	-
大腸炎						
Total Pts with at least one AE	-	-	-	-	-	-
大腸炎	-	-	-	-	-	-
胚・胎児毒性						
Total Pts with at least one AE	-	-	-	-	-	-
成長障害	-	-	-	-	-	-
乳腺炎	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Atezolizumab (Actual) : N = 609

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
ぶどう膜炎						
Total Pts with at least one AE	-	-	-	-	-	-
ぶどう膜炎	-	-	-	-	-	-
腎炎						
Total Pts with at least one AE	-	-	-	-	-	-
ヘノッホ・シェーンライン紫斑病性腎炎	-	-	-	-	-	-
膵炎						
Total Pts with at least one AE	-	-	-	-	-	-
膵炎	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period 76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
No. of Pts treated in each period	105	98	86	63	48	35
ALL AE of Special Interest Medical Concept						
Total Pts with at least one AE	-	-	-	-	-	-
発疹						
Total Pts with at least one AE	-	-	-	-	-	-
脱毛症	-	-	-	-	-	-
発疹	-	-	-	-	-	-
皮膚乾燥	-	-	-	-	-	-
爪の障害	-	-	-	-	-	-
爪変色	-	-	-	-	-	-
そう痒症	-	-	-	-	-	-
爪甲脱落症	-	-	-	-	-	-
紅斑	-	-	-	-	-	-
手掌・足底発赤知覚不全症候群	-	-	-	-	-	-
爪毒性	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
斑状丘疹状皮疹	-	-	-	-	-	-
ざ瘡様皮膚炎	-	-	-	-	-	-
寝汗	-	-	-	-	-	-
皮膚色素過剰	-	-	-	-	-	-
皮膚剥脱	-	-	-	-	-	-
湿疹	-	-	-	-	-	-
多汗症	-	-	-	-	-	-
爪甲離床症	-	-	-	-	-	-
爪線状隆起	-	-	-	-	-	-
皮膚炎	-	-	-	-	-	-
そう痒性皮疹	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-
接触性皮膚炎	-	-	-	-	-	-
爪ジストロフィー	-	-	-	-	-	-
爪痛	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
皮膚毒性	-	-	-	-	-	-
皮膚反応	-	-	-	-	-	-
嵌入爪	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-
ざ瘡	-	-	-	-	-	-
アトピー性皮膚炎	-	-	-	-	-	-
過角化	-	-	-	-	-	-
乾癬	-	-	-	-	-	-
光線角化症	-	-	-	-	-	-
紅色症	-	-	-	-	-	-
紅斑性皮疹	-	-	-	-	-	-
黒皮症	-	-	-	-	-	-
脂漏性皮膚炎	-	-	-	-	-	-
手掌紅斑	-	-	-	-	-	-
色素沈着障害	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
全身性皮疹	-	-	-	-	-	-
爪床出血	-	-	-	-	-	-
爪破損	-	-	-	-	-	-
点状出血	-	-	-	-	-	-
皮膚亀裂	-	-	-	-	-	-
皮膚刺激	-	-	-	-	-	-
皮膚腫瘤	-	-	-	-	-	-
皮膚色素減少	-	-	-	-	-	-
皮膚軟化	-	-	-	-	-	-
皮膚粘膜発疹	-	-	-	-	-	-
皮膚嚢腫	-	-	-	-	-	-
皮膚病変	-	-	-	-	-	-
皮膚疼痛	-	-	-	-	-	-
睫毛眉毛脱落症	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
発疹						
褥瘡性潰瘍	-	-	-	-	-	-
Infusion reaction						
Total Pts with at least one AE	-	-	-	-	-	-
呼吸困難	-	-	-	-	-	-
発熱	-	-	-	-	-	-
低血圧	-	-	-	-	-	-
潮紅	-	-	-	-	-	-
過敏症	-	-	-	-	-	-
顔面浮腫	-	-	-	-	-	-
悪寒	-	-	-	-	-	-
頻脈	-	-	-	-	-	-
注入に伴う反応	-	-	-	-	-	-
喘鳴	-	-	-	-	-	-
薬物過敏症	-	-	-	-	-	-
アナフィラキシー反応	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
Infusion reaction						
眼球浮腫	-	-	-	-	-	-
顔面腫脹	-	-	-	-	-	-
蕁麻疹	-	-	-	-	-	-
眼部腫脹	-	-	-	-	-	-
眼窩周囲浮腫	-	-	-	-	-	-
気管支痙攣	-	-	-	-	-	-
口唇腫脹	-	-	-	-	-	-
舌腫脹	-	-	-	-	-	-
舌浮腫	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
糖尿病						
Total Pts with at least one AE	-	-	-	-	-	-
高血糖	-	-	-	-	-	-
血中ブドウ糖増加	-	-	-	-	-	-
糖尿病	-	-	-	-	-	-
２型糖尿病	-	-	-	-	-	-
尿中ブドウ糖陽性	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名 : MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period					
	76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
肝炎						
Total Pts with at least one AE	-	-	-	-	-	-
アラニンアミノトランスフェラーゼ増加	-	-	-	-	-	-
アスパラギン酸アミノトランスフェラーゼ増加	-	-	-	-	-	-
γ－グルタミルトランスフェラーゼ増加	-	-	-	-	-	-
肝機能異常	-	-	-	-	-	-
血中ビリルビン増加	-	-	-	-	-	-
肝臓痛	-	-	-	-	-	-
急性肝不全	-	-	-	-	-	-
食道静脈瘤	-	-	-	-	-	-
食道静脈瘤出血	-	-	-	-	-	-
肺臓炎						
Total Pts with at least one AE	-	-	-	-	-	-
肺臓炎	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Adverse Events by Time Period (First Onset) (GO28915:OAK)
Protocol: GO28915
Population: All Safety Evaluable Patients

