2.7.4 臨床的安全性

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略号一覧

略号	省略していない表現 (英)	省略していない表現 (日)
aGVHD	acute graft versus host disease	急性移植片対宿主病
ALL	acute lymphoblastic leukemia	急性リンパ性白血病
ALP	alkaline phosphatase	アルカリホスファターゼ
ALT	alanine aminotransferase	アラニンアミノトランスフェラーゼ
AML	acute myeloid leukemia	急性骨髄性白血病
ANC	absolute neutrophils count	好中球絶対数
AST	aspartate aminotransferase	アスパラギン酸アミノトランスフェラーゼ
ATG	anti-thymocyte globulin	抗胸腺細胞グロブリン
AUC	area under the concentration-time curve	濃度－時間曲線下面積
BAT	Best Available Therapy	現状で利用可能な最良の治療
BID	bis in diem/twice a day	1 日 2 回
BMI	body mass index	体格指数
BOR	best overall response	最良総合効果
BSA	body surface area	体表面積
CAS	crossover analysis set	クロスオーバー解析対象集団
CCDS	company core data sheet	企業中核データシート
cGVHD	chronic graft versus host disease	慢性移植片対宿主病
CI	confidence interval	信頼区間
CIBMTR	Center for International Blood and Marrow Transplant Research	−
CMH	Cochran-Mantel-Haenszel	コクラン-マンテル-ヘンツェル
CML	chronic myelogenous leukemia	慢性骨髄性白血病
CMV	cytomegalovirus	サイトメガロウイルス
CNI	calcineurin inhibitor	カルシニューリン阻害薬
COVID-19	coronavirus disease 2019	新型コロナウイルス感染症
CR	complete response	完全奏効
CRF	case report form	症例報告書
CSR	clinical study report	治験総括報告書
CTCAE	Common Terminology Criteria for Adverse Events	有害事象共通用語規準
CYP	cytochrome P450	チトクローム P450
DMC	data monitoring committee	データモニタリング委員会
DOR	duration of response	奏効期間
DORR	durable overall response rate	−
EAIR	exposure-adjusted incidence rate	曝露期間で調整した発現率
ECOG	Eastern Cooperative Oncology Group	−
ECP	extracorporeal photopheresis	体外循環式光化学療法
EFS	event-free survival	無イベント生存期間
EMA	European Medicines Agency	欧州医薬品庁
EOT	end of treatment	投与終了時
EQ-5D-5L	EuroQOL 5-dimension 5-level	−

略号	省略していない表現 (英)	省略していない表現 (日)
EU	European Union	欧州連合
FACT-BMT	functional assessment of cancer therapy - bone marrow transplantation	−
FAS	full analysis set	最大の解析対象集団
FDA	Food and Drug Administration	米国食品医薬品局
FEV_1%	forced expiratory volume in one second	1 秒率
FFS	failure-free survival	治療成功生存期間
GCP	good clinical practice	医薬品の臨床試験の実施の基準
GFR	glomerular filtration rate	糸球体濾過量
GGT	gamma glutamyltransferase	γ-グルタミルトランスフェラーゼ
GVHD	graft versus host disease	移植片対宿主病
GVT	graft versus tumor	移植片対腫瘍
HCT-CI	hematopoietic cell transplantation comorbidity index	造血細胞移植特異的合併症指数
HLA	human leukocyte antigen	ヒト白血球抗原
HSCT	hematopoietic stem cell transplantation	造血幹細胞移植
ICF	informed consent form	同意説明文書及び同意書
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for human use	医薬品規制調和国際会議
IFN	interferon	インターフェロン
IL	interleukin	インターロイキン
IRT	interactive response technology	双方向自動応答技術
ITT	intention-to-treat	−
JAK	Janus kinase	−
LFT	liver function tests	肝機能検査
LLN	lower limit of normal	基準値下限
LSS	Lee symptom scale	Lee 症状スケール
MAGIC	The Mount Sinai Acute GVHD International Consortium	−
MDS	myelodysplastic syndrome	骨髄異形成症候群
MedDRA	Medical Dictionary for Regulatory Activities	ICH 国際医薬用語集
MF	myelofibrosis	骨髄線維症
mLSS	modified Lee symptom scale	修正版 LEE 症状スケール
MMF	mycophenolate mofetil	ミコフェノール酸モフェチル
MR	malignancy relapse/progression	悪性腫瘍の再発又は進行
MSC	mesenchymal stromal cells	間葉系間質細胞
mTOR	mammalian target of rapamycin	哺乳類のラパマイシン標的蛋白質
MTX	methotrexate	メトトレキサート
NA	not applicable	該当なし
NCI	National Cancer Institute	米国国立がん研究所
NE	not evaluable	−
NIH	National Institute of Health	米国国立衛生研究所
NMSC	non-melanoma skin cancer	非黒色腫皮膚癌

略号	省略していない表現 (英)	省略していない表現 (日)
NRM	non-relapse mortality	非再発死亡期間
ORR	overall response rate	奏効率
OS	overall survival	全生存期間
PAS	pharmacokinetic analysis set	薬物動態解析対象集団
PK	pharmacokinetics	薬物動態
PMDA	Pharmaceuticals and Medical Devices Agency	独立行政法人 医薬品医療機器総合機構
PPS	per-protocol set	治験実施計画書に適合した対象集団
PR	partial response	部分奏効
PSUR	periodic safety update report	定期的安全性最新報告
PT	preferred term	基本語
PV	polycythemia vera	真性多血症
QD	quaque die, once a day	1 日 1 回
QoL	quality of life	生活の質
RDI	relative dose intensity	相対的用量強度
RMP	risk management plan	医薬品リスク管理計画
RR	response rate	奏効が得られた被験者の割合
RUX	ruxolitinib	ルキソリチニブ
SAF	safety analysis population	安全性解析対象集団
SD	standard deviation	標準偏差
SOC	system organ class	器官別大分類
SR-aGVHD	steroid-refractory acute graft versus host disease	ステロイド抵抗性急性移植片対宿主病
TBL	total bilirubin	総ビリルビン
Teff	effector T cell	エフェクターT 細胞
TNF-α	tumor necrosis factor alpha	腫瘍壊死因子 α
TSS	total symptom score	合計症状スコア
ULN	upper limit of normal	基準値上限
VAS	visual analogue scale	ビジュアルアナログスケール
VGPR	very good partial response	最良部分奏効

用語の定義一覧

用語	定義
試験名	各試験名は，本書では以下のとおり表記した。 • CINC424C2301 試験 → C2301 試験 • CINC424D2301 試験 → D2301 試験 • INCB 18424-271 試験 → 271 試験

1 医薬品への曝露

1.1 総括的安全性評価計画及び安全性試験の記述

1.1.1 安全性に関する臨床試験及び情報源の概観

移植片対宿主病（GVHD）は，同種造血幹細胞移植において多く認められる，最も重要な合併症であり，病理組織学的所見又は臨床徴候により急性 GVHD と慢性 GVHD の 2 種類に分けられる。本書では，GVHD 患者に対するルキソリチニブリン酸塩（RUX）の安全性を，急性 GVHD と慢性 GVHD に分けて評価した。

急性 GVHD に対する安全性評価では，12 歳以上のステロイド抵抗性急性 GVHD 患者を対象とした C2301 試験を評価資料とした。C2301 試験は，治験担当医師が選択した Best Available Therapy（現状で利用可能な最良の治療，BAT）を対照とする国際共同試験であり，日本も参加した。本承認申請時点で進行中である。C2301 試験は，全被験者が Day 56 の評価を終了又はそれ以前に中止した時点で 1 回目のデータカットオフ 1（2019 年 7 月 25 日）を行い，主要評価項目及び主要な副次評価項目を含む主要解析を実施した。また，全被験者が約 6 ヵ月間の治験治療を終了又はそれ以前に中止した時点で 2 回目のデータカットオフ 2（2020 年 1 月 6 日）を行い，その他の副次評価項目を含む解析を実施した。本書では，2 回目の解析結果を安全性評価に用いた。また，参考資料として，C2301 試験とは開始用量が異なるものの，12 歳以上のステロイド抵抗性急性 GVHD 患者を対象とした単群試験である外国第 II 相試験（271 試験）の最終解析の結果も参照した。

慢性 GVHD の安全性評価では，12 歳以上のステロイド抵抗性慢性 GVHD 患者を対象とした D2301 試験を評価資料とした。D2301 試験は BAT を対照とする国際共同試験であり，日本も参加した。本承認申請時点で進行中である。全被験者が第 7 サイクル Day 1（C7D1，1 サイクルは 28 日間）の評価を終了又はそれ以前に中止した時点でデータカットオフ（2020 年 5 月 8 日）を行い，その解析結果を安全性評価に用いた。

日本人患者に対する安全性は，C2301 試験及び D2301 試験の日本人部分集団の結果に基づき評価した。

安全性評価に使用した臨床試験の一覧を Table 1-1 に示す。

Table 1-1 安全性評価に使用した臨床試験の一覧

評価/参考	試験番号/対象	実施地域	デザイン	治験薬/投与量/投与経路	安全性解析対象[日本人]（名）	曝露期間の中央値（最小値～最大値）[a]
評価	C2301/ステロイド抵抗性急性 GVHD	国際共同	第 III 相，多施設共同，ランダム化，非盲検，並行群間比較，BAT 対照	RUX/10 mg BID/経口 BAT/治験担当医師判断	RUX 群 152 [9] BAT 群 150 [21] 合計 302 [30]	RUX 群 63.0（6.0～463.0）日 BAT 群 29.0（1.0～188.0）日
評価	D2301/	国際共同	第 III 相，多施設共	RUX/10 mg BID/経口	RUX 群 165 [22]	RUX 群

評価/参考	試験番号/対象	実施地域	デザイン	治験薬/投与量/投与経路	安全性解析対象[日本人]（名）	曝露期間の中央値（最小値～最大値）[a]
	ステロイド抵抗性慢性 GVHD		同，ランダム化，非盲検，並行群間比較，BAT 対照	BAT/治験担当医師判断	BAT 群 158 [15] 合計 323 [37]	41.3（0.7～127.3）週 BAT 群 24.1（0.6～108.4）週
参考	271	外国	第 II 相，多施設共同，単群，非盲検	RUX/5 mg BID (Day 1～3) 10 mg BID (Day 4～) [b]/経口	71 [0]	46.0（4-811）日

Source: 5.2，5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.1，5.3.5.1-2-D2301 試験-Table 14.3-1.1，5.3.5.2-1-271 試験-Table 3.1.1，5.3.5.3-1-Table 14.3-1.1j，5.3.5.3-2-Table 14.3-1.1j
BAT：現状で利用可能な最良の治療，BID：1 日 2 回
a) C2301 試験（進行中）データカットオフ日：全被験者が約 6 ヵ月間の治験治療を終了又はそれ以前に中止した時点（2020 年 1 月 6 日），D2301 試験（進行中）データカットオフ日：全被験者が第 C7D1 の評価を終了又はそれ以前に中止した時点（2020 年 5 月 8 日），271 試験（完了）データカットオフ日：被験者の 75%が血液疾患の 2 年間の非再発死亡達成，死亡，又は追跡不能となった時点（2019 年 6 月 5 日）
b) Day 3 までの投与で血液学的検査値の悪化及び副作用がみられなかった場合には，10 mg BID に増量可とした。

1.1.1.1 評価資料の試験デザインの概略

個々の試験の詳細は「2.7.6 個々の試験のまとめ」に示す。

1.1.1.1.1 急性 GVHD 対象の国際共同第 III 相試験（C2301 試験）

本試験は，同種 HSCT 歴のある 12 歳以上でステロイド抵抗性のグレード II から IV の急性 GVHD 患者を対象に，BAT を対照として RUX の有効性及び安全性を評価することを目的とした，第 III 相，多施設共同，ランダム化，非盲検，並行群間比較試験である。本試験は，スクリーニング期（28 日間），治療期（24 週間），安全性追跡調査期（最終投与後 30 日間），及び長期追跡調査期（最終投与時来院から Month 24 まで）の 4 期で構成された。

目標ランダム化被験者数は 308 名であった。急性 GVHD と診断された患者からスクリーニング同意取得後，スクリーニングを開始した。治験実施計画書に規定されたステロイド抵抗性基準を満たしすべての適格性が確認された被験者は，本試験の同意を取得した後，Day 1 に急性 GVHD の重症度（グレード II，III，IV）を層別因子として RUX 群又は BAT 群に 1：1 の比でランダム化され，投与開始となった。BAT は，ランダム化前に治験担当医師が決定した。

RUX の用法・用量は 10 mg 1 日 2 回（BID）経口投与とした。RUX と関連のある臨床検査値異常又は有害事象が認められた被験者では，治験実施計画書に規定された用量調節基準に従って RUX を減量又は休薬した。回復後の再増量は可能であったが，10 mg BID を超えないこととした。他の急性 GVHD 治療薬［全身副腎皮質ステロイド± CNI ± 全身療法（急性 GVHD 診断前から予防目的で投与されていた場合に限る）］をスクリーニング期に使用していた場合は継続可とした。また，抗感染症薬，輸血等，HSCT 後の標準的な支持療法は併用可とした。RUX 及び BAT の投与は，急性 GVHD 治療の効果不十分，慢性 GVHD の徴候又は症状の発現，原疾患である血液疾患の再発又は進行，許容できない毒性，又はその他の理由による中止基準に合致した場合に中止した。投与中に完全奏効（CR）又は部分奏効（PR）を達成した被験者では，Day 7 以降に副腎皮質ステロイドの漸減が許容された。また，副腎皮質ステロイドの中止後，CNI 及び RUX の漸減

（RUX は Day 56 以降）も許容された。RUX の漸減は Week 24 までの完了が望ましいとされたが，急性 GVHD 再燃又は安全性上の懸念により難しい場合は，Week 96 までの延長が許容された。BAT 群の被験者は，Day 28 以降 Week 24 までに以下の 1 又は 2 に合致し，かつ慢性 GVHD（重複型，進行型，又は de novo 型）の徴候又は症状がない場合には，同期間内に RUX への切換え（クロスオーバー）を可能とした。

1）Day 28 に主要評価項目の奏効基準（CR 又は PR）未達成

2）効果が消失し，かつ，進行，混合奏効，又は無効の基準を満たし，急性 GVHD に対する追加の全身免疫抑制療法が必要

クロスオーバーした被験者では，RUX 初回投与日を Crossover Day 1 とし，RUX 群と同じ投与方法及び漸減方法に従って Crossover Week 24 まで RUX を投与した。

RUX 又は BAT の最終投与後 30 日間で安全性追跡調査を行い，その後 Month 6，9，12，18 及び 24 時点で長期追跡調査として生存状況，血液疾患の再発又は進行等を調査した。

1.1.1.1.2 慢性 GVHD 対象の国際共同第 III 相試験（D2301 試験）

本試験は，同種 HSCT 歴のある 12 歳以上でステロイド抵抗性の中等症又は重症の慢性 GVHD 患者を対象に，BAT を対照として RUX の有効性及び安全性を評価することを目的とした，第 III 相，多施設共同，ランダム化，非盲検，並行群間比較試験である。本試験は，スクリーニング期（28 日間），治療期［最長 156 週間：主要な治療期間（24 週間），継続治療期間（132 週間）］，安全性追跡調査期（最終投与後 30 日間）の 3 期で構成された。

目標ランダム化被験者数は 324 名であった。治験実施計画書に規定されたステロイド抵抗性の基準を満たす慢性 GVHD 患者から同意を取得した。スクリーニング期に全適格性が確認された被験者は，Day 1 に慢性 GVHD の重症度（中等症，重症）を層別因子として RUX 群又は BAT 群に 1：1 の比でランダム化され，投与開始となった。BAT は，ランダム化前に治験担当医師が決定した。

RUX の用法・用量は 10 mg BID 経口投与とした。RUX と関連のある臨床検査値異常又は有害事象が認められた被験者では，治験実施計画書に規定された用量調節基準に従って RUX を減量又は休薬した。回復後の再増量は可能であったが，10 mg BID を超えないこととした。他の慢性 GVHD 治療薬［全身副腎皮質ステロイド± CNI ± 全身療法（組入れ前から慢性 GVHD の予防目的で投与されていた場合に限る）］をスクリーニング期に使用していた場合は継続可とした。また，抗感染症薬，輸血等，HSCT 後の標準的な支持療法は併用可とした。RUX 及び BAT の投与は，慢性 GVHD 治療の効果不十分，原疾患である血液疾患の再発又は進行，許容できない毒性，21 日間を超える休薬，又はその他の理由による試験中止基準に合致した場合に中止した。投与中に CR 又は PR を達成した被験者では，時期を問わず副腎皮質ステロイドの漸減が許容された。また，副腎皮質ステロイドの中止後，CNI 及び RUX の漸減（いずれも C7D1 以降）も許容された。BAT 群の被験者のうち，C7D1 以降の継続治療期間に 1）疾患進行，2）混合奏効，3）不変，4）

BAT による許容できない毒性，5）慢性 GVHD 再燃　のいずれかに合致した場合には，RUX へのクロスオーバーを可能とした。クロスオーバーした被験者では，RUX 初回投与日を Crossover Day 1 とし，RUX 群と同じ投与方法及び漸減方法に従って Crossover Cycle 33 Day 28（1 サイクル：28 日間）まで RUX を投与した。

CR 又は PR を達成し，Cycle 39 以前に治験治療を漸減完了した被験者では，治療期の調査を Cycle 39 まで実施した。CR 又は PR 達成以外の理由で Cycle 39 以前に投与中止した被験者では，最終投与後 30 日間で安全性追跡調査を行い，その後 Cycle 39 まで 3 ヵ月ごとに長期追跡調査として生存状況及び新たな慢性 GVHD 療法の開始を調査した。

1.1.1.2　参考資料の試験デザインの概略

1.1.1.2.1 急性 GVHD 対象の外国第 II 相試験（271 試験）

本試験は，同種 HSCT 歴のある 12 歳以上でステロイド抵抗性のグレード II から IV の急性 GVHD 患者を対象に，RUX の有効性及び安全性を評価することを目的とした，第 II 相，多施設共同，非盲検，単群試験である。本試験は，スクリーニング期（28 日間），治療期（約 9 ヵ月間），安全性追跡調査期（最終投与後 30～35 日間），及び長期追跡調査期（投与終了から，死亡，同意撤回，又は試験終了のいずれか早い日まで）で構成された。

目標被験者数は 70 名であった。治験実施計画書に規定されたステロイド抵抗性の基準を満たす急性 GVHD 患者から同意を取得し，スクリーニング期に全適格性が確認された被験者は，Day 1 から RUX を投与した。

RUX の開始用法・用量は 5 mg BID 経口投与とし，Day 3 までの投与で血液学的検査値の悪化，かつ副作用がみられなかった場合には，10 mg BID に増量可とした。安全性上必要な場合は，治験実施計画書に規定された用量調節基準に従い，RUX の減量又は最長 14 日間の休薬を可とした。回復後の再増量は可能であったが，20 mg/日は超えないこととした。抗感染症薬，GVHD 予防薬（CNI 等），輸血，及び局所ステロイドをスクリーニング期に使用していた場合は継続可とした。RUX の投与は，RUX の漸減完了，治療不成功（無効，又は GVHD の進行に対して全身療法の追加が必要），原疾患である血液腫瘍の進行，許容できない毒性の発現，同意撤回，治験担当医師判断による投与中止，又は死亡が認められるまで継続した。副腎皮質ステロイドは Day 1 から投与し，時期を問わず漸減が許容された。RUX は，Day 180 以降に CR 又は VGPR を達成し，かつ，副腎皮質ステロイドを 8 週間以上中止している場合には漸減が許容された。

RUX の投与終了後 30～35 日間で安全性追跡調査を行った後，死亡，同意撤回，試験終了のいずれか早い日まで，8 週間ごとに長期追跡調査を行った。GVHD の進行以外の理由で RUX を投与中止した被験者では，安全性追跡調査時及び以降 28 日ごとに GVHD のステージ及びグレードを評価した。

1.1.1.3 安全性に関するその他の情報源

承認申請時点の安全性に関するその他の情報源の要約を Table 1-2 に示す。

Table 1-2 安全性に関するその他の情報源の要約

項目	報告日	評価期間	添付資料番号
Jakavi/Jakafi PSUR 10	2020 年 4 月 20 日	2019 年 2 月 23 日～2020 年 2 月 22 日	5.3.6-1
EU Risk Management Plan（EU-RMP）Version 11.1	2019 年 12 月 19 日	—	1.11.2

1.1.2 安全性の評価方法

各試験の安全性評価項目及び評価方法の詳細は第 5 部に添付する試験総括報告書に示す。

1.1.2.1 安全性の評価項目

1.1.2.1.1 有害事象

有害事象の定義

有害事象とは，同意書取得後に生じたあらゆる好ましくない徴候，症状，又は医療上の状態の発現又は悪化と定義した。臨床検査値又はその他の検査結果の異常は，それらが臨床的徴候又は症状を伴う場合，臨床的に重要と判断される場合，治療を要する場合，又は治験薬の用量変更を要する場合に限り有害事象とした。

有害事象の収集方法

いずれの試験でも，治験担当医師は，来院時の被験者に対する誘導的でない質問，被験者の自発報告，診察，臨床検査，その他の検査により有害事象の情報を収集した。

対象疾患（C2301 試験：急性 GVHD，D2301 試験：慢性 GVHD）の進行又は再燃，慢性 GVHD の発現（C2301 試験のみ），原疾患である血液疾患の再発又は進行に関する事象は，転帰が死亡のものも含め，有害事象として報告しないよう規定した（ただし，治験担当医師が症例報告書（CRF）で有害事象として報告した場合は集計に含めた）。271 試験ではこの規定はなかった。271 試験で疾患進行が発現した場合，他の随伴する有害事象が確認されない場合に限り，疾患進行を有害事象として報告するよう規定した。

有害事象の判定基準

- 重症度

有害事象の重症度は米国国立がん研究所（NCI）有害事象共通用語規準（CTCAE）第 4.03 版に基づき Grade 1～5 で評価した。該当する有害事象が NCI-CTCAE に掲載されていない場合は，下記の定義に準じて Grade 1～5 で評価した。

- Grade 1：軽度
- Grade 2：中等度

- Grade 3：高度
- Grade 4：生命を脅かすまたは活動不能とする有害事象
- Grade 5：有害事象による死亡

271 試験では CTCAE Grade 1～4 で評価し，死亡に至った有害事象も Grade 1～4 で評価した上で転帰を死亡と報告した。

- 治験治療との関連

C2301 試験及び 271 試験では，RUX，BAT（以下，治験治療），又は治験治療と併用する副腎皮質ステロイド，CNI，又は予防目的の全身療法（以下，他の急性 GVHD 治療薬）と有害事象の関連を以下の 4 つのいずれかに分類した。

- 関連なし
- 関連あり：治験治療
- 関連あり：他の急性 GVHD 治療薬
- 関連あり：両方又は判別不可能

これらのうち「関連あり：治験治療」又は「関連あり：両方又は判別不可能」と分類された有害事象を副作用とした。

D2301 試験では，治験治療，又は治験治療と併用する副腎皮質ステロイド，CNI，又は予防目的の全身療法）（以下，他の慢性 GVHD 治療薬）と有害事象の関連を以下の 5 つのいずれかに分類した。

- 関連なし
- 関連あり
- 関連あり：治験治療
- 関連あり：他の慢性 GVHD 治療薬
- 関連あり：両方又は判別不可能

これらのうち「関連あり」，「関連あり：治験治療」，又は「関連あり：両方又は判別不可能」と分類された有害事象を副作用とした。

- 重篤性

以下の 5 つの基準のいずれかに該当する有害事象を重篤な有害事象と定義した。

- 死亡又は生命を脅かすもの
- 永続的又は顕著な障害・機能不全に陥るもの
- 先天異常又は出生時欠損を来すもの
- 医学的に重要なもの，すなわち被験者を危険にさらすか，又は上記のような結果に至ることを防止するために内科的又は外科的処置を必要とするような事象と定義されるもの
- 入院又は入院期間の延長が必要となるもの。ただし，次の場合を除いた。
    - 対象疾患に関する規定どおりの治療又は観察のための入院であって，状態の悪化を伴わない場合

- 対象疾患には無関係な既存の病態に対する待機的治療又は以前から計画された治療のための入院であって，同意取得以降に悪化していない場合
- 全身状態の悪化を伴わない，社会的事由及び介護者の一時休息のための入院

救急外来での治療を要したものの入院に至らず上記の定義のいずれにも合致しない事象は，重篤な有害事象として報告しないこととした。

使用した有害事象の辞書

有害事象の標準化には ICH 国際医薬用語集（MedDRA）を使用した。また，有害事象の日本語への翻訳には，標準化に使用した辞書に対応する MedDRA 日本語版を使用した。有害事象は特に記載のない限り，基本語（PT）を記載した。

その他の重要な有害事象

治験治療の投与中止に至った有害事象，治験治療の用量調節又は休薬に至った有害事象，及び治療を要した有害事象をその他の重要な有害事象として定義した。なお，C2301 試験及び D2301 試験の治験実施計画書では，用量調節及び休薬の基準を RUX のみに対して規定し，BAT の用量調節及び休薬は治験担当医師の判断に基づいて実施された。

臨床的に注目すべき有害事象

RUX の作用機序，非臨床成績，及び既承認の適応症でのデータから想定，懸念される，Table 1-3 に示す事象を，臨床的に注目すべき有害事象とした。関連する有害事象を Table 7-1 の定義に従ってグループ化し，包括的に評価した。感染症については，病原体別（ウイルス，細菌，真菌，不明）に Table 7-1 の定義に従ってグループ化した結果も検討した。これらの結果は 2.1.5 項「器官別又は症候群別有害事象」に示した。

Table 1-3 臨床的に注目すべき有害事象

カテゴリ	臨床的に注目すべき有害事象
感染症 [a]	感染症（結核を除く），肺炎，日和見感染，サイトメガロウイルス感染／感染症，尿路感染，敗血症／敗血症性ショック，結核，帯状疱疹，B 型肝炎の再活性化，進行性多巣性白質脳症
血球減少	血小板減少症，赤血球減少症，白血球減少症，その他の血球減少
出血性事象	出血性事象，胃腸出血，挫傷，頭蓋内出血，その他の出血性事象
その他	トランスアミナーゼ上昇
	脂質異常
	高血圧
	血栓塞栓症
	悪性腫瘍
	非黒色腫皮膚癌（NMSC）
	めまい
	骨折
	成長遅延

カテゴリ	臨床的に注目すべき有害事象
	体重増加

a) 病原体別（ウイルス，細菌，真菌，不明）の感染症，及びその他の感染も検討した。

1.1.2.1.2 臨床検査値

評価した臨床検査項目を Table 1-4 に示す。

Table 1-4 臨床検査項目一覧

検査区分	検査項目
血液学的検査	ヘモグロビン，血小板数，白血球数，白血球分画（好塩基球，好酸球，リンパ球，単球，好中球）
血液生化学的検査	アルブミン，ALP，ALT，AST，GGT[c]，カルシウム，クレアチニン，マグネシウム[c]，リン[c]，クロール[a]，ナトリウム，カリウム，総ビリルビン（基準範囲外の場合は間接ビリルビン[b]），血中尿素窒素又は尿素，総コレステロール[c]，総蛋白，トリグリセリド[c]，アミラーゼ[c]，膵リパーゼ[c]，グルコース（空腹時）
凝固検査[c]	プロトロンビン時間（国際標準化比），部分トロンボプラスチン時間又は活性化部分トロンボプラスチン時間，フィブリノゲン

a) D2301 試験では測定しなかった。
b) D2301 試験では直接ビリルビン及び間接ビリルビン
c) 271 試験では測定しなかった。

1.1.2.1.3 バイタルサイン

坐位血圧，坐位脈拍，体温，及び体重を測定した。

1.1.3 安全性解析における集団及びグループ分け

1.1.3.1 安全性データの併合

急性 GVHD の C2301 試験と慢性 GVHD の D2301 試験は，対象疾患，曝露期間，有害事象のプロファイルが試験間で異なったことから，本書ではこれらの試験のデータは併合せず，試験ごとに評価した。いずれも急性 GVHD 患者が対象である C2301 試験及び 271 試験（参考資料）は併合したが，試験デザインや曝露期間が試験間で異なったことから併合データは本書で使用せず，各試験の集計結果を併記して示した。さらに，C2301 試験，D2301 試験，及び 271 試験の 3 試験も併合したが，本書では使用しなかった。急性 GVHD の 2 試験の併合データ及び全 3 試験の併合データは第 5 部に添付する。

1.1.3.2 安全性の解析方法

各試験の安全性の解析方法の詳細は第 5 部に添付する試験総括報告書に示す。

1.1.3.2.1 安全性解析対象集団

各試験の解析対象集団の定義を Table 1-5 に示す。本書での安全性解析対象集団（SAF）には，C2301 試験及び D2301 試験の SAF 及びクロスオーバー解析対象集団，並びに 271 試験の安全性評価可能集団を含め，実施された治験治療に基づき解析した。

Table 1-5 解析対象集団の定義

試験	解析対象集団	定義
C2301 試験 D2301 試験	最大の解析対象集団（FAS）[a]	ランダム化された全被験者。Intent-to-treat の原則に従い，割り付けられた治験治療及び層別因子別に解析した。
	安全性解析対象集団（SAF）	治験治療を 1 回以上実施された全被験者。実施された治験治療（割り付けられた治験治療が 1 回以上実施された場合はその治験治療，割り付けられた治験治療が 1 回も実施されなかった場合は最初に実施された治験治療）に基づき解析した。
	クロスオーバー解析対象集団	BAT に割り付けられて BAT を実施された後，クロスオーバーして RUX を 1 回以上投与された全被験者
271 試験（参考）	有効性評価可能集団 [a]	組み入れられた全被験者
	安全性評価可能集団	組み入れられた被験者のうち，治験薬を 1 回以上投与された全被験者

a) 被験者の内訳及び投与群別の被験者背景の解析に用いた。

安全性データの集計及び提示の要約を Table 1-6 に示す。

C2301 試験では，BAT 群の被験者は Day 28 以降に RUX へクロスオーバーすることが許容され，約 3 割の被験者がクロスオーバーした。両群の安全性プロファイルを適切に評価するために，群間比較には主に Day 28 までの結果を用いた。さらに，長期投与での RUX の安全性を評価するために，データカットオフ 2 までの結果を用い，RUX 群と BAT からクロスオーバーした被験者のデータを併合した RUX overall の被験者の安全性を評価した。

D2301 試験では，C7D1 以降に BAT から RUX へのクロスオーバーが許容され，BAT 群の約 4 割の被験者がクロスオーバーした。両群の安全性プロファイルを適切に評価するために，群間比較には主に C7D1 までの結果を用いた。また，データカットオフまでの結果を用いて RUX overall の被験者の安全性を評価した。

Table 1-6 安全性データの集計及び提示の要約

試験	集計データ	提示した群又は集団	被験者数	RUX の用法用量
C2301 試験	Day 28 まで	RUX 群	152	10 mg BID
	Day 28 まで	BAT 群	150	—
	データカットオフ 2[a]まで	RUX 群	152	10 mg BID
	データカットオフ 2[a]まで	BAT 群[c]	150	—
	データカットオフ 2[a]まで	RUX crossover の被験者[d]	49	10 mg BID
	データカットオフ 2[a]まで	RUX overall の被験者[e]	201	10 mg BID
D2301 試験	C7D1 まで	RUX 群	165	10 mg BID
	C7D1 まで	BAT 群	158	—
	データカットオフ[b]まで	RUX 群	165	10 mg BID
	データカットオフ[b]まで	BAT 群[c]	158	—
	データカットオフ[b]まで	RUX crossover の被験者[d]	61	10 mg BID
	データカットオフ[b]まで	RUX overall の被験者[e]	226	10 mg BID
271 試験	最終解析結果	RUX 群	71	開始用量 5 mg BID,

試験	集計データ	提示した群又は集団	被験者数	RUX の用法用量
（参考）				最高用量 10 mg BID

a) 全被験者が約 6 ヵ月間の治験治療を終了又はそれ以前に中止した時点（2020 年 1 月 6 日）
b) 全被験者が C7D1 の評価を終了又はそれ以前に中止した時点（2020 年 5 月 8 日）
c) クロスオーバー以降のデータは解析に含めなかった。
d) BAT から RUX に切り換えた被験者。クロスオーバー以降のデータを解析に含めた。
e) RUX 群と RUX crossover の被験者の併合

1.1.3.2.2 有害事象

本書では，有害事象の標準化に以下の MedDRA version を用いた。なお，version 22.1 では PT「サイトメガロウイルス感染」には感染再燃も含まれたのに対し，version 23.0 では感染再燃は PT「サイトメガロウイルス感染再燃」にコーディングされ，PT「サイトメガロウイルス感染」と区別して集計された。

- C2301 試験の RUX 群，BAT 群，RUX crossover の被験者：version 22.1
- D2301 試験の RUX 群，BAT 群，RUX crossover の被験者：version 23.0
- C2301 試験及び D2301 試験の RUX overall の被験者：version 23.0
- 271 試験：version 23.0

治験治療下で発現した有害事象の発現被験者数及び発現率を群別に集計した。治験治療下とは，治験治療の開始から最終投与後 30 日又は治療期終了日のうちいずれか遅い方までとした。BAT に割り付けられクロスオーバーした被験者では，BAT の開始から最終投与後 30 日又は RUX 初回投与日の前日のうちいずれか早い方までに発現した事象は BAT 群で集計し，RUX の投与開始から最終投与後 30 日又は Crossover 治療期終了日のうちいずれか遅い方までに発現した事象は RUX crossover で集計した。有害事象は，器官別大分類（SOC）別及び PT 別に示した。同一の被験者が同一の有害事象を複数回発現した場合，該当する SOC 及び PT は 1 名と集計した。同一の被験者が複数の重症度（Grade）の同一の有害事象を発現した場合，最悪 Grade で 1 名と集計した。

発現率（%）は，安全性解析対象被験者数（N）に対する有害事象発現被験者数（n）の割合とした。データカットオフまでの集計では，治験治療の曝露期間で調整した有害事象発現率（EAIR）も示した。EAIR は 100 人年あたりの有害事象発現被験者数であり，［有害事象の発現被験者数/曝露期間の合計（人年）］× 100 により算出した。曝露期間の合計（人年）は「全被験者の曝露日数の合計/ 365.25」と定義し，各被験者の曝露日数は，有害事象が発現した被験者は当該事象の初回発現までの曝露日数を，有害事象が発現しなかった被験者は全曝露日数をカウントした。さらに，投与期間別の有害事象発現率を示した。その際，発現率は当該区間で有害事象を発現するリスクのある被験者総数を推定して算出した。すなわち，投与期間別の発現率は［当該区間で有害事象を発現した被験者数 /（当該区間開始時の被験者数 − 当該区間終了時までに投与中止した被験者の半数）］× 100 として算出した。

死亡は治験治療下の死亡を評価した。また，時期を問わない死亡も示した。

- C2301 試験及び D2301 試験では，CRF の死亡ページに記録された死因（死亡の主因。各被験者で 1 事象）を集計した。死因は「対象疾患関連」と「その他」に分けて集計した。
- 271 試験では，CRF の死亡ページで主因に限定せずに死因を収集したため，対象疾患関連の死因のみを集計した。

さらに，いずれの試験も，死亡に至った有害事象も評価した。死亡に至った有害事象は，CRF の有害事象ページに記録された有害事象のうち転帰が死亡の事象を集計した。死亡に至った有害事象が複数認められた被験者では，全事象を集計に含めた。治験治療下で発現した有害事象を評価した。治験治療との関連も評価した。なお，C2301 試験及び D2301 試験では，対象疾患の進行又は再燃，慢性 GVHD の発現（C2301 試験のみ），原疾患の再発又は進行は原則として有害事象として報告しないよう規定したため（1.1.2.1.1 項），これらの事象は集計に含まれない。ただし，治験担当医師が CRF で有害事象として報告した場合は集計に含めた。271 試験では同様の規定がなかったため，これらの事象も集計に含まれた。

1.1.3.2.3 臨床検査値

臨床検査値（血液学的検査，血液生化学的検査）は NCI-CTCAE 第 4.03 版の重症度分類に基づき，ベースライン後に新たに発現又は悪化した異常値の基準に該当した被験者数とその割合を集計した。同一の被験者が複数の重症度（Grade）に該当した場合，最悪 Grade で 1 名と集計した。また，投与期間中の検査値の推移を図示した。

1.1.3.2.4 バイタルサイン

バイタルサイン及び体重はベースラインからの変化量の記述統計量を算出した。また，Table 1-7 に示す臨床的に注目すべきバイタルサインの異常の基準に該当した被験者数とその割合を集計した。

Table 1-7　　臨床的に注目すべきバイタルサインの異常の基準

	上昇	低下
収縮期血圧	≥ 180 mmHg かつベースラインからの上昇幅が ≥ 20 mmHg	≤ 90 mmHg かつベースラインからの低下幅が ≥ 20 mmHg
拡張期血圧	≥ 105 mmHg かつベースラインからの上昇幅が ≥ 15 mmHg	≤ 50 mmHg かつベースラインからの低下幅が ≥ 15 mmHg
脈拍	≥ 100 bpm かつベースラインからの増加幅が > 25%	≤ 50 bpm かつベースラインからの減少幅が> 25%
体温	> 39.1°C	–
体重	ベースラインからの増加幅が> 10%	ベースラインからの減少幅が> 10%

1.1.3.2.5 部分集団

急性 GVHD は C2301 試験のデータカットオフ 2 までの RUX overall の被験者のデータ，慢性 GVHD は D2301 試験のデータカットオフまでの RUX overall の被験者のデータを対象に，Table 1-8 に示す要因別に，有害事象，重篤な有害事象の部分集団解析を実施した。また，日本人部分集

団として，日本の実施医療機関で組み入れられた被験者を対象に，投与群別（RUX 群，BAT 群）及び RUX overall の被験者の結果を示した。

Table 1-8　　部分集団の定義及び評価した項目

要因	カテゴリー
日本人	—
青少年（12 歳以上 18 歳未満）	—
年齢	12 歳以上 18 歳未満，18 歳以上 65 歳以下，65 歳超
性別	男性，女性
人種	White，Asian，その他
地域	アジア（日本以外），日本，その他（欧州，オーストラリア，カナダ，米国を含む）
ベースラインの肝機能障害の程度	正常，軽度（TBL > 1.0～1.5 × ULN），中等度（TBL 1.5～3 × ULN），重度（TBL > 3 × ULN），不明
ベースラインの腎機能障害の程度	正常，軽度（GFR 60～89 mL/min），中等度（GFR 30～59 mL/min），重度（GFR < 30 mL/min），不明
シクロスポリン併用	あり，なし
ランダム化時の急性 GVHD の臓器障害発生部位（急性 GVHD のみ）	皮膚，肝臓，上部消化管，下部消化管

GFR = 糸球体濾過量，TBL = 総ビリルビン，ULN = 基準値上限

1.1.3.3　安全性データの提示

本書に提示した安全性データの一覧を Table 1-9 に示す。

Table 1-9　　本書に提示した安全性データの一覧

	急性 GVHD		慢性 GVHD
	C2301 試験（評価）	271 試験（参考）	D2301 試験（評価）
曝露状況	○	○	○
人口統計学的データ	○	○	○
有害事象			
有害事象 [a]	○	○	○
副作用	○	○	○
重症度別 [a]	○	○	○
投与期間別	○	—	○
死亡	○	○	○
重篤な有害事象 [a]	○	○	○
投与中止に至った有害事象	○	○	○
用量調節又は休薬に至った有害事象	○	○	○
治療を要した有害事象	○	○	○
臨床的に注目すべき有害事象 [a]	○	○	○
臨床検査	○	○	○
バイタルサイン	○	○	○

	急性 GVHD		慢性 GVHD
	C2301 試験（評価）	271 試験（参考）	D2301 試験（評価）
日本人での安全性	○	—	○
青少年での安全性	○	○	○
部分集団での検討	○	○	○

a) C2301 試験及び D2301 試験では EAIR も示した。

1.2 全般的な曝露状況

1.2.1 被験者の内訳

1.2.1.1 急性 GVHD

C2301 試験で 620 名がスクリーニングされ，そのうち 310 名が RUX 群又は BAT 群にランダム化された。310 名中 1 名（BAT 群）は，スクリーニング同意書には署名していたものの誤って治験同意書への署名前にランダム化されたため，すべての解析から除外した。残りの 309 名（RUX 群 154 名，BAT 群 155 名，以下同順）のうち 302 名に治験治療が 1 回以上実施された（2.7.3-Table 3-1）。データカットオフ 2 までに 309 名のうち 250 名が割り付けられた治験治療を中止し，その割合は RUX 群で BAT 群と比べて低かった（75.3%，86.5%）。中止理由は RUX 群では効果不十分（20.8%，44.5%），有害事象（17.5%，3.9%）の順に多く，BAT 群では効果不十分，死亡（16.2%，13.5%）の順に多かった。RUX 群では BAT 群と比べて効果不十分による中止が少なく，有害事象による中止が多かった。その他の理由は群間で大きな違いはなかった。3 名（いずれも RUX 群）が割り付けられた治験治療を継続中であった。

BAT 群 155 名中 49 名（31.6%）が RUX へクロスオーバーし，このうち 36 名がクロスオーバー後に投与を中止した。中止理由は有害事象（12/49 名，24.5%）が最も多かった。2 名が RUX 投与を継続中であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.1-1.2）。

ランダム化された 310 名のうち治験同意書への署名前にランダム化された 1 名を除く 309 名（154 名，155 名）が FAS に，治験同意書への署名後に治験治療が実施された 302 名（152 名，150 名）が SAF に含まれた（5.3.5.1-1-C2301 試験 CSR2-Table 14.1-5.1）。

1.2.1.2 慢性 GVHD

D2301 試験で 404 名がスクリーニングされ，そのうち 329 名が RUX 群又は BAT 群にランダム化された（RUX 群 165 名，BAT 群 164 名，以下同順）。329 名のうち 323 名（165 名，158 名）に治験治療が 1 回以上実施された（2.7.3-Table 3-2）。データカットオフまでに 329 名のうち 204 名が割り付けられた治験治療を中止し，その割合は RUX 群で BAT 群と比べて低かった（49.7%，74.4%）。中止理由は RUX 群では有害事象（17.0%，4.9%），効果不十分（14.5%，42.7%）の順に多く，BAT 群では効果不十分，医師による判断（2.4%，8.5%）の順に多かった。RUX 群では BAT 群と比べて効果不十分による中止が少なく，有害事象による中止が多かった。その他の理由は群間で大きな違いはなかった。125 名が割り付けられた治験治療を継続中であった。

BAT 群 164 名中 61 名（37.2%）が RUX へクロスオーバーし，このうち 15 名がクロスオーバー後に投与を中止した。中止理由は有害事象及び効果不十分（各 4/61 名，6.6%）が最も多かった。46 名が RUX 投与を継続中であった（5.3.5.1-2-D2301 試験-Table 14.1-1.2）。

ランダム化された 329 名（165 名，164 名）が FAS に，治験治療が実施された 323 名（165 名，158 名）が SAF に含まれた（5.3.5.1-2-D2301 試験-Table 14.1-5.1）。

1.2.2 総合的な曝露の程度

急性 GVHD

C2301 試験のデータカットオフ 2 時点で，治験治療の曝露期間の中央値（最小値～最大値）は RUX 群が 63.0（6.0～463.0）日，BAT 群が 29.0（1.0～188.0）日であり，RUX 群で BAT 群と比べて 2 倍以上長かった（Table 1-10）。総曝露期間は RUX 群（39.5 人年）で BAT 群（19.0 人年）と比べて長かった。RUX 群の RUX の用量強度の中央値は Day 28 までが 20.0 mg/日，データカットオフ 2 までが 16.6 mg/日であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.3.1，Table 14.3-1.3.3）。

BAT 群の被験者の治療は治験担当医師がランダム化前に選択し，Day 28 までは変更可であった。被験者の 79.3%で，1 種類のみの BAT が実施された。曝露期間［中央値（最小値～最大値）］が最も長かった BAT はエベロリムス［133.5（103.0～164.0）日］であり，次いで体外循環式光化学療法（ECP）［47.5（2.0～173.0）日］，間葉系間質細胞（MSC）［28.5（4.0～62.0）日］であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.2，Table 14.3-1.3）。

RUX overall の被験者では，RUX の総曝露期間は 51.8 人年であり，39 名が 6 ヵ月間を超えて（最長 66.1 週間）RUX を投与された（Table 1-12）。

慢性 GVHD

D2301 試験の C7D1 までの治験治療の曝露期間の中央値（最小値～最大値）は RUX 群が 25.6（0.7～25.6）週，BAT 群が 24.0（0.6～25.6）週であり，群間で同程度であった（Table 1-11）。

データカットオフ時点で，曝露期間の中央値（最小値～最大値）は RUX 群が 41.3（0.7～127.3）週，BAT 群が 24.1（0.6～108.4）週であり，RUX 群で BAT 群と比べて 1.5 倍以上長かった。総曝露期間は RUX 群（1748.0 人月）で BAT 群（1061.8 人月）と比べて長かった。RUX 群の RUX の用量強度の中央値は C7D1 までが 19.6 mg/日，データカットオフまでが 18.6 mg/日であった（5.3.5.1-2-D2301 試験-Table 14.3-1.4，Table 14.3-1.5）。

BAT 群の被験者の治療は治験担当医師がランダム化前に選択し，C7D1 までは変更可であった。被験者の 80.4%で，1 種類のみの BAT が実施された。曝露期間［中央値（最小値～最大値）］が最も長かった BAT は ECP［24.8（1.4～100.4）週］であり，次いでシロリムス［24.5（2.4～68.6）週］，ミコフェノール酸モフェチル（MMF）［24.1（2.1～108.4）週］であった（5.3.5.1-2-D2301 試験-Table 14.3-1.2，Table 14.3-1.3）。

RUX overall の被験者では，RUX の総曝露期間は 195.1 人年であり，155 名が 6 ヵ月間を超えて（最長 127.3 週間）RUX を投与された（Table 1-12）。

Table 1-10 急性 GVHD の曝露状況（C2301 試験，SAF，データカットオフ 2 まで）

	RUX N = 152	BAT N = 150	RUX crossover N = 49
Duration of exposure (days)			
Mean (SD)	94.9 (89.73)	46.3 (44.64)	91.4 (84.20)
Median (Min - Max)	63.0 (6.0-463.0)	29.0 (1.0-188.0)	61.0 (2.0-383.0)
Patient-time (years)	39.5	19.0	12.3
Duration of exposure categories -n (%)			
≤ 28 days	43 (28.3)	73 (48.7)	14 (28.6)
> 28 - 56 days	28 (18.4)	37 (24.7)	10 (20.4)
> 56 - 112 days	29 (19.1)	24 (16.0)	8 (16.3)
> 112 - 168 days	24 (15.8)	11 (7.3)	6 (12.2)
> 168 - 336 days	25 (16.4)	5 (3.3)	10 (20.4)
> 336 - 672 days	3 (2.0)	0	1 (2.0)
> 672 days	0	0	0

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.1，Table 14.3-1.5
Patient-time (years) is the sum of each patient's treatment exposure in years.

Table 1-11 慢性 GVHD の曝露状況（D2301 試験，SAF，データカットオフ）

	RUX N = 165	BAT N = 158	RUX crossover N = 61
Duration of exposure up to C7D1 (weeks)			
Mean (SD)	20.8 (7.65)	19.7 (7.91)	-
Median (Min - Max)	25.6 (0.7-25.6)	24.0 (0.6-25.6)	-
Duration of exposure up to the data cut-off (weeks)			
Mean (SD)	46.1 (32.84)	29.2 (22.24)	42.3 (25.19)
Median (Min - Max)	41.3 (0.7-127.3)	24.1 (0.6-108.4)	42.3 (2.6-98.7)
Patient-time (months)	1748.0	1061.8	593.5
Duration of exposure categories -n (%)			
≤ 4 weeks	9 (5.5)	23 (14.6)	2(3.3)
> 4 - 8 weeks	9 (5.5)	14 (8.9)	3(4.9)
> 8 - 12 weeks	13 (7.9)	11 (7.0)	3(4.9)
> 12 - 16 weeks	10 (6.1)	12 (7.6)	2(3.3)
> 16 - 20 weeks	5 (3.0)	11 (7.0)	4(6.6)
> 20 - 24 weeks	8 (4.8)	22 (13.9)	3(4.9)
> 24 weeks	111 (67.3)	65 (41.1)	44 (72.1)

Source: 5.3.5.1-2-D2301 試験-Table 14.3-1.1，Table 14.3-1.6
Patient-time (months) is the sum of each patient's treatment exposure in months.

Table 1-12 曝露状況（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
Duration of exposure (weeks)			
Mean (SD)	13.4 (12.60)	18.8 (26.24)	45.1 (30.95)
Median (Min - Max)	8.9 (0.3-66.1)	6.6 (0.6-115.9)	41.4 (0.7-127.3)
Patient-time (years)	51.8	25.6	195.1
Duration of exposure categories -n (%)			
≤ 4 weeks	57 (28.4)	29 (40.8)	11 (4.9)
> 4 - 8 weeks	38 (18.9)	14 (19.7)	12 (5.3)
> 8 - 12 weeks	27 (13.4)	2 (2.8)	16 (7.1)
> 12 - 16 weeks	10 (5.0)	4 (5.6)	12 (5.3)
> 16 - 20 weeks	7 (3.5)	2 (2.8)	9 (4.0)
> 20 - 24 weeks	23 (11.4)	2 (2.8)	11 (4.9)
> 24 - 36 weeks	27 (13.4)	2 (2.8)	29 (12.8)
> 36 - 48 weeks	8 (4.0)	8 (11.3)	29 (12.8)
> 48 weeks	4 (2.0)	8 (11.3)	97 (42.9)

Source: 5.3.5.3-4-Table 1.2-1.2
Patient-time (years) is the sum of each patient's treatment exposure in years.
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

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

1.3.1 人口統計学的特性及び疾患特性

急性 GVHD

C2301 試験での投与群別の人口統計学的特性及び疾患特性は，FAS を対象に評価した（2.7.3-3.1.4.1 項）。FAS の RUX 群と BAT 群で人口統計学的特性及び疾患特性に大きな違いはなかった。また，移植前処置を除いて HSCT に関連する背景因子に群間で大きな違いはなく，臓器障害発生部位を除いて急性 GVHD の病歴に群間で大きな違いはなかった。SOC 別の主な既往歴又は合併症（いずれかの群で 60%以上）は，感染症および寄生虫症（RUX 群 65.6%，BAT 群 62.6%，以下同順），代謝および栄養障害（61.0%，60.6%），胃腸障害（52.6%，63.9%）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.1-8.1）。

SAF の RUX overall の被験者の年齢の中央値は 53.0 歳であり，18 歳以上 65 歳以下が 82.6%，青少年被験者（12 歳以上 18 歳未満）が 3.0%（6 名）を占めた（Table 1-13）。性別は男性が 57.7%，人種は White が 70.1%を占めた。BMI の平均値は 23.4 kg/m^2 であった。

慢性 GVHD

D2301 試験での投与群別の人口統計学的特性及び疾患特性は，FAS を対象に評価した（2.7.3-3.1.4.2 項）。FAS の RUX 群と BAT 群で人口統計学的特性及び疾患特性に大きな違いはなかった。

また，HSCT に関連する背景因子，慢性 GVHD の病歴に群間で大きな違いはなかった。SOC 別の主な既往歴又は合併症（いずれかの群で 40%以上）は，代謝および栄養障害（46.1%，47.6%），感染症および寄生虫症（44.2%，44.5%）であった（5.3.5.1-2-D2301 試験-Table 14.1-8.1）。なお，FAS の集計結果では，12 名（3.6%）が 18 歳未満，317 名（96.4%）が 18 歳以上に含まれた。この集計は CRF で収集した各被験者の誕生年に基づいているが，誕生年月日に基づく場合，12 名中 1 名（BAT 群，被験者番号 [redacted]）は実際はランダム化時点で 1[redacted]歳，317 名中 1 名（RUX 群，被験者番号 [redacted]）は 1[redacted]歳であった。

SAF の RUX overall の被験者の年齢の中央値は 48.0 歳であり，18 歳以上 65 歳以下が 85.4%，青少年被験者（12 歳以上 18 歳未満）が 3.5%（8 名）を占めた（Table 1-13）。性別は男性が 64.6%，人種は White が 75.2%を占めた。BMI の平均値は 23.4 kg/m^2 であった。

Table 1-13 主な人口統計学的特性（C2301 試験，271 試験，及び D2301 試験，SAF）

Demographic variable	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
Age (years)			
n	201	71	226
Mean (SD)	49.0 (15.76)	52.9 (14.18)	45.5 (15.83)
Median (Min - Max)	53.0 (12.0-73.0)	58.0 (18.0-73.0)	48.0 (12.0-73.0)
Age category -n (%)			
Adolescents, 12 - < 18 years	6 (3.0)	0	8 (3.5)
18 - 65 years	166 (82.6)	62 (87.3)	193 (85.4)
> 65 years	29 (14.4)	9 (12.7)	25 (11.1)
Sex -n (%)			
Female	85 (42.3)	36 (50.7)	80 (35.4)
Male	116 (57.7)	35 (49.3)	146 (64.6)
Race -n (%)			
White	141 (70.1)	66 (93.0)	170 (75.2)
Black or African American	0	3 (4.2)	2 (0.9)
Asian	26 (12.9)	2 (2.8)	36 (15.9)
American Indian or Alaska Native	0	0	2 (0.9)
Other	8 (4.0)	0	11 (4.9)
Unknown	26 (12.9)	0	5 (2.2)
Ethnicity -n (%)			
Hispanic/Latino	11 (5.5)	9 (12.7)	19 (8.4)
Not Hispanic/Latino	115 (57.2)	60 (84.5)	159 (70.4)
Not Reported	43 (21.4)	2 (2.8)	37 (16.4)
Unknown	32 (15.9)	0	11 (4.9)
Body mass index (kg/m^2)			
n	191	66	199
Mean (SD)	23.4 (4.32)	26.8 (6.19)	23.4 (5.07)
Median (Min - Max)	23.2 (13.5-35.7)	25.4 (18.4-46.6)	22.8 (13.0-38.7)

Source: 5.3.5.3-4-Table 1.3-1.2

1.3.2 併用薬

急性 GVHD

C2301 試験でデータカットオフ 2 までに併用薬又は併用療法を使用した被験者の割合は RUX 群で 98.7%，BAT 群で 100%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3-2.13.1）。副腎皮質ステロイド及び CNI 以外で多く使用された併用薬又は併用療法は，いずれの群でも感染症治療薬，消化管運動改善薬，電解質液であった。PT 別では，RUX 群で最も多く使用されたものはスルファメトキサゾール・トリメトプリム製剤（71.1%，63.3%），次いでアシクロビル（61.2%，56.7%），ウルソデオキシコール酸（56.6%，57.3%）であり，BAT 群ではスルファメトキサゾール・トリメトプリム製剤が最も多く，次いでフロセミド（46.1%，58.7%），ウルソデオキシコール酸であった。副腎皮質ステロイド（65.8%，67.3%）で最も多く使用されたものは，いずれの群でもブデソニド（33.6%，43.3%）であり，次いでヒドロコルチゾン（15.1%，14.7%）であった。CNI（45.4%，18.0%）はシクロスポリン（29.6%，10.0%），タクロリムス（17.1%，8.7%）が多く使用された。併用薬又は併用療法に群間で大きな違いはみられなかった。

慢性 GVHD

D2301 試験でデータカットオフまでに併用薬を使用した被験者の割合は RUX 群で 100%，BAT 群で 99.4%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3-2.1）。副腎皮質ステロイド及び CNI 以外で多く使用された併用薬又は併用療法は，いずれの群でも感染症治療薬，胃腸薬（胆汁酸製剤等），鎮静薬（ベンゾジアゼピン等）であった。PT 別では，最も多く使用された併用薬はいずれの群でもスルファメトキサゾール・トリメトプリム製剤（66.1%，62.0%）であり，次いでアシクロビル（60.0%，50.6%），ウルソデオキシコール酸（40.0%，34.8%）であった。副腎皮質ステロイド（59.4%，55.1%）で最も多く使用されたものは，いずれの群でもデキサメタゾン（13.3%，19.0%）であり，次いでヒドロコルチゾン（12.1%，10.1%），ブデソニド（8.5%，13.9%）であった。CNI（27.3%，19.0%）では，シクロスポリン（17.6%，12.0%），タクロリムス（10.9%，8.2%）が多く使用された。併用薬又は併用療法に群間で大きな違いはみられなかった。

1.3.3 COVID-19 パンデミックの影響

急性 GVHD

C2301 試験のデータカットオフ 2（2020 年 1 月 6 日）までの結果及び 271 試験（最終解析のデータカットオフ日：2019 年 6 月 5 日）の結果に基づく安全性評価に対する COVID-19 パンデミックの影響はなかった。

慢性 GVHD

D2301 試験では，COVID-19 パンデミックに対してとられた手順変更の適切な記録及び保管を 20[redacted]年[redacted]月[redacted]日に実施医療機関に依頼し，また，逸脱集計のカテゴリに COVID-19 関連を追加した。その結果，データカットオフ（2020 年 5 月 8 日）までのパンデミックに関する主な逸脱の内容は，実施医療機関外での評価（FAS の 8.2%），治験薬交付方法の変更（5.5%）であり，来院未実施は 3 名（0.9%）と少なく，COVID-19 に関連する治験治療の中断や試験参加の中止はなかった。SAF の RUX 群 165 名中 1 名（0.6%）に COVID-19 が発現したが，Grade 2 で，処置なく消失した（5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。総じて安全性評価に対するパンデミックの影響は最小限であった。逸脱の詳細は試験総括報告書に示した。

2 有害事象

2.1 有害事象の解析

有害事象の定義，収集方法，使用した有害事象の辞書，及び解析方法は 1.1.2.1.1 項及び 1.1.3.2.2 項に示す。

本項では，各小項目の中で急性 GVHD，慢性 GVHD の順に結果を示す。

2.1.1 比較的よくみられる有害事象

Day 28 又は C7D1 までの集計では RUX 群又は BAT 群で，データカットオフまでの集計では RUX overall の被験者で，発現率が 10%以上の有害事象を「比較的よくみられる有害事象」，2%以上の副作用を「比較的よくみられる副作用」と定義した。

2.1.1.1 有害事象

2.1.1.1.1 急性 GVHD

SOC 別

C2301 試験の Day 28 までの全有害事象の発現率は，RUX 群で 96.1%，BAT 群で 94.7%（以下同順）と群間で同程度であり，いずれの群でもほとんどの被験者で有害事象が認められた（Table 2-1）。RUX 群で BAT 群と比べて発現率が 10%以上高かった事象は血液およびリンパ系障害（58.6%，44.7%）であった。

データカットオフ 2 までの全有害事象の発現率は，RUX 群で 99.3%，BAT 群で 98.7%であった。RUX 群の曝露期間は BAT 群と比べて長く（1.2.2 項），曝露期間で調整した有害事象発現率である EAIR を検討した結果，全有害事象の EAIR に RUX 群と BAT 群で大きな違いはなかった（4991.2，4712.9）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.11，Table 14.3.1-1.23）。

データカットオフ 2 までの，RUX overall の被験者での全有害事象の発現率は 98.5%であった（Table 2-2）。SOC 別で発現率が最も高かった有害事象は感染症および寄生虫症（78.6%）であり，次いで血液およびリンパ系障害（69.2%），胃腸障害（58.7%）であった。

Table 2-1 Day 28 までの急性 GVHD の SOC 別有害事象（C2301 試験，SAF）

SOC	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	146 (96.1)	142 (94.7)
感染症および寄生虫症	93 (61.2)	88 (58.7)
血液およびリンパ系障害	89 (58.6)	67 (44.7)
臨床検査	67 (44.1)	59 (39.3)
胃腸障害	66 (43.4)	56 (37.3)
代謝および栄養障害	65 (42.8)	69 (46.0)
一般・全身障害および投与部位の状態	49 (32.2)	58 (38.7)
腎および尿路障害	32 (21.1)	24 (16.0)
血管障害	31 (20.4)	28 (18.7)
筋骨格系および結合組織障害	29 (19.1)	27 (18.0)
呼吸器，胸郭および縦隔障害	28 (18.4)	29 (19.3)
精神障害	24 (15.8)	27 (18.0)
神経系障害	21 (13.8)	30 (20.0)
皮膚および皮下組織障害	18 (11.8)	17 (11.3)
傷害，中毒および処置合併症	17 (11.2)	14 (9.3)
肝胆道系障害	11 (7.2)	13 (8.7)
免疫系障害	11 (7.2)	15 (10.0)
心臓障害	9 (5.9)	18 (12.0)
内分泌障害	4 (2.6)	5 (3.3)
眼障害	4 (2.6)	11 (7.3)
生殖系および乳房障害	4 (2.6)	2 (1.3)
耳および迷路障害	2 (1.3)	3 (2.0)
製品の問題	1 (0.7)	0
良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.7)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.2
MedDRA version 22.1
RUX 群の発現率の降順

Table 2-2 急性 GVHD の SOC 別の有害事象（C2301 試験及び 271 試験，SAF）

SOC	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
合計	198 (98.5)	71 (100.0)
感染症および寄生虫症	158 (78.6)	58 (81.7)
血液およびリンパ系障害	139 (69.2)	52 (73.2)
胃腸障害	118 (58.7)	59 (83.1)
臨床検査	112 (55.7)	56 (78.9)
一般・全身障害および投与部位の状態	100 (49.8)	57 (80.3)
代謝および栄養障害	96 (47.8)	58 (81.7)
呼吸器，胸郭および縦隔障害	75 (37.3)	51 (71.8)
神経系障害	61 (30.3)	38 (53.5)
腎および尿路障害	58 (28.9)	40 (56.3)
血管障害	56 (27.9)	33 (46.5)
筋骨格系および結合組織障害	55 (27.4)	45 (63.4)
皮膚および皮下組織障害	51 (25.4)	30 (42.3)
精神障害	48 (23.9)	36 (50.7)
傷害，中毒および処置合併症	38 (18.9)	33 (46.5)
心臓障害	29 (14.4)	35 (49.3)
免疫系障害	23 (11.4)	10 (14.1)
肝胆道系障害	21 (10.4)	13 (18.3)
眼障害	16 (8.0)	24 (33.8)
内分泌障害	9 (4.5)	6 (8.5)
良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）	7 (3.5)	6 (8.5)
生殖系および乳房障害	7 (3.5)	7 (9.9)
耳および迷路障害	7 (3.5)	6 (8.5)
製品の問題	3 (1.5)	0
外科および内科処置	0	1 (1.4)

Source: 5.3.5.3-4-Table 2.1-3.2
MedDRA version 23.0
RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

PT 別

Day 28 までの RUX 群で BAT 群に比べて発現率が 10%以上高かった事象は血小板減少症（RUX 群 32.9%，BAT 群 18.7%，以下同順）であった（Table 2-3）。

データカットオフ 2 までの RUX overall の被験者で発現率が最も高かった PT 別有害事象は貧血（37.8%）であり，次いで血小板減少症（35.3%），好中球減少症（23.4%）であった（Table 2-4）。

Table 2-3 Day 28 までの急性 GVHD の PT 別の有害事象（いずれかの群で発現率 10%以上）（C2301 試験，SAF）

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	146 (96.1)	142 (94.7)
血小板減少症	50 (32.9)	28 (18.7)
貧血	46 (30.3)	42 (28.0)
サイトメガロウイルス感染 [a]	39 (25.7)	31 (20.7)
末梢性浮腫	28 (18.4)	26 (17.3)
血小板数減少	26 (17.1)	21 (14.0)
好中球減少症	24 (15.8)	19 (12.7)
低カリウム血症	21 (13.8)	25 (16.7)
高血圧	16 (10.5)	14 (9.3)
低アルブミン血症	16 (10.5)	16 (10.7)
低マグネシウム血症	16 (10.5)	19 (12.7)
発熱	16 (10.5)	18 (12.0)
下痢	14 (9.2)	15 (10.0)
好中球数減少	10 (6.6)	15 (10.0)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.2
MedDRA version 22.1
RUX 群の発現率の降順
a) サイトメガロウイルスへの感染，感染再燃ともに，MedDRA version 22.1 では PT サイトメガロウイルス感染にコーディングされた。

Table 2-4 急性 GVHD の PT 別の有害事象（RUX overall の被験者で発現率 10%以上）（C2301 試験及び 271 試験，SAF）

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
合計	198 (98.5)	71 (100)
貧血	76 (37.8)	46 (64.8)
血小板減少症	71 (35.3)	14 (19.7)
好中球減少症	47 (23.4)	6 (8.5)
低カリウム血症	45 (22.4)	35 (49.3)
サイトメガロウイルス感染再燃	45 (22.4)	4 (5.6)
発熱	43 (21.4)	17 (23.9)
末梢性浮腫	42 (20.9)	33 (46.5)
血小板数減少	37 (18.4)	32 (45.1)
悪心	33 (16.4)	23 (32.4)
低マグネシウム血症	29 (14.4)	24 (33.8)
下痢	28 (13.9)	21 (29.6)
嘔吐	28 (13.9)	18 (25.4)

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
高血圧	27 (13.4)	16 (22.5)
敗血症	25 (12.4)	10 (14.1)
白血球数減少	24 (11.9)	21 (29.6)
腹痛	24 (11.9)	15 (21.1)
好中球数減少	23 (11.4)	28 (39.4)
急性腎障害	23 (11.4)	17 (23.9)
肺炎	21 (10.4)	11 (15.5)

Source: 5.3.5.3-4-Table 2.1-3.2
MedDRA version 23.0
RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

2.1.1.1.2 慢性 GVHD

SOC 別

D2301 試験の C7D1 までの全有害事象の発現率は，RUX 群で 97.6%，BAT 群で 91.8%（以下同順）と群間で同程度であり，いずれの群でもほとんどの被験者で有害事象が認められた（Table 2-5）。RUX 群で BAT 群と比べて発現率が 10%以上高かった事象は臨床検査（50.3%，32.3%），血液およびリンパ系障害（41.8%，22.2%）であった。

データカットオフまでの全有害事象の発現率は，RUX 群で 98.2%，BAT 群で 92.4%であった。RUX 群の曝露期間は BAT 群と比べて長く（1.2.2 項），EAIR を検討した結果，全有害事象の EAIR は RUX 群で BAT 群と比べて高かった（1055.9，863.3）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.16，Table 14.3.1-1.27）。

データカットオフまでの RUX overall の被験者の全有害事象の発現率は 94.7%であった（Table 2-6）。SOC 別で発現率が最も高かった有害事象は感染症および寄生虫症（68.6%）であり，次いで臨床検査（49.1%），血液およびリンパ系障害（42.5%）であった。

Table 2-5 C7D1 までの慢性 GVHD の SOC 別の有害事象（D2301 試験，SAF）

SOC	RUX N = 165 n (%)	BAT N = 158 n (%)
合計	161 (97.6)	145 (91.8)
感染症および寄生虫症	102 (61.8)	92 (58.2)
臨床検査	83 (50.3)	51 (32.3)
血液およびリンパ系障害	69 (41.8)	35 (22.2)
代謝および栄養障害	65 (39.4)	51 (32.3)
一般・全身障害および投与部位の状態	62 (37.6)	48 (30.4)
胃腸障害	61 (37.0)	61 (38.6)

SOC	RUX N = 165 n (%)	BAT N = 158 n (%)
呼吸器，胸郭および縦隔障害	60 (36.4)	48 (30.4)
筋骨格系および結合組織障害	44 (26.7)	42 (26.6)
神経系障害	35 (21.2)	32 (20.3)
血管障害	34 (20.6)	31 (19.6)
皮膚および皮下組織障害	24 (14.5)	21 (13.3)
精神障害	21 (12.7)	22 (13.9)
眼障害	18 (10.9)	24 (15.2)
腎および尿路障害	16 (9.7)	17 (10.8)
傷害，中毒および処置合併症	15 (9.1)	15 (9.5)
心臓障害	11 (6.7)	19 (12.0)
耳および迷路障害	5 (3.0)	7 (4.4)
免疫系障害	5 (3.0)	4 (2.5)
内分泌障害	4 (2.4)	6 (3.8)
肝胆道系障害	4 (2.4)	5 (3.2)
生殖系および乳房障害	4 (2.4)	3 (1.9)
良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (1.8)	4 (2.5)
社会環境	1 (0.6)	0
製品の問題	0	1 (0.6)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-1.3
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-6 慢性 GVHD の SOC 別の有害事象（D2301 試験，SAF，データカットオフまで）

SOC	RUX overall N = 226 n (%)
合計	214 (94.7)
感染症および寄生虫症	155 (68.6)
臨床検査	111 (49.1)
血液およびリンパ系障害	96 (42.5)
代謝および栄養障害	90 (39.8)
一般・全身障害および投与部位の状態	89 (39.4)
胃腸障害	87 (38.5)
呼吸器，胸郭および縦隔障害	86 (38.1)
筋骨格系および結合組織障害	71 (31.4)
神経系障害	53 (23.5)
血管障害	43 (19.0)
皮膚および皮下組織障害	36 (15.9)
眼障害	34 (15.0)
精神障害	31 (13.7)

SOC	RUX overall N = 226 n (%)
傷害，中毒および処置合併症	23 (10.2)
腎および尿路障害	19 (8.4)
心臓障害	18 (8.0)
耳および迷路障害	9 (4.0)
良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）	9 (4.0)
肝胆道系障害	7 (3.1)
生殖系および乳房障害	6 (2.7)
免疫系障害	5 (2.2)
内分泌障害	5 (2.2)
先天性，家族性および遺伝性障害	1 (0.4)
社会環境	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-3.2
MedDRA version 23.0
発現率の降順

PT 別

C7D1 までの RUX 群で BAT 群と比べて発現率が 10%以上高かった事象は貧血（RUX 群 29.1%，BAT 群 12.7%，以下同順），アラニンアミノトランスフェラーゼ増加（15.2%，4.4%）であった（Table 2-7）。

データカットオフまでの RUX overall の被験者で発現率が最も高かった PT 別有害事象は貧血（28.8%）であり，次いで発熱（18.1%），高血圧，肺炎（各 14.6%）であった（Table 2-8）。

Table 2-7 C7D1 までの慢性 GVHD の PT 別の有害事象（いずれかの群で発現率 10%以上）（D2301 試験，SAF）

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
合計	161 (97.6)	145 (91.8)
貧血	48 (29.1)	20 (12.7)
高血圧	26 (15.8)	20 (12.7)
発熱	26 (15.8)	15 (9.5)
アラニンアミノトランスフェラーゼ増加	25 (15.2)	7 (4.4)
血中クレアチニン増加	23 (13.9)	7 (4.4)
好中球減少症	18 (10.9)	8 (5.1)
肺炎	18 (10.9)	20 (12.7)
血小板減少症	18 (10.9)	14 (8.9)
咳嗽	17 (10.3)	11 (7.0)
下痢	17 (10.3)	21 (13.3)
疲労	17 (10.3)	12 (7.6)
血小板数減少	17 (10.3)	9 (5.7)

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
悪心	15 (9.1)	16 (10.1)
低カリウム血症	13 (7.9)	16 (10.1)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-1.3
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-8 慢性 GVHD の PT 別の有害事象（発現率 10%以上）（D2301 試験，SAF，データカットオフまで）

PT	RUX overall N = 226 n (%)
合計	214 (94.7)
貧血	65 (28.8)
発熱	41 (18.1)
高血圧	33 (14.6)
肺炎	33 (14.6)
下痢	32 (14.2)
アラニンアミノトランスフェラーゼ増加	32 (14.2)
好中球減少症	30 (13.3)
咳嗽	30 (13.3)
上気道感染	30 (13.3)
血中クレアチニン増加	29 (12.8)
血小板減少症	26 (11.5)
疲労	26 (11.5)
頭痛	23 (10.2)

Source: 5.3.5.3-4-Table 2.1-3.2
MedDRA version 23.0
発現率の降順

2.1.1.2 治験薬との関連を否定できない有害事象（副作用）

2.1.1.2.1 急性 GVHD

C2301 試験の Day 28 までの全副作用の発現率は，RUX 群で 52.0%，BAT 群で 28.7%（以下同順）であり，RUX 群で BAT 群と比べて高かった（Table 2-9）。RUX 群で BAT 群と比べて発現率が 5%以上高かった副作用は，血小板減少症（19.1%，4.0%），貧血（11.2%，3.3%），血小板数減少（11.2%，4.7%），好中球減少症（7.2%，1.3%）であった。

データカットオフ 2 までの RUX overall の被験者の全副作用の発現率は 66.2%であった（Table 2-10）。発現率が最も高かった副作用は血小板減少症（21.9%）であり，次いで貧血（15.9%），血小板数減少，好中球減少症（各 12.9%）であった。

Table 2-9 Day 28 までの急性 GVHD の PT 別の副作用（いずれかの群で発現率 2%以上）（C2301 試験，SAF）

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	79 (52.0)	43 (28.7)
血小板減少症	29 (19.1)	6 (4.0)
貧血	17 (11.2)	5 (3.3)
血小板数減少	17 (11.2)	7 (4.7)
好中球減少症	11 (7.2)	2 (1.3)
白血球数減少	9 (5.9)	7 (4.7)
好中球数減少	8 (5.3)	4 (2.7)
サイトメガロウイルス感染 [a]	7 (4.6)	7 (4.7)
白血球減少症	6 (3.9)	2 (1.3)
汎血球減少症	5 (3.3)	0
アラニンアミノトランスフェラーゼ増加	4 (2.6)	1 (0.7)
エプスタイン・バーウイルス感染	4 (2.6)	0
γ-グルタミルトランスフェラーゼ増加	4 (2.6)	0
高血圧	4 (2.6)	1 (0.7)
敗血症	4 (2.6)	1 (0.7)
低アルブミン血症	3 (2.0)	1 (0.7)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.3
MedDRA version 22.1
RUX 群の発現率の降順
a) サイトメガロウイルスへの感染，感染再燃ともに，MedDRA version 22.1 では PT サイトメガロウイルス感染にコーディングされた。

Table 2-10 急性 GVHD の PT 別の副作用（RUX overall の被験者で発現率 2%以上）（C2301 試験及び 271 試験，SAF）

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
合計	133 (66.2)	54 (76.1)
血小板減少症	44 (21.9)	11 (15.5)
貧血	32 (15.9)	25 (35.2)
血小板数減少	26 (12.9)	23 (32.4)
好中球減少症	26 (12.9)	3 (4.2)
白血球数減少	17 (8.5)	14 (19.7)
好中球数減少	16 (8.0)	19 (26.8)
白血球減少症	10 (5.0)	0
敗血症	8 (4.0)	4 (5.6)
汎血球減少症	8 (4.0)	0
サイトメガロウイルス感染再燃	8 (4.0)	2 (2.8)

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
肺炎	6 (3.0)	4 (5.6)
点状出血	6 (3.0)	0
アラニンアミノトランスフェラーゼ増加	5 (2.5)	8 (11.3)
γ-グルタミルトランスフェラーゼ増加	5 (2.5)	1 (1.4)
高血圧	4 (2.0)	2 (2.8)
尿路感染	4 (2.0)	1 (1.4)
アスパラギン酸アミノトランスフェラーゼ増加	4 (2.0)	4 (5.6)
下痢	4 (2.0)	3 (4.2)
鼻出血	4 (2.0)	2 (2.8)
サイトメガロウイルス感染	4 (2.0)	1 (1.4)
発熱	4 (2.0)	4 (5.6)
頭痛	4 (2.0)	2 (2.8)

Source: 5.3.5.3-4-Table 2.1-4.2
MedDRA version 23.0
RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

2.1.1.2.2 慢性 GVHD

D2301 試験の C7D1 までの全副作用の発現率は，RUX 群で 63.0%，BAT 群で 28.5%（以下同順）であり，RUX 群で BAT 群と比べて高かった（Table 2-11）。RUX 群で BAT 群と比べて発現率が 5%以上高かった副作用は，貧血（21.8%，3.2%），好中球減少症（8.5%，2.5%），アラニンアミノトランスフェラーゼ増加（7.9%，0.6%）であった。

データカットオフまでの RUX overall の被験者の全副作用の発現率は 60.2%であった（Table 2-12）。発現率が最も高かった副作用は貧血（21.7%）であり，次いで好中球減少症（10.2%），血小板減少症（8.4%）であった。

Table 2-11 C7D1 までの慢性 GVHD の PT 別の副作用（いずれかの群で発現率 2%以上）（D2301 試験，SAF）

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
合計	104 (63.0)	45 (28.5)
貧血	36 (21.8)	5 (3.2)
好中球減少症	14 (8.5)	4 (2.5)
血小板減少症	14 (8.5)	6 (3.8)
アラニンアミノトランスフェラーゼ増加	13 (7.9)	1 (0.6)
血小板数減少	10 (6.1)	3 (1.9)
肺炎	10 (6.1)	5 (3.2)

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
血中クレアチニン増加	9 (5.5)	2 (1.3)
アスパラギン酸アミノトランスフェラーゼ増加	7 (4.2)	1 (0.6)
γ-グルタミルトランスフェラーゼ増加	7 (4.2)	1 (0.6)
頭痛	5 (3.0)	1 (0.6)
白血球減少症	5 (3.0)	0
発熱	5 (3.0)	1 (0.6)
尿路感染	5 (3.0)	2 (1.3)
アミラーゼ増加	4 (2.4)	1 (0.6)
白血球数減少	4 (2.4)	2 (1.3)
下痢	2 (1.2)	4 (2.5)
悪心	2 (1.2)	4 (2.5)
高血圧	1 (0.6)	4 (2.5)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-1.4
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-12 慢性 GVHD の PT 別の副作用（発現率 2%以上）（D2301 試験, SAF，データカットオフまで）

PT	RUX overall N = 226 n (%)
合計	136 (60.2)
貧血	49 (21.7)
好中球減少症	23 (10.2)
血小板減少症	19 (8.4)
アラニンアミノトランスフェラーゼ増加	18 (8.0)
肺炎	13 (5.8)
血小板数減少	11 (4.9)
血中クレアチニン増加	11 (4.9)
アスパラギン酸アミノトランスフェラーゼ増加	9 (4.0)
γ-グルタミルトランスフェラーゼ増加	7 (3.1)
発熱	7 (3.1)
白血球数減少	6 (2.7)
血中クレアチンホスホキナーゼ増加	6 (2.7)
上気道感染	6 (2.7)
尿路感染	6 (2.7)
白血球減少症	5 (2.2)
アミラーゼ増加	5 (2.2)
下気道感染	5 (2.2)
リパーゼ増加	5 (2.2)
疲労	5 (2.2)

PT	RUX overall N = 226 n (%)
頭痛	5 (2.2)
下痢	5 (2.2)
高コレステロール血症	5 (2.2)