Docetaxel (Actual) ; N = 578

AE of Special Interest Medical Concept/ MedDRA Preferred Term	Period 76 <- 80w No. (%)	80 <- 84w No. (%)	84 <- 88w No. (%)	88 <- 92w No. (%)	92 <- 96w No. (%)	96w <- No. (%)
胚・胎児毒性						
Total Pts with at least one AE	-	-	-	-	-	-
成長障害	-	-	-	-	-	-
表皮融解	-	-	-	-	-	-
甲状腺機能低下症						
Total Pts with at least one AE	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	-	-	-	-	-	-
甲状腺機能低下症	-	-	-	-	-	-
大腸炎						
Total Pts with at least one AE	-	-	-	-	-	-
大腸炎	-	-	-	-	-	-
甲状腺機能亢進症						
Total Pts with at least one AE	-	-	-	-	-	-
血中甲状腺刺激ホルモン増加	-	-	-	-	-	-

Multiple occurrences of the same AE in one individual counted only once in new onset period.
AEs collected after first treatment dose are included.
事象名：MedDRA ver. 19.0
Data Cut-off: 7 Jul 2016; RAVE Data Extracted: 19 Aug 2016.

Program: /opt/BIOSTAT/prod/cdt7692j/j28915a/aepn_aesi.sas / Output: /opt/BIOSTAT/prod/cdt7692j/j28915a/reports/aepn_aesi_GO28915_SE.out
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［5.3.5.1-3 aepn_aesi_GO28915_SE を再掲］

2.7.4.7.8 死亡した被験者の一覧

(1) 死亡した被験者の一覧（OAK 試験）
5.3.5.1-1 l_ael04_SE に示した。

(2) 死亡した被験者の一覧（POPLAR 試験）
5.3.5.1-2 l_ael04_SE_dc8May2015に示した。

(3) 死亡した被験者の一覧（BIRCH 試験）
5.3.5.2-1 l_dd_SE に示した。

(4) 死亡した被験者の一覧（FIR 試験）
5.3.5.2-2 l_dd_SE に示した。

(5) 死亡した被験者の一覧（PCD4989g 試験，非小細胞肺癌コホート）
5.3.3.2-1 l_dd_NSCLC_SE に示した。

(6) 死亡した被験者の一覧（JO28944試験）
治験期間中の死亡は認められなかった。

2.7.4.7.9 重篤な有害事象を発現した被験者の一覧

(1) 重篤な有害事象を発現した被験者の一覧（OAK 試験）
5.3.5.1-1 l_ael03_SE に示した。

(2) 重篤な有害事象を発現した被験者の一覧（POPLAR 試験）
5.3.5.1-2 l_ael03_SE_dc8May2015に示した。

(3) 重篤な有害事象を発現した被験者の一覧（BIRCH 試験）
5.3.5.3-1 l_sae_GO28754_SE に示した。

(4) 重篤な有害事象を発現した被験者の一覧（FIR 試験）
5.3.5.3-1 l_sae_GO28625_SE に示した。

(5) 重篤な有害事象を発現した被験者の一覧（PCD4989g 試験，非小細胞肺癌コホート）
5.3.3.2-1 l_ae_ser_NSCLC_SER_SE に示した。

(6) 重篤な有害事象を発現した被験者の一覧（試験）
5.3.3.2-2 Listing16.2-19に示した。