Source: 5.3.5.3-4-Table 2.1-4.2
MedDRA version 23.0
発現率の降順

2.1.1.3 有害事象の重症度

2.1.1.3.1 急性 GVHD

C2301 試験の Day 28 までの Grade 3 以上の有害事象の発現率は，RUX 群で 78.3%，BAT 群で 79.3%（以下同順）であり，群間で同程度であった（Table 2-13）。RUX 群で BAT 群と比べて発現率が 10%以上高かった事象は血小板減少症（27.0%，16.0%）であった。Grade 3 以上の副作用の発現率は RUX 群で 40.8%，BAT 群で 20.0%であり，RUX 群で BAT 群と比べて発現率が 5%以上高かった事象は血小板減少症（14.5%，4.0%），貧血（7.9%，2.0%），血小板数減少（10.5%，4.7%）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.3）。

データカットオフ 2 までの Grade 3 以上の有害事象の発現率は，RUX 群で 91.4%，BAT 群で 87.3%であった。EAIR は，RUX 群と BAT 群で大きな違いはなかった（1299.1，1428.7）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.23）。

データカットオフ 2 までの RUX overall の被験者の Grade 3 以上の有害事象の発現率は 91.0%であった（Table 2-14）。発現率が最も高かった PT 別事象は血小板減少症（31.8%）であり，次いで貧血（31.3%），好中球減少症（21.4%）であった。Grade 3 以上の副作用の発現率は 56.2%であり，発現率が高かった事象は血小板減少症（19.4%），貧血（12.4%），血小板数減少（11.9%）であった（5.3.5.3-4-Table 2.1-4.2）。

Table 2-13 Day 28 までの急性 GVHD の Grade 3 以上の有害事象（いずれかの群で発現率 5%以上）（C2301 試験，SAF）

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	119 (78.3)	119 (79.3)
血小板減少症	41 (27.0)	24 (16.0)
貧血	34 (22.4)	28 (18.7)
血小板数減少	22 (14.5)	20 (13.3)
好中球減少症	20 (13.2)	14 (9.3)
サイトメガロウイルス感染 [a]	11 (7.2)	12 (8.0)
白血球数減少	11 (7.2)	11 (7.3)
敗血症	10 (6.6)	5 (3.3)

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
好中球数減少	10 (6.6)	12 (8.0)
低カリウム血症	9 (5.9)	9 (6.0)
高血圧	9 (5.9)	6 (4.0)
低アルブミン血症	6 (3.9)	10 (6.7)
高血糖	5 (3.3)	8 (5.3)
γ-グルタミルトランスフェラーゼ増加	3 (2.0)	8 (5.3)
血中ビリルビン増加	3 (2.0)	8 (5.3)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.2
MedDRA version 22.1
RUX 群の発現率の降順
a) サイトメガロウイルスへの感染，感染再燃ともに，MedDRA version 22.1 では PT サイトメガロウイルス感染にコーディングされた。

Table 2-14 急性 GVHD の Grade 3 以上の有害事象（RUX overall の被験者で発現率 5%以上）（C2301 試験及び 271 試験，SAF）

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
合計	183 (91.0)	69 (97.2)
血小板減少症	64 (31.8)	10 (14.1)
貧血	63 (31.3)	36 (50.7)
好中球減少症	43 (21.4)	6 (8.5)
血小板数減少	31 (15.4)	29 (40.8)
白血球数減少	23 (11.4)	12 (16.9)
好中球数減少	21 (10.4)	23 (32.4)
敗血症	21 (10.4)	9 (12.7)
低カリウム血症	19 (9.5)	13 (18.3)
肺炎	14 (7.0)	10 (14.1)
呼吸不全	13 (6.5)	10 (14.1)
敗血症性ショック	13 (6.5)	4 (5.6)
下痢	12 (6.0)	5 (7.0)
白血球減少症	12 (6.0)	0
高血圧	11 (5.5)	10 (14.1)
サイトメガロウイルス感染再燃	11 (5.5)	2 (2.8)
急性腎障害	10 (5.0)	6 (8.5)
低アルブミン血症	10 (5.0)	10 (14.1)
γ-グルタミルトランスフェラーゼ増加	10 (5.0)	1 (1.4)
汎血球減少症	10 (5.0)	0

Source: 5.3.5.3-4-Table 2.1-3.2
MedDRA version 23.0
RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

2.1.1.3.2 慢性 GVHD

D2301 試験の C7D1 までの Grade 3 以上の有害事象の発現率は，RUX 群で 57.0%，BAT 群で 57.6%（以下同順）であり，群間で同程度であった（Table 2-15）。PT 別で，RUX 群で BAT 群と比べて発現率が 10%以上高い事象はなかった。Grade 3 以上の副作用の発現率は RUX 群で 33.9%，BAT 群で 14.6%であり，RUX 群で BAT 群と比べて発現率が 5%以上高かった事象は貧血（9.1%，1.3%），血小板減少症（7.9%，1.3%）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.4）。

データカットオフまでの Grade 3 以上の有害事象の発現率は，RUX 群で 66.1%，BAT 群で 58.9%であった。EAIR は，RUX 群で BAT 群と比べて低かった（123.7，149.0）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.27）。

データカットオフまでの RUX overall の被験者の Grade 3 以上の有害事象の発現率は 61.5%であった（Table 2-16）。発現率が最も高かった PT 別事象は貧血（13.7%）であり，次いで肺炎（11.9%），好中球減少症（10.2%）であった。Grade 3 以上の副作用の発現率は 36.3%であり，発現率が高かった事象は貧血（9.7%），血小板減少症（7.1%），好中球減少症（6.6%）であった（5.3.5.3-4-Table 2.1-4.2）。

Table 2-15 C7D1 までの慢性 GVHD の Grade 3 以上の有害事象（いずれかの群で発現率 5%以上）（D2301 試験，SAF）

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
合計	94 (57.0)	91 (57.6)
貧血	21 (12.7)	12 (7.6)
血小板減少症	17 (10.3)	9 (5.7)
好中球減少症	14 (8.5)	6 (3.8)
肺炎	14 (8.5)	15 (9.5)
γ-グルタミルトランスフェラーゼ増加	11 (6.7)	3 (1.9)
高血圧	8 (4.8)	11 (7.0)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-1.3
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-16 慢性 GVHD の Grade 3 以上の有害事象（発現率 5%以上）（D2301 試験，SAF，データカットオフまで）

PT	RUX overall N = 226 n (%)
合計	139 (61.5)
貧血	31 (13.7)
肺炎	27 (11.9)
好中球減少症	23 (10.2)
血小板減少症	22 (9.7)
γ-グルタミルトランスフェラーゼ増加	13 (5.8)

Source: 5.3.5.3-4-Table 2.1-3.2
MedDRA version 23.0
発現率の降順

2.1.1.4 投与期間別の有害事象

2.1.1.4.1 急性 GVHD

C2301 試験のデータカットオフ 2 までの RUX overall の被験者で，投与期間別（RUX 投与開始後 31 日以内，31 日超から 59 日以内，59 日超から 6 ヵ月以内，6 ヵ月超から 12 ヵ月以内，12 ヵ月超）に有害事象を発現するリスクのある被験者総数を推定して算出した有害事象発現率を Table 2-17 に示す。各区間の長さが均等でないため区間の間で厳密に比較できないが，RUX 投与開始後 6 ヵ月以内の発現率の推移に特定の傾向は認められず，6 ヵ月以降は発現率が低下した。また，主な PT 別有害事象は，ほとんどが 6 ヵ月以降に発現率が低下し，投与期間の延長に伴う発現率の上昇はみられなかった。

なお，臨床的に注目すべき有害事象の発現時期は 2.1.5 項で評価した。

Table 2-17 急性 GVHD の投与期間別の有害事象発現率（全体の RUX overall の被験者で発現率 10%以上）（C2301 試験，SAF，データカットオフ 2 まで）

	RUX overall				
PT	0-31 days N* = 189.0 n (%)	> 31-59 days N* = 151.0 n (%)	> 59 days to 6 months N* = 93.0 n (%)	> 6 months to 12 months N* = 32.5 n (%)	> 12 months N* = 2.0 n (%)
合計	188 (99.5)	148 (98.0)	106 (114.0)	26 (80.0)	1 (50.0)
血小板減少症	60 (31.7)	28 (18.5)	17 (18.3)	0	0
貧血	55 (29.1)	35 (23.2)	26 (28.0)	2 (6.2)	0
サイトメガロウイルス感染再燃	39 (20.6)	7 (4.6)	10 (10.8)	1 (3.1)	0
好中球減少症	30 (15.9)	18 (11.9)	17 (18.3)	1 (3.1)	0
血小板数減少	30 (15.9)	18 (11.9)	15 (16.1)	0	0
末梢性浮腫	30 (15.9)	11 (7.3)	11 (11.8)	0	0
低カリウム血症	29 (15.3)	19 (12.6)	10 (10.8)	1 (3.1)	0

PT	0-31 days N* = 189.0 n (%)	> 31-59 days N* = 151.0 n (%)	RUX overall > 59 days to 6 months N* = 93.0 n (%)	> 6 months to 12 months N* = 32.5 n (%)	> 12 months N* = 2.0 n (%)
発熱	23 (12.2)	17 (11.3)	7 (7.5)	5 (15.4)	0
高血圧	21 (11.1)	5 (3.3)	1 (1.1)	0	0
低マグネシウム血症	19 (10.1)	9 (6.0)	9 (9.7)	0	0
下痢	17 (9.0)	6 (4.0)	8 (8.6)	1 (3.1)	0
白血球数減少	16 (8.5)	14 (9.3)	8 (8.6)	0	0
悪心	15 (7.9)	10 (6.6)	12 (12.9)	1 (3.1)	0
敗血症	14 (7.4)	8 (5.3)	7 (7.5)	1 (3.1)	0
好中球数減少	13 (6.9)	15 (9.9)	6 (6.5)	2 (6.2)	0
腹痛	13 (6.9)	6 (4.0)	4 (4.3)	3 (9.2)	0
急性腎障害	13 (6.9)	5 (3.3)	6 (6.5)	1 (3.1)	0
嘔吐	12 (6.3)	9 (6.0)	9 (9.7)	3 (9.2)	0
肺炎	7 (3.7)	5 (3.3)	12 (12.9)	1 (3.1)	0

Source: 5.3.5.3-4-Table 2.1-23.2
N* = 当該区間開始時の被験者数 − 当該区間終了時までに投与中止した被験者の半数
n = 当該区間で有害事象を発現した被験者数
各区間の n/N* (%) を示した。
MedDRA version 23.0
0-31 days の発現率の降順

2.1.1.4.2 慢性 GVHD

D2301 試験のデータカットオフまでの RUX overall の被験者で，投与期間別に有害事象を発現するリスクのある被験者総数を推定して算出した有害事象発現率を Table 2-18 に示す。各区間の長さが均等でないため区間の間で厳密に比較できないが，RUX 投与開始後 12 ヵ月以内の全有害事象の発現率の推移に特定の傾向は認められなかった。また，主な PT 別有害事象で，投与期間が長くなることによる発現率の上昇はみられなかった。

Table 2-18 慢性 GVHD の投与期間別の有害事象発現率（全体の RUX overall の被験者で発現率 10%以上）（D2301 試験，SAF，データカットオフまで）

PT	0-31 days N* = 224.0 n/N* (%)	> 31-59 days N* = 217.0 n/N* (%)	RUX overall > 59 days to 6 months N* = 184.5 n/N* (%)	> 6 months to 12 months N* = 126.5 n/N* (%)	> 12 months N* = 48.0 n/N* (%)
合計	169 (75.4)	126 (58.1)	163 (88.3)	105 (83.0)	60 (125.0)
貧血	21 (9.4)	24 (11.1)	40 (21.7)	14 (11.1)	10 (20.8)
アラニンアミノトランスフェラーゼ増加	20 (8.9)	6 (2.8)	9 (4.9)	6 (4.7)	2 (4.2)
血小板減少症	17 (7.6)	12 (5.5)	11 (6.0)	2 (1.6)	1 (2.1)
発熱	14 (6.3)	7 (3.2)	17 (9.2)	9 (7.1)	5 (10.4)

PT	0-31 days N* = 224.0 n/N* (%)	> 31-59 days N* = 217.0 n/N* (%)	RUX overall > 59 days to 6 months N* = 184.5 n/N* (%)	> 6 months to 12 months N* = 126.5 n/N* (%)	> 12 months N* = 48.0 n/N* (%)
好中球減少症	13 (5.8)	9 (4.1)	11 (6.0)	8 (6.3)	2 (4.2)
血中クレアチニン増加	10 (4.5)	8 (3.7)	14 (7.6)	4 (3.2)	3 (6.3)
肺炎	10 (4.5)	6 (2.8)	15 (8.1)	9 (7.1)	4 (8.3)
下痢	10 (4.5)	3 (1.4)	11 (6.0)	7 (5.5)	4 (8.3)
疲労	10 (4.5)	3 (1.4)	11 (6.0)	3 (2.4)	2 (4.2)
頭痛	9 (4.0)	3 (1.4)	9 (4.9)	4 (3.2)	3 (6.3)
高血圧	8 (3.6)	7 (3.2)	14 (7.6)	3 (2.4)	1 (2.1)
上気道感染	8 (3.6)	3 (1.4)	10 (5.4)	10 (7.9)	3 (6.3)
咳嗽	7 (3.1)	6 (2.8)	16 (8.7)	7 (5.5)	3 (6.3)

Source: 5.3.5.3-4-Table 2.1-23.2
N* = 当該区間開始時の被験者数 − 当該区間終了時までに投与中止した被験者の半数
n = 当該区間で有害事象を発現した被験者数
各区間の n/N* (%) を示した。
MedDRA version 23.0
0-31 days の発現率の降順

2.1.2 死亡

本項では，死亡に加えて，死亡に至った有害事象を評価した。それぞれの解析方法は 1.1.3.2.2 項に示す。

2.1.2.1 死亡

2.1.2.1.1 急性 GVHD

C2301 試験

死亡の一覧を Table 7-3 に示す。

治験治療下の死亡

Day 28 までに，RUX 群で 15 名（9.9%），BAT 群で 21 名（14.0%）（以下同順）が治験治療下で死亡し，その割合は群間で同程度であった（Table 2-19）。最も多かった死因はいずれの群も対象疾患である急性 GVHD（急性 GVHD 又は急性 GVHD 治療に伴う合併症）（9 名，17 名）であり，その他の死因はいずれも 1 名での発現であった。

データカットオフ 2 までに，RUX 群で 43 名（28.3%），BAT 群で 36 名（24.0%）が治験治療下で死亡し，その割合は群間で同程度であった（Table 7-2）。最も多かった死因はいずれの群も急性 GVHD（21 名，21 名）であった。その他の死因のうちいずれかの群で 2 名以上に認められたものは，RUX 群では敗血症（3 名），心停止，疾患進行，多臓器機能不全症候群，敗血症性ショック（各 2 名），BAT 群では敗血症性ショック（2 名）であった。RUX crossover の被験者では，19 名（38.8%）が治験治療下で死亡した。最も多かった死因は急性 GVHD（8 名）であり，その

他の死因は呼吸不全（2 名）を除きいずれも 1 名での発現であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.3）。

RUX 群と RUX crossover の被験者を併合した RUX overall の被験者としては，データカットオフ 2 までに 62 名（30.8%）が治験治療下で死亡した（Table 2-20）。最も多かった死因は急性 GVHD（29 名）であった。その他の死因（33 名）のうち 2 名以上に認められたものは，敗血症（4 名），呼吸不全（3 名），心停止，疾患進行，多臓器機能不全症候群，敗血症性ショック（各 2 名）であった。

時期を問わない死亡

データカットオフ 2 までに，SAF の RUX 群で 152 名中 82 名（53.9%），BAT に割り付けられた被験者（クロスオーバー後に死亡した被験者を含む）で 150 名中 86 名（57.3%）が死亡した（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.4）。RUX crossover の被験者では 49 名中 29 名（59.2%）が死亡した。RUX overall の被験者としては，201 名中 111 名（55.2%）が死亡した（5.3.5.3-4-Table 2.1-21.1）。

Table 2-19 Day 28 までの急性 GVHD の治験治療下の死亡（C2301 試験，SAF）

	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	15 (9.9)	21 (14.0)
死因：対象疾患関連		
急性 GVHD	9 (5.9)	17 (11.3)
死因：その他（PT）	6 (3.9)	4 (2.7)
心停止	1 (0.7)	0
感染	1 (0.7)	0
呼吸障害	1 (0.7)	0
呼吸不全	1 (0.7)	0
気道感染	1 (0.7)	0
敗血症性ショック	1 (0.7)	1 (0.7)
誤嚥	0	1 (0.7)
脳梗塞	0	1 (0.7)
易感染性宿主の感染	0	1 (0.7)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.1
MedDRA version 22.1.
RUX 群の発現率の降順

Table 2-20 急性 GVHD の治験治療下の死亡（C2301 試験，SAF，データカットオフ 2 まで）

	RUX overall N = 201 n (%)
合計	62 (30.8)
死因：対象疾患関連	29 (14.4)
急性 GVHD	29 (14.4)
GVHD 進行	-
死因：その他（PT）	33 (16.4)
敗血症	4 (2.0)
呼吸不全	3 (1.5)
多臓器機能不全症候群	2 (1.0)
心停止	2 (1.0)
疾患進行	2 (1.0)
敗血症性ショック	2 (1.0)
肺出血	1 (0.5)
急性骨髄性白血病	1 (0.5)
再発急性骨髄性白血病	1 (0.5)
アデノウイルス感染	1 (0.5)
心肺不全	1 (0.5)
脳血管発作	1 (0.5)
昏睡	1 (0.5)
状態悪化	1 (0.5)
死亡	1 (0.5)
全身健康状態異常	1 (0.5)
特発性肺炎症候群	1 (0.5)
感染	1 (0.5)
肺障害	1 (0.5)
肺臓炎	1 (0.5)
腎機能障害	1 (0.5)
呼吸障害	1 (0.5)
気道感染	1 (0.5)
ウイルス感染	1 (0.5)

Source: 5.3.5.3-4-Table 2.1-20.2
MedDRA version 23.0.
発現率の降順

271 試験（参考資料）

死亡の一覧を Table 7-7 に示す。

治験治療下の死亡

治験治療下の死亡は，71 名中 25 名（35.2%）に認められた（5.3.5.3-4-Table 2.1-20.2）。このうち 7 名で死因は GVHD 進行であった。

時期を問わない死亡

30 名（42.3%）が死亡した（5.3.5.3-4-Table 2.1-21.1）。このうち 10 名で死因は GVHD 進行であった。

2.1.2.1.2 慢性 GVHD

D2301 試験の死亡の一覧を Table 7-10 に示す。

治験治療下の死亡

C7D1 までに，RUX 群で 13 名（7.9%），BAT 群で 9 名（5.7%）（以下同順）が治験治療下で死亡し，その割合は同程度であった（Table 2-21）。最も多かった死因はいずれの群も対象疾患である慢性 GVHD（慢性 GVHD 又は慢性 GVHD 治療に伴う合併症）であり（12 名，6 名），その他の死因はいずれも 1 名での発現であった。

データカットオフまでに，RUX 群で 16 名（9.7%），BAT 群で 11 名（7.0%）が治験治療下で死亡し，その割合は群間で同程度であった（Table 7-9）。最も多かった死因はいずれの群も慢性 GVHD（14 名，7 名）であり，その他の死因は 1 名での発現であった。RUX crossover の被験者では，3 名（4.9%）が治験治療下で死亡した。最も多かった死因は慢性 GVHD（2 名）であり，その他の死因は 1 名での発現であった（5.3.5.1-2-D2301 試験-Table 14.3.1-2.3）。

RUX 群と RUX crossover の被験者を併合した RUX overall の被験者としては，データカットオフまでに 19 名（8.4%）が治験治療下で死亡した（Table 2-22）。最も多かった死因は慢性 GVHD（16 名）であり，その他の死因は全身健康状態悪化，頭蓋内出血，シュードモナス性敗血症が各 1 名であった。

時期を問わない死亡

データカットオフまでに FAS の RUX 群で 165 名中 31 名（18.8%），BAT 群に割り付けられた被験者（クロスオーバー後に死亡した被験者を含む）で 164 名中 27 名（16.5%）が死亡した（5.3.5.1-2-D2301 試験-Table 14.3.1-2.7）。RUX crossover の被験者では 61 名中 5 名が死亡した。RUX overall の被験者としては，226 名中 36 名（15.9%）が死亡した（5.3.5.3-4-Table 2.1-21.2）。

Table 2-21 C7D1 までの慢性 GVHD の治験治療下の死亡（D2301 試験，SAF）

	RUX N = 165 n (%)	BAT N = 158 n (%)
合計	13 (7.9)	9 (5.7)
死因：対象疾患関連		
慢性 GVHD	12 (7.3)	6 (3.8)
死因：その他（PT）	1 (0.6)	3 (1.9)
全身健康状態悪化	1 (0.6)	0
肺炎	0	1 (0.6)

	RUX N = 165 n (%)	BAT N = 158 n (%)
敗血症	0	1 (0.6)
全身性感染	0	1 (0.6)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-2.1
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-22 データカットオフまでの慢性 GVHD の治験治療下の死亡（D2301 試験，SAF）

	RUX overall N = 226 n (%)
合計	19 (8.4)
死因：対象疾患関連	
慢性 GVHD	16 (7.1)
死因：その他（PT）	3 (1.3)
全身健康状態悪化	1 (0.4)
頭蓋内出血	1 (0.4)
シュードモナス性敗血症	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-20.2
MedDRA version 23.0

2.1.2.2 死亡に至った有害事象

2.1.2.2.1 急性 GVHD

C2301 試験

Day 28 までに，死亡に至った有害事象は RUX 群で 152 名中 12 名（7.9%），BAT 群で 150 名中 17 名（11.3%）（以下同順）に認められ，発現率は群間で同程度であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.5）。これらの被験者のうち RUX 群 6 名，BAT 群 13 名では，死因（CRF の死亡ページに記録された死亡の主因）は対象疾患（急性 GVHD）と報告された。PT 別で，いずれかの群で 2 名以上に認められた死亡に至った有害事象は，敗血症（3 名，2 名），敗血症性ショック（3 名，3 名），肺炎（1 名，3 名），呼吸不全（1 名，3 名），移植片対宿主病（0 名，3 名）であった。死亡に至った副作用はいずれの群でも少なく（2 名，3 名），RUX 群ではシュードモナス性敗血症，敗血症（各 1 名），BAT 群では敗血症，肝不全，多臓器機能不全症候群，腎盂腎炎（各 1 名）であった。

データカットオフ 2 までに，死亡に至った有害事象は RUX 群で 33 名（21.7%），BAT 群で 32 名（21.3%）に認められ，発現率は群間で同程度であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.6）。いずれかの群で 3 名以上に認められた PT 別事象は敗血症（8 名，4 名），敗

血症性ショック（7 名，4 名），肺炎（2 名，4 名），呼吸不全（1 名，4 名），多臓器機能不全症候群（2 名，3 名），移植片対宿主病（0 名，3 名）であった。死亡に至った副作用は RUX 群で 10 名，BAT 群で 4 名に認められた。RUX 群の 10 名中 7 名では，RUX と他の急性 GVHD 治療薬（副腎皮質ステロイド± CNI ± 予防目的の全身療法）の両方に関連するか，又は判別不可能と判断された（敗血症 3 名，敗血症性ショック 2 名，シュードモナス性敗血症 1 名，ウイルス感染 1 名）。残る 3 名では RUX のみに関連すると判断され，内訳は下部消化管出血，細菌性敗血症，肺炎が各 1 名であった。ただし，下部消化管出血が認められた 1 名（日本人，被験者番号 [redacted]）の死因は急性 GVHD であり，ステージ 3 の消化管病変を伴っていた。細菌性敗血症の 1 名（被験者番号 [redacted]）では直近の外傷性損傷による入院，免疫抑制療法の併用があった。肺炎が認められた 1 名（被験者番号 [redacted]）には肺炎の重要なリスク因子があった（グレード IV の急性 GVHD，プレドニゾロン及びタクロリムスの併用）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.6，Table 14.3.1-3.1，Listing 16.2.7-1.1，C2301 試験 CSR1-Section 14.3.3）。

RUX crossover の被験者では，死亡に至った有害事象は 49 名中 15 名（30.6%）に認められ，呼吸不全（4 名，8.2%）及び敗血症（2 名，4.1%）を除き，いずれも 1 名での発現であった。死亡に至った副作用は 4 名に認められた。このうち 2 名では，RUX と他の急性 GVHD 治療薬の両方に関連するか判別不可能と判断された（アデノウイルス感染，呼吸不全，各 1 名）。残る 2 名では RUX のみに関連ありと判断され，内訳は敗血症，呼吸不全が各 1 名であった。ただし，敗血症が認められた 1 名（被験者番号 [redacted]）では，MMF 及び副腎皮質ステロイドを併用しており，RUX 投与に伴う好中球数低値がみられていた。呼吸不全の 1 名（被験者番号 [redacted]）では，本事象は緑膿菌肺炎に起因しており，エタネルセプト投与下での緑膿菌感染歴，RUX 投与下での好中球数低値がみられていた（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.8，Table 14.3.1-3.2，Listing 16.2.8-1.1a，Section 14.3.3）。

データカットオフ 2 までに RUX overall の被験者で死亡に至った有害事象は 201 名中 48 名（23.9%）に認められた（5.3.5.3-4-Table 2.1-22.2）。48 名のうち 20 名では，死因は対象疾患（急性 GVHD）と報告された。PT 別で最も多かった死亡に至った有害事象は敗血症（7 名）であり，次いで敗血症性ショック，呼吸不全（各 4 名）であった。死亡に至った副作用は 14 名に認められた。

271 試験（参考資料）

死亡に至った有害事象は 71 名中 28 名（39.4%）に認められた。2 名以上に認められた PT 別事象は呼吸不全（6 名），敗血症，疾患進行，多臓器機能不全症候群，肝不全（各 2 名）であった。死亡に至った副作用は 2 名（肺出血，敗血症，各 1 名）に発現し，いずれの事象も RUX と副腎皮質ステロイドの両方に関連ありと判断された。ただし，肺出血が認められた 1 名では，RUX 以外の因子として，全身状態悪化，対象疾患，浸潤性真菌性副鼻腔炎の悪化，副腎皮質ステロイドの併用，肺毒性のある化学療法（シクロホスファミド，イホスファミド，カルムスチン等）の

使用歴，直近の肺炎も死亡に関連したと考えられた。敗血症が認められた 1 名では，RUX 以外の因子として，全身状態悪化，対象疾患，免疫抑制剤の併用（MMF，シロリムス），汎血球減少症の併発，直近の股関節部骨折及び手術，穿孔を伴う好中球減少性大腸炎も死亡に関連したと考えられた。RUX のみに関連すると判断された死亡に至った事象はなかった（5.3.5.2-1-271 試験-Table 3.2.8，Section 15，Table 7-7）。

2.1.2.2.2 慢性 GVHD

D2301 試験の C7D1 までの死亡に至った有害事象は RUX 群で 165 名中 12 名（7.3%），BAT 群で 158 名中 8 名（5.1%）（以下同順）に認められ，発現率は群間で同程度であった（5.3.5.1-2-D2301 試験-Table 14.3.1-2.4）。これらの被験者のうち RUX 群 11 名，BAT 群 5 名では，死因は対象疾患（慢性 GVHD）と報告された。PT 別で，いずれかの群で 2 名以上に認められた死亡に至った有害事象は，肺炎（5 名，3 名），敗血症性ショック（0 名，3 名）であった。死亡に至った副作用はいずれの群でも少なく（7 名，4 名），RUX 群では肺炎（4 名），気管支肺アスペルギルス症，細菌性肺炎，呼吸不全，敗血症（各 1 名），BAT 群では肺炎，敗血症性ショック（各 2 名）であった。

データカットオフまでに，死亡に至った有害事象は RUX 群で 15 名（9.1%），BAT 群で 10 名（6.3%）に認められ，群間で発現率は同程度であった（5.3.5.1-2-D2301 試験-Table 14.3.1-2.5）。いずれかの群で 2 名以上に認められた PT 別事象は，肺炎（5 名，3 名），敗血症性ショック（0 名，3 名），呼吸不全（1 名，2 名）であった。死亡に至った副作用は RUX 群で 8 名（4.8%），BAT 群で 4 名（2.5%）に認められた。RUX 群の 8 名中 5 名では，RUX と他の慢性 GVHD 治療薬（副腎皮質ステロイド ± CNI ± 予防目的の全身療法）の両方に関連するか，又は判別不可能と判断された（肺炎 3 名，細菌性肺炎，敗血症，呼吸不全各 1 名）。残る 3 名では RUX のみに関連すると判断され，内訳は肺炎，頭蓋内出血，気管支肺アスペルギルス症が各 1 名であった。ただし，肺炎が認められた 1 名（被験者番号 [redacted]）では，CNI 及び副腎皮質ステロイドを併用していた。頭蓋内出血の 1 名（被験者番号 [redacted]）では，浸透圧性下痢に続発する重度の脱水，静脈虚脱，全身状態悪化，血小板減少症の Grade 4 への悪化が認められていた。気管支肺アスペルギルス症の 1 名（被験者番号 [redacted]）では，副腎皮質ステロイドを併用していた（5.3.5.1-2-D2301 試験-Table 14.3.1-2.5，Listing 16.2.7-1，Section 14.3.3）。

RUX crossover の被験者では，死亡に至った有害事象は 61 名中 2 名（3.3%）に認められ，アスペルギルス感染，頭蓋内出血（各 1 名）であった。死亡に至った副作用はなかった（5.3.5.1-2-D2301 試験-Table 14.3.1-2.6）。

データカットオフまでに RUX overall の被験者で死亡に至った有害事象は 226 名中 17 名（7.5%）に認められた（5.3.5.3-4-Table 2.1-22.2）。17 名のうち 14 名では，死因は対象疾患（慢性 GVHD）と報告された。最も多かった PT 別事象は肺炎（5 名）であり，その他の事象は 1 名での発現であった。死亡に至った副作用は 8 名に認められた。

2.1.3 その他の重篤な有害事象

2.1.3.1 急性 GVHD

C2301 試験

重篤な有害事象の一覧を Table 7-5 に示す。

Day 28 までの重篤な有害事象の発現率は RUX 群で 37.5%，BAT 群で 34.0%であり，群間で同程度であった（Table 2-23）。PT 別の各事象の発現率は群間で同程度であった。重篤な副作用の発現率は RUX 群で 11.2%，BAT 群で 8.0%であり，群間で同程度であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.5）。

データカットオフ 2 までの重篤な有害事象の発現率は RUX 群で 66.4%，BAT 群で 53.3%（以下同順）であった（Table 7-4）。重篤な有害事象の EAIR は RUX 群で BAT 群と比べて低かった（319.4，422.7）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.24）。いずれかの群で発現率が 5%以上であった PT 別事象は，敗血症（7.9%，7.3%），発熱（6.6%，4.0%），敗血症性ショック（6.6%，5.3%），下痢（5.3%，2.0%），肺炎（4.6%，5.3%），サイトメガロウイルス感染（3.9%，5.3%）であった。各事象の発現率は群間で同程度であった。RUX crossover の被験者では，重篤な有害事象の発現率は 77.6%であり，主な事象は敗血症（14.3%），呼吸不全（12.2%），敗血症性ショック，サイトメガロウイルス感染（各 6.1%）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.27）。RUX crossover の被験者で特有の事象は認められなかった。

データカットオフ 2 までの RUX overall の被験者の重篤な有害事象の発現率は 69.2%であった（Table 2-24）。発現率が最も高かった事象は敗血症（9.5%）であり，次いで敗血症性ショック（6.5%），呼吸不全（6.0%）であった。重篤な有害事象のうち，RUX のみと関連ありと判断された事象は 27 名で報告された。27 名中 11 名は重篤な有害事象により投与を中止し（好中球数減少，移植片機能損失，血小板減少症，ウイルス感染，胃腸出血，ウイルス性膀胱炎，肺炎，下部消化管出血，脳炎，トランスアミナーゼ上昇，細菌性敗血症，各 1 名），うち 3 名（肺炎，細菌性敗血症，脳炎）は転帰が死亡（脳炎は RUX 最終投与後 30 日より後の死亡），2 名（好中球数減少，移植片機能損失）は最終報告時点で転帰が未消失であった。その他の被験者では，RUX のみと関連する重篤な副作用は，RUX の用量調節，休薬，又は加療により投与継続が可能であった（5.3.5.1-1-C2301 試験 CSR2-Listing 16.2.7-1.1）。

Table 2-23 Day 28 までの急性 GVHD の重篤な有害事象（RUX 群で発現率 2%以上）（C2301 試験，SAF）

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	57 (37.5)	51 (34.0)
敗血症	8 (5.3)	3 (2.0)
下痢	5 (3.3)	1 (0.7)

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
サイトメガロウイルス感染 [a]	4 (2.6)	5 (3.3)
呼吸不全	4 (2.6)	4 (2.7)
敗血症性ショック	4 (2.6)	4 (2.7)
汎血球減少症	3 (2.0)	0
肺炎	3 (2.0)	3 (2.0)
発熱	3 (2.0)	2 (1.3)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.4
MedDRA version 22.1.
RUX 群の発現率の降順
a) サイトメガロウイルスへの感染，感染再燃ともに，MedDRA version 22.1 では PT サイトメガロウイルス感染にコーディングされた。

Table 2-24 急性 GVHD の重篤な有害事象（RUX overall の被験者で発現率 2%以上）（C2301 試験及び 271 試験，SAF）

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
合計	139 (69.2)	59 (83.1)
敗血症	19 (9.5)	9 (12.7)
敗血症性ショック	13 (6.5)	3 (4.2)
呼吸不全	12 (6.0)	7 (9.9)
発熱	10 (5.0)	8 (11.3)
肺炎	9 (4.5)	9 (12.7)
下痢	8 (4.0)	3 (4.2)
急性腎障害	5 (2.5)	4 (5.6)
呼吸窮迫	5 (2.5)	0
サイトメガロウイルス感染再燃	5 (2.5)	0
胃腸出血	4 (2.0)	1 (1.4)
血小板減少症	4 (2.0)	1 (1.4)
サイトメガロウイルス感染	4 (2.0)	0
汎血球減少症	4 (2.0)	0

Source: 5.3.5.3-4-Table 2.1-5.2
MedDRA version 23.0
RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

271 試験（参考資料）

重篤な有害事象の一覧を Table 7-8 に示す。

重篤な有害事象の発現率は 83.1%であった。最も多かった事象は肺炎，敗血症（各 12.7%）であり，次いで発熱（11.3%），呼吸不全（9.9%）であった（Table 2-24）。

2.1.3.2 慢性 GVHD

D2301 試験の重篤な有害事象の一覧を Table 7-12 に示す。

C7D1 までの重篤な有害事象の発現率は RUX 群で 33.3%，BAT 群で 36.7%であり，群間で同程度であった（Table 2-25）。PT 別の各事象の発現率は群間で同程度であった。重篤な副作用の発現率は RUX 群で 16.4%，BAT 群で 10.1%であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.6）。

データカットオフまでの重篤な有害事象の発現率は RUX 群で 43.6%，BAT 群で 39.9%（以下同順）であり，群間で同程度であった（Table 7-11）。重篤な有害事象の EAIR は RUX 群で BAT 群と比べて低かった（60.3，76.6）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.28）。いずれかの群で発現率が 2%以上であった PT 別事象は，肺炎（12.7%，8.9%），発熱（6.7%，2.5%），下気道感染（2.4%，0.6%），気管支肺アスペルギルス症（1.2%，2.5%）であった。各事象の発現率は群間で同程度であった。RUX crossover の被験者では，重篤な有害事象の発現率は 36.1%であり，主な事象は肺炎，発熱（各 6.6%），貧血（4.9%）であった。RUX crossover の被験者で特有の事象は認められなかった。

データカットオフまでの RUX overall の被験者の重篤な有害事象の発現率は 41.6%であった（Table 2-26）。発現率が最も高かった事象は肺炎（11.1%）であり，次いで発熱（6.6%），呼吸困難，下気道感染（各 2.2%）であった。重篤な有害事象のうち，RUX のみと関連ありと判断された事象は 21 名で報告された。21 名中 5 名は重篤な有害事象により投与を中止し（同一被験者で発現した血中クレアチニン増加及び血小板減少症，各 1 名に発現した頭蓋内出血，肺炎，急性腎障害，心房粗動），うち 1 名（頭蓋内出血）は転帰が死亡であった。その他の被験者では，RUX のみと関連する重篤な副作用は，RUX の用量調節，休薬，又は加療により投与継続が可能であった（5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。

Table 2-25 C7D1 までの慢性 GVHD の重篤な有害事象（RUX 群で発現率 1%以上）（D2301 試験，SAF）

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
合計	55 (33.3)	58 (36.7)
肺炎	13 (7.9)	13 (8.2)
発熱	8 (4.8)	3 (1.9)
下気道感染	4 (2.4)	0
発熱性好中球減少症	3 (1.8)	2 (1.3)
急性腎障害	2 (1.2)	3 (1.9)
背部痛	2 (1.2)	0
気管支肺アスペルギルス症	2 (1.2)	4 (2.5)
サイトメガロウイルス感染再燃	2 (1.2)	1 (0.6)
脱水	2 (1.2)	0
呼吸困難	2 (1.2)	2 (1.3)
低血圧	2 (1.2)	0

PT	RUX N = 165 n (%)	BAT N = 158 n (%)
気胸	2 (1.2)	0
肺塞栓症	2 (1.2)	3 (1.9)
呼吸不全	2 (1.2)	0
敗血症	2 (1.2)	1 (0.6)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-1.5
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-26 慢性 GVHD の重篤な有害事象（発現率 1%以上）（D2301 試験, SAF, データカットオフまで）

PT	RUX overall N = 226 n (%)
合計	94 (41.6)
肺炎	25 (11.1)
発熱	15 (6.6)
呼吸困難	5 (2.2)
下気道感染	5 (2.2)
発熱性好中球減少症	4 (1.8)
腹痛	4 (1.8)
貧血	4 (1.8)
気道感染	4 (1.8)
敗血症	3 (1.3)
呼吸不全	3 (1.3)
肺塞栓症	3 (1.3)
上気道感染	3 (1.3)
背部痛	3 (1.3)
帯状疱疹	3 (1.3)
気胸	3 (1.3)

Source: 5.3.5.3-4-Table 2.1-5.2
MedDRA version 23.0
発現率の降順

2.1.4 その他の重要な有害事象

2.1.4.1 投与中止に至った有害事象

2.1.4.1.1 急性 GVHD

C2301 試験の Day 28 までの投与中止に至った有害事象の発現率は RUX 群で 11.2%，BAT 群で 4.0%であった（Table 2-27）。PT 別事象は，RUX 群ではいずれの事象も発現率は 2%以下と低く，BAT 群ではいずれの事象も 1 名（0.7%）での発現であった。

データカットオフ 2 までの RUX overall の被験者の投与中止に至った有害事象の発現率は29.4%であった（Table 2-28）。発現率が最も高かった事象は血小板減少症（3.0%）であり，次いで敗血症，好中球減少症（各 2.5%）であった。投与中止に至った有害事象のうち，RUX のみと関連ありと判断された事象は 20 名で報告され，その内訳は血小板減少症（3 名），好中球減少症，白血球減少症，貧血（各 2 名），細菌性敗血症，血小板数減少，全血球数減少，好中球数減少，汎血球減少症，胃腸出血，下部消化管出血，ウイルス感染，ウイルス性膀胱炎，肺炎，脳炎，肝細胞損傷，移植片機能損失，トランスアミナーゼ上昇（各 1 名）であった。このうち，肺炎，細菌性敗血症，脳炎は転帰が死亡であり（脳炎は RUX 最終投与後 30 日より後の死亡），好中球減少症（2 名），好中球数減少，血小板減少症，血小板数減少，全血球数減少，汎血球減少症，肝細胞損傷，移植片機能損失（各 1 名）は最終報告時点で転帰が未消失であった（5.3.5.1-1-C2301 試験 CSR2-Listing 16.2.7-1.1）。

Table 2-27 Day 28 までの急性 GVHD の投与中止に至った有害事象（C2301 試験, SAF）

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
合計	17 (11.2)	6 (4.0)
貧血	3 (2.0)	1 (0.7)
血小板減少症	3 (2.0)	0
汎血球減少症	2 (1.3)	0
心停止	1 (0.7)	0
認知障害	1 (0.7)	0
ウイルス性膀胱炎	1 (0.7)	0
全身健康状態異常	1 (0.7)	0
低酸素症	1 (0.7)	0
腸閉塞	1 (0.7)	0
白血球減少症	1 (0.7)	0
微小血管症	1 (0.7)	0
好中球数減少	1 (0.7)	0
クレブシエラ菌性肺炎	1 (0.7)	0
シュードモナス性敗血症	1 (0.7)	0
肺塞栓症	1 (0.7)	0
発熱	1 (0.7)	0
細菌性気道感染	1 (0.7)	0
敗血症	1 (0.7)	0
頻脈	1 (0.7)	0
ウイルス感染	1 (0.7)	0
急性呼吸不全	0	1 (0.7)
エプスタイン・バーウイルス感染	0	1 (0.7)
溶血	0	1 (0.7)

PT	RUX N = 152 n (%)	BAT N = 150 n (%)
ミオパチー	0	1 (0.7)
肺炎	0	1 (0.7)
腎盂腎炎	0	1 (0.7)
呼吸不全	0	1 (0.7)
敗血症性ショック	0	1 (0.7)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.6
MedDRA version 22.1
RUX 群の発現率の降順

Table 2-28 急性 GVHD の投与中止に至った有害事象（RUX overall の被験者で発現率 1%以上）（C2301 試験及び 271 試験，SAF）

PT	C2301 試験 RUX overall N = 201 n (%)	271 試験 RUX N = 71 n (%)
合計	59 (29.4)	23 (32.4)
血小板減少症	6 (3.0)	1 (1.4)
敗血症	5 (2.5)	4 (5.6)
好中球減少症	5 (2.5)	0
呼吸不全	3 (1.5)	2 (2.8)
貧血	3 (1.5)	1 (1.4)
汎血球減少症	3 (1.5)	0
血小板数減少	3 (1.5)	1 (1.4)
細菌性敗血症	2 (1.0)	0
サイトメガロウイルス性大腸炎	2 (1.0)	0
胃腸出血	2 (1.0)	0
腸閉塞	2 (1.0)	0
白血球減少症	2 (1.0)	0
好中球数減少	2 (1.0)	0
移植片機能損失	2 (1.0)	0

Source: 5.3.5.3-4-Table 2.1-7.2
MedDRA version 23.0
RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

2.1.4.1.2 慢性 GVHD

D2301 試験の C7D1 までの投与中止に至った有害事象の発現率は RUX 群で 16.4%，BAT 群で 7.0%であった（Table 2-29）。PT 別の各事象の発現率は群間で同程度であった。

データカットオフまでの RUX overall の被験者の投与中止に至った有害事象の発現率は 18.1%であった（Table 2-30）。肺炎（4.0%）を除き，いずれの事象も発現率は 1%未満と低かった。投

与中止に至った有害事象のうち，RUX のみと関連ありと判断された事象は 11 名で報告され，その内訳はアラニンアミノトランスフェラーゼ増加（2 名），好中球数減少，血小板減少症，貧血，肺炎，頭蓋内出血，皮膚のつっぱり感，体温上昇，腎不全，急性腎障害，心房粗動，血中クレアチニン増加（各 1 名）であった。このうち，頭蓋内出血は転帰が死亡であり，皮膚のつっぱり感，体温上昇，腎不全（各 1 名）は最終報告時点で転帰が未消失であった（5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。

Table 2-29 C7D1 までの慢性 GVHD の投与中止に至った有害事象（D2301 試験，SAF）

PT	RUX N=165 n (%)	BAT N=158 n (%)
合計	27 (16.4)	11 (7.0)
肺炎	8 (4.8)	2 (1.3)
気胸	2 (1.2)	0
急性腎障害	1 (0.6)	0
アラニンアミノトランスフェラーゼ増加	1 (0.6)	0
貧血	1 (0.6)	1 (0.6)
心房粗動	1 (0.6)	0
体温上昇	1 (0.6)	0
脳膿瘍	1 (0.6)	0
クッシング様症状	1 (0.6)	0
全身健康状態悪化	1 (0.6)	1 (0.6)
イレウス	1 (0.6)	0
ウイルス性髄膜炎	1 (0.6)	0
好中球減少症	1 (0.6)	1 (0.6)
好中球数減少	1 (0.6)	0
細菌性肺炎	1 (0.6)	0
移植後リンパ増殖性障害	1 (0.6)	0
発熱	1 (0.6)	0
腎不全	1 (0.6)	0
呼吸不全	1 (0.6)	0
敗血症	1 (0.6)	0
敗血症性ショック	1 (0.6)	1 (0.6)
血栓症	1 (0.6)	0
中毒性表皮壊死融解症	1 (0.6)	0
非定型溶血性尿毒症症候群	0	1 (0.6)
下痢	0	1 (0.6)
微小血管症	0	1 (0.6)
多臓器機能不全症候群	0	1 (0.6)
血小板数減少	0	1 (0.6)
肺塞栓症	0	1 (0.6)

PT	RUX N=165 n (%)	BAT N=158 n (%)
血小板減少症	0	1 (0.6)
血栓性微小血管症	0	1 (0.6)
嘔吐	0	1 (0.6)
白血球数減少	0	1 (0.6)

Source: 5.3.5.1-2-D2301 試験-Table 14.3.1-1.7
MedDRA version 23.0
RUX 群の発現率の降順

Table 2-30 慢性 GVHD の投与中止に至った有害事象（2 名以上に発現）（D2301 試験，SAF，データカットオフまで）

PT	RUX overall N = 226 n (%)
合計	41 (18.1)
肺炎	9 (4.0)
血小板減少症	2 (0.9)
貧血	2 (0.9)
敗血症性ショック	2 (0.9)
アラニンアミノトランスフェラーゼ増加	2 (0.9)
頭蓋内出血	2 (0.9)
気胸	2 (0.9)

Source: 5.3.5.3-4-Table 2.1-7.2
MedDRA version 23.0
発現率の降順

2.1.4.2 用量調節又は休薬に至った有害事象

2.1.4.2.1 急性 GVHD

C2301 試験の Day 28 までの用量調節又は休薬に至った有害事象の発現率は RUX 群で 36.8%，BAT 群で 9.3%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.7）。RUX 群で発現率が最も高かった事象は血小板減少症（9.9%，0.7%）であり，次いで好中球減少症（8.6%，0.7%），血小板数減少（7.9%，2.0%）であった。BAT 群では血小板数減少を除き各事象 1～2 名（2%未満）での発現であった。なお，C2301 試験の治験実施計画書では用量調節及び休薬の基準を RUX のみに対して規定し，BAT の用量調節及び休薬は治験担当医師の判断による標準治療として実施されたことから，BAT 群との比較結果の解釈には注意を要する。

データカットオフ 2 までの RUX overall の被験者の用量調節又は休薬に至った有害事象の発現率は 53.7%であった（5.3.5.3-4-Table 2.1-8.2）。発現率が最も高かった事象は血小板減少症（14.9%）であり，次いで血小板数減少（10.4%），好中球減少症（9.0%）であった。

2.1.4.2.2 慢性 GVHD

D2301 試験の C7D1 までの用量調節又は休薬に至った有害事象の発現率は RUX 群で 37.6%，BAT 群で 16.5%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.8）。RUX 群で発現率が最も高かった事象は貧血（7.9%，0.6%）であり，次いで血中クレアチニン増加（6.1%，0%），好中球減少症（4.8%，1.3%）であった。BAT 群では発熱（2.4%，1.9%），悪心（0%，1.9%）を除き各事象 1～2 名（2%未満）での発現であった。なお，D2301 試験の治験実施計画書では用量調節及び休薬の基準を RUX のみに対して規定し，BAT の用量調節は治験担当医師の判断による標準治療として実施されたことから，BAT 群との比較結果の解釈には注意を要する。

データカットオフまでの RUX overall の被験者の用量調節又は休薬に至った有害事象の発現率は 39.8%であった（5.3.5.3-4-Table 2.1-8.2）。発現率が最も高かった事象は貧血（8.8%）であり，次いで好中球減少症（6.6%），血中クレアチニン増加（4.9%）であった。

2.1.4.3 治療を要した有害事象

2.1.4.3.1 急性 GVHD

C2301 試験のデータカットオフ 2 までの治療を要した有害事象の発現率は RUX 群で 97.4%，BAT 群で 93.3%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.18）。RUX 群で発現率が最も高かった事象は貧血（31.6%，26.0%）であり，次いでサイトメガロウイルス感染（30.3%，26.7%），血小板減少症（23.7%，15.3%）であった。各事象の発現率は群間で同程度であった。

データカットオフ 2 までの RUX overall の被験者の治療を要した有害事象の発現率は 97.0%であった（5.3.5.3-4-Table 2.1-9.2）。RUX 群で最も多かった事象は貧血（28.4%）であり，次いでサイトメガロウイルス感染再燃（21.9%），血小板減少症（20.4%）であった。

2.1.4.3.2 慢性 GVHD

D2301 試験の C7D1 までの治療を要した有害事象の発現率は RUX 群で 83.6%，BAT 群で 82.9%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.9）。RUX 群で発現率が最も高かった事象は高血圧（12.7%，9.5%）であり，次いで貧血（11.5%，7.0%），発熱（11.5%，8.2%），肺炎（9.7%，12.0%）であった。各事象の発現率は群間で同程度であった。

データカットオフまでの RUX overall の被験者の治療を要した有害事象の発現率は 85.4%であった（5.3.5.3-4-Table 2.1-9.2）。RUX 群で最も多かった事象は発熱（15.0%）であり，次いで肺炎（14.2%），貧血（13.7%）であった。

2.1.5 器官別又は症候群別有害事象の解析

急性 GVHD 患者，慢性 GVHD 患者での RUX に関連した臨床的に注目すべき有害事象を検討するため，Table 1-3 に示す事象を包括的に評価した。結果概要を Table 2-31 に示し，各事象の詳細を以降の各項で急性 GVHD，慢性 GVHD の順に示す。臨床的に注目すべき有害事象の発現状況

は RUX の既知の安全性プロファイルと類似しており，感染症及び血球減少が高頻度で認められた。なお，成長遅延，進行性多巣性白質脳症，及び結核は C2301 試験，D2301 試験，271 試験のいずれの試験でも認められなかった。NMSC の発現は少なかったため，悪性腫瘍（2.1.5.4.5 項）で評価した。

Table 2-31 臨床的に注目すべき有害事象の要約（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201		271 試験 RUX N = 71		D2301 試験 RUX overall N = 226	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
感染症						
感染症（結核を除く）	159 (79.1)	104 (51.7)	58 (81.7)	46 (64.8)	157 (69.5)	59 (26.1)
肺炎	36 (17.9)	26 (12.9)	17 (23.9)	15 (21.1)	47 (20.8)	36 (15.9)
日和見感染	67 (33.3)	26 (12.9)	15 (21.1)	7 (9.9)	26 (11.5)	7 (3.1)
サイトメガロウイルス感染／感染症	65 (32.3)	23 (11.4)	14 (19.7)	6 (8.5)	20 (8.8)	3 (1.3)
尿路感染	36 (17.9)	13 (6.5)	10 (14.1)	6 (8.5)	21 (9.3)	3 (1.3)
敗血症／敗血症性ショック	51 (25.4)	44 (21.9)	16 (22.5)	15 (21.1)	8 (3.5)	8 (3.5)
帯状疱疹	4 (2.0)	2 (1.0)	0	0	4 (1.8)	3 (1.3)
B 型肝炎の再活性化	1 (0.5)	0	0	0	1 (0.4)	0
その他の感染	128 (63.7)	60 (29.9)	42 (59.2)	30 (42.3)	131 (58.0)	26 (11.5)
血球減少						
血小板減少症	107 (53.2)	94 (46.8)	44 (62.0)	38 (53.5)	45 (19.9)	33 (14.6)
赤血球減少症	78 (38.8)	64 (31.8)	46 (64.8)	36 (50.7)	65 (28.8)	31 (13.7)
白血球減少症	89 (44.3)	82 (40.8)	42 (59.2)	35 (49.3)	50 (22.1)	37 (16.4)
その他の血球減少	18 (9.0)	14 (7.0)	0	0	2 (0.9)	1 (0.4)
出血性事象						
出血性事象	74 (36.8)	25 (12.4)	35 (49.3)	14 (19.7)	26 (11.5)	6 (2.7)
胃腸出血	33 (16.4)	16 (8.0)	19 (26.8)	9 (12.7)	2 (0.9)	2 (0.9)
挫傷	21 (10.4)	2 (1.0)	10 (14.1)	1 (1.4)	9 (4.0)	0
頭蓋内出血	2 (1.0)	2 (1.0)	1 (1.4)	0	2 (0.9)	2 (0.9)
その他の出血性事象	35 (17.4)	5 (2.5)	22 (31.0)	4 (5.6)	15 (6.6)	2 (0.9)
その他						
トランスアミナーゼ上昇	30 (14.9)	13 (6.5)	22 (31.0)	6 (8.5)	39 (17.3)	14 (6.2)
脂質異常	21 (10.4)	11 (5.5)	9 (12.7)	3 (4.2)	40 (17.7)	13 (5.8)
高血圧	27 (13.4)	11 (5.5)	16 (22.5)	10 (14.1)	34 (15.0)	13 (5.8)
血栓塞栓症	25 (12.4)	14 (7.0)	16 (22.5)	9 (12.7)	10 (4.4)	5 (2.2)
悪性腫瘍	4 (2.0)	3 (1.5)	5 (7.0)	3 (4.2)	4 (1.8)	1 (0.4)
NMSC	0	0	1 (1.4)	0	3 (1.3)	1 (0.4)
めまい	12 (6.0)	0	10 (14.1)	0	7 (3.1)	0
骨折	7 (3.5)	3 (1.5)	5 (7.0)	2 (2.8)	8 (3.5)	1 (0.4)

	C2301 試験 RUX overall N = 201		271 試験 RUX N = 71		D2301 試験 RUX overall N = 226	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
体重増加	3 (1.5)	0	3 (4.2)	1 (1.4)	8 (3.5)	0

Source: 5.3.5.3-4-Table 2.1-10.2
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
MedDRA version 23.0

2.1.5.1 感染症

感染症は HSCT 後の患者で高頻度に認められる合併症である。HSCT 後の患者では，GVHD 罹患，並びに GVHD の予防又は治療のための免疫抑制剤の使用により，ウイルスや真菌に対して易感染状態となる。また，骨髄破壊的移植前処置による骨髄抑制，サイトメガロウイルス感染，及び治療に伴って，細菌感染の頻度が増加する可能性がある（García-Cadenas et al. 2017，Young et al. 2016）。

感染症（結核を除く）について，関連する PT 別事象をグループ化して定義し（5.3.5.3-4-Listing 1），評価した結果を以下に示す。また，肺炎，日和見感染，サイトメガロウイルス感染／感染症，尿路感染，敗血症／敗血症性ショック，結核，帯状疱疹，B 型肝炎の再活性化の関連する PT 別事象をグループ化して定義し，別途検討した結果も示す。さらに，病原体別（ウイルス，細菌，真菌，不明）の感染症について検討した結果を示す。なお，複数のグループで定義される PT 別事象もある。「その他の感染」は，「感染症（結核を除く）」と重複する PT が多いため，「感染症（結核を除く）」で評価した。

急性 GVHD

C2301 試験の Day 28 までの感染症（結核を除く）の発現率は RUX 群で 61.2%，BAT 群で 58.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.10）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 32.2%，BAT 群 37.3%，以下同順）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率に群間で大きな違いはなかった（17.1%，8.7%）。死亡に至った事象の発現率は群間で同程度であり（5.9%，5.3%），RUX 群での主な PT 別事象は敗血症（2.0%，1.3%），敗血症性ショック（2.0%，2.0%）で，いずれの事象も発現率は群間で同程度であった。重篤な事象の発現率は群間で同程度であり（21.7%，17.3%），敗血症を除き各事象 3%未満と低かった。重篤な敗血症の発現率は群間で同程度であった（5.3%，2.0%）。投与中止に至った事象の発現率は低かった（3.3%，2.0%）。

データカットオフ 2 までの感染症（結核を除く）の発現率は RUX 群で 82.2%，BAT 群で 71.3%であった。EAIR は RUX 群で BAT 群と比べて低かった（681.9，787.0）（5.3.5.3-4-Table 2.1-12.10）。

データカットオフ 2 までの RUX overall の被験者の感染症（結核を除く）の発現率は 79.1%であった（Table 2-32）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-1）。副作用の発現率は 24.9%であり，最も多かった事象はサイトメガロウイルス感染再燃，敗血症（各 4.0%）であった（5.3.5.3-4-Table 2.1-13.10）。死亡に至った事象の発現率は 12.9%（26 名）であり，敗血症（5.0%），敗血症性ショック（3.5%），肺炎，シュードモナス性敗血症（各 1.0%）を除き各事象 1 名での発現であった。このうち 3 名（敗血症，肺炎，細菌性敗血症，各 1 名）では，死亡に至った事象は RUX に関連すると判断されたが，これらの被験者では急性 GVHD の症状，直近の外傷性損傷による入院，免疫抑制療法の併用があった（2.1.2.2.1 項）。重篤な事象の発現率は 39.8%であり，敗血症（9.5%），敗血症性ショック（6.5%），肺炎（4.5%）が多かった。投与中止に至った事象は 8.5%（17 名）で認められたが，このうち RUX と関連ありと判断された事象は 5 名に認められ，うち 2 名は加療により回復した。感染症の多くは RUX の用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-32 急性 GVHD の感染症（結核を除く）（RUX overall の被験者で発現率 5%以上）（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	159 (79.1)	58 (81.7)
95% CI	(72.8, 84.5)	(70.7, 89.9)
EAIR, n (incidence rate per 100 patient treatment years)	159 (652.2)	58 (652.6)
重症度, n (%)		
Grade 3	55 (27.4)	26 (36.6)
Grade 4	23 (11.4)	20 (28.2)
Grade 5	26 (12.9)	NA
副作用, n (%)	50 (24.9)	21 (29.6)
重篤な有害事象, n (%)	80 (39.8)	36 (50.7)
治験治療に対する処置, n (%)		
投与中止	17 (8.5)	9 (12.7)
減量	2 (1.0)	2 (2.8)
増量	0	0
休薬	20 (10.0)	8 (11.3)
不変/NA/不明	153 (76.1)	46 (64.8)
治療を要した有害事象, n (%)	150 (74.6)	56 (78.9)
転帰, n (%)		
回復/消失	116 (57.7)	42 (59.2)
軽快	11 (5.5)	5 (7.0)
未回復/未消失	69 (34.3)	29 (40.8)
回復/消失したが後遺症あり	5 (2.5)	1 (1.4)
死亡	26 (12.9)	10 (14.1)
不明	3 (1.5)	0

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
PT 別有害事象		
サイトメガロウイルス感染再燃	45 (22.4)	4 (5.6)
敗血症	25 (12.4)	10 (14.1)
肺炎	21 (10.4)	11 (15.5)
尿路感染	17 (8.5)	6 (8.5)
サイトメガロウイルス感染	15 (7.5)	5 (7.0)
医療機器関連感染	14 (7.0)	4 (5.6)
敗血症性ショック	13 (6.5)	4 (5.6)

Source: 5.3.5.3-4-Table 2.1-13.10
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果
治験治療に対する処置及び転帰は，複数の有害事象を発現した被験者ではすべての該当カテゴリでカウントした。

慢性 GVHD

D2301 試験の C7D1 までの感染症（結核を除く）の発現率は RUX 群で 62.4%，BAT 群で 58.2%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.10）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 20.6%，BAT 群 20.9%，以下同順）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなかった（27.3%，11.4%）。死亡に至った事象の発現率は群間で同程度であり（5.5%，4.4%），RUX 群での主な PT 別事象は肺炎（3.0%，1.9%）で，いずれの事象も発現率は群間で同程度であった。重篤な事象の発現率は群間で同程度であり（20.6%，20.3%），肺炎を除き各事象 3%未満と低かった。重篤な肺炎の発現率は群間で同程度であった（7.9%，8.2%）。投与中止に至った事象の発現率は RUX 群で 8.5%，BAT 群で 1.9%であった。

データカットオフまでの感染症（結核を除く）の発現率は RUX 群で 72.1%，BAT 群で 65.8%であった。EAIR は RUX 群で BAT 群と比べて低かった（169.0，185.0）（5.3.5.3-4-Table 2.1-12.10）。

データカットオフまでの RUX overall の被験者の感染症（結核を除く）の発現率は 69.5%であった（Table 2-33）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-1）。副作用の発現率は 26.5%であり，最も多かった事象は肺炎（5.8%）であった（5.3.5.3-4-Table 2.1-13.10）。死亡に至った事象の発現率は 5.3%（12 名）であり，肺炎（2.2%）を除き各事象 1 名での発現であった。このうち RUX と関連ありと判断された事象は 3 名（肺炎 2 名，気管支肺アスペルギルス症 1 名）で認められた（5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。重篤な事象の発現率は 27.0%であり，肺炎（11.1%），下気道感染（2.2%），気道感染（1.8%）が多かった。投与中止に至った事象は 8.0%で認められたが，このうち RUX と関連ありと判断された事象は 1 名のみ

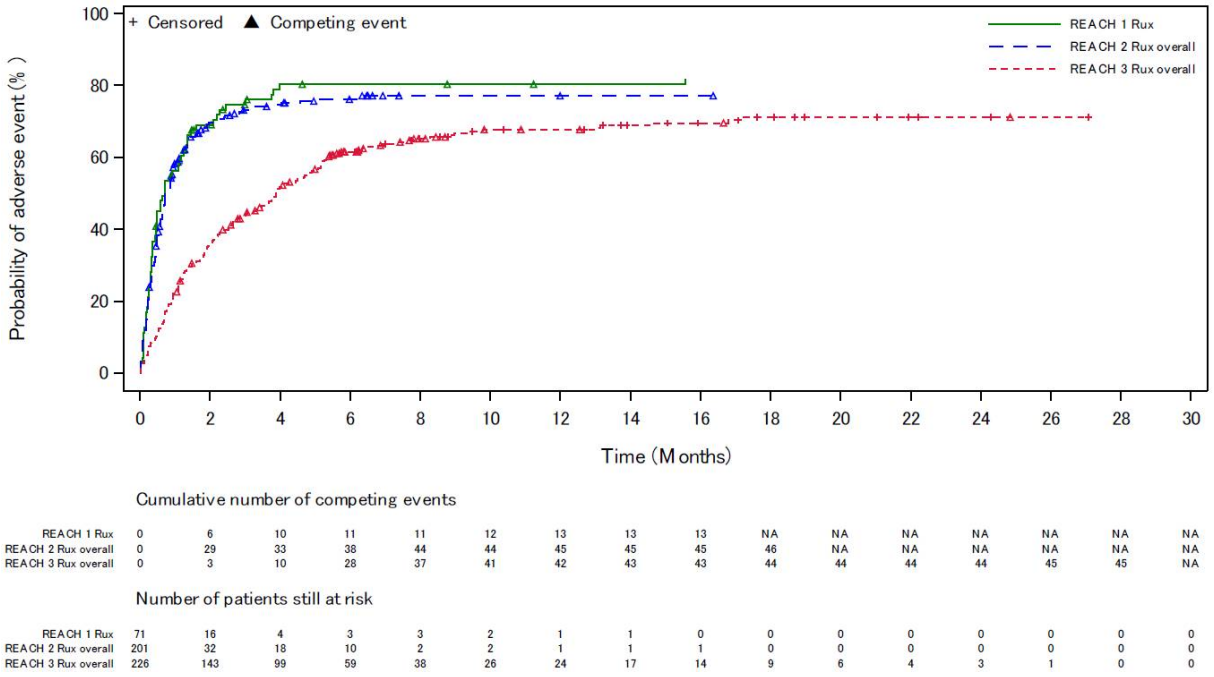
であり，加療により軽快した。感染症の多くは RUX の用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-33 慢性 GVHD の感染症（結核を除く）（発現率 5%以上）（D2301 試験, SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	157 (69.5)
95% CI	(63.0, 75.4)
EAIR, n (incidence rate per 100 patient treatment years)	157 (161.2)
重症度, n (%)	
Grade 3	42 (18.6)
Grade 4	5 (2.2)
Grade 5	12 (5.3)
副作用, n (%)	60 (26.5)
重篤な有害事象, n (%)	61 (27.0)
治験治療に対する処置, n (%)	
投与中止	18 (8.0)
減量	11 (4.9)
増量	1 (0.4)
休薬	18 (8.0)
不変/NA/不明	148 (65.5)
治療を要した有害事象, n (%)	139 (61.5)
転帰, n (%)	
回復/消失	131 (58.0)
軽快	16 (7.1)
未回復/未消失	32 (14.2)
回復/消失したが後遺症あり	2 (0.9)
死亡	12 (5.3)
不明	0
欠測	2 (0.9)
PT 別有害事象	
肺炎	33 (14.6)
上気道感染	30 (13.3)
インフルエンザ	18 (8.0)
上咽頭炎	16 (7.1)
尿路感染	15 (6.6)
気管支炎	15 (6.6)
サイトメガロウイルス感染再燃	12 (5.3)
結膜炎	12 (5.3)

Source: 5.3.5.3-4-Table 2.1-13.10
MedDRA version 23.0
PT は発現率の降順

Figure 2-1　感染症（結核を除く）の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Cumulative number of competing events

REACH 1 Rux	0	6	10	11	11	12	13	13	13	NA	NA	NA	NA	NA	NA	NA
REACH 2 Rux overall	0	29	33	38	44	44	45	45	45	46	NA	NA	NA	NA	NA	NA
REACH 3 Rux overall	0	3	10	28	37	41	42	43	43	44	44	44	44	45	45	NA

Number of patients still at risk

REACH 1 Rux	71	16	4	3	3	2	1	1	0	0	0	0	0	0	0	0
REACH 2 Rux overall	201	32	18	10	2	2	1	1	1	0	0	0	0	0	0	0
REACH 3 Rux overall	226	143	99	59	38	26	24	17	14	9	6	4	3	1	0	0

Source: 5.3.5.3-4-Figure 2.1-7.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.1.1 肺炎

急性 GVHD

C2301 試験の Day 28 までの肺炎の発現率は RUX 群で 7.2%，BAT 群で 10.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.15）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 5.9%，BAT 群 8.0%，以下同順）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率はいずれの群も低かった（2.6%，2.0%）。死亡に至った事象の発現率はいずれの群も低く（0.7%，2.0%），PT 別事象はいずれの群も肺炎であった。重篤な肺炎の発現率は群間で同程度であった（3.9%，4.0%）。

データカットオフ 2 までの肺炎の発現率は RUX 群で 17.8%，BAT 群で 17.3%であった。EAIR は，RUX 群で 60.4，BAT 群で 92.4 であった（5.3.5.3-4-Table 2.1-12.15）。

データカットオフ 2 までの RUX overall の被験者の肺炎の発現率は 17.9%であった（Table 2-34）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-2）。副作用の発現率は 6.0%であった。死亡に至った事象の発現率は 2.0%であり，PT 別事象は肺炎（1.0%），特発性肺炎症候群，肺臓炎（各 0.5%）であった。重篤な事象の発現率は 10.4%であり，肺炎（4.5%），気管支肺アスペルギルス症，特発性肺炎症候群，肺臓炎，クレブシエラ菌性肺炎（各

1.0%）を除き各事象 1 名での発現であった。本事象により RUX の投与を中止した被験者は少なく（1.5%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-34 急性 GVHD の肺炎（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	36 (17.9)	17 (23.9)
95% CI	(12.9, 23.9)	(14.6, 35.5)
EAIR, n (incidence rate per 100 patient treatment years)	36 (61.7)	17 (67.3)
重症度, n (%)		
Grade 3	15 (7.5)	10 (14.1)
Grade 4	7 (3.5)	5 (7.0)
Grade 5	4 (2.0)	NA
副作用, n (%)	12 (6.0)	4 (5.6)
重篤な有害事象, n (%)	21 (10.4)	11 (15.5)
治験治療に対する処置, n (%)		
投与中止	3 (1.5)	1 (1.4)
減量	0	1 (1.4)
増量	0	0
休薬	6 (3.0)	0
不変/NA/不明	31 (15.4)	16 (22.5)
治療を要した有害事象, n (%)	35 (17.4)	16 (22.5)
転帰, n (%)		
回復/消失	21 (10.4)	8 (11.3)
軽快	1 (0.5)	1 (1.4)
未回復/未消失	14 (7.0)	6 (8.5)
回復/消失したが後遺症あり	0	1 (1.4)
死亡	4 (2.0)	3 (4.2)
不明	0	0
PT 別有害事象		
肺炎	21 (10.4)	11 (15.5)
気管支肺アスペルギルス症	4 (2.0)	3 (4.2)
特発性肺炎症候群	3 (1.5)	0
肺臓炎	2 (1.0)	1 (1.4)
ニューモシスチス・イロベチイ肺炎	2 (1.0)	0
真菌性下気道感染	2 (1.0)	0
クレブシエラ菌性肺炎	2 (1.0)	0
メタニューモウイルス感染	1 (0.5)	0
細菌性肺炎	1 (0.5)	1 (1.4)
真菌性肺炎	1 (0.5)	0
器質化肺炎	1 (0.5)	0
ウイルス性下気道感染	1 (0.5)	0

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
肺硬化	1 (0.5)	0
肺炎球菌性肺炎	1 (0.5)	0
RS ウイルス肺炎	1 (0.5)	0
レンサ球菌性肺炎	1 (0.5)	0
細菌性下気道感染	0	1 (1.4)
肺浸潤	0	1 (1.4)
誤嚥性肺炎	0	1 (1.4)
レジオネラ菌性肺炎	0	1 (1.4)

Source: 5.3.5.3-4-Table 2.1-13.15
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの肺炎の発現率は RUX 群で 19.4%，BAT 群で 17.1%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.15）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同じであった（RUX 群 13.3%，BAT 群 13.3%，以下同順）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなかった（10.3%，4.4%）。死亡に至った事象の発現率は群間で同程度であり（4.2%，1.9%），内訳は肺炎（3.0%，1.9%），気管支肺アスペルギルス症，細菌性肺炎（各 0.6%，0%）であった。重篤な事象の発現率は群間で同程度であり（13.9%，12.0%），肺炎を除き各事象 3%未満と低かった。重篤な肺炎の発現率は群間で同程度であった（7.9%，8.2%）。

データカットオフまでの肺炎の発現率は RUX 群で 23.6%，BAT 群で 17.7%であった。EAIR は RUX 群で 27.5，BAT 群で 29.0 であった（5.3.5.3-4-Table 2.1-12.15）。

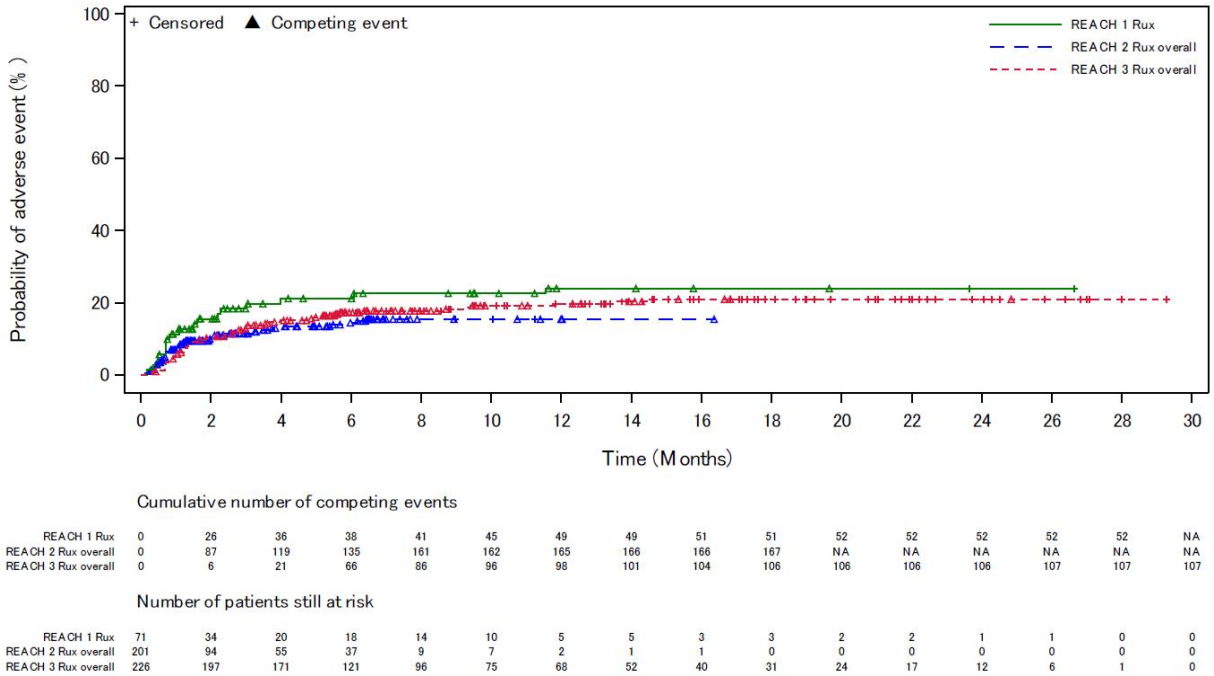
データカットオフまでの RUX overall の被験者の肺炎の発現率は 20.8%であった（Table 2-35）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-2）。副作用の発現率は 10.2%であった。死亡に至った事象の発現率は 3.1%であり，内訳は肺炎（2.2%），気管支肺アスペルギルス症，細菌性肺炎（各 0.4%）であった。重篤な事象の発現率は 15.5%であり，肺炎（11.1%），下気道感染（2.2%）を除き各事象 1～2 名での発現であった。本事象により RUX の投与を中止した被験者は少なく（4.4%），多くの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-35 慢性 GVHD の肺炎（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	47 (20.8)
95% CI	(15.7, 26.7)
EAIR, n (incidence rate per 100 patient treatment years)	47 (25.0)
重症度, n (%)	
Grade 3	27 (11.9)
Grade 4	2 (0.9)
Grade 5	7 (3.1)
副作用, n (%)	23 (10.2)
重篤な有害事象, n (%)	35 (15.5)
治験治療に対する処置, n (%)	
投与中止	10 (4.4)
減量	5 (2.2)
増量	0
休薬	9 (4.0)
不変/NA/不明	35 (15.5)
治療を要した有害事象, n (%)	47 (20.8)
転帰, n (%)	
回復/消失	28 (12.4)
軽快	6 (2.7)
未回復/未消失	8 (3.5)
回復/消失したが後遺症あり	1 (0.4)
死亡	7 (3.1)
不明	0
PT 別有害事象	
肺炎	33 (14.6)
下気道感染	7 (3.1)
肺臓炎	3 (1.3)
気管支肺アスペルギルス症	2 (0.9)
メタニューモウイルス感染	2 (0.9)
真菌性肺炎	2 (0.9)
ニューモシスチス・イロベチイ肺炎	1 (0.4)
細菌性肺炎	1 (0.4)
器質化肺炎	1 (0.4)
サイトメガロウイルス性肺炎	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.15
MedDRA version 23.0
PT は発現率の降順

Figure 2-2　　肺炎の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-10.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.1.2 日和見感染

急性 GVHD

C2301 試験の Day 28 までの日和見感染の発現率は RUX 群で 27.0%，BAT 群で 22.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.14）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 4.6%，BAT 群 4.0%，以下同順）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率に群間で大きな違いはなかった（5.9%，4.7%）。死亡に至った事象はなく，重篤な事象の発現率は群間で同程度であった（4.6%，4.0%）。

データカットオフ 2 までの日和見感染の発現率は RUX 群で 34.9%，BAT 群で 26.7%であった。EAIR は RUX 群で 148.9，BAT 群で 166.8 であった（5.3.5.3-4-Table 2.1-12.14）。

データカットオフ 2 までの RUX overall の被験者の日和見感染の発現率は 33.3%であった（Table 2-36）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-3）。副作用の発現率は 7.5%であった。死亡に至った事象はなく，重篤な事象の発現率は 7.5%であり，サイトメガロウイルス感染再燃（2.5%），サイトメガロウイルス性大腸炎（1.5%），気管支肺アスペルギルス症，ムコール症（各 1.0%），アスペルギルス感染，ニューモシスチス・イロベチイ肺炎，脳アスペルギルス症，サイトメガロウイルス性小腸炎，RS ウイルス肺炎（各 0.5%）で

あった。本事象により RUX の投与を中止した被験者は少なく（1.5%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-36 急性 GVHD の日和見感染（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	67 (33.3)	15 (21.1)
95% CI	(26.9, 40.3)	(12.3, 32.4)
EAIR, n (incidence rate per 100 patient treatment years)	67 (145.9)	15 (58.2)
重症度, n (%)		
Grade 3	25 (12.4)	5 (7.0)
Grade 4	1 (0.5)	2 (2.8)
Grade 5	0	NA
副作用, n (%)	15 (7.5)	4 (5.6)
重篤な有害事象, n (%)	15 (7.5)	3 (4.2)
治験治療に対する処置, n (%)		
投与中止	3 (1.5)	0
減量	0	1 (1.4)
増量	0	0
休薬	1 (0.5)	1 (1.4)
不変/NA/不明	66 (32.8)	13 (18.3)
治療を要した有害事象, n (%)	62 (30.8)	15 (21.1)
転帰, n (%)		
回復/消失	40 (19.9)	6 (8.5)
軽快	5 (2.5)	1 (1.4)
未回復/未消失	25 (12.4)	7 (9.9)
回復/消失したが後遺症あり	2 (1.0)	1 (1.4)
死亡	0	0
不明	0	0
PT 別有害事象		
サイトメガロウイルス感染再燃	45 (22.4)	4 (5.6)
エプスタイン・バーウイルス感染再燃	9 (4.5)	0
気管支肺アスペルギルス症	4 (2.0)	3 (4.2)
サイトメガロウイルス性大腸炎	4 (2.0)	0
サイトメガロウイルス血症	2 (1.0)	4 (5.6)
サイトメガロウイルス性小腸炎	2 (1.0)	0
ニューモシスチス・イロベチイ肺炎	2 (1.0)	0
ムコール症	2 (1.0)	0
全身性カンジダ	2 (1.0)	0
RS ウイルス感染	1 (0.5)	2 (2.8)
アスペルギルス感染	1 (0.5)	0
食道カンジダ症	1 (0.5)	1 (1.4)

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
カンジダ性敗血症	1 (0.5)	0
脳アスペルギルス症	1 (0.5)	0
サイトメガロウイルス性消化管感染	1 (0.5)	0
フサリウム感染	1 (0.5)	0
RS ウイルス肺炎	1 (0.5)	0
クリプトスポリジウム感染	0	1 (1.4)
サイトメガロウイルス性脈絡網膜炎	0	1 (1.4)

Source: 5.3.5.3-4-Table 2.1-13.14
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの日和見感染の発現率は RUX 群で 11.5%，BAT 群で 12.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.14）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 3.0%，BAT 群 3.2%，以下同順）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなかった（3.6%，1.9%）。死亡に至った事象は少なく（0.6%，0%），重篤な事象の発現率は群間で同程度であった（3.6%，3.8%）。

データカットオフまでの日和見感染の発現率は RUX 群で 12.7%，BAT 群で 13.3%であった。EAIR は RUX 群で 14.1，BAT 群で 22.2 であった（5.3.5.3-4-Table 2.1-12.14）。

データカットオフまでの RUX overall の被験者の日和見感染の発現率は 11.5%であった（Table 2-37）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-3）。副作用の発現率は 4.0%であった。死亡に至った事象の発現率は 0.9%であり，アスペルギルス感染，気管支肺アスペルギルス症（各 0.4%）であった。重篤な事象の発現率は 3.5%であり，サイトメガロウイルス感染再燃，気管支肺アスペルギルス症（各 0.9%），アスペルギルス感染，ニューモシスチス・イロベチイ肺炎，クリプトコッカス性髄膜炎，マイコバクテリア感染，サイトメガロウイルス性肺炎（各 0.4%）であった。本事象により RUX の投与を中止した被験者は少なく（0.4%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

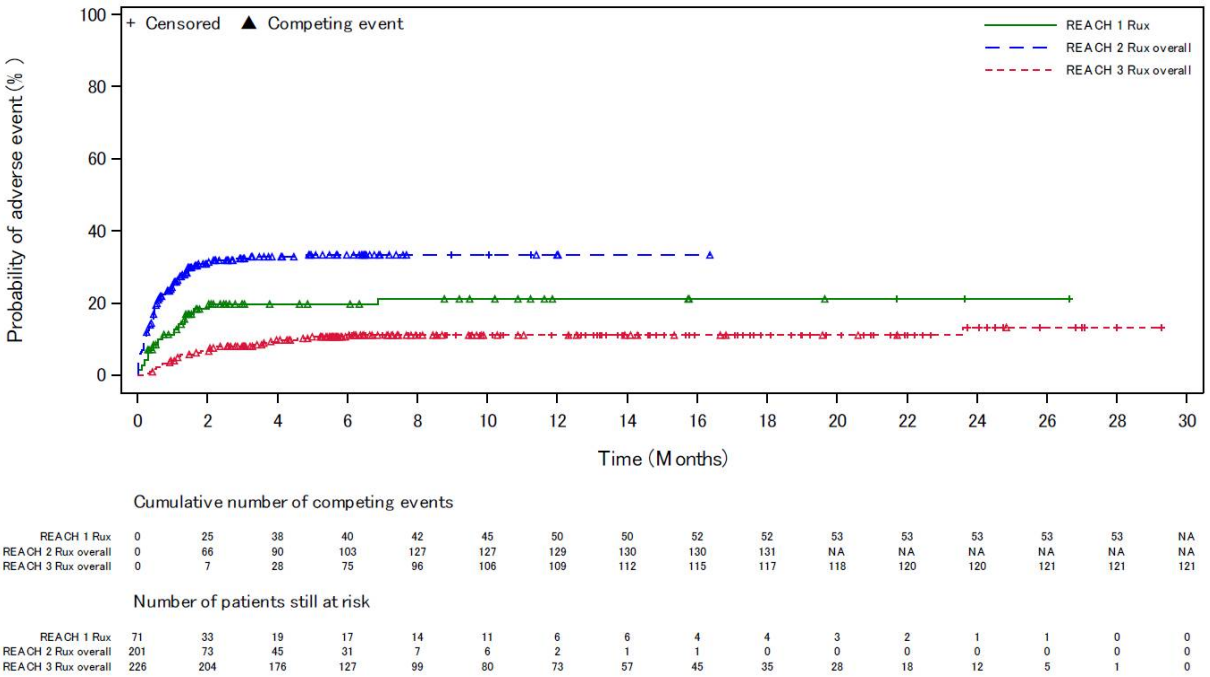
Table 2-37　慢性 GVHD の日和見感染（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	26 (11.5)
95% CI	(7.7, 16.4)
EAIR, n (incidence rate per 100 patient treatment years)	26 (13.0)
重症度, n (%)	

	RUX overall N = 226
Grade 3	5 (2.2)
Grade 4	0
Grade 5	2 (0.9)
副作用, n (%)	9 (4.0)
重篤な有害事象, n (%)	8 (3.5)
治験治療に対する処置, n (%)	
投与中止	1 (0.4)
減量	2 (0.9)
増量	0
休薬	2 (0.9)
不変/NA/不明	23 (10.2)
治療を要した有害事象, n (%)	21 (9.3)
転帰, n (%)	
回復/消失	20 (8.8)
軽快	2 (0.9)
未回復/未消失	3 (1.3)
回復/消失したが後遺症あり	0
死亡	2 (0.9)
不明	0
PT 別有害事象	
サイトメガロウイルス感染再燃	12 (5.3)
RS ウイルス感染	5 (2.2)
アスペルギルス感染	3 (1.3)
エプスタイン・バーウイルス感染再燃	2 (0.9)
気管支肺アスペルギルス症	2 (0.9)
サイトメガロウイルス血症	2 (0.9)
サイトメガロウイルス性小腸炎	1 (0.4)
ニューモシスチス・イロベチイ肺炎	1 (0.4)
クリプトコッカス性髄膜炎	1 (0.4)
マイコバクテリア感染	1 (0.4)
サイトメガロウイルス性肺炎	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.14
MedDRA version 23.0
PT は発現率の降順

Figure 2-3　日和見感染の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Cumulative number of competing events

REACH 1 Rux	0	25	38	40	42	45	50	50	52	52	53	53	53	53	53	NA
REACH 2 Rux overall	0	66	90	103	127	127	129	130	130	131	NA	NA	NA	NA	NA	NA
REACH 3 Rux overall	0	7	28	75	96	106	109	112	115	117	118	120	120	121	121	121

Number of patients still at risk

REACH 1 Rux	71	33	19	17	14	11	6	6	4	4	3	2	1	1	0	0
REACH 2 Rux overall	201	73	45	31	7	6	2	1	1	0	0	0	0	0	0	0
REACH 3 Rux overall	226	204	176	127	99	80	73	57	45	35	28	18	12	5	1	0

Source: 5.3.5.3-4-Figure 2.1-9.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.1.3 サイトメガロウイルス感染／感染症

C2301 試験の投与群別の解析とその他の解析では MedDRA version が異なり，サイトメガロウイルス感染再燃がコーディングされる PT が異なるが（1.1.3.2.2 項），いずれの解析でも「サイトメガロウイルス感染／感染症」の定義には感染再燃も含まれた。

急性 GVHD

C2301 試験の FAS では，ベースラインの既往歴又は合併症として，サイトメガロウイルス感染が RUX 群で BAT 群と比べて多く認められた（RUX 群 23.4%，BAT 群 18.1%，以下同順）（5.3.5.1-1-C2301 試験 CSR2-Table 14.1-8.1，MedDRA version 22.1）。

SAF の Day 28 までのサイトメガロウイルス感染／感染症の発現率は RUX 群で 28.3%，BAT 群で 24.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.20）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（9.2%，10.0%）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率に群間で大きな違いはなかった（5.9%，5.3%）。死亡に至った事象や投与中止に至った事象はなく，重篤な事象の発現率は群間で同程度であった（3.9%，4.0%）。

データカットオフ 2 までのサイトメガロウイルス感染／感染症の発現率は RUX 群で 35.5%，BAT 群で 32.0%であった。EAIR は RUX 群で BAT 群と比べて低かった（154.0，214.5）（5.3.5.3-4-Table 2.1-12.20）。

データカットオフ 2 までの RUX overall の被験者のサイトメガロウイルス感染／感染症の発現率は 32.3%であった（Table 2-38）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-4）。副作用の発現率は 7.0%であった。死亡に至った事象はなく，重篤な事象の発現率は 7.0%であり，サイトメガロウイルス感染再燃（2.5%），サイトメガロウイルス感染（2.0%），サイトメガロウイルス性大腸炎（1.5%），サイトメガロウイルス性小腸炎，サイトメガロウイルス検査陽性（各 0.5%）であった。RUX の投与中止に至った事象の発現率は 1.0%と低く，サイトメガロウイルス感染／感染症の大部分は用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-38 急性 GVHD のサイトメガロウイルス感染／感染症（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	65 (32.3)	14 (19.7)
95% CI	(25.9, 39.3)	(11.2, 30.9)
EAIR, n (incidence rate per 100 patient treatment years)	65 (142.3)	14 (55.5)
重症度, n (%)		
Grade 3	22 (10.9)	6 (8.5)
Grade 4	1 (0.5)	0
Grade 5	0	NA
副作用, n (%)	14 (7.0)	4 (5.6)
重篤な有害事象, n (%)	14 (7.0)	1 (1.4)
治験治療に対する処置, n (%)		
投与中止	2 (1.0)	1 (1.4)
減量	1 (0.5)	0
増量	0	0
休薬	2 (1.0)	1 (1.4)
不変/NA/不明	63 (31.3)	12 (16.9)
治療を要した有害事象, n (%)	64 (31.8)	14 (19.7)
転帰, n (%)		
回復/消失	43 (21.4)	9 (12.7)
軽快	6 (3.0)	0
未回復/未消失	18 (9.0)	5 (7.0)
回復/消失したが後遺症あり	1 (0.5)	0
死亡	0	0
不明	0	0

PT 別有害事象

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
サイトメガロウイルス感染再燃	45 (22.4)	4 (5.6)
サイトメガロウイルス感染	15 (7.5)	5 (7.0)
サイトメガロウイルス検査陽性	4 (2.0)	0
サイトメガロウイルス性大腸炎	4 (2.0)	0
サイトメガロウイルス血症	2 (1.0)	4 (5.6)
サイトメガロウイルス性小腸炎	2 (1.0)	0
サイトメガロウイルス性消化管感染	1 (0.5)	0
サイトメガロウイルス性脈絡網膜炎	0	1 (1.4)

Source: 5.3.5.3-4-Table 2.1-13.20
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の FAS では，ベースラインの既往歴又は合併症として，PT サイトメガロウイルス感染再燃は RUX 群，BAT 群で同程度に認められ（RUX 群 5.5%，BAT 群 4.3%，以下同順），PT サイトメガロウイルス感染（0.6%，1.8%）は少なかった（5.3.5.1-2-D2301 試験-Table 14.1-8.1，MedDRA version 23.0）。

SAF の C7D1 までのサイトメガロウイルス感染／感染症の発現率は RUX 群で 9.1%，BAT 群で 10.8%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.20）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（1.8%，1.9%）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなかった（3.6%，1.9%）。死亡に至った事象や投与中止に至った事象はなく，重篤な事象の発現率は群間で同程度であった（2.4%，1.9%）。

データカットオフまでのサイトメガロウイルス感染／感染症の発現率は RUX 群で 9.7%，BAT 群で 11.4%であった。EAIR は RUX 群で BAT 群と比べて低かった（10.7，18.4）（5.3.5.3-4-Table 2.1-12.20）。

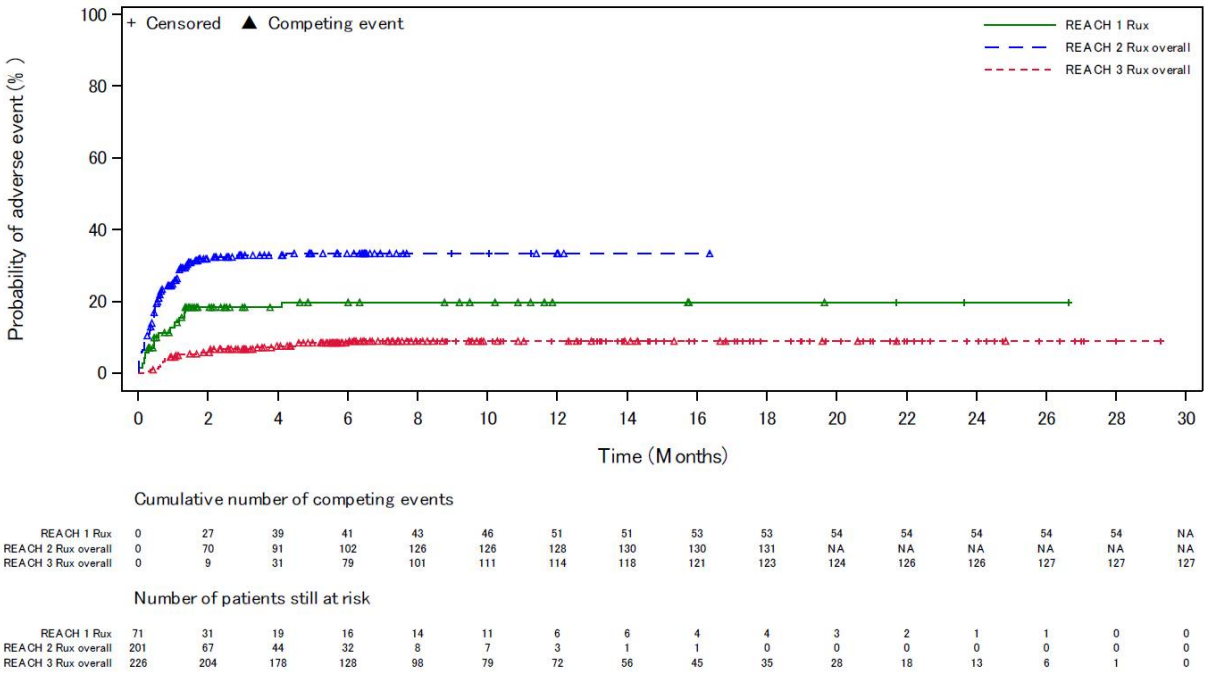
データカットオフまでの RUX overall の被験者のサイトメガロウイルス感染／感染症の発現率は 8.8%であった（Table 2-39）。ほとんどの事象は RUX 投与開始後 6 ヵ月以内に初回発現した（Figure 2-4）。副作用の発現率は 3.1%であった。死亡に至った事象はなく，重篤な事象の発現率は 1.8%であり，サイトメガロウイルス感染再燃（0.9%），サイトメガロウイルス感染，サイトメガロウイルス性肺炎（各 0.4%）であった。本事象による RUX の投与中止はなく，ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-39 慢性 GVHD のサイトメガロウイルス感染／感染症（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	20 (8.8)
95% CI	(5.5, 13.3)
EAIR, n (incidence rate per 100 patient treatment years)	20 (10.0)
重症度, n (%)	
Grade 3	3 (1.3)
Grade 4	0
Grade 5	0
副作用, n (%)	7 (3.1)
重篤な有害事象, n (%)	4 (1.8)
治験治療に対する処置, n (%)	
投与中止	0
減量	0
増量	0
休薬	1 (0.4)
不変/NA/不明	20 (8.8)
治療を要した有害事象, n (%)	19 (8.4)
転帰, n (%)	
回復/消失	17 (7.5)
軽快	0
未回復/未消失	2 (0.9)
回復/消失したが後遺症あり	0
死亡	0
不明	0
欠測	1 (0.4)
PT 別有害事象	
サイトメガロウイルス感染再燃	12 (5.3)
サイトメガロウイルス検査陽性	3 (1.3)
サイトメガロウイルス感染	2 (0.9)
サイトメガロウイルス血症	2 (0.9)
サイトメガロウイルス性小腸炎	1 (0.4)
サイトメガロウイルス性肺炎	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.20
MedDRA version 23.0
PT は発現率の降順

Figure 2-4　サイトメガロウイルス感染／感染症の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5. 3-4-Figure 2.1-13.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.1.4 尿路感染

急性 GVHD

C2301 試験の Day 28 までの尿路感染の発現率は RUX 群で 9.9%，BAT 群で 10.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.12）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 3.3%，BAT 群で 6.7%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率はいずれの群も低かった（2.6%，1.3%）。死亡に至った事象は RUX 群では認められず（0%，0.7%），重篤な事象の発現率はいずれの群も低かった（1.3%，2.0%）。

データカットオフ 2 までの尿路感染の発現率は RUX 群で 19.1%，BAT 群で 14.0%であった。EAIR は RUX 群で 69.3，BAT 群で 78.2 であった（5.3.5.3-4-Table 2.1-12.12）。

データカットオフ 2 までの RUX overall の被験者の尿路感染の発現率は 17.9%であった（Table 2-40）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-5）。副作用の発現率は 4.5%であった。死亡に至った事象はなく，重篤な事象の発現率は 2.0%であり，各事象 1～2 名での発現であった。本事象により RUX の投与を中止した被験者は少なく（0.5%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-40 急性 GVHD の尿路感染（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	36 (17.9)	10 (14.1)
95% CI	(12.9, 23.9)	(7.0, 24.4)
EAIR, n (incidence rate per 100 patient treatment years)	36 (65.4)	10 (38.2)
重症度, n (%)		
Grade 3	12 (6.0)	6 (8.5)
Grade 4	1 (0.5)	0
Grade 5	0	NA
副作用, n (%)	9 (4.5)	3 (4.2)
重篤な有害事象, n (%)	4 (2.0)	3 (4.2)
治験治療に対する処置, n (%)		
投与中止	1 (0.5)	0
減量	0	0
増量	0	0
休薬	1 (0.5)	0
不変/NA/不明	34 (16.9)	10 (14.1)
治療を要した有害事象, n (%)	27 (13.4)	10 (14.1)
転帰, n (%)		
回復/消失	25 (12.4)	9 (12.7)
軽快	0	1 (1.4)
未回復/未消失	11 (5.5)	1 (1.4)
回復/消失したが後遺症あり	0	0
死亡	0	0
不明	1 (0.5)	0
PT 別有害事象		
尿路感染	17 (8.5)	6 (8.5)
膀胱炎	9 (4.5)	1 (1.4)
ウイルス性膀胱炎	3 (1.5)	1 (1.4)
細菌性尿路感染	2 (1.0)	2 (2.8)
腎盂腎炎	2 (1.0)	0
大腸菌性尿路感染	1 (0.5)	1 (1.4)
ウイルス性尿路感染	1 (0.5)	0
尿路性敗血症	1 (0.5)	0
ウイルス性出血性膀胱炎	1 (0.5)	0
腎感染	0	1 (1.4)

Source: 5.3.5.3-4-Table 2.1-13.12
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの尿路感染の発現率は RUX 群で 8.5%，BAT 群で 6.3%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.12）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 1.2%，BAT 群 1.3%，以下同順）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率は群間で同程度であった（4.2%，2.5%）。死亡に至った事象はなく，重篤な事象は RUX 群のみで認められ（0.6%，0%），発現率は低かった。

データカットオフまでの尿路感染の発現率は RUX 群で 10.9%，BAT 群で 9.5%であった。EAIR は RUX 群で 12.6，BAT 群で 15.3 であった（5.3.5.3-4-Table 2.1-12.12）。

データカットオフまでの RUX overall の被験者の尿路感染の発現率は 9.3%であった（Table 2-41）。ほとんどの事象は RUX 投与開始後 6 ヵ月以内に初回発現した（Figure 2-5）。副作用の発現率は 4.0%であった。死亡に至った事象はなかった。重篤な事象の発現率は 0.9%と低く，尿路感染，腎盂腎炎（各 0.4%）であった。本事象により RUX の投与を中止した被験者はなく，ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

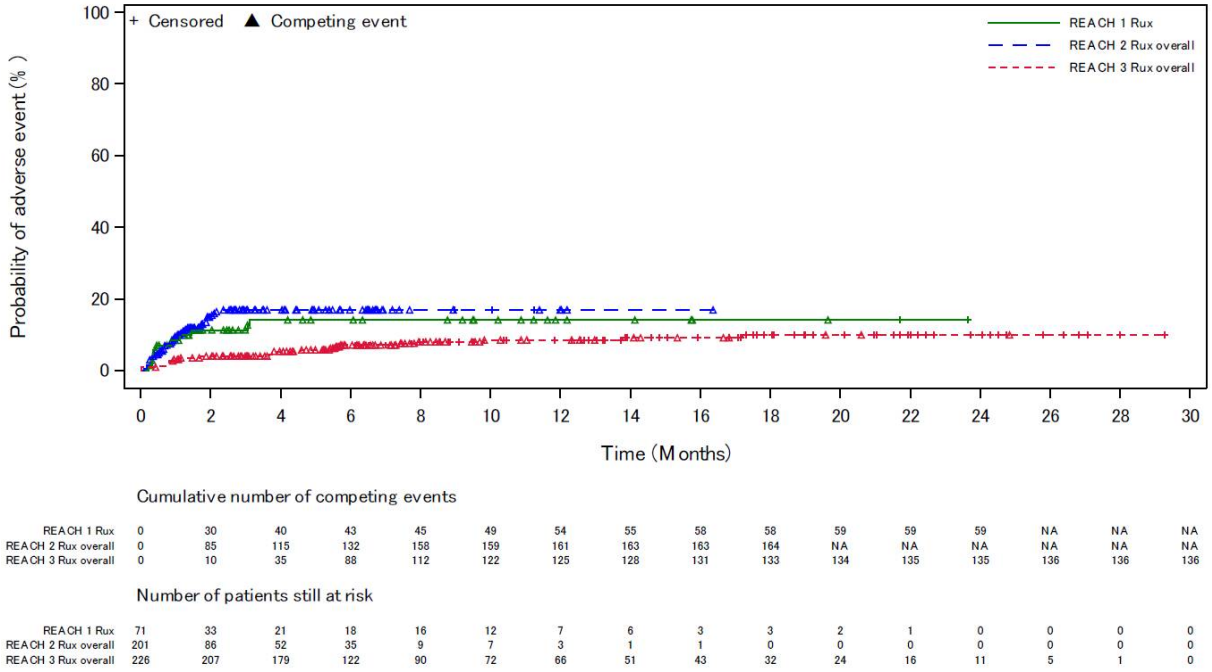
Table 2-41　慢性 GVHD の尿路感染（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	21 (9.3)
95% CI	(5.8, 13.9)
EAIR, n (incidence rate per 100 patient treatment years)	21 (11.0)
重症度, n (%)	
Grade 3	3 (1.3)
Grade 4	0
Grade 5	0
副作用, n (%)	9 (4.0)
重篤な有害事象, n (%)	2 (0.9)
治験治療に対する処置, n (%)	
投与中止	0
減量	1 (0.4)
増量	0
休薬	0
不変/NA/不明	21 (9.3)
治療を要した有害事象, n (%)	18 (8.0)
転帰, n (%)	
回復/消失	17 (7.5)
軽快	0
未回復/未消失	3 (1.3)
回復/消失したが後遺症あり	1 (0.4)
死亡	0

	RUX overall N = 226
不明	0
PT 別有害事象	
尿路感染	15 (6.6)
膀胱炎	4 (1.8)
腎盂腎炎	1 (0.4)
ウイルス性尿路感染	1 (0.4)
尿道炎	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.12
MedDRA version 23.0
PT は発現率の降順

Figure 2-5 尿路感染の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5. 3.5.3-4-Figure 2.1-8.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.1.5 敗血症／敗血症性ショック

急性 GVHD

C2301 試験の Day 28 までの敗血症／敗血症性ショックの発現率は RUX 群で 12.5%，BAT 群で 8.7%であり，群間で大きな違いはなかった（5.3.5.3-4-Table 2.1-11.16）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の発現率は RUX 群で 11.2%，BAT 群で 6.0%（以下

同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。死亡に至った事象の発現率は群間で同程度であり（4.6%，3.3%），PT 別の事象は，敗血症性ショック（3 名，3 名），敗血症（3 名，2 名），シュードモナス性敗血症（1 名，0 名）で，いずれの事象も発現率は群間で同程度であった。重篤な事象の発現率は群間で同程度であり（10.5%，5.3%），RUX 群の敗血症（5.3%，2.0%）を除き各事象 3%未満と低かった。重篤な敗血症の発現率は群間で同程度であった。投与中止に至った事象の発現率は低かった（1.3%，0.7%）。

データカットオフ 2 までの敗血症／敗血症性ショックの発現率は RUX 群で 24.3%，BAT 群で 20.7%であった。EAIR は RUX 群で BAT 群と比べて低かった（79.4，111.3）（5.3.5.3-4-Table 2.1-12.16）。

データカットオフ 2 までの RUX overall の被験者の敗血症／敗血症性ショックの発現率は 25.4%であった（Table 2-42）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-6）。副作用の発現率は 7.5%であった。死亡に至った事象の発現率は 10.0%であり，敗血症（10 名），敗血症性ショック（7 名），シュードモナス性敗血症（2 名），細菌性敗血症（1 名）であった。このうち 2 名（細菌性敗血症，敗血症，各 1 名）では，死亡に至った事象は RUX に関連すると判断されたが，これらの被験者では直近の外傷性損傷による入院歴，免疫抑制療法の併用があった（2.1.2.2.1 項）。重篤な事象の発現率は 19.9%であり，敗血症（9.5%），敗血症性ショック（6.5%），シュードモナス性敗血症（1.5%）を除き各事象 1～2 名での発現であった。投与中止に至った事象の発現率は 4.0%と低く，敗血症／敗血症性ショックの大部分は RUX の用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-42 急性 GVHD の敗血症／敗血症性ショック（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	51 (25.4)	16 (22.5)
95% CI	(19.5, 32.0)	(13.5, 34.0)
EAIR, n (incidence rate per 100 patient treatment years)	51 (84.4)	16 (60.2)
重症度, n (%)		
Grade 3	8 (4.0)	3 (4.2)
Grade 4	16 (8.0)	12 (16.9)
Grade 5	20 (10.0)	NA
副作用, n (%)	15 (7.5)	4 (5.6)
重篤な有害事象, n (%)	40 (19.9)	14 (19.7)
治験治療に対する処置, n (%)		
投与中止	8 (4.0)	5 (7.0)
減量	0	0
増量	0	0
休薬	10 (5.0)	6 (8.5)

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
不変/NA/不明	39 (19.4)	7 (9.9)
治療を要した有害事象, n (%)	45 (22.4)	13 (18.3)
転帰, n (%)		
回復/消失	23 (11.4)	8 (11.3)
軽快	1 (0.5)	0
未回復/未消失	7 (3.5)	4 (5.6)
回復/消失したが後遺症あり	1 (0.5)	0
死亡	20 (10.0)	4 (5.6)
不明	1 (0.5)	0
PT別有害事象		
敗血症	25 (12.4)	10 (14.1)
敗血症性ショック	13 (6.5)	4 (5.6)
大腸菌性敗血症	4 (2.0)	0
シュードモナス性敗血症	3 (1.5)	0
細菌性敗血症	2 (1.0)	0
ブドウ球菌性敗血症	2 (1.0)	1 (1.4)
カンジダ性敗血症	1 (0.5)	0
クロストリジウム性敗血症	1 (0.5)	0
医療機器関連敗血症	1 (0.5)	0
エンテロバクター性敗血症	1 (0.5)	0
真菌性敗血症	1 (0.5)	0
クレブシエラ性敗血症	1 (0.5)	0
レンサ球菌性敗血症	1 (0.5)	0
尿路性敗血症	1 (0.5)	0
腸球菌性敗血症	0	1 (1.4)

Source: 5.3.5.3-4-Table 2.1-13.16
MedDRA version 23.0
PTは RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの敗血症／敗血症性ショックの発現率は RUX 群で 2.4%，BAT 群で 6.3%であり，RUX 群の方が低い傾向がみられた（5.3.5.3-4-Table 2.1-11.16）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の発現率は RUX 群で 2.4%，BAT 群で 5.7%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率は群間で同程度であった（1.8%，1.9%）。死亡に至った事象の発現率は群間で同程度であり（0.6%，1.9%），PT 別の事象は，敗血症（1 名，0 名），敗血症性ショック（0 名，3 名）であった。重篤な事象の発現率は群間で同程度であり（1.8%，4.4%），いずれの事象も 2%未満と低かった。投与中止に至った事象の発現率は低かった（1.2%，0.6%）。

データカットオフまでの敗血症／敗血症性ショックの発現率は RUX 群で 4.2%，BAT 群で 7.0%であった。EAIR は RUX 群で BAT 群と比べて低かった（4.5，10.9）（5.3.5.3-4-Table 2.1-12.16）。

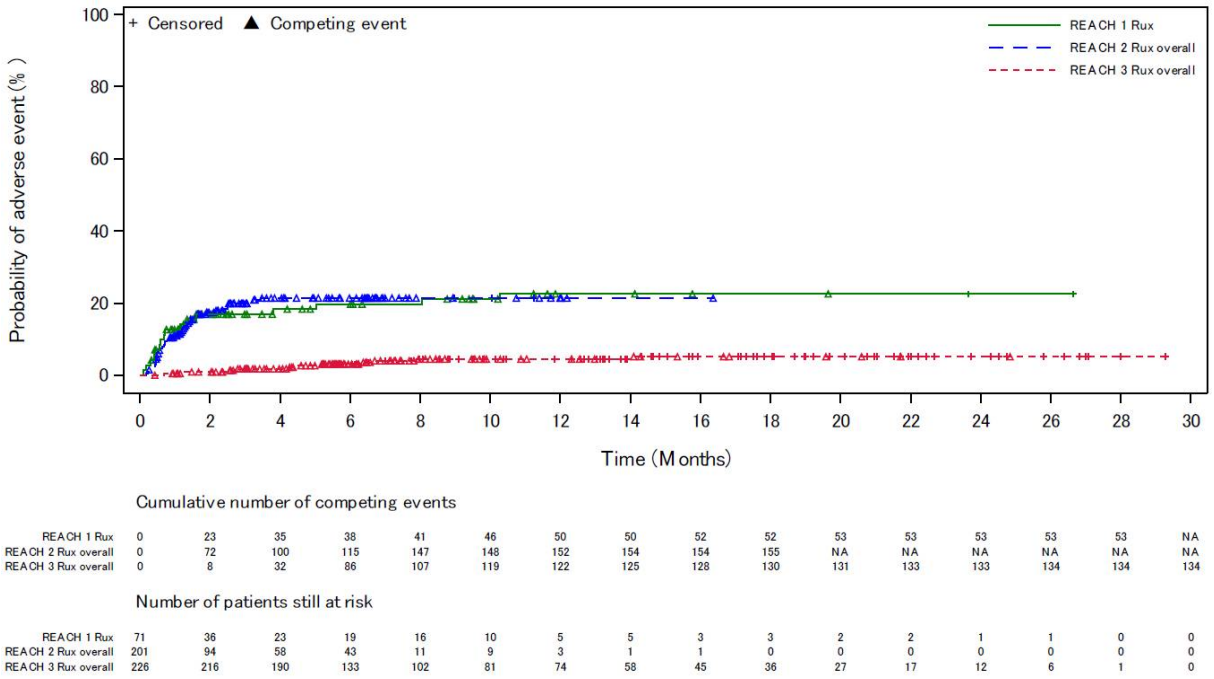
データカットオフまでの RUX overall の被験者の敗血症／敗血症性ショックの発現率は 3.5%であった（Table 2-43）。副作用の発現率は 1.8%であった。死亡に至った事象の発現率は 0.9%であり，内訳は敗血症，シュードモナス性敗血症（各 1 名）であった。重篤な事象の発現率は 3.1%であり，敗血症（3 名）を除き各事象 1～2 名での発現であった。投与中止に至った事象の発現率は 1.8%と低かった。

Table 2-43 慢性 GVHD の敗血症／敗血症性ショック（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	8 (3.5)
95% CI	(1.5, 6.9)
EAIR, n (incidence rate per 100 patient treatment years)	8 (3.9)
重症度, n (%)	
Grade 3	3 (1.3)
Grade 4	3 (1.3)
Grade 5	2 (0.9)
副作用, n (%)	4 (1.8)
重篤な有害事象, n (%)	7 (3.1)
治験治療に対する処置, n (%)	
投与中止	4 (1.8)
減量	2 (0.9)
増量	0
休薬	0
不変/NA/不明	4 (1.8)
治療を要した有害事象, n (%)	8 (3.5)
転帰, n (%)	
回復/消失	4 (1.8)
軽快	0
未回復/未消失	2 (0.9)
回復/消失したが後遺症あり	0
死亡	2 (0.9)
不明	0
PT 別有害事象	
敗血症	3 (1.3)
敗血症性ショック	2 (0.9)
大腸菌性敗血症	1 (0.4)
シュードモナス性敗血症	1 (0.4)
細菌性敗血症	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.16
MedDRA version 23.0
PT は発現率の降順

Figure 2-6　敗血症／敗血症性ショックの累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-11.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.1.6 結核，帯状疱疹，B 型肝炎の再活性化，進行性多巣性白質脳症

結核，進行性多巣性白質脳症は C2301 試験，D2301 試験，271 試験のいずれでも認められなかった。帯状疱疹，B 型肝炎の再活性化は RUX 投与被験者での発現が少なく，詳細は各試験の総括報告書に示した。

2.1.5.1.7 病原体別

急性 GVHD

C2301 試験の Day 28 までの病原体別感染症の発現率は，ウイルス感染が RUX 群で BAT 群と比べて高い傾向であったが，明らかな違いはなかった。その他の病原体カテゴリは RUX 群，BAT 群（以下同順）で同程度であった（ウイルス：39.5%，32.0%，細菌：15.8%，15.3%，真菌：5.9%，5.3%，病原体不明：28.3%，26.0%）（5.3.5.3-4-Table 2.1-11.31～Table 2.1-11.34）。病原体不明のうち，いずれかの群で発現率が 3%以上であった PT 別事象は，敗血症（7.2%，4.0%），尿路感染（5.3%，4.7%），医療機器関連感染（3.9%，3.3%），肺炎（3.9%，5.3%）であった。

データカットオフ 2 までの病原体別感染症の発現率は，ウイルスが 53.9%，40.7%，細菌が 25.7%，19.3%，真菌が 13.2%，10.7%，病原体不明が 53.3%，42.0%であった。EAIR は，ウイルスが 316.6，292.5，細菌が 91.9，113.4，真菌が 44.2，58.0，病原体不明が 250.3，288.5 であった（5.3.5.3-4-Table 2.1-12.31～Table 2.1-12.34）。

データカットオフ 2 までの RUX overall の被験者での病原体別感染症の発現状況を Table 2-44 に示す。

Table 2-44　急性 GVHD の病原体別感染症の概要（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201				271 試験 RUX N = 71			
	ウイルス	細菌	真菌	不明	ウイルス	細菌	真菌	不明
有害事象, n (%)	98 (48.8)	54 (26.9)	28 (13.9)	107 (53.2)	22 (31.0)	23 (32.4)	10 (14.1)	42 (59.2)
95% CI	(41.7, 55.9)	(20.9, 33.6)	(9.5, 19.5)	(46.1, 60.3)	(20.5, 43.1)	(21.8, 44.5)	(7.0, 24.4)	(46.8, 70.7)
EAIR, n (incidence rate per 100 patient treatment years)	98 (281.4)	54 (99.5)	28 (47.7)	107 (251.0)	22 (113.1)	23 (93.7)	10 (35.3)	42 (262.3)
重症度, n (%)								
Grade 3	38 (18.9)	27 (13.4)	13 (6.5)	24 (11.9)	10 (14.1)	15 (21.1)	4 (5.6)	15 (21.1)
Grade 4	2 (1.0)	6 (3.0)	3 (1.5)	18 (9.0)	0	5 (7.0)	4 (5.6)	17 (23.9)
Grade 5	2 (1.0)	4 (2.0)	0	21 (10.4)	NA	NA	NA	NA
副作用, n (%)	22 (10.9)	12 (6.0)	8 (4.0)	27 (13.4)	9 (12.7)	6 (8.5)	3 (4.2)	13 (18.3)
重篤な有害事象, n (%)	27 (13.4)	21 (10.4)	7 (3.5)	47 (23.4)	4 (5.6)	12 (16.9)	4 (5.6)	28 (39.4)
治験治療に対する処置, n (%)								
投与中止	5 (2.5)	4 (2.0)	1 (0.5)	7 (3.5)	1 (1.4)	1 (1.4)	1 (1.4)	7 (9.9)
減量	2 (1.0)	0	0	0	0	0	1 (1.4)	2 (2.8)
増量	0	0	0	0	0	0	0	0
休薬	4 (2.0)	5 (2.5)	0	12 (6.0)	1 (1.4)	2 (2.8)	1 (1.4)	6 (8.5)
不変/NA/不明	95 (47.3)	46 (22.9)	28 (13.9)	101 (50.2)	20 (28.2)	21 (29.6)	8 (11.3)	30 (42.3)
治療を要した有害事象, n (%)	86 (42.8)	52 (25.9)	28 (13.9)	91 (45.3)	20 (28.2)	22 (31.0)	10 (14.1)	38 (53.5)
転帰, n (%)								
回復/消失	63 (31.3)	34 (16.9)	16 (8.0)	73 (36.3)	14 (19.7)	18 (25.4)	4 (5.6)	29 (40.8)
軽快	8 (4.0)	1 (0.5)	1 (0.5)	1 (0.5)	1 (1.4)	1 (1.4)	1 (1.4)	2 (2.8)
未回復/未消失	35 (17.4)	16 (8.0)	13 (6.5)	29 (14.4)	12 (16.9)	5 (7.0)	4 (5.6)	11 (15.5)
回復/消失したが後遺症あり	3 (1.5)	0	1 (0.5)	1 (0.5)	0	0	1 (1.4)	0
死亡	2 (1.0)	4 (2.0)	0	21 (10.4)	0	3 (4.2)	1 (1.4)	8 (11.3)
不明	2 (1.0)	2 (1.0)	0	0	0	0	0	0

Source: 5.3.5.3-4-Table 2.1-13.31～Table 2.1-13.34
MedDRA version 23.0
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの病原体別感染症の発現率は，ウイルス感染が RUX 群で BAT 群と比べて高い傾向であったが，明らかな違いはなかった。その他の病原体カテゴリは，RUX 群，BAT 群（以下同順）で同程度であった（ウイルス：28.5%，23.4%，細菌：6.1%，6.3%，真菌：6.1%，5.7%，病原体不明：44.2%，43.7%）（5.3.5.3-4-Table 2.1-11.31～Table 2.1-11.34）。病原体

不明のうち，いずれかの群で発現率が 3%以上であった PT 別事象は，尿路感染（6.7%，3.2%），肺炎（10.9%，12.7%），上気道感染（8.5%，8.2%），気管支炎（3.6%，1.3%），結膜炎（4.8%，2.5%），下気道感染（3.6%，1.3%），上咽頭炎（6.1%，3.8%）であった。

データカットオフまでの病原体別感染症の発現率は，ウイルスが 35.8%，27.2%，細菌が 9.1%，7.0%，真菌が 6.7%，6.3%，病原体不明が 55.2%，50.0%であった。EAIR は，ウイルスが 49.9，51.5，細菌が 10.0，11.0，真菌が 7.1，9.9，病原体不明が 99.7，113.7 であった（5.3.5.3-4-Table 2.1-12.31～Table 2.1-12.34）。

データカットオフまでの RUX overall の被験者での病原体別感染症の発現状況を Table 2-45 に示す。

Table 2-45 慢性 GVHD の病原体別感染症の概要（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226			
	ウイルス	細菌	真菌	不明
有害事象, n (%)	75 (33.2)	18 (8.0)	12 (5.3)	124 (54.9)
95% CI	(27.1, 39.7)	(4.8, 12.3)	(2.8, 9.1)	(48.1, 61.5)
EAIR, n (incidence rate per 100 patient treatment years)	75 (45.6)	18 (9.0)	12 (5.8)	124 (103.4)
重症度, n (%)				
Grade 3	12 (5.3)	6 (2.7)	3 (1.3)	36 (15.9)
Grade 4	1 (0.4)	0	0	4 (1.8)
Grade 5	1 (0.4)	3 (1.3)	3 (1.3)	6 (2.7)
副作用, n (%)	27 (11.9)	6 (2.7)	5 (2.2)	39 (17.3)
重篤な有害事象, n (%)	12 (5.3)	8 (3.5)	7 (3.1)	47 (20.8)
治験治療に対する処置, n (%)				
投与中止	3 (1.3)	2 (0.9)	1 (0.4)	12 (5.3)
減量	2 (0.9)	1 (0.4)	2 (0.9)	8 (3.5)
増量	0	0	0	1 (0.4)
休薬	7 (3.1)	0	3 (1.3)	11 (4.9)
不変/NA/不明	67 (29.6)	17 (7.5)	9 (4.0)	114 (50.4)
治療を要した有害事象, n (%)	51 (22.6)	16 (7.1)	11 (4.9)	112 (49.6)
転帰, n (%)				
回復/消失	62 (27.4)	12 (5.3)	5 (2.2)	105 (46.5)
軽快	2 (0.9)	1 (0.4)	3 (1.3)	10 (4.4)
未回復/未消失	15 (6.6)	3 (1.3)	4 (1.8)	18 (8.0)
回復/消失したが後遺症あり	0	0	0	2 (0.9)
死亡	1 (0.4)	3 (1.3)	3 (1.3)	6 (2.7)
不明	0	0	0	0
欠測	0	0	0	2 (0.9)

Source: 5.3.5.3-4-Table 2.1-13.31～Table 2.1-13.34
MedDRA version 23.0

2.1.5.2 血球減少

HSCT 後の患者では，ウイルス感染，GVHD 罹患，骨髄毒性のある治療（例：ガンシクロビル）といった血球減少要因を有することが多く，血小板減少症，貧血，好中球減少症等の血球減少の合併が高頻度に認められる（Nakamae et al. 2011）。また，血球減少は，RUX の薬理作用に基づく既知の副作用である。なお，C2301 試験及び D2301 試験の治験実施計画書では，RUX に起因する 500/mm^3 以上 750/mm^3 未満の好中球数減少又は 15,000/mm^3 以上 20,000/mm^3 未満の血小板数減少がみられた場合に RUX を減量し，RUX に起因する 500/mm^3 未満の好中球数減少又は 15,000/mm^3 未満の血小板数減少がみられた場合に RUX を休薬することを規定していた。

血小板減少症，赤血球減少症，白血球減少症，その他の血球減少について，関連する PT 別事象をグループ化して定義し（5.3.5.3-4-Listing 1），評価した結果を以下に示す。なお，複数のグループで定義される PT 別事象もある。

2.1.5.2.1 血小板減少症

急性 GVHD

C2301 試験の Day 28 までの血小板減少症の発現率は RUX 群で 50.0%，BAT 群で 32.7%であり，RUX 群で BAT 群と比べて高かった（5.3.5.3-4-Table 2.1-11.01）。Grade 3 以上の事象の発現率は RUX 群で BAT 群と比べて高かった（RUX 群 41.4%，BAT 群 29.3%，以下同順）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率は RUX 群で BAT 群と比べて高かった（30.3%，8.7%）。死亡に至った事象はなく，重篤な事象の発現率はいずれの群も低かった（0.7%，1.3%）。臨床検査では，Grade 3 及び Grade 4 の血小板数低値に該当した被験者の割合は，いずれも群間で同程度であった（3.1 項）。

データカットオフ 2 までの血小板減少症の発現率は RUX 群で 56.6%，BAT 群で 36.7%であった。EAIR は RUX 群で BAT 群と比べて高かった（319.0，251.0）（5.3.5.3-4-Table 2.1-12.01）。

データカットオフ 2 までの RUX overall の被験者の血小板減少症の発現率は 53.2%であった（Table 2-46）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-7）。副作用の発現率は 34.3%であった。死亡に至った事象はなく，重篤な事象の発現率は 2.5%と低かった。RUX の投与中止に至った事象の発現率は 4.5%と低く，血小板減少症の大部分は用量調節，休薬，加療により管理可能であった。臨床検査では，Grade 3 及び Grade 4 の血小板数低値に該当した被験者の割合は，それぞれ 31.3%及び 47.7%であった。血小板数の平均値は一過性の低下を示した後ベースライン程度まで回復した（3.1 項）。

慢性 GVHD

D2301 試験の C7D1 までの血小板減少症の発現率は RUX 群で 21.2%，BAT 群で 14.6%であり，RUX 群で BAT 群と比べて高い傾向が認められた（5.3.5.3-4-Table 2.1-11.01）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で BAT 群と比べて

高い傾向が認められた（RUX 群 15.2%，BAT 群 10.1%，以下同順）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率は RUX 群で BAT 群と比べて高かった（14.5%，5.7%）。死亡に至った事象はなく，重篤な事象（0%，0.6%）は RUX 群では認められなかった。臨床検査では，Grade 3 及び Grade 4 の血小板数低値に該当した被験者の割合は，いずれも群間で同程度であった（3.1 項）。

データカットオフまでの血小板減少症の発現率は RUX 群で 23.0%，BAT 群で 15.8%であった。EAIR は群間で同程度であった（27.4，26.3）（5.3.5.3-4-Table 2.1-12.01）。

データカットオフまでの RUX overall の被験者の血小板減少症の発現率は 19.9%であった（Table 2-46）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-7）。副作用の発現率は 13.3%であった。死亡に至った事象はなく，重篤な事象の発現率は 1.8%と低かった。RUX の投与中止に至った事象の発現率は 1.3%と低く，血小板減少症の多くは用量調節又は休薬が不要で，加療により管理可能であった。臨床検査では，Grade 3 及び Grade 4 の血小板数低値に該当した被験者の割合は，それぞれ 5.9%及び 10.7%であった。血小板数の平均値は増加傾向を示した（3.1 項）。

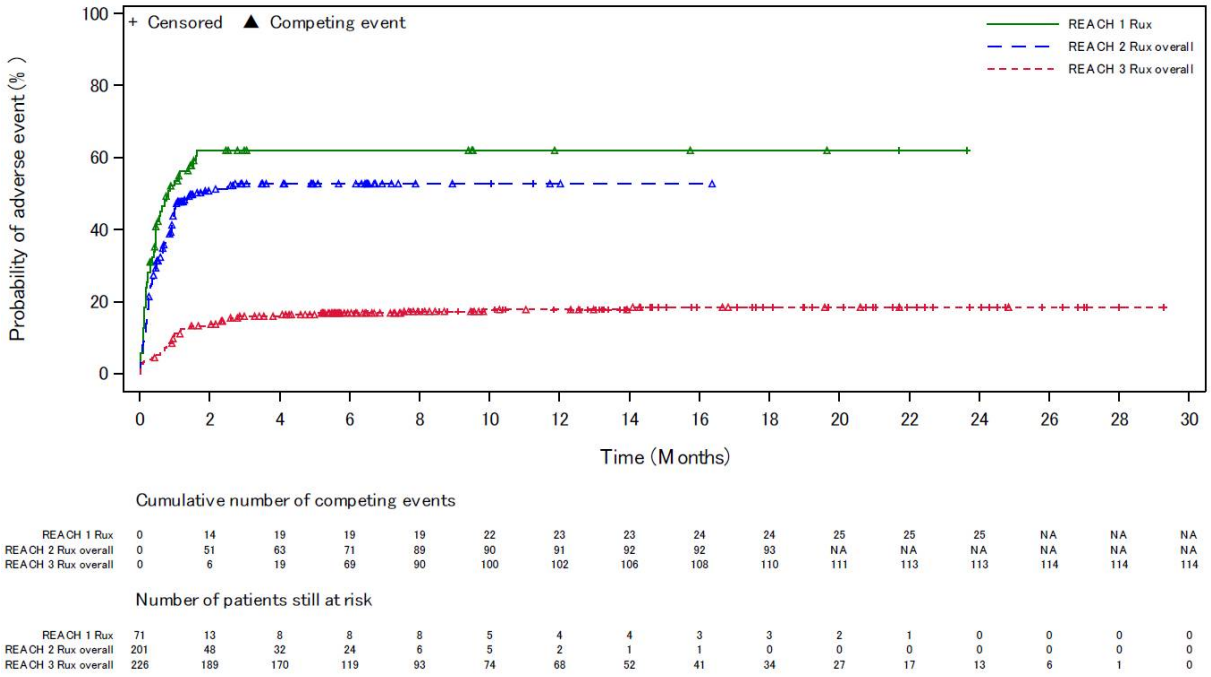
Table 2-46　　血小板減少症（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
有害事象, n (%)	107 (53.2)	44 (62.0)	45 (19.9)
95% CI	(46.1, 60.3)	(49.7, 73.2)	(14.9, 25.7)
EAIR, n (incidence rate per 100 patient treatment years)	107 (294.3)	44 (312.4)	45 (24.1)
重症度, n (%)			
Grade 3	26 (12.9)	10 (14.1)	11 (4.9)
Grade 4	68 (33.8)	28 (39.4)	22 (9.7)
Grade 5	0	NA	0
副作用, n (%)	69 (34.3)	33 (46.5)	30 (13.3)
重篤な有害事象, n (%)	5 (2.5)	3 (4.2)	4 (1.8)
治験治療に対する処置, n (%)			
投与中止	9 (4.5)	2 (2.8)	3 (1.3)
減量	32 (15.9)	13 (18.3)	4 (1.8)
増量	3 (1.5)	1 (1.4)	0
休薬	25 (12.4)	9 (12.7)	5 (2.2)
不変/NA/不明	82 (40.8)	35 (49.3)	42 (18.6)
治療を要した有害事象, n (%)	65 (32.3)	16 (22.5)	18 (8.0)
転帰, n (%)			
回復/消失	49 (24.4)	15 (21.1)	22 (9.7)
軽快	7 (3.5)	1 (1.4)	6 (2.7)
未回復/未消失	48 (23.9)	28 (39.4)	17 (7.5)
回復/消失したが後遺症あり	3 (1.5)	0	0

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
死亡	0	0	0
不明	0	1 (1.4)	0

Source: 5.3.5.3-4-Table 2.1-13.01
MedDRA version 23.0
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 2-7　血小板減少症の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-1.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.2.2 赤血球減少症

急性 GVHD

C2301 試験の Day 28 までの赤血球減少症の発現率は RUX 群で 30.3%，BAT 群で 29.3%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.02）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 22.4%，BAT 群で 20.0%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用は貧血（11.2%，3.3%）のみであった。重篤な事象は認められなかった。臨床検査では，Grade 3 のヘモグロビン低値に該当した被験者の割合は，いずれも群間で同程度であった（3.1 項）。

データカットオフ 2 までの赤血球減少症の発現率は RUX 群で 40.8%，BAT 群で 34.0%であった。EAIR は RUX 群で BAT 群と比べて低かった（184.8，233.2）（5.3.5.3-4-Table 2.1-12.02）。

データカットオフ 2 までの RUX overall の被験者の赤血球減少症の発現率は 38.8%であった（Table 2-47）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-8）。副作用の発現率は 15.9%であった。重篤な事象は認められなかった。RUX の投与中止に至った事象の発現率は 1.5%と低く，赤血球減少症の多くは用量調節又は休薬が不要で，加療により管理可能であった。臨床検査では，Grade 3 のヘモグロビン低値に該当した被験者の割合は 51.6%であった。ヘモグロビンの平均値は一過性の低下を示した後ベースライン程度まで回復した（3.1 項）。

慢性 GVHD

D2301 試験の C7D1 までの赤血球減少症の発現率は RUX 群で 29.7%，BAT 群で 12.7%であり，RUX 群で高かった（5.3.5.3-4-Table 2.1-11.02）。Grade 3 以上の事象の発現率は RUX 群で 12.7%，BAT 群で 7.6%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率は RUX 群で BAT 群と比べて高かった（21.8%，3.2%）。死亡に至った事象は認められなかった。重篤な事象は RUX 群の 1 名（0.6%）で貧血が認められた。臨床検査では，Grade 3 のヘモグロビン低値に該当した被験者の割合は群間で同程度であった（3.1 項）。

データカットオフまでの赤血球減少症の発現率は RUX 群で 32.1%，BAT 群で 13.9%であった。EAIR は RUX 群で BAT 群と比べて高かった（43.0，23.3）（5.3.5.3-4-Table 2.1-12.02）。

データカットオフまでの RUX overall の被験者の赤血球減少症の発現率は 28.8%であった（Table 2-47）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-8）。副作用の発現率は 21.7%であった。死亡に至った事象はなく，重篤な事象は貧血（1.8%）のみであった。RUX の投与中止に至った事象の発現率は 0.9%と低く，赤血球減少症の多くは用量調節，休薬，加療により管理可能であった。臨床検査では，Grade 3 のヘモグロビン低値に該当した被験者の割合は 14.8%であった。ヘモグロビンの平均値は一過性の低下を示した後ベースライン程度まで回復した（3.1 項）。

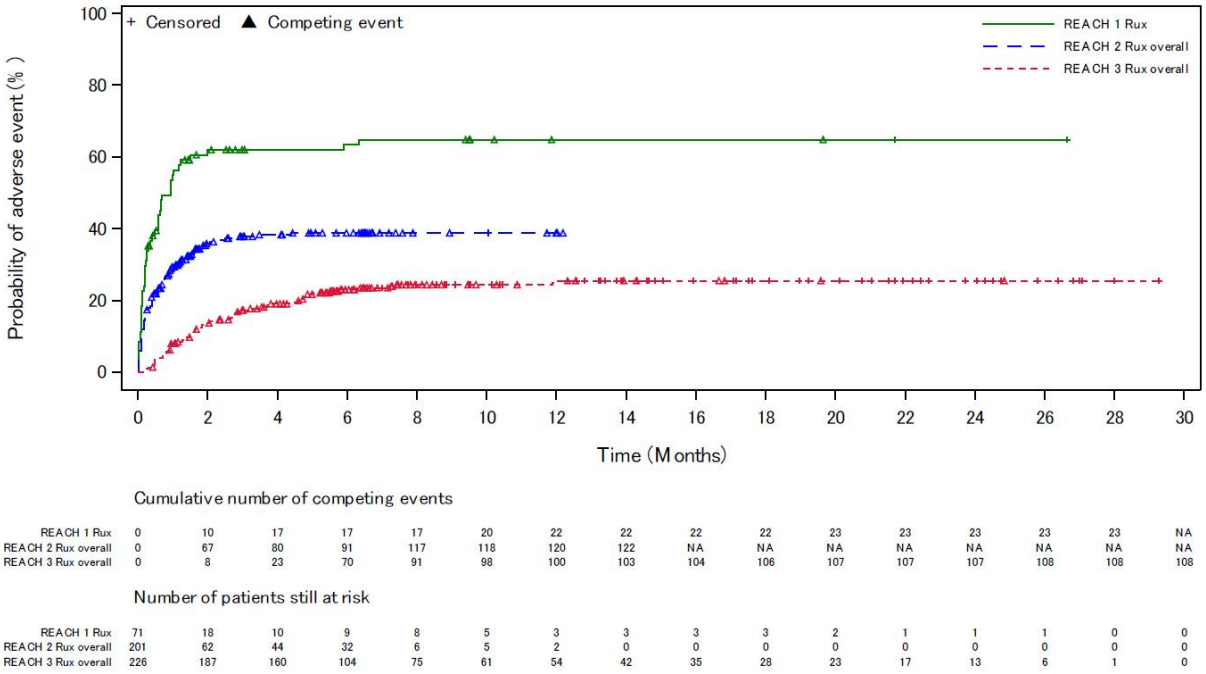
Table 2-47 赤血球減少症（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
有害事象, n (%)	78 (38.8)	46 (64.8)	65 (28.8)
95% CI	(32.0, 45.9)	(52.5, 75.8)	(23.0, 35.1)
EAIR, n (incidence rate per 100 patient treatment years)	78 (180.1)	46 (306.7)	65 (39.1)
重症度, n (%)			
Grade 3	61 (30.3)	36 (50.7)	30 (13.3)
Grade 4	3 (1.5)	0	1 (0.4)
Grade 5	0	NA	0
副作用, n (%)	32 (15.9)	25 (35.2)	49 (21.7)

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
重篤な有害事象, n (%)	0	2 (2.8)	4 (1.8)
治験治療に対する処置, n (%)			
投与中止	3 (1.5)	1 (1.4)	2 (0.9)
減量	6 (3.0)	4 (5.6)	14 (6.2)
増量	0	0	0
休薬	3 (1.5)	2 (2.8)	7 (3.1)
不変/NA/不明	72 (35.8)	44 (62.0)	57 (25.2)
治療を要した有害事象, n (%)	58 (28.9)	13 (18.3)	31 (13.7)
転帰, n (%)			
回復/消失	42 (20.9)	19 (26.8)	36 (15.9)
軽快	7 (3.5)	1 (1.4)	9 (4.0)
未回復/未消失	27 (13.4)	25 (35.2)	16 (7.1)
回復/消失したが後遺症あり	2 (1.0)	1 (1.4)	1 (0.4)
死亡	0	0	0
不明	0	0	0
欠測	0	0	4 (1.8)

Source: 5.3.5.3-4-Table 2.1-13.02
MedDRA version 23.0
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 2-8　赤血球減少症の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-2.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.2.3 白血球減少症

急性 GVHD

C2301 試験の Day 28 までの白血球減少症の発現率は RUX 群で 32.9%，BAT 群で 26.7%であり，RUX 群の方が高い傾向がみられた（5.3.5.3-4-Table 2.1-11.03）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 28.9%，BAT 群で 22.0%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率は RUX 群で BAT 群と比べて高かった（18.4%，7.3%）。死亡に至った事象は認められなかった。重篤な事象の発現率は群間で同程度であり（0.7%，2.0%），2 名以上で認められた事象はなかった。臨床検査では，Grade 3 及び Grade 4 の白血球数低値，リンパ球数低値，好中球数低値に該当した被験者の割合は，いずれも群間で同程度であった（3.1 項）。

データカットオフ 2 までの白血球減少症の発現率は RUX 群で 46.7%，BAT 群で 32.0%であった。EAIR は群間で同程度であった（217.5，213.6）（5.3.5.3-4-Table 2.1-12.03）。

データカットオフ 2 までの RUX overall の被験者の白血球減少症の発現率は 44.3%であった（Table 2-48）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-9）。副作用の発現率は 28.4%であった。死亡に至った事象が 1 名（0.5%，発熱性好中球減少症）で報告された。重篤な事象の発現率は 4.0%であり，発熱性好中球減少症及び好中球減少症（各 3 名）を除き各事象 1～2 名での発現であった。RUX の投与中止に至った事象の発現率は 4.5%と低く，白血球減少症の多くは用量調節，休薬，加療により管理可能であった。臨床検査では，Grade 3 及び Grade 4 の白血球数低値に該当した被験者の割合は，それぞれ 34.8%及び 22.8%，Grade 3 及び Grade 4 のリンパ球数低値に該当した被験者の割合は，それぞれ 37.8%及び 60.3%，Grade 3 及び Grade 4 の好中球数低値に該当した被験者の割合は，それぞれ 17.9%及び 20.6%であった。好中球数の平均値は試験期間を通してベースラインより低く推移したが，リンパ球数は増加傾向であり，白血球数は一過性の低下を示した後ベースライン程度まで回復した（3.1 項）。

慢性 GVHD

D2301 試験の C7D1 までの白血球減少症の発現率は RUX 群で 18.8%，BAT 群で 13.9%であり，RUX 群の方が高い傾向がみられた（5.3.5.3-4-Table 2.1-11.03）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 12.7%，BAT 群で 10.8%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなく（12.7%，5.7%），いずれの事象も発現率は群間で同程度であった。死亡に至った事象はなかった。重篤な事象の発現率は群間で同程度であり（2.4%，1.3%），両群ともに主な事象は発熱性好中球減少症であった（1.8%，1.3%）。臨床検査では，Grade 3 及び Grade 4 の白血球数低値，

リンパ球数低値，好中球数低値に該当した被験者の割合は，いずれも群間で同程度であった（3.1 項）。

データカットオフまでの白血球減少症の発現率は RUX 群で 23.6%，BAT 群で 14.6%であった。EAIR は群間で同程度であった（29.0，23.8）（5.3.5.3-4-Table 2.1-12.03）。

データカットオフまでの RUX overall の被験者の白血球減少症の発現率は 22.1%であった（Table 2-48）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-9）。副作用の発現率は 15.0%であった。死亡に至った事象はなかった。重篤な事象の発現率は 3.1%であり，発熱性好中球減少症（4 名）を除き各事象 1～2 名での発現であった。RUX の投与中止に至った事象の発現率は 0.9%と低く，白血球減少症の多くは用量調節，休薬，加療により管理可能であった。臨床検査では，Grade 3 及び Grade 4 の白血球数低値に該当した被験者の割合は，それぞれ 6.8%及び 5.8%，Grade 3 及び Grade 4 のリンパ球数低値に該当した被験者の割合は，それぞれ 16.9%及び 7.2%，Grade 3 及び Grade 4 の好中球数低値に該当した被験者の割合は，それぞれ 9.5%及び 6.7%であった。白血球数，好中球数の平均値は試験期間を通してベースラインより低く推移したが，リンパ球数はベースラインより高く推移した（3.1 項）。

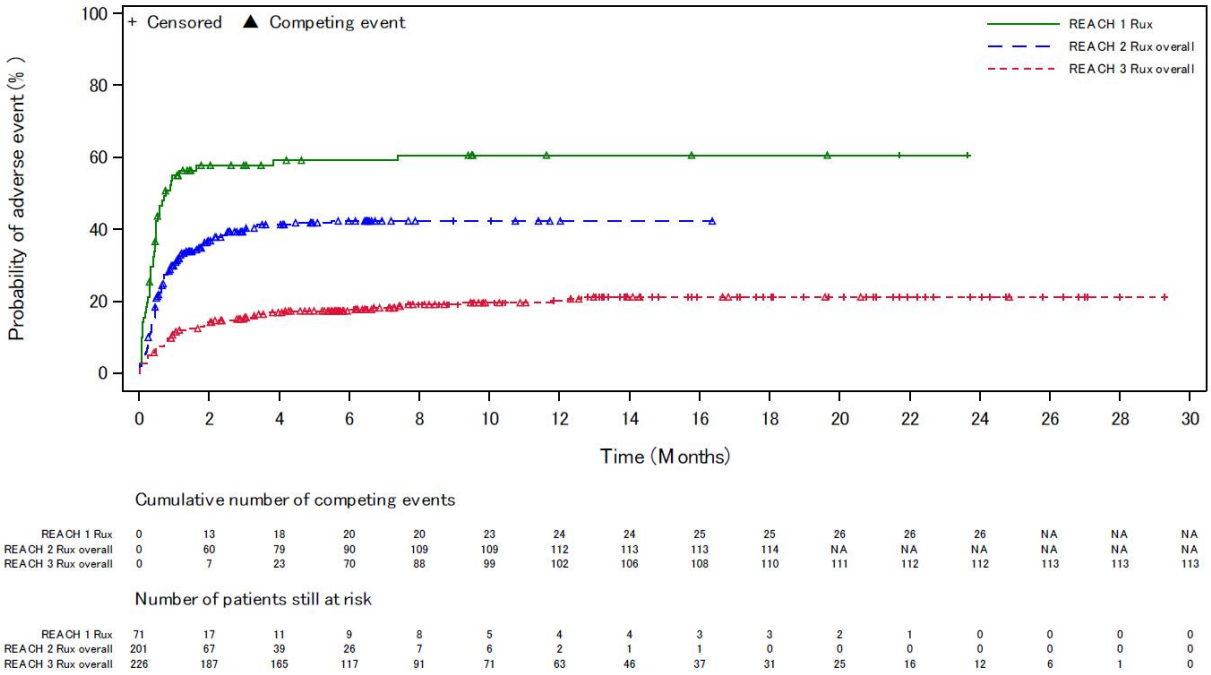
Table 2-48 白血球減少症（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
有害事象, n (%)	89 (44.3)	43 (60.6)	50 (22.1)
95% CI	(37.3, 51.4)	(48.3, 72.0)	(16.9, 28.1)
EAIR, n (incidence rate per 100 patient treatment years)	89 (205.4)	43 (276.8)	50 (27.6)
重症度, n (%)			
Grade 3	41 (20.4)	17 (23.9)	16 (7.1)
Grade 4	40 (19.9)	18 (25.4)	21 (9.3)
Grade 5	1 (0.5)	NA	0
副作用, n (%)	57 (28.4)	29 (40.8)	34 (15.0)
重篤な有害事象, n (%)	8 (4.0)	1 (1.4)	7 (3.1)
治験治療に対する処置, n (%)			
投与中止	9 (4.5)	1 (1.4)	2 (0.9)
減量	22 (10.9)	14 (19.7)	13 (5.8)
増量	0	0	0
休薬	23 (11.4)	7 (9.9)	14 (6.2)
不変/NA/不明	71 (35.3)	37 (52.1)	41 (18.1)
治療を要した有害事象, n (%)	63 (31.3)	27 (38.0)	24 (10.6)
転帰, n (%)			
回復/消失	56 (27.9)	34 (47.9)	37 (16.4)
軽快	6 (3.0)	2 (2.8)	6 (2.7)
未回復/未消失	30 (14.9)	11 (15.5)	12 (5.3)
回復/消失したが後遺症あり	0	0	0

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
死亡	1 (0.5)	0	0
不明	1 (0.5)	1 (1.4)	0
欠測	0	0	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.03
MedDRA version 23.0
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 2-9　白血球減少症の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-3.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.2.4 その他の血球減少

急性 GVHD

C2301 試験の Day 28 までのその他の血球減少の発現率は RUX 群で 5.9%，BAT 群で 4.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.04）。データカットオフ 2 までのその他の血球減少の発現率は RUX 群で 8.6%，BAT 群で 6.0%であり，EAIR は RUX 群で 27.7，BAT 群で 31.2 であった（5.3.5.3-4-Table 2.1-12.04）。RUX overall の被験者での発現率は 9.0%であった（5.3.5.3-

4-Table 2.1-13.04）。最も多かった PT 別事象は汎血球減少症（6.5%）であった。副作用の発現率は 5.0%，重篤な事象の発現率は 2.5%であった。

慢性 GVHD

D2301 試験の C7D1 までのその他の血球減少の発現率は RUX 群で 1.2%，BAT 群で 1.3%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.04）。データカットオフまでのその他の血球減少の発現率は RUX 群で 1.2%，BAT 群で 1.3%であり，EAIR は RUX 群で 1.3，BAT 群で 1.9 であった（5.3.5.3-4-Table 2.1-12.04）。RUX overall の被験者での発現率は 0.9%であった（5.3.5.3-4-Table 2.1-13.04）。PT 別で，汎血球減少症は少なかった（0.9%）。副作用の発現率は 0.4%と低く，重篤な事象は認められなかった。

2.1.5.3 出血性事象

HSCT 後の患者で，骨髄破壊的移植前処置歴，高グレードの急性 GVHD，高度の血小板減少症の持続といった出血要因を多く伴う場合，出血は高頻度に認められる合併症である。出血部位は，胃腸及び泌尿生殖器が最も多くみられる（Labrador et al. 2015）。

出血性事象について，関連する PT 別事象をグループ化して定義し（5.3.5.3-4-Listing 1），評価した結果を以下に示す。また，胃腸出血，挫傷，頭蓋内出血，その他の出血性事象に関連する PT 別事象をグループ化して定義し，別途検討した結果も示す。なお，複数のグループで定義される PT 別事象もある。

急性 GVHD

C2301 試験の Day 28 までの出血性事象の発現率は RUX 群で 25.0%，BAT 群で 22.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.05）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 4.6%，BAT 群で 2.7%（以下同順）であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率に群間で大きな違いはなく（6.6%，1.3%），いずれの事象も発現率は群間で同程度であった。死亡に至った事象はなく，重篤な事象の発現率はいずれの群も低かった（2.0%，1.3%）。

データカットオフ 2 までの出血性事象の発現率は RUX 群で 40.1%，BAT 群で 28.0%であった。EAIR は RUX 群で 158.2，BAT 群で 174.3 であった（5.3.5.3-4-Table 2.1-12.05）。

データカットオフ 2 までの RUX overall の被験者の出血性事象の発現率は 36.8%であった（Table 2-49）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-10）。副作用の発現率は 10.4%であり，最も多かった事象は点状出血（3.0%）であった（5.3.5.3-4-Table 2.1-13.05）。死亡に至った事象の発現率は 1.0%と低く，下部消化管出血，肺出血（各 0.5%）であった。重篤な事象の発現率は 7.0%であり，胃腸出血（2.0%），下部消化管出血（1.0%）を除き各事象 1 名での発現であった。本事象により RUX の投与を中止した被験者は少なく（2.0%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

Table 2-49 急性 GVHD の出血性事象（RUX overall の被験者で 2 名以上）（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	74 (36.8)	36 (50.7)
95% CI	(30.1, 43.9)	(38.6, 62.8)
EAIR, n (incidence rate per 100 patient treatment years)	74 (143.3)	36 (201.6)
重症度, n (%)		
Grade 3	17 (8.5)	10 (14.1)
Grade 4	6 (3.0)	5 (7.0)
Grade 5	2 (1.0)	NA
副作用, n (%)	21 (10.4)	6 (8.5)
重篤な有害事象, n (%)	14 (7.0)	8 (11.3)
治験治療に対する処置, n (%)		
投与中止	4 (2.0)	1 (1.4)
減量	0	0
増量	0	0
休薬	4 (2.0)	2 (2.8)
不変/NA/不明	70 (34.8)	36 (50.7)
治療を要した有害事象, n (%)	36 (17.9)	16 (22.5)
転帰, n (%)		
回復/消失	50 (24.9)	19 (26.8)
軽快	5 (2.5)	0
未回復/未消失	26 (12.9)	20 (28.2)
回復/消失したが後遺症あり	1 (0.5)	0
死亡	2 (1.0)	3 (4.2)
不明	2 (1.0)	1 (1.4)
PT 別有害事象		
血尿	13 (6.5)	12 (16.9)
鼻出血	10 (5.0)	8 (11.3)
点状出血	9 (4.5)	1 (1.4)
胃腸出血	7 (3.5)	1 (1.4)
挫傷	6 (3.0)	5 (7.0)
メレナ	6 (3.0)	0
血腫	4 (2.0)	3 (4.2)
血便排泄	4 (2.0)	2 (2.8)
出血性膀胱炎	4 (2.0)	1 (1.4)
紫斑	3 (1.5)	1 (1.4)
直腸出血	3 (1.5)	0
下部消化管出血	2 (1.0)	12 (16.9)
肛門出血	2 (1.0)	1 (1.4)
播種性血管内凝固	2 (1.0)	1 (1.4)

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
胃出血	2 (1.0)	1 (1.4)
喀血	2 (1.0)	1 (1.4)
上部消化管出血	2 (1.0)	1 (1.4)
腸出血	2 (1.0)	0
口腔血性水疱	2 (1.0)	0

Source: 5.3.5.3-4-Table 2.1-13.05
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの出血性事象の発現率は RUX 群で 11.5%，BAT 群で 14.6%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.05）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 2.4%，BAT 群で 1.9%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなく（1.2%，3.2%），いずれの事象も 1～2 名での発現であった。死亡に至った事象はなかった。重篤な事象の発現率は群間で同程度であり（2.4%，1.3%），いずれの事象も 1～2 名での発現であった。

データカットオフまでの出血性事象の発現率は RUX 群で 12.7%，BAT 群で 16.5%であった。EAIR は RUX 群で 14.8，BAT 群で 27.4 であった（5.3.5.3-4-Table 2.1-12.05）。

データカットオフまでの RUX overall の被験者の出血性事象の発現率は 11.5%であった（Table 2-50）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-10）。副作用の発現率は 1.3%であり，各事象 1 名での発現であった（5.3.5.3-4-Table 2.1-13.05）。死亡に至った事象の発現率は 0.9%であり，頭蓋内出血が 2 名（0.9%）で報告された。重篤な事象の発現率は 2.7%であり，頭蓋内出血（0.9%）を除き各事象 1 名での発現であった。本事象により RUX の投与を中止した被験者は少なく（0.9%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

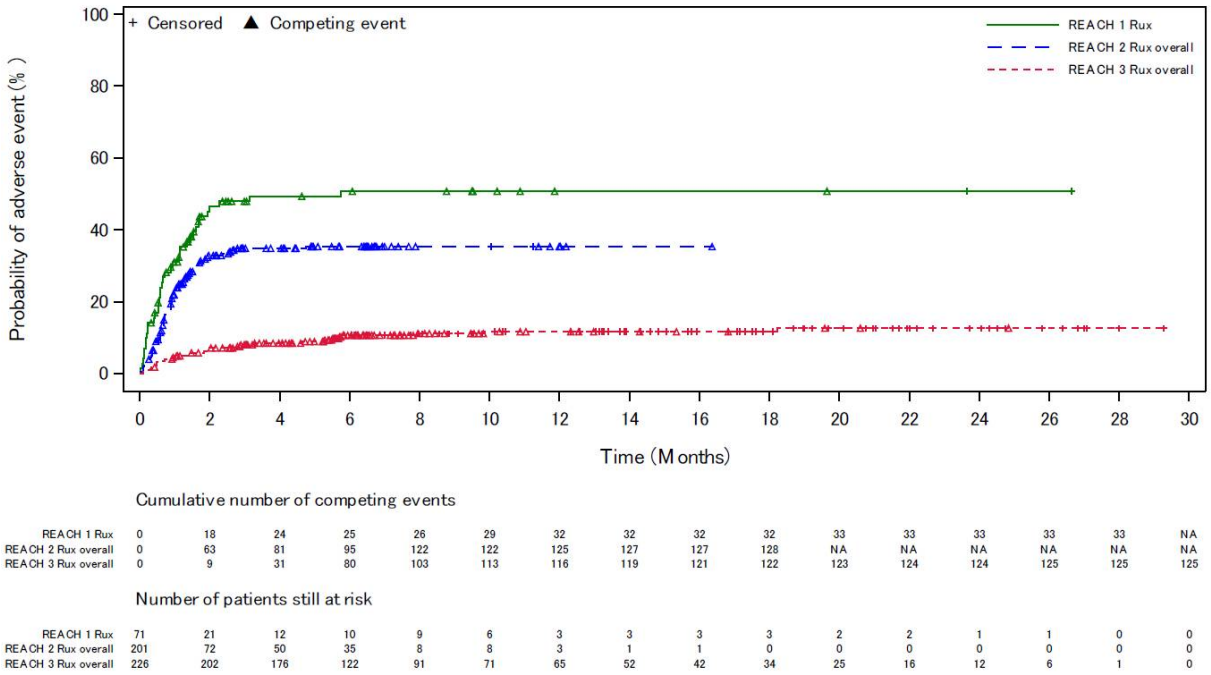
Table 2-50　慢性 GVHD の出血性事象（発現被験者数 2 名以上）（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	26 (11.5)
95% CI	(7.7, 16.4)
EAIR, n (incidence rate per 100 patient treatment years)	26 (13.6)
重症度, n (%)	
Grade 3	4 (1.8)
Grade 4	0
Grade 5	2 (0.9)

	RUX overall N = 226
副作用, n (%)	3 (1.3)
重篤な有害事象, n (%)	6 (2.7)
治験治療に対する処置, n (%)	
投与中止	2 (0.9)
減量	0
増量	0
休薬	4 (1.8)
不変/NA/不明	23 (10.2)
治療を要した有害事象, n (%)	7 (3.1)
転帰, n (%)	
回復/消失	20 (8.8)
軽快	1 (0.4)
未回復/未消失	4 (1.8)
回復/消失したが後遺症あり	0
死亡	2 (0.9)
不明	0
PT 別有害事象	
鼻出血	6 (2.7)
血尿	3 (1.3)
点状出血	3 (1.3)
挫傷	2 (0.9)
血腫	2 (0.9)
斑状出血	2 (0.9)
頭蓋内出血	2 (0.9)
腟出血	2 (0.9)

Source: 5.3.5.3-4-Table 2.1-13.05
MedDRA version 23.0
PT は発現率の降順

Figure 2-10 出血性事象の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Cumulative number of competing events

REACH 1 Rux	0	18	24	25	26	29	32	32	32	32	33	33	33	33	33	NA
REACH 2 Rux overall	0	63	81	95	122	122	125	127	127	128	NA	NA	NA	NA	NA	NA
REACH 3 Rux overall	0	9	31	80	103	113	116	119	121	122	123	124	124	125	125	125

Number of patients still at risk

REACH 1 Rux	71	21	12	10	9	6	3	3	3	3	2	2	1	1	0	0
REACH 2 Rux overall	201	72	50	35	8	8	3	1	1	0	0	0	0	0	0	0
REACH 3 Rux overall	226	202	176	122	91	71	65	52	42	34	25	16	12	6	1	0

Source: 5. 3.5.3-4-Figure 2.1-4.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.3.1 胃腸出血

急性 GVHD

C2301 試験の Day 28 までの胃腸出血の発現率は RUX 群で 9.2%，BAT 群で 6.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.07）。副作用の発現率（RUX 群 2.6%，BAT 群 0.7%，以下同順），重篤な事象の発現率（1.3%，0.7%）は群間で同程度であった。

データカットオフ 2 までの胃腸出血の発現率は RUX 群で 18.4%，BAT 群で 9.3%であった。EAIR は RUX 群で 61.8，BAT 群で 48.2 であった（5.3.5.3-4-Table 2.1-12.07）。

データカットオフ 2 までの RUX overall の被験者の胃腸出血関連の発現率は 16.4%であった（Table 2-51）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-11）。副作用の発現率は 4.0%，重篤な事象の発現率は 4.5%であった。本事象により RUX の投与を中止した被験者は少なく（2.0%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

慢性 GVHD

D2301 試験の C7D1 までの胃腸出血の発現率は RUX 群で 1.2%，BAT 群で 3.2%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.07）。胃腸出血関連の副作用の発現率（RUX 群 0%，BAT 群 1.9%，以下同順），重篤な事象の発現率（1.2%，1.3%）は群間で同程度であった。

データカットオフまでの胃腸出血の発現率は RUX 群で 1.2%，BAT 群で 3.2%であった。EAIR は RUX 群で 1.3，BAT 群で 4.8 であった（5.3.5.3-4-Table 2.1-12.07）。

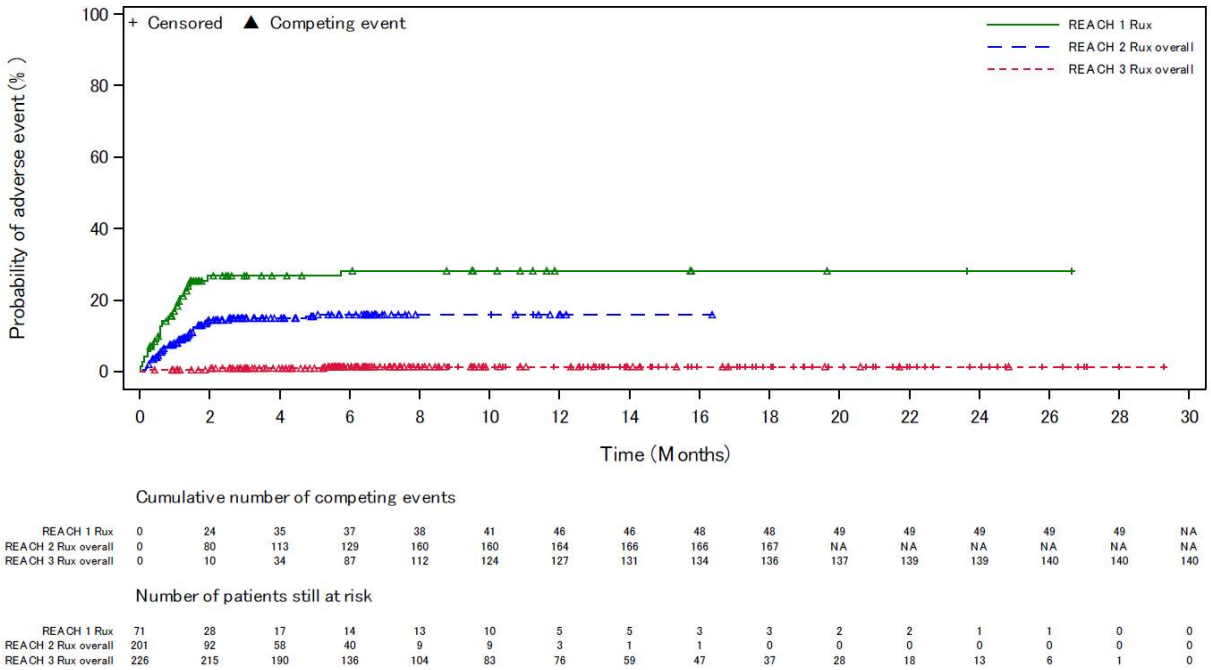
データカットオフまでの RUX overall の被験者の胃腸出血の発現率は 0.9%（2 名）であり，いずれの被験者でも重篤であった（Table 2-51）。副作用，RUX の投与中止に至った事象はなかった。

Table 2-51 胃腸出血（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 Rux overall N=226
有害事象, n (%)	33 (16.4)	20 (28.2)	2 (0.9)
95% CI	(11.6, 22.3)	(18.1, 40.1)	(0.1, 3.2)
EAIR, n (incidence rate per 100 patient treatment years)	33 (55.0)	20 (86.2)	2 (1.0)
重症度, n (%)			
Grade 3	9 (4.5)	7 (9.9)	2 (0.9)
Grade 4	6 (3.0)	3 (4.2)	0
Grade 5	1 (0.5)	NA	0
副作用, n (%)	8 (4.0)	1 (1.4)	0
重篤な有害事象, n (%)	9 (4.5)	6 (8.5)	2 (0.9)
治験治療に対する処置, n (%)			
投与中止	4 (2.0)	1 (1.4)	0
減量	0	0	0
増量	0	0	0
休薬	2 (1.0)	1 (1.4)	0
不変/NA/不明	29 (14.4)	19 (26.8)	2 (0.9)
治療を要した有害事象, n (%)	18 (9.0)	10 (14.1)	1 (0.4)
転帰, n (%)			
回復/消失	18 (9.0)	9 (12.7)	2 (0.9)
軽快	3 (1.5)	0	0
未回復/未消失	10 (5.0)	10 (14.1)	0
回復/消失したが後遺症あり	1 (0.5)	0	0
死亡	1 (0.5)	2 (2.8)	0
不明	0	0	0

Source: 5.3.5.3-4-Table 2.1-13.07
MedDRA version 23.0
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 2-11　胃腸出血の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-5.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.3.2 挫傷

急性 GVHD

C2301 試験の Day 28 までの挫傷の発現率は RUX 群で 5.9%，BAT 群で 6.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.06）。副作用（RUX 群 2.0%，BAT 群 0%，以下同順），重篤な事象（0.7%，0%）の発現率は低かった。

データカットオフ 2 までの挫傷の発現率は RUX 群で 9.2%，BAT 群で 7.3%であった。EAIR は RUX 群で 30.5，BAT 群で 39.3 であった（5.3.5.3-4-Table 2.1-12.06）。

データカットオフ 2 までの RUX overall の被験者の挫傷の発現率は 10.4%であった（Table 2-52）。副作用の発現率は 4.0%であり，重篤な事象の発現率は低く（1.0%），RUX の投与中止に至った事象はなかった。

慢性 GVHD

D2301 試験の C7D1 までの挫傷の発現率は RUX 群で 4.2%，BAT 群で 2.5%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.06）。挫傷の副作用の発現率はいずれの群も 0.6%であった。重篤な事象はなかった。

データカットオフまでの挫傷の発現率は RUX 群で 4.8%，BAT 群で 3.2%であった。EAIR は RUX 群で 5.3，BAT 群で 4.9 であった（5.3.5.3-4-Table 2.1-12.06）。

データカットオフまでの RUX overall の被験者の挫傷の発現率は 4.0%であった（Table 2-52）。挫傷の副作用の発現率は低く（0.4%），重篤な事象，RUX の投与中止に至った事象はなかった。

Table 2-52 挫傷（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 Rux overall N=226
有害事象, n (%)	21 (10.4)	10 (14.1)	9 (4.0)
95% CI	(6.6, 15.5)	(7.0, 24.4)	(1.8, 7.4)
EAIR, n (incidence rate per 100 patient treatment years)	21 (35.3)	10 (39.4)	9 (4.5)
重症度, n (%)			
Grade 3	2 (1.0)	1 (1.4)	0
Grade 4	0	0	0
Grade 5	0	NA	0
副作用, n (%)	8 (4.0)	2 (2.8)	1 (0.4)
重篤な有害事象, n (%)	2 (1.0)	0	0
治験治療に対する処置, n (%)			
投与中止	0	0	0
減量	0	0	0
増量	0	0	0
休薬	1 (0.5)	0	1 (0.4)
不変/NA/不明	21 (10.4)	10 (14.1)	9 (4.0)
治療を要した有害事象, n (%)	5 (2.5)	2 (2.8)	0
転帰, n (%)			
回復/消失	13 (6.5)	5 (7.0)	7 (3.1)
軽快	2 (1.0)	0	0
未回復/未消失	6 (3.0)	4 (5.6)	2 (0.9)
回復/消失したが後遺症あり	0	0	0
死亡	0	0	0
不明	2 (1.0)	1 (1.4)	0

Source: 5.3.5.3-4-Table 2.1-13.06
MedDRA version 23.0
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

2.1.5.3.3 頭蓋内出血

急性 GVHD

C2301 試験の Day 28 までの頭蓋内出血は RUX 群では認められず，BAT 群で 0.7%に認められた（5.3.5.3-4-Table 2.1-11.08）。データカットオフ 2 までの RUX overall の被験者での発現率は

1.0%であった（5.3.5.3-4-Table 2.1-13.08）。副作用及び重篤な事象の発現率は，いずれも 0.5%で低かった。

慢性 GVHD

D2301 試験の C7D1 までの頭蓋内出血はいずれの群でも認められなかった（5.3.5.3-4-Table 2.1-11.08）。データカットオフまでの RUX overall の被験者での発現率は 0.9%，副作用は 0.4%であった（5.3.5.3-4-Table 2.1-13.08）。いずれの事象も重篤であった。

2.1.5.3.4 その他の出血性事象

急性 GVHD

C2301 試験の Day 28 までのその他の出血性事象の発現率は RUX 群で 13.2%，BAT 群で 10.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.09）。

データカットオフ 2 までのその他の出血性事象の発現率は RUX 群で 19.1%，BAT 群で 16.7%であった。EAIR は RUX 群で 65.0，BAT 群で 93.7 であった（5.3.5.3-4-Table 2.1-12.09）。

データカットオフ 2 までの RUX overall の被験者のその他の出血性事象の発現率は 17.4%であった（Table 2-53）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に発現した（Figure 2-12）。副作用の発現率は 4.5%であり，重篤な事象の発現率は低く（1.0%），RUX の投与中止に至った事象はなかった。

慢性 GVHD

D2301 試験の C7D1 までのその他の出血性事象の発現率は RUX 群で 6.7%，BAT 群で 10.1%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.09）。

データカットオフまでのその他の出血性事象の発現率は RUX 群で 7.3%，BAT 群で 11.4%であった。EAIR は RUX 群で 8.1，BAT 群で 18.4 であった（5.3.5.3-4-Table 2.1-12.09）。

データカットオフまでの RUX overall の被験者のその他の出血性事象の発現率は 6.6%であった（Table 2-53）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-12）。副作用（0.4%）及び重篤な事象（0.9%）の発現率は低く，RUX の投与中止に至った事象はなかった。

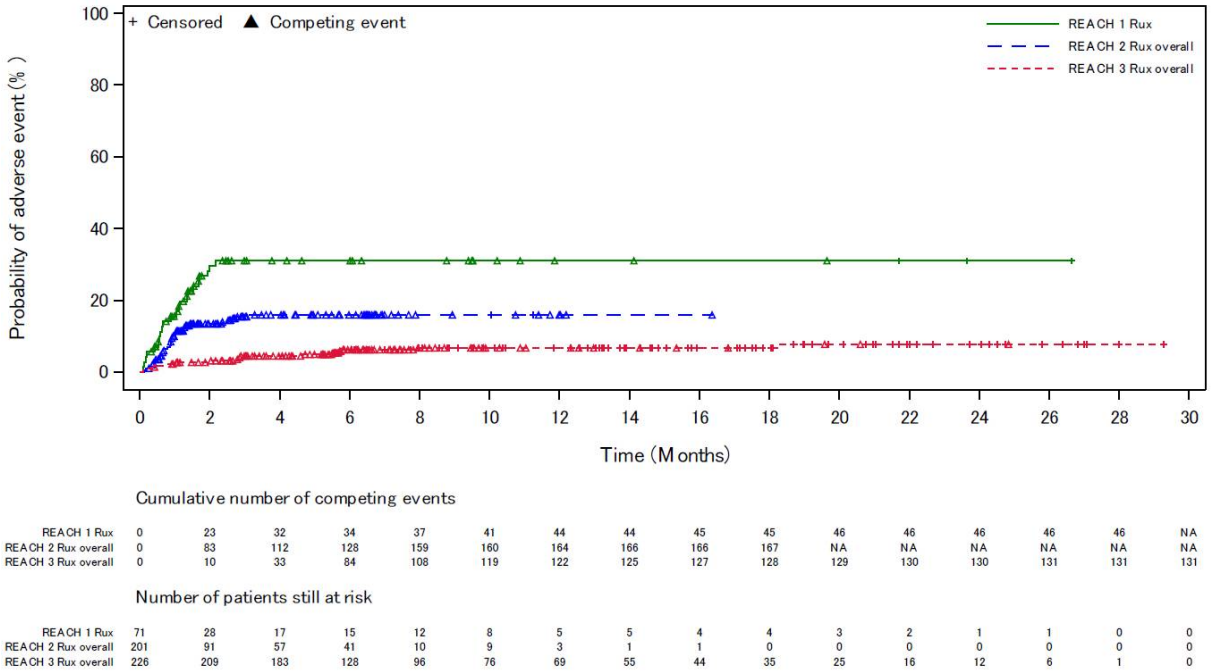
Table 2-53 その他の出血性事象（C2301 試験，271 試験，及び D2301 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
有害事象, n (%)	35 (17.4)	22 (31.0)	15 (6.6)
95% CI	(12.4, 23.4)	(20.5, 43.1)	(3.8, 10.7)
EAIR, n (incidence rate per 100 patient treatment years)	35 (59.1)	22 (95.7)	15 (7.6)
重症度, n (%)			
Grade 3	4 (2.0)	2 (2.8)	2 (0.9)

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71	D2301 試験 RUX overall N = 226
Grade 4	0	2 (2.8)	0
Grade 5	1 (0.5)	NA	0
副作用, n (%)	9 (4.5)	5 (7.0)	1 (0.4)
重篤な有害事象, n (%)	2 (1.0)	2 (2.8)	2 (0.9)
治験治療に対する処置, n (%)			
投与中止	0	0	0
減量	0	0	0
増量	0	0	0
休薬	1 (0.5)	1 (1.4)	1 (0.4)
不変/NA/不明	34 (16.9)	22 (31.0)	14 (6.2)
治療を要した有害事象, n (%)	15 (7.5)	6 (8.5)	4 (1.8)
転帰, n (%)			
回復/消失	27 (13.4)	11 (15.5)	12 (5.3)
軽快	0	0	1 (0.4)
未回復/未消失	11 (5.5)	12 (16.9)	2 (0.9)
回復/消失したが後遺症あり	0	0	0
死亡	1 (0.5)	1 (1.4)	0
不明	0	0	0

Source: 5.3.5.3-4-Table 2.1-13.09
MedDRA version 23.0
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 2-12　その他の出血性事象の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-6.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.4　その他の臨床的に注目すべき有害事象

2.1.5.4.1 トランスアミナーゼ上昇

急性 GVHD

C2301 試験の Day 28 までのトランスアミナーゼ上昇の発現率は RUX 群で 10.5%，BAT 群で 8.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.21）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（RUX 群 2.0%，BAT 群 2.7%，以下同順）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率に群間で大きな違いはなかった（3.3%，0.7%）。重篤な事象は認められなかった。

データカットオフ 2 までのトランスアミナーゼ上昇の発現率は RUX 群で 17.8%，BAT 群で 10.0%であった。EAIR は RUX 群で 63.4，BAT 群で 56.3 であった（5.3.5.3-4-Table 2.1-12.21）。

データカットオフ 2 までの RUX overall の被験者のトランスアミナーゼ上昇の発現率は 14.9%であった（Table 2-54）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-13）。副作用の発現率は 4.0%であった。死亡に至った事象はなかった。重篤な事象の発現率は 1.0%と低く，PT 別事象は肝機能検査異常，トランスアミナーゼ上昇（各 0.5%）であった。本事

象により RUX の投与を中止した被験者は少なく（0.5%），多くの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

肝機能検査の結果及び Hy's law に該当した被験者については 3.2.1 項に記載した。

Table 2-54 急性 GVHD のトランスアミナーゼ上昇（C2301 試験及び 271 試験, SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	30 (14.9)	22 (31.0)
95% CI	(10.3, 20.6)	(20.5, 43.1)
EAIR, n (incidence rate per 100 patient treatment years)	30 (52.8)	22 (112.9)
重症度, n (%)		
Grade 3	9 (4.5)	6 (8.5)
Grade 4	4 (2.0)	0
Grade 5	0	NA
副作用, n (%)	8 (4.0)	8 (11.3)
重篤な有害事象, n (%)	2 (1.0)	1 (1.4)
治験治療に対する処置, n (%)		
投与中止	1 (0.5)	0
減量	5 (2.5)	3 (4.2)
増量	0	0
休薬	1 (0.5)	3 (4.2)
不変/NA/不明	26 (12.9)	20 (28.2)
治療を要した有害事象, n (%)	7 (3.5)	0
転帰, n (%)		
回復/消失	17 (8.5)	13 (18.3)
軽快	3 (1.5)	1 (1.4)
未回復/未消失	10 (5.0)	8 (11.3)
回復/消失したが後遺症あり	0	0
死亡	0	0
不明	0	0
PT 別有害事象		
アラニンアミノトランスフェラーゼ増加	18 (9.0)	19 (26.8)
アスパラギン酸アミノトランスフェラーゼ増加	10 (5.0)	18 (25.4)
肝機能検査値上昇	3 (1.5)	0
肝酵素上昇	2 (1.0)	0
薬物性肝障害	2 (1.0)	0
トランスアミナーゼ上昇	1 (0.5)	0
肝機能検査異常	1 (0.5)	0

Source: 5.3.5.3-4-Table 2.1-13.21
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までのトランスアミナーゼ上昇の発現率は RUX 群で 18.2%，BAT 群で 7.6%であり，RUX 群で BAT 群と比べて高かった（5.3.5.3-4-Table 2.1-11.21）。PT 別で，アラニンアミノトランスフェラーゼ増加の発現率は RUX 群で BAT 群と比べて高く，その他の PT 別事象は群間で同程度であった。Grade 3 以上の事象の発現率は RUX 群で 6.7%，BAT 群で 0.6%（以下同順）であった（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率も RUX 群で高い傾向が認められた（9.7%，1.3%）。死亡に至った事象はなく，重篤な事象（0.6%，0%）は RUX 群のみで認められ，1 名での発現であった。

データカットオフまでのトランスアミナーゼ上昇の発現率は RUX 群で 20.6%，BAT 群で 7.6%であった。EAIR は RUX 群で 26.0，BAT 群で 12.3 であった（5.3.5.3-4-Table 2.1-12.21）。

データカットオフまでの RUX overall の被験者のトランスアミナーゼ上昇の発現率は 17.3%であった（Table 2-55）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-13）。副作用の発現率は 9.3%であった。死亡に至った事象はなく，重篤な事象の発現率は 0.4%（1 名）と低かった。本事象により RUX の投与を中止した被験者は少なく（0.9%），ほとんどの被験者で用量調節又は休薬が不要で，加療により管理可能であった。

肝機能検査の結果は 3.2.1 項に記載した。RUX 群で Hy's law に該当した被験者はいなかった。

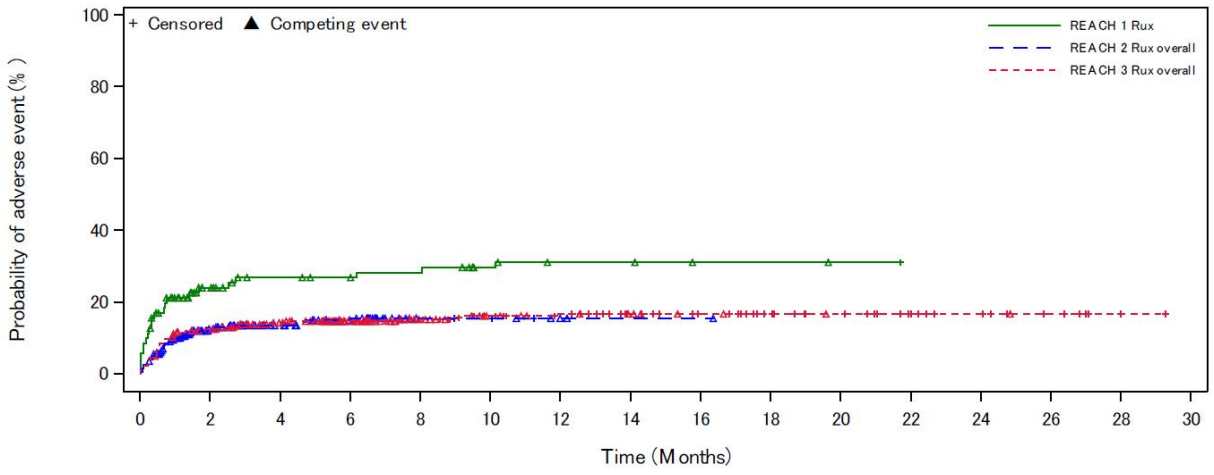
Table 2-55 慢性 GVHD のトランスアミナーゼ上昇（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	39 (17.3)
95% CI	(12.6, 22.8)
EAIR, n (incidence rate per 100 patient treatment years)	39 (21.9)
重症度, n (%)	
Grade 3	12 (5.3)
Grade 4	2 (0.9)
Grade 5	0
副作用, n (%)	21 (9.3)
重篤な有害事象, n (%)	1 (0.4)
治験治療に対する処置, n (%)	
投与中止	2 (0.9)
減量	3 (1.3)
増量	0
休薬	7 (3.1)
不変/NA/不明	35 (15.5)
治療を要した有害事象, n (%)	7 (3.1)
転帰, n (%)	
回復/消失	32 (14.2)
軽快	0

	RUX overall N = 226
未回復/未消失	9 (4.0)
回復/消失したが後遺症あり	1 (0.4)
死亡	0
不明	0
PT 別有害事象	
アラニンアミノトランスフェラーゼ増加	32 (14.2)
アスパラギン酸アミノトランスフェラーゼ増加	18 (8.0)
トランスアミナーゼ上昇	4 (1.8)
高トランスアミナーゼ血症	2 (0.9)
肝酵素上昇	1 (0.4)
肝機能検査異常	1 (0.4)
アラニンアミノトランスフェラーゼ異常	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.21
MedDRA version 23.0
PT は発現率の降順

Figure 2-13　トランスアミナーゼ上昇の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Cumulative number of competing events

REACH 1 Rux	0	29	36	38	39	43	45	45	47	47	48	48	NA	NA	NA	NA
REACH 2 Rux overall	0	88	121	134	162	162	165	166	166	167	NA	NA	NA	NA	NA	NA
REACH 3 Rux overall	0	8	27	76	100	109	112	114	117	118	119	119	119	120	120	120

Number of patients still at risk

REACH 1 Rux	71	25	16	14	12	7	4	4	2	2	1	0	0	0	0	0
REACH 2 Rux overall	201	88	53	37	8	7	2	1	1	0	0	0	0	0	0	0
REACH 3 Rux overall	226	190	167	117	87	67	59	47	38	29	22	16	12	6	1	0

Source: 5.3.5.3-4-Figure 2.1-14.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.4.2 脂質異常

急性 GVHD

C2301 試験の Day 28 までの脂質異常の発現率は RUX 群で 3.9%，BAT 群で 4.0%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.26）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率はいずれの群も 1.3%であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用は RUX 群のみで 2 名（1.3%）に認められた。重篤な事象はなかった。

データカットオフ 2 までの脂質異常の発現率は RUX 群で 9.9%，BAT 群で 7.3%であった。EAIR は RUX 群で 34.1，BAT 群で 39.1 であった（5.3.5.3-4-Table 2.1-12.26）。

データカットオフ 2 までの RUX overall の被験者の脂質異常の発現率は 10.4%であった（Table 2-56）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-14）。副作用の発現率は 2.5%であり，最も多かった事象は血中コレステロール増加（1.5%）であった（5.3.5.3-4-Table 2.1-13.26）。重篤な事象，RUX の投与中止に至った事象はなかった。

脂質検査の結果は 3.2.2 項に示した。

Table 2-56　急性 GVHD の脂質異常（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	21 (10.4)	9 (12.7)
95% CI	(6.6, 15.5)	(6.0, 22.7)
EAIR, n (incidence rate per 100 patient treatment years)	21 (36.5)	9 (40.8)
重症度, n (%)		
Grade 3	7 (3.5)	1 (1.4)
Grade 4	4 (2.0)	2 (2.8)
Grade 5	0	NA
副作用, n (%)	5 (2.5)	2 (2.8)
重篤な有害事象, n (%)	0	0
治験治療に対する処置, n (%)		
投与中止	0	0
減量	1 (0.5)	0
増量	0	0
休薬	0	0
不変/NA/不明	21 (10.4)	9 (12.7)
治療を要した有害事象, n (%)	10 (5.0)	3 (4.2)
転帰, n (%)		
回復/消失	6 (3.0)	3 (4.2)
軽快	5 (2.5)	1 (1.4)
未回復/未消失	13 (6.5)	6 (8.5)
回復/消失したが後遺症あり	0	0
死亡	0	0

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
不明	0	0
PT 別有害事象		
高トリグリセリド血症	11 (5.5)	9 (12.7)
血中コレステロール増加	6 (3.0)	1 (1.4)
高脂血症	5 (2.5)	0
高コレステロール血症	2 (1.0)	0
脂質異常症	1 (0.5)	0
血中トリグリセリド増加	1 (0.5)	0

Source: 5.3.5.3-4-Table 2.1-13.26
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの脂質異常の発現率は RUX 群で 18.8%，BAT 群で 14.6%（以下同順）であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.26）。いずれの PT 別事象も発現率は群間で同程度であった。Grade 3 以上の事象の発現率は群間で同程度であった（7.3%，7.0%）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率に群間で大きな違いはなく（4.2%，1.3%），いずれの事象も発現率は低かった。重篤な事象は認められなかった。

データカットオフまでの脂質異常の発現率は RUX 群で 20.6%，BAT 群で 14.6%であった。EAIR は RUX 群で 26.4，BAT 群で 25.1 であった（5.3.5.3-4-Table 2.1-12.26）。

データカットオフまでの RUX overall の被験者の脂質異常の発現率は 17.7%であった（Table 2-57）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-14）。副作用の発現率は 4.4%であり，最も多かった事象は高コレステロール血症（2.2%）であった（5.3.5.3-4-Table 2.1-13.26）。重篤な事象，RUX の投与中止に至った事象はなかった。

脂質検査の結果は 3.2.2 項に示した。

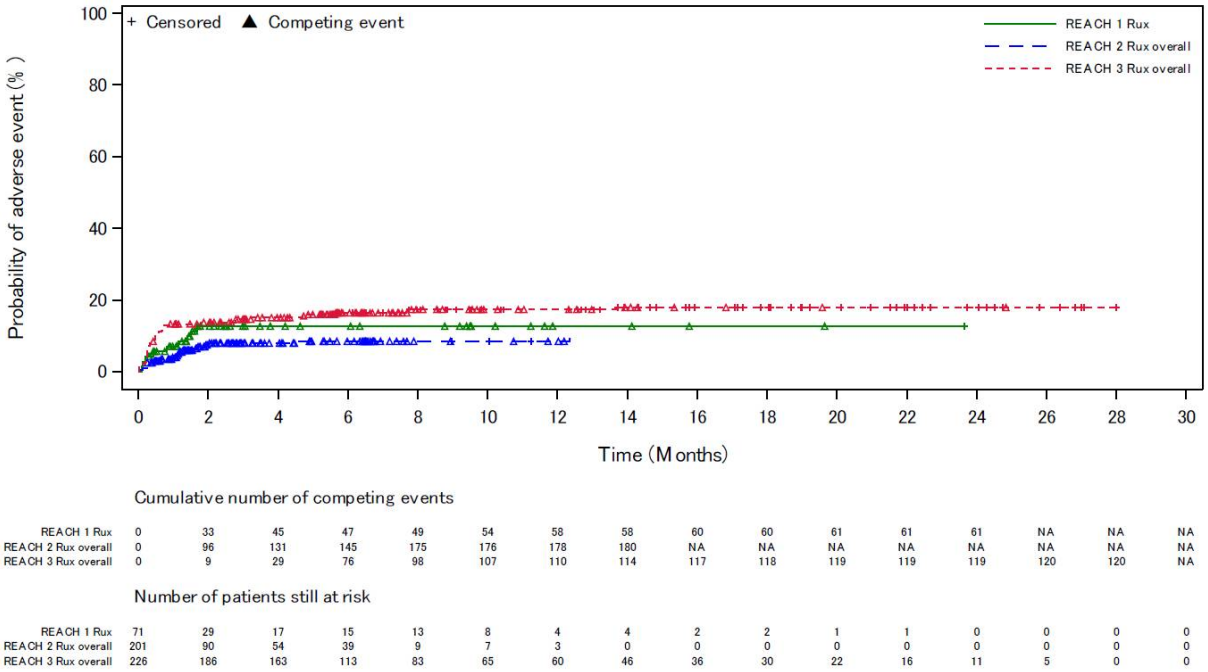
Table 2-57 慢性 GVHD の脂質異常（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	40 (17.7)
95% CI	(13.0, 23.3)
EAIR, n (incidence rate per 100 patient treatment years)	40 (22.8)
重症度, n (%)	
Grade 3	9 (4.0)
Grade 4	4 (1.8)
Grade 5	0
副作用, n (%)	10 (4.4)

	RUX overall N = 226
重篤な有害事象, n (%)	0
治験治療に対する処置, n (%)	
投与中止	0
減量	0
増量	0
休薬	0
不変/NA/不明	40 (17.7)
治療を要した有害事象, n (%)	27 (11.9)
転帰, n (%)	
回復/消失	18 (8.0)
軽快	1 (0.4)
未回復/未消失	21 (9.3)
回復/消失したが後遺症あり	1 (0.4)
死亡	0
不明	0
欠測	2 (0.9)
PT 別有害事象	
高トリグリセリド血症	19 (8.4)
血中コレステロール増加	13 (5.8)
高コレステロール血症	16 (7.1)
高脂血症	4 (1.8)
脂質異常症	1 (0.4)
低比重リポ蛋白増加	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.26
MedDRA version 23.0
PT は発現率の降順

Figure 2-14　脂質異常の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Cumulative number of competing events

REACH 1 Rux	0	33	45	47	49	54	58	58	60	60	61	61	61	NA	NA	NA
REACH 2 Rux overall	0	96	131	145	175	176	178	180	NA	NA	NA	NA	NA	NA	NA	NA
REACH 3 Rux overall	0	9	29	76	98	107	110	114	117	118	119	119	119	120	120	NA

Number of patients still at risk

REACH 1 Rux	71	29	17	15	13	8	4	4	2	2	1	1	0	0	0	0
REACH 2 Rux overall	201	90	54	39	9	7	3	0	0	0	0	0	0	0	0	0
REACH 3 Rux overall	226	186	163	113	83	65	60	46	36	30	22	16	11	5	0	0

Source: 5. 3.5.3-4-Figure 2.1-15.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.4.3 高血圧

急性 GVHD

C2301 試験の Day 28 までの高血圧の発現率は RUX 群で 10.5%，BAT 群で 9.3%（以下同順）であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.27）。Grade 3 以上の事象の発現率は群間で同程度であった（5.9%，4.0%）（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-1.8）。副作用の発現率に群間で大きな違いはなかった（2.6%，0.7%）。重篤な事象は認められなかった。

データカットオフ 2 までの高血圧の発現率は RUX 群で 13.8%，BAT 群で 12.7%であった。EAIR は RUX 群で 48.2，BAT 群で 73.0 であった（5.3.5.3-4-Table 2.1-12.27）。

データカットオフ 2 までの RUX overall の被験者の高血圧の発現率は 13.4%であった（Table 2-58）。ほとんどの事象は RUX 投与開始後 2 ヵ月以内に初回発現した（Figure 2-15）。副作用の発現率は 2.0%と低かった（5.3.5.3-4-Table 2.1-13.27）。重篤な事象，RUX の投与中止に至った事象はなかった。

臨床的に注目すべき血圧上昇の結果は 4.1.1 項に示した。

Table 2-58 急性 GVHD の高血圧（C2301 試験及び 271 試験，SAF）

	C2301 試験 RUX overall N = 201	271 試験 RUX N = 71
有害事象, n (%)	27 (13.4)	16 (22.5)
95% CI	(9.0, 18.9)	(13.5, 34.0)
EAIR, n (incidence rate per 100 patient treatment years)	27 (47.2)	16 (58.5)
重症度, n (%)		
Grade 3	11 (5.5)	10 (14.1)
Grade 4	0	0
Grade 5	0	NA
副作用, n (%)	4 (2.0)	2 (2.8)
重篤な有害事象, n (%)	0	0
治験治療に対する処置, n (%)		
投与中止	0	0
減量	0	0
増量	0	0
休薬	0	0
不変/NA/不明	27 (13.4)	16 (22.5)
治療を要した有害事象, n (%)	25 (12.4)	15 (21.1)
転帰, n (%)		
回復/消失	11 (5.5)	8 (11.3)
軽快	0	0
未回復/未消失	16 (8.0)	8 (11.3)
回復/消失したが後遺症あり	0	0
死亡	0	0
不明	0	0
PT 別有害事象		
高血圧	27 (13.4)	16 (22.5)

Source: 5.3.5.3-4-Table 2.1-13.27
MedDRA version 23.0
PT は RUX overall の被験者の発現率の降順
C2301 試験はデータカットオフ 2 までの結果

慢性 GVHD

D2301 試験の C7D1 までの高血圧の発現率は RUX 群で 16.4%，BAT 群で 12.7%（以下同順）であり，RUX 群で BAT 群と比べて高い傾向がみられた（5.3.5.3-4-Table 2.1-11.27）。Grade 3 以上の事象の発現率は群間で同程度であった（6.1%，7.0%）（5.3.5.1-2-D2301 試験-Table 14.3.1-1.11）。副作用の発現率はいずれの群も低かった（1.2%，2.5%）。重篤な事象は認められなかった。

データカットオフまでの高血圧の発現率は RUX 群で 18.2%，BAT 群で 13.3%であった。EAIR は RUX 群で 21.6，BAT 群で 22.4 であった（5.3.5.3-4-Table 2.1-12.27）。

データカットオフまでの RUX overall の被験者の高血圧の発現率は 15.0%であった（Table 2-59）。ほとんどの事象は RUX 投与開始後 4 ヵ月以内に初回発現した（Figure 2-15）。副作用は高血圧及び血圧上昇で各 1 名に認められた。死亡に至った事象はなかった。重篤な事象は高血圧（1 名）のみであった。RUX の投与中止に至った事象はなかった。

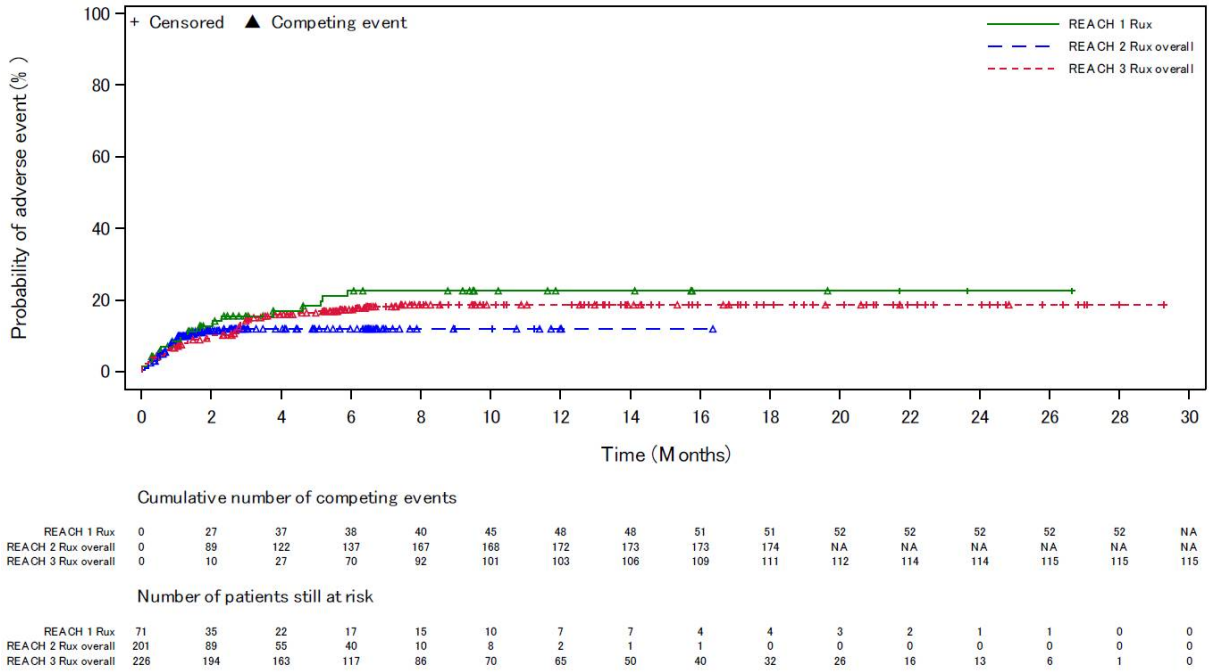
臨床的に注目すべき血圧上昇の結果は 4.1.2 項に示した。

Table 2-59 慢性 GVHD の高血圧（D2301 試験，SAF，データカットオフまで）

	RUX overall N = 226
有害事象, n (%)	34 (15.0)
95% CI	(10.6, 20.4)
EAIR, n (incidence rate per 100 patient treatment years)	34 (18.0)
重症度, n (%)	
Grade 3	13 (5.8)
Grade 4	0
Grade 5	0
副作用, n (%)	2 (0.9)
重篤な有害事象, n (%)	1 (0.4)
治験治療に対する処置, n (%)	
投与中止	0
減量	0
増量	0
休薬	0
不変/NA/不明	34 (15.0)
治療を要した有害事象, n (%)	27 (11.9)
転帰, n (%)	
回復/消失	20 (8.8)
軽快	1 (0.4)
未回復/未消失	10 (4.4)
回復/消失したが後遺症あり	2 (0.9)
死亡	0
不明	0
欠測	2 (0.9)
PT 別有害事象	
高血圧	33 (14.6)
血圧異常	1 (0.4)
血圧上昇	1 (0.4)

Source: 5.3.5.3-4-Table 2.1-13.27
MedDRA version 23.0
PT は発現率の降順

Figure 2-15　　高血圧の累積発現率（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 2.1-16.2
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果
各被験者での当該事象の初回発現時期を示す。死亡，理由を問わない投与中止を競合リスクとした。

2.1.5.4.4 血栓塞栓症

急性 GVHD

C2301 試験の Day 28 までの血栓塞栓症の発現率は RUX 群で 8.6%，BAT 群で 6.7%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.28）。データカットオフ 2 までの血栓塞栓症の発現率は RUX 群で 12.5%，BAT 群で 11.3%であり，EAIR は RUX 群で 41.8，BAT 群で 61.0 であった（5.3.5.3-4-Table 2.1-12.28）。RUX overall の被験者での発現率は 12.4%であった（5.3.5.3-4-Table 2.1-13.28）。副作用の発現率は低く（1.0%），重篤な事象の発現率は 5.0%，RUX の投与中止に至った事象は 1.5%であった。

慢性 GVHD

D2301 試験の C7D1 までの血栓塞栓症の発現率は RUX 群で 4.8%，BAT 群で 7.6%であり，群間で同程度であった（5.3.5.3-4-Table 2.1-11.28）。データカットオフまでの血栓塞栓症の発現率は RUX 群で 6.1%，BAT 群で 7.6%であり，EAIR は RUX 群で 6.6，BAT 群で 11.6 であった（5.3.5.3-4-Table 2.1-12.28）。RUX overall の被験者での発現率は 4.4%であった（5.3.5.3-4-Table 2.1-13.28）。血栓塞栓症の副作用（0.4%），重篤な事象（1.3%），RUX の投与中止に至った事象（0.4%）の発現率は低かった。

2.1.5.4.5 悪性腫瘍

NMSC の発現は少なかったため，悪性腫瘍で評価した。NMSC の定義に含まれる PT 別事象はすべて悪性腫瘍の定義に含まれた（5.3.5.3-4-Listing 1）。

急性 GVHD

C2301 試験の Day 28 までに悪性腫瘍はいずれの群でも認められなかった（5.3.5.3-4-Table 2.1-11.22）。データカットオフ 2 までに悪性腫瘍は RUX overall の被験者で 4 名（2.0%）に認められ，PT 別事象は中枢神経系リンパ腫，びまん性大細胞型 B 細胞性リンパ腫，多形性神経膠芽細胞腫，白血病再発（各 1 名）であった。びまん性大細胞型 B 細胞性リンパ腫は RUX と他の急性 GVHD 治療薬の両方に関連するか，又は判別不可能と判断された。死亡に至った事象はなく，中枢神経系リンパ腫及び多形性神経膠芽細胞腫は重篤であった。4 名全員が悪性腫瘍により RUX の投与を中止した（5.3.5.1-1-C2301 試験 CSR2-Listing 16.2.7-1.1，5.3.5.3-4-Table 2.1-13.22）。

慢性 GVHD

D2301 試験の C7D1 までに悪性腫瘍は RUX 群で 2 名（1.2%）に認められ，BAT 群では認められなかった。RUX 群で認められた事象はいずれも NMSC であった（5.3.5.3-4-Table 2.1-11.23，Table 2.1-11.22）。データカットオフまでに悪性腫瘍は RUX overall の被験者で 4 名（1.8%）に認められた。PT 別事象は基底細胞癌（2 名），カポジ肉腫，皮膚有棘細胞癌（各 1 名）であり，いずれも RUX と関連なしと判断された。カポジ肉腫を除き NMSC であった。死亡に至った事象はなく，基底細胞癌及びカポジ肉腫は重篤であった。1 名で悪性腫瘍（カポジ肉腫）により RUX の投与を中止した（5.3.5.1-2-D2301 試験-Listing 16.2.7-1，5.3.5.3-4-Table 2.1-13.23，Table 2.1-13.22）。

2.1.5.4.6 めまい

急性 GVHD

C2301 試験の Day 28 までのめまいの発現率は RUX 群（2.6%）と BAT 群（2.0%）で同程度であった（5.3.5.3-4-Table 2.1-11.24）。データカットオフ 2 までの RUX overall の被験者での発現率は 6.0%であった。重篤な事象は 1 名（0.5%）で認められた（5.3.5.3-4-Table 2.1-13.24）。

慢性 GVHD

D2301 試験の C7D1 までのめまいの発現率は RUX 群（2.4%）と BAT 群（2.5%）で同程度であった（5.3.5.3-4-Table 2.1-11.24）。データカットオフまでの RUX overall の被験者での発現率は 3.1%であった。重篤な事象はなかった（5.3.5.3-4-Table 2.1-13.24）。

2.1.5.4.7 骨折

急性 GVHD

C2301 試験の Day 28 までの骨折の発現率は RUX 群（2.0%）と BAT 群（0.7%）で同程度であった（5.3.5.3-4-Table 2.1-11.29）。データカットオフ 2 までの RUX overall の被験者での発現率は 3.5%であった。副作用は 1 名（0.5%），重篤な事象は 3 名（1.5%）で認められた（5.3.5.3-4-Table 2.1-13.29）。

慢性 GVHD

D2301 試験の C7D1 までの骨折の発現率は RUX 群（2.4%）と BAT 群（3.8%）で同程度であった（5.3.5.3-4-Table 2.1-11.29）。データカットオフまでの RUX overall の被験者での発現率は 3.5%であった。副作用は認められず，重篤な事象は 1 名（0.4%）のみで認められた（5.3.5.3-4-Table 2.1-13.29）。

2.1.5.4.8 体重増加

急性 GVHD

C2301 試験の Day 28 までの体重増加の発現率は RUX 群（2.0%）と BAT 群（2.0%）で同じであった（5.3.5.3-4-Table 2.1-11.25）。

データカットオフ 2 までの RUX overall の被験者での発現率は 1.5%と低く，いずれの事象も Grade 3 未満であった（5.3.5.3-4-Table 2.1-13.25）。副作用は 1 名（0.5%）で，重篤な事象はなかった。臨床的に注目すべき体重増加の結果は 4.1.1 項に示した。

慢性 GVHD

D2301 試験の C7D1 までの体重増加の発現率は RUX 群（4.8%）と BAT 群（2.5%）で同程度であった（5.3.5.3-4-Table 2.1-11.25）。

データカットオフまでの RUX overall の被験者での発現率は 3.5%と低く，いずれの事象も Grade 3 未満であった（5.3.5.3-4-Table 2.1-13.25）。副作用は 2 名（0.9%）で，重篤な事象はなかった。臨床的に注目すべき体重増加の結果は 4.1.2 項に示した。

2.2 個別有害事象の文章による説明

死亡，その他の重篤な有害事象並びに他の重要な有害事象の叙述は，すべて各試験の試験総括報告書に示した。評価資料とした C2301 試験及び D2301 試験の RUX 投与被験者の死亡，日本人 RUX 投与被験者の重篤な有害事象の叙述を「2.7.6 個々の試験のまとめ」に示した。

3 臨床検査値の評価

臨床検査値の異常値の基準，統計解析手法，解析データの提示方法は 1.1.3.2.3 項に示す。本項では，各小項目の中で急性 GVHD，慢性 GVHD の順に結果を示す。

3.1 血液学的検査

急性 GVHD

C2301 試験の血液学的検査では，いずれの項目も，ベースラインで Grade 0～2 であった被験者の割合は RUX 群と BAT 群で同程度であった（5.3.5.3-4-Table 3.3-6）。ベースラインで発現率が高かった（いずれかの群で 10%以上）Grade 3 又は 4 の異常は，Grade 3 のヘモグロビン低値（RUX 群 8.6%，BAT 群 11.3%，以下同順），Grade 3 のリンパ球数低値（38.2%，35.3%），Grade 4 のリンパ球数低値（21.1%，29.3%），Grade 3 の血小板数低値（18.4%，22.0%）であった。

Day 28 までに新たに発現又はベースラインに比べて Grade 3 又は 4 の低値に悪化した血液学的検査値異常は，ヘモグロビン低値（Grade 3：31.2%，32.1%），白血球数低値（Grade 3：26.8%，22.9%，Grade 4：16.0%，17.6%），リンパ球数低値（Grade 3：36.7%，38.5%，Grade 4：53.8%，53.8%），好中球数低値（Grade 3：10.3%，16.0%，Grade 4：12.3%，10.4%），血小板数低値（Grade 3：36.1%，41.0%，Grade 4：32.4%，35.8%）であり，いずれの項目も発現率は群間で同程度であった（5.3.5.3-4-Table 3.3-5）。

データカットオフ 2 までの，RUX overall の被験者で新たに発現又はベースラインに比べて悪化した血液学的検査値異常を Table 3-1 に示す。発現率が高かった（30%以上）Grade 3 の異常はヘモグロビン低値（47.7%），白血球数低値（34.8%），リンパ球数低値（37.8%），血小板数低値（31.3%）であり，Grade 4 の異常はリンパ球数低値（60.3%），血小板数低値（47.7%）であった。

検査値の平均値（Figure 3-1～Figure 3-5）は，ヘモグロビンは Week 4 まではベースラインよりも低く推移し，Week 8 以降は増加した。白血球数は Week 2 から減少し，Week 4 以降は徐々に増加して Week 48 にベースライン程度まで回復した。リンパ球数は Week 4 までベースラインと同程度に推移し，Week 8 から Week 36 まで増加した。好中球数は Week 1 から減少し，試験期間を通してベースラインより低く推移した。血小板数は Week 4 まで減少した後 Week 12 にベースライン程度まで回復し，その後増加した。

慢性 GVHD

D2301 試験の血液学的検査では，いずれの項目も，ベースラインで Grade 2 以下の低値又は正常値であった被験者の割合は RUX 群と BAT 群で同程度であった（5.3.5.1-2-D2301 試験-Table 14.3-3.1）。ベースラインで発現率が高かった（いずれかの群で 5%以上）Grade 3 又は 4 の

異常は，Grade 3 のリンパ球数低値（RUX 群 11.5%，BAT 群 11.4%，以下同順），Grade 3 の血小板数低値（3.0%，5.7%）であった。

C7D1 までに新たに発現又はベースラインに比べて Grade 3 又は 4 の低値に悪化した血液学的検査値異常は，ヘモグロビン低値（Grade 3：14.1%，9.7%），白血球数低値（Grade 3：6.2%，6.5%，Grade 4：5.5%，1.9%），リンパ球数低値（Grade 3：15.4%，15.2%，Grade 4：9.3%，10.7%），好中球数低値（Grade 3：6.8%，3.9%，Grade 4：5.5%，6.5%），血小板数低値（Grade 3：8.2%，8.3%，Grade 4：10.4%，7.8%）であり，いずれの項目も発現率は群間で同程度であった（5.3.5.3-4-Table 3.3-5）。

データカットオフまでの，RUX overall の被験者で新たに発現又はベースラインに比べて悪化した血液学的検査値異常を Table 3-1 に示す。発現率が高かった（10%以上）Grade 3 の異常はヘモグロビン低値（14.8%），リンパ球数低値（16.9%）であり，Grade 4 の異常は血小板数低値（10.7%）であった。

検査値の平均値（Figure 3-1～Figure 3-5）は，ヘモグロビンは Week 2 から Week 16 まで減少した後増加し，Week 48 にベースライン程度まで回復した。白血球数は Week 1 から減少し，試験期間を通してベースラインより低く推移した。リンパ球数は Week 1 に増加した後，試験期間を通して変動はみられなかった。好中球数は Week 1 から減少し，試験期間を通してベースラインより低く推移した。血小板数は Week 8 以降増加した。

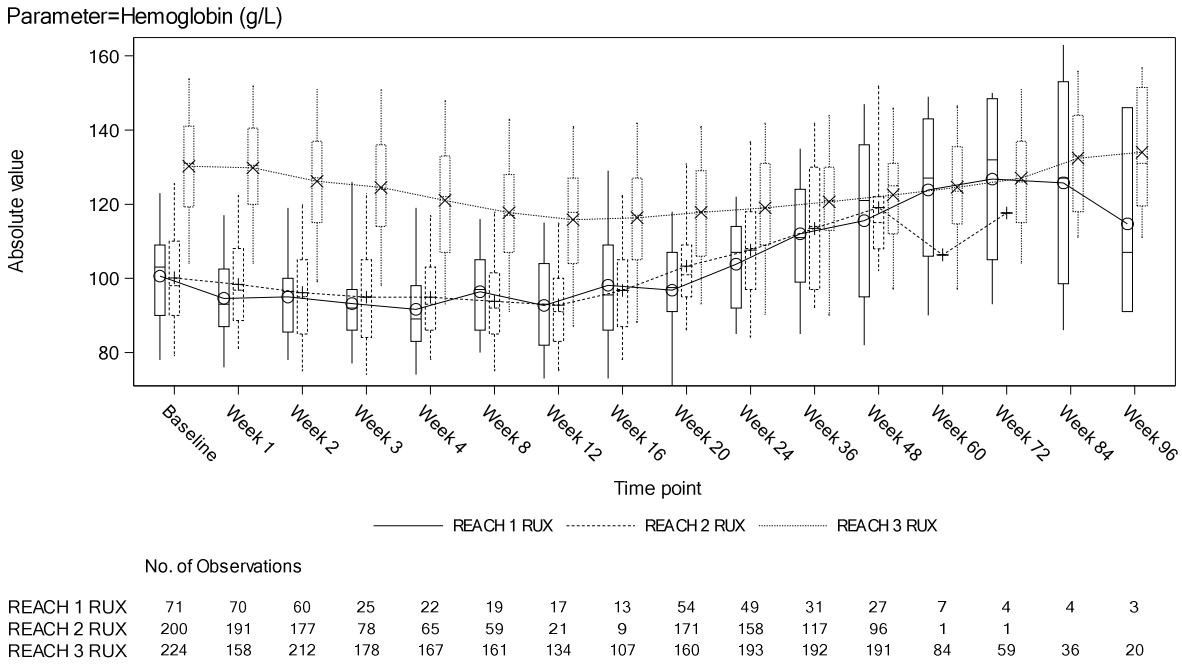
Table 3-1　新たに発現又はベースラインに比べて悪化した血液学的検査値異常（C2301 試験，271 試験，及び D2301 試験，SAF）

	Worsening from baseline to	C2301 試験 RUX overall N = 201 n/m (%)	271 試験 RUX N = 71 n/m (%)	D2301 試験 RUX overall N = 226 n/m (%)
ヘモグロビン低値	Grade 1	7/16 (43.8)	2/8 (25.0)	64/132 (48.5)
	Grade 2	41/95 (43.2)	20/41 (48.8)	56/208 (26.9)
	Grade 3	84/176 (47.7)	32/62 (51.6)	33/223 (14.8)
	Any grade	132/176 (75.0)	54/62 (87.1)	153/223 (68.6)
白血球数低値	Grade 1	20/130 (15.4)	5/43 (11.6)	37/206 (18.0)
	Grade 2	36/154 (23.4)	15/54 (27.8)	36/217 (16.6)
	Grade 3	62/178 (34.8)	24/64 (37.5)	15/222 (6.8)
	Grade 4	44/193 (22.8)	11/68 (16.2)	13/224 (5.8)
	Any grade	162/193 (83.9)	55/68 (80.9)	101/224 (45.1)
リンパ球数低値	Grade 1	1/31 (3.2)	0/12	16/139 (11.5)
	Grade 2	6/44 (13.6)	1/15 (6.7)	34/164 (20.7)
	Grade 3	28/74 (37.8)	10/30 (33.3)	33/195 (16.9)
	Grade 4	91/151 (60.3)	31/53 (58.5)	16/221 (7.2)
	Any grade	126/151 (83.4)	42/53 (79.2)	99/221 (44.8)
好中球数低値	Grade 1	12/161 (7.5)	5/57 (8.8)	12/213 (5.6)
	Grade 2	39/171 (22.8)	10/59 (16.9)	33/216 (15.3)

	Worsening from baseline to	C2301 試験 RUX overall N = 201 n/m (%)	271 試験 RUX N = 71 n/m (%)	D2301 試験 RUX overall N = 226 n/m (%)
	Grade 3	33/184 (17.9)	19/65 (29.2)	21/221 (9.5)
	Grade 4	39/189 (20.6)	11/69 (15.9)	15/224 (6.7)
	Any grade	123/189 (65.1)	45/69 (65.2)	81/224 (36.2)
血小板数低値	Grade 1	6/36 (16.7)	1/9 (11.1)	28/153 (18.3)
	Grade 2	20/87 (23.0)	9/35 (25.7)	12/208 (5.8)
	Grade 3	40/128 (31.3)	12/50 (24.0)	13/219 (5.9)
	Grade 4	84/176 (47.7)	31/63 (49.2)	24/224 (10.7)
	Any grade	150/176 (85.2)	53/63 (84.1)	77/224 (34.4)

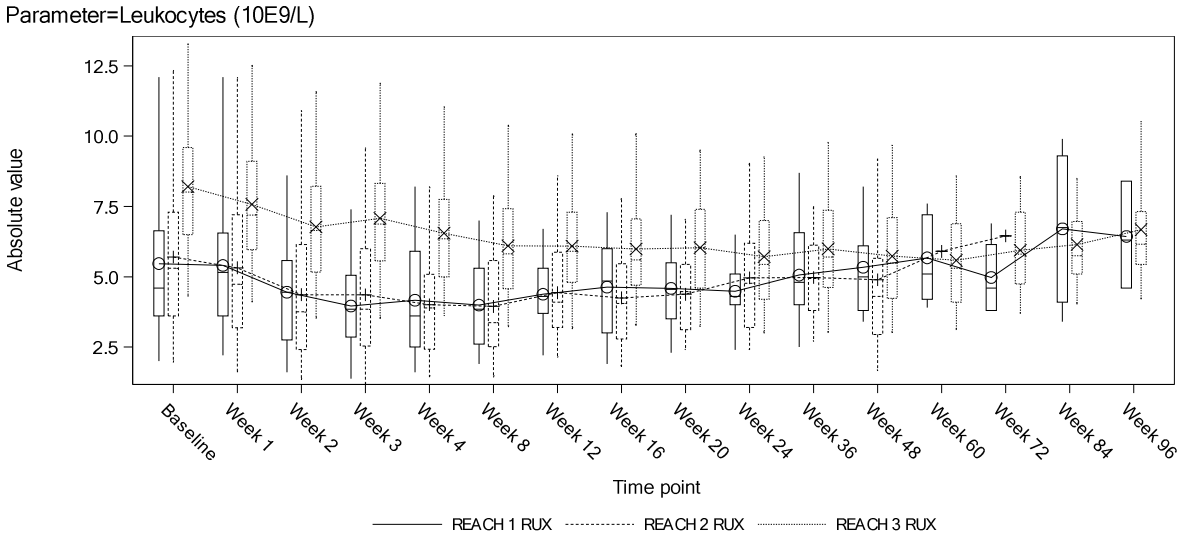
Source: 5.3.5.3-4-Table 3.3-2.2
n = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に Grade x に悪化した被験者数
m = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に少なくとも 1 回測定された被験者数
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 3-1 ヘモグロビンの推移（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 3.3-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

Figure 3-2 白血球数の推移（C2301 試験，271 試験，及び D2301 試験，SAF）

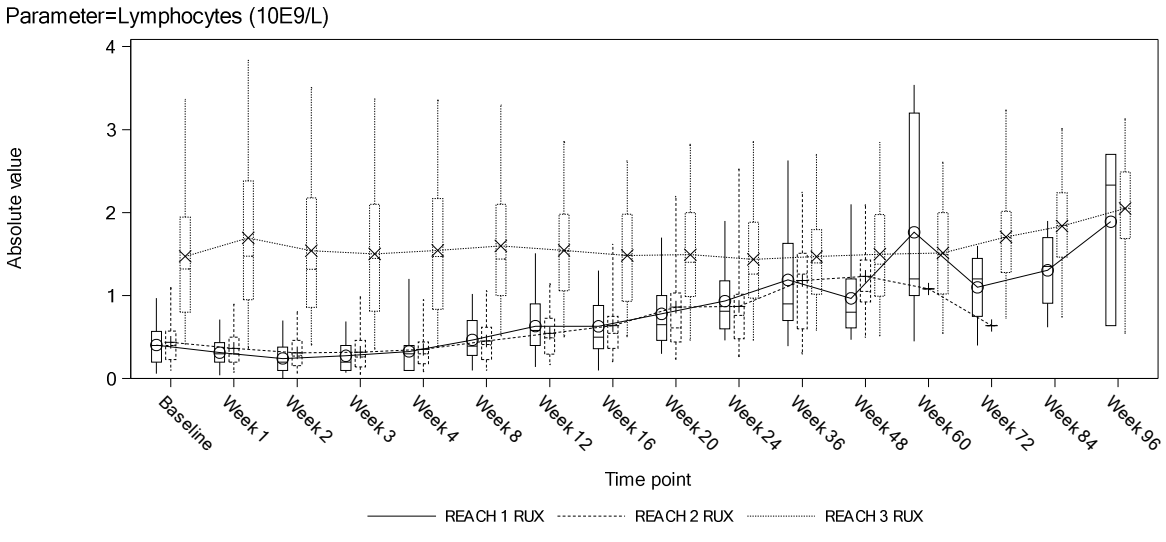


No. of Observations

REACH 1 RUX	71	70	60	49	54	31	27	25	17	19	22	13	7	4	4	3
REACH 2 RUX	200	191	177	158	171	115	95	78	21	59	65	9	1	1		
REACH 3 RUX	224	158	211	194	160	194	191	178	134	161	167	107	84	59	36	20

Source: 5.3.5.3-4-Figure 3.3-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

Figure 3-3 リンパ球数の推移（C2301 試験，271 試験，及び D2301 試験，SAF）

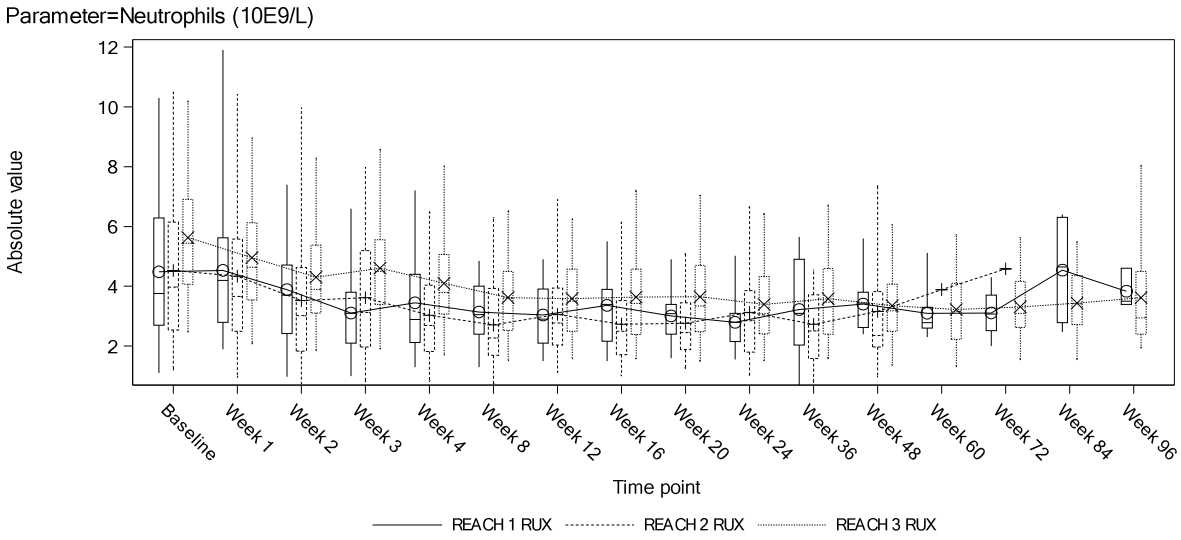


No. of Observations

REACH 1 RUX	60	70	30	25	22	19	17	70	53	49	27	13	7	4	4	3
REACH 2 RUX	167	195	117	76	63	59	19	179	160	152	94	9	1	1		
REACH 3 RUX	211	225	192	178	166	160	134	159	158	190	190	107	83	59	36	20

Source: 5.3.5.3-4-Figure 3.3-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

Figure 3-4 好中球数の推移（C2301 試験，271 試験，及び D2301 試験，SAF）

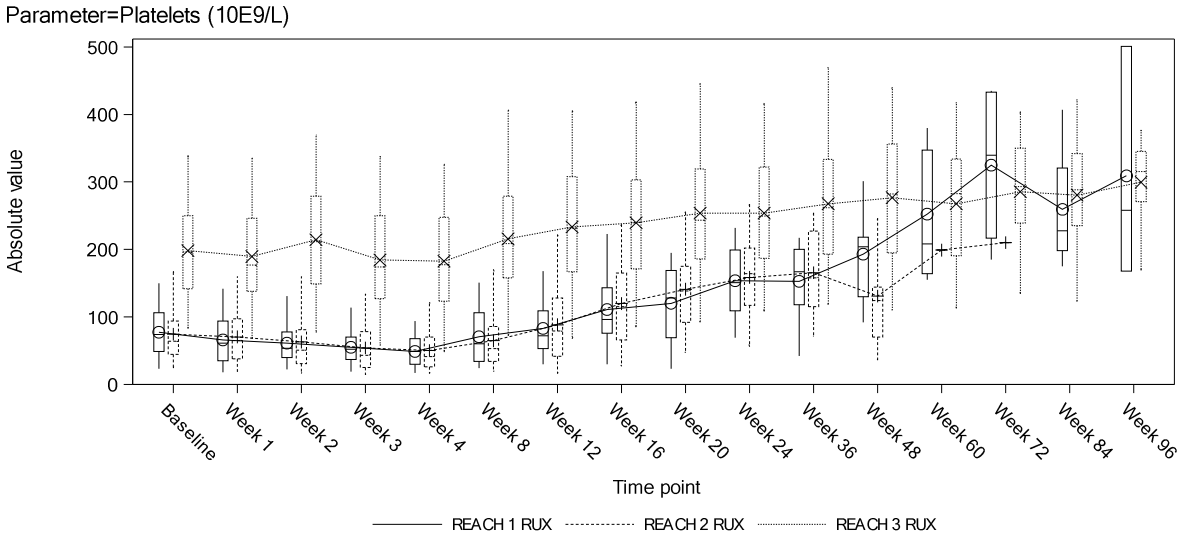


No. of Observations

REACH 1 RUX	70	49	70	60	31	27	25	17	53	19	22	13	7	4	4	3
REACH 2 RUX	198	155	185	168	115	95	77	20	160	59	64	9	1	1		
REACH 3 RUX	225	190	158	210	192	191	178	134	159	160	166	107	83	59	36	20

Source: 5.3.5.3-4-Figure 3.3-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

Figure 3-5　　血小板数の推移（C2301 試験，271 試験，及び D2301 試験，SAF）



No. of Observations

REACH 1 RUX	71	70	60	54	49	31	22	19	17	13	27	25	7	4	4	3
REACH 2 RUX	201	191	177	171	158	117	66	60	21	9	98	79	1	1		
REACH 3 RUX	225	159	212	160	194	192	166	161	134	107	192	178	84	59	36	20

Source: 5.3.5.3-4-Figure 3.3-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

3.2　　血液生化学的検査

3.2.1　　肝機能検査

急性 GVHD

C2301 試験の肝機能検査で，ベースライン後 Day 28 までに認められた ALT，AST，ビリルビン，及び ALP の高値への悪化の大部分は RUX 群，BAT 群のいずれの群でも Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-4）。Grade 3 の高値に悪化した被験者の割合は群間で同程度であり，Grade 4 はいずれの群でも 2%未満と低かった。なお，肝臓は対象疾患の標的臓器の 1 つである。

データカットオフ 2 までに，RUX 群の 152 名中 8 名（5.3%），BAT 群の 150 名中 18 名（12.0%）が Hy's law（ALT 又は AST が基準値上限の 3 倍を超え，かつビリルビンが基準値上限の 2 倍を超え，かつ ALP が基準値上限の 2 倍未満）に該当した（5.3.5.1-1-C2301 試験 CSR2-Table 14.3-3.3.1a）。RUX 群の 8 名のうち，1 名（被験者番号 [redacted]）ではスルファメトキサゾール・トリメトプリム，レダホリン，及びバラシクロビルの併用による肝性胆汁うっ滞に続発したものであった。別の 1 名（被験者番号 [redacted]）では進行性の肝 GVHD の影響が考えられた。2 名（被験者番号 [redacted]，[redacted]）では，感染症を発現し抗生物質が併用されたことにより肝機能検査値が上昇した可能性が考えられた。残る 4 名（被験者番号 [redacted]，[redacted]，[redacted]，

[redacted]）では，Day 1 に Hy's law に該当又は肝機能検査値の異常高値が認められており，治験治療開始前から肝機能検査値が高値であった（5.3.5.1-1-C2301 試験 CSR2-12.4.2.1 項）。

RUX overall の被験者でベースライン後に認められた ALT，AST，ビリルビン，及び ALP 高値への悪化の大部分はいずれの群も Grade 1 又は 2 であった（Table 3-2）。Grade 3 の高値に悪化した被験者の割合は ALT（17.6%）を除きいずれも 10%未満であり，Grade 4 はいずれの群でも 3%未満と低かった。

ALT 及び AST の平均値（Figure 3-6，Figure 3-7）は，いずれも Week 60 までベースラインと同程度に推移した。

慢性 GVHD

D2301 試験の肝機能検査で，ベースライン後 C7D1 までに認められた ALT，AST，ビリルビン，及び ALP の高値への悪化の大部分は RUX 群，BAT 群のいずれの群でも Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-4）。Grade 3 の高値に悪化した被験者の割合は群間で同程度であり，Grade 4 の割合はいずれの群でも 2%未満と低かった。

データカットオフまでに RUX 群で Hy's law に該当した被験者はなく，BAT 群で 4 名が該当した（5.3.5.1-2-D2301 試験-Table 14.3-3.3，Table 14.3-3.6）。

RUX overall の被験者でベースライン後に認められた ALT，AST，ビリルビン，及び ALP の高値への悪化の大部分は Grade 1 又は 2 であった（Table 3-2）。Grade 3 の高値に悪化した被験者の割合はいずれも 5%未満であり，Grade 4 は 1%未満と低かった。

ALT 及び AST の平均値は，いずれも Week 60 までベースラインと同程度に推移した（Figure 3-6，Figure 3-7）。

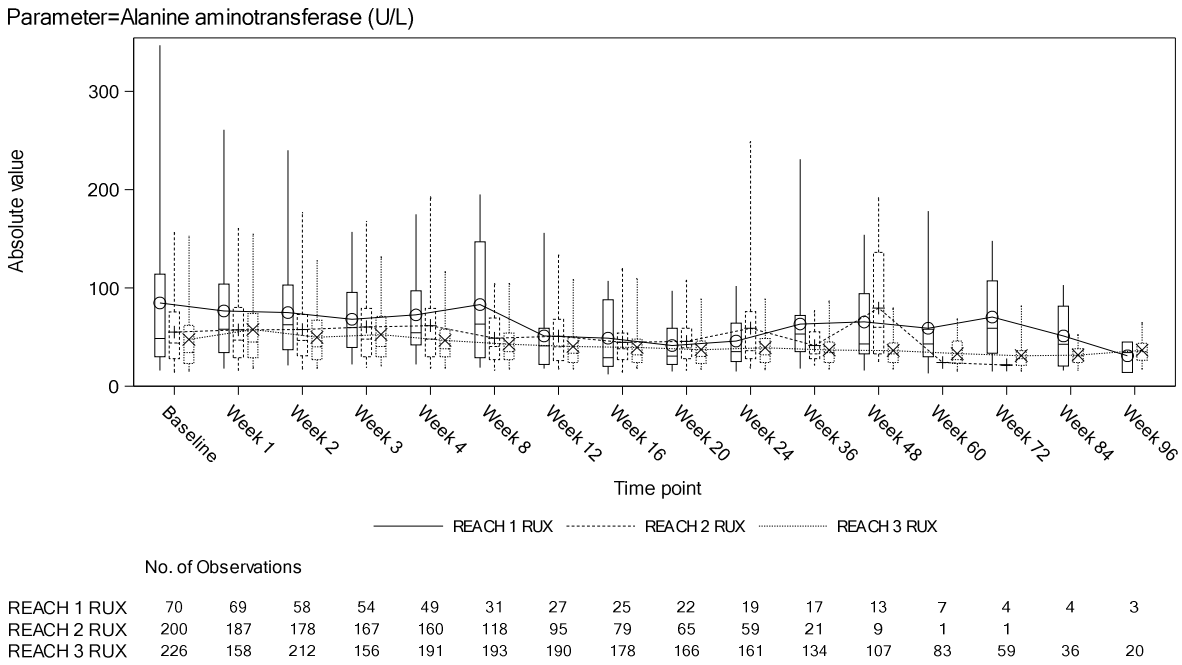
Table 3-2　新たに発現又はベースラインに比べて悪化した肝機能検査値異常（C2301 試験，271 試験，及び D2301 試験，SAF）

		C2301 試験 RUX overall N = 201 n/m (%)	271 試験 RUX N = 71 n/m (%)	D2301 試験 RUX overall N = 226 n/m (%)
	Worsening from baseline to			
ALT 高値	Grade 1	42/92 (45.7)	20/36 (55.6)	65/132 (49.2)
	Grade 2	30/171 (17.5)	9/54 (16.7)	20/199 (10.1)
	Grade 3	32/182 (17.6)	6/61 (9.8)	10/212 (4.7)
	Grade 4	3/195 (1.5)	0/69	2/225 (0.9)
	Any grade	107/195 (54.9)	35/69 (50.7)	97/225 (43.1)
AST 高値	Grade 1	58/138 (42.0)	21/43 (48.8)	96/171 (56.1)
	Grade 2	30/187 (16.0)	11/64 (17.2)	13/215 (6.0)
	Grade 3	15/193 (7.8)	4/69 (5.8)	7/223 (3.1)
	Grade 4	0/197	0/71	2/226 (0.9)
	Any grade	103/197 (52.3)	36/71 (50.7)	118/226 (52.2)
ALP 高値	Grade 1	48/144 (33.3)	24/52 (46.2)	42/158 (26.6)

	Worsening from baseline to	C2301 試験 RUX overall N = 201 n/m (%)	271 試験 RUX N = 71 n/m (%)	D2301 試験 RUX overall N = 226 n/m (%)
	Grade 2	34/184 (18.5)	7/64 (10.9)	14/218 (6.4)
	Grade 3	10/195 (5.1)	5/71 (7.0)	2/221 (0.9)
	Grade 4	0/197	0/71	0/223
	Any grade	92/197 (46.7)	36/71 (50.7)	58/223 (26.0)
ビリルビン高値	Grade 1	13/128 (10.2)	6/48 (12.5)	22/205 (10.7)
	Grade 2	28/149 (18.8)	12/52 (23.1)	6/219 (2.7)
	Grade 3	16/176 (9.1)	2/59 (3.4)	3/223 (1.3)
	Grade 4	5/191 (2.6)	5/69 (7.2)	1/226 (0.4)
	Any grade	62/191 (32.5)	25/69 (36.2)	32/226 (14.2)

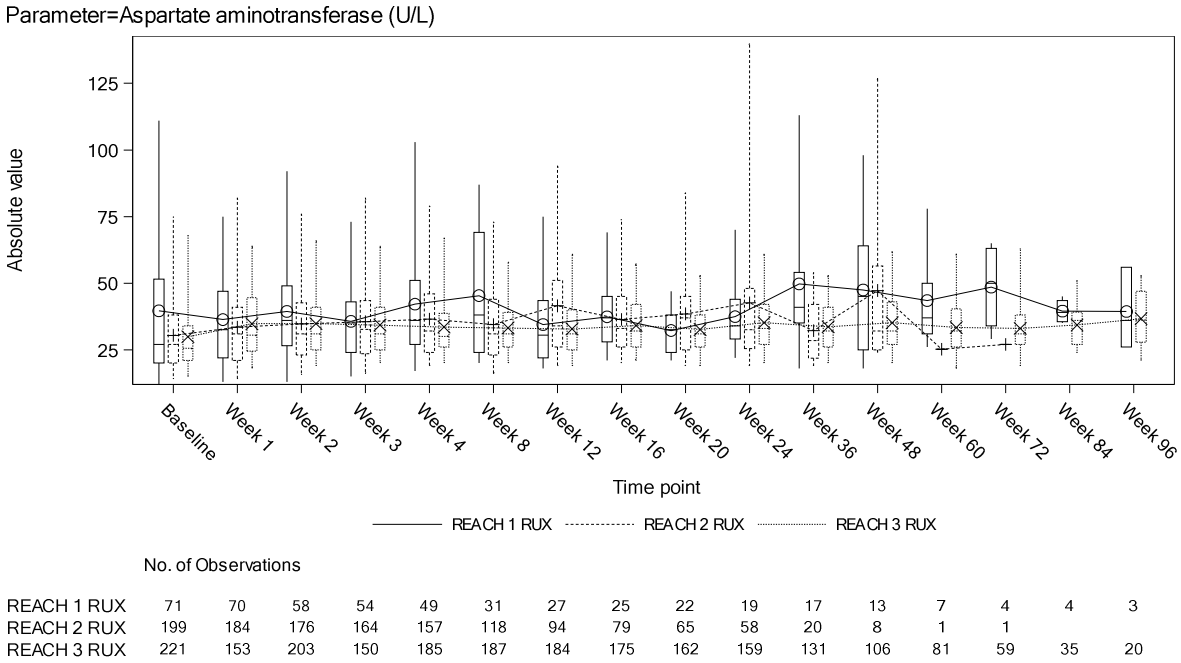
Source: 5.3.5.3-4-Table 3.4-2.2
n = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に Grade x に悪化した被験者数
m = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に少なくとも 1 回測定された被験者数
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 3-6 ALT の推移（C2301 試験，271 試験，及び D2301 試験，SAF）



Source: 5.3.5.3-4-Figure 3.4-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

Figure 3-7　　AST の推移（C2301 試験，271 試験，及び D2301 試験，SAF）



No. of Observations

REACH 1 RUX	71	70	58	54	49	31	27	25	22	19	17	13	7	4	4	3
REACH 2 RUX	199	184	176	164	157	118	94	79	65	58	20	8	1	1		
REACH 3 RUX	221	153	203	150	185	187	184	175	162	159	131	106	81	59	35	20

Source: 5.3.5.3-4-Figure 3.4-1
REACH 1= 271 試験，REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

3.2.2　　脂質検査

急性 GVHD

C2301 試験の脂質検査で，ベースライン後 Day 28 までに認められたコレステロール及びトリグリセリドの高値への悪化の大部分は RUX 群，BAT 群のいずれの群でも Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-4）。Grade 3 の高値に悪化した被験者の割合は群間で同程度であり，Grade 4 はいずれの群でも 5%以下と低かった。

データカットオフ 2 までに，RUX overall の被験者でベースライン後に認められたコレステロール及びトリグリセリドの高値への悪化の大部分は Grade 1 又は 2 であった（Table 3-3）。ベースライン後に Grade 3 又は 4 の高値に悪化した被験者の割合は，トリグリセリドの Grade 3（15.9%）を除き，いずれの項目も 10%未満であった。

コレステロールの平均値は，Week 1 には増加を示し，Week 12 まで増加した後，Week 36 まで同程度に推移した（Figure 3-8）。

慢性 GVHD

D2301 試験の脂質検査で，ベースライン後 C7D1 までに認められたコレステロール及びトリグリセリドの高値への悪化の大部分は RUX 群，BAT 群のいずれの群でも Grade 1 又は 2 であった

（5.3.5.3-4-Table 3.4-4）。Grade 3 の高値に悪化した被験者の割合は群間で同程度であり，Grade 4 はいずれの群でも 3%未満と低かった。

データカットオフまでに，RUX overall の被験者でベースライン後に認められたコレステロール及びトリグリセリドの高値への悪化の大部分は Grade 1 又は 2 であった（Table 3-3）。Grade 3 の高値に悪化した被験者の割合はいずれも 10%未満であり，Grade 4 は 2%未満と低かった。

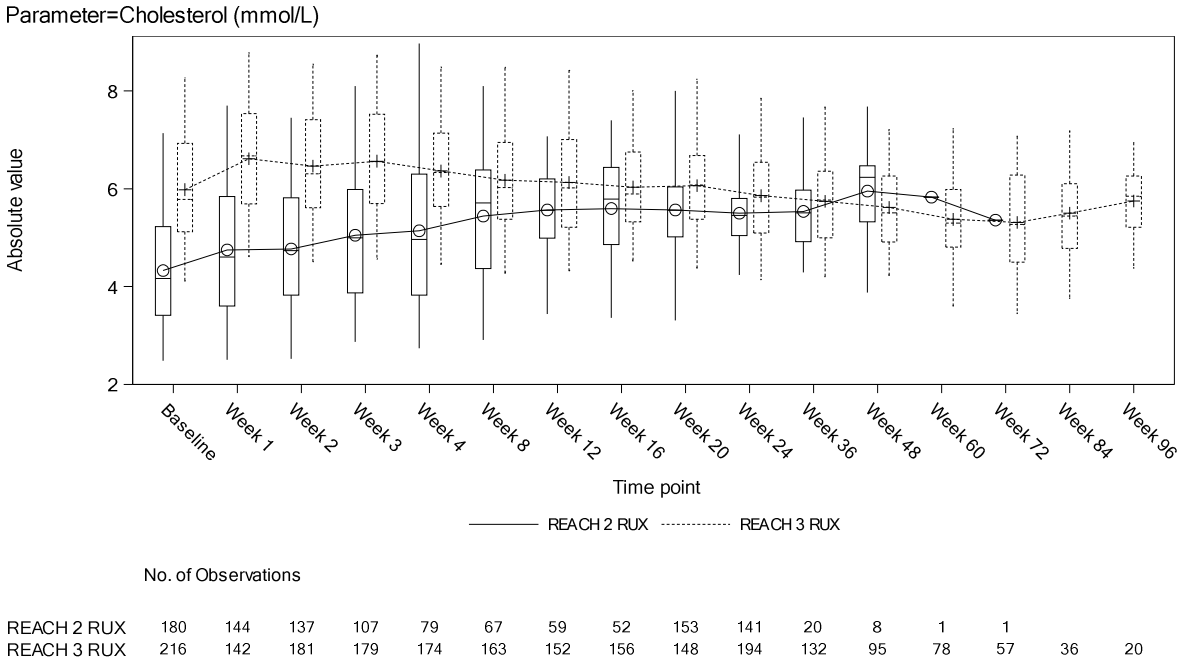
コレステロールの平均値は，Week 1 に増加を示した後，Week 60 まで減少した（Figure 3-8）。

Table 3-3 新たに発現又はベースラインに比べて悪化した脂質検査値異常（C2301 試験及び D2301 試験，SAF）

		C2301 試験 RUX overall N = 201 n/m (%)	D2301 試験 RUX overall N = 226 n/m (%)
	Worsening from baseline to		
コレステロール高値	Grade 1	54/140 (38.6)	51/87 (58.6)
	Grade 2	21/171 (12.3)	52/192 (27.1)
	Grade 3	6/184 (3.3)	12/220 (5.5)
	Grade 4	11/187 (5.9)	1/222 (0.5)
	Any grade	92/187 (49.2)	116/222 (52.3)
トリグリセリド高値	Grade 1	26/53 (49.1)	54/103 (52.4)
	Grade 2	49/133 (36.8)	41/196 (20.9)
	Grade 3	28/176 (15.9)	14/218 (6.4)
	Grade 4	6/189 (3.2)	4/224 (1.8)
	Any grade	109/189 (57.7)	113/224 (50.4)

Source: 5.3.5.3-4-Table 3.4-2.2
n = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に Grade x に悪化した被験者数
m = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に少なくとも 1 回測定された被験者数
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 3-8　　コレステロールの推移（C2301 試験及び D2301 試験，SAF）



No. of Observations

REACH 2 RUX	180	144	137	107	79	67	59	52	153	141	20	8	1	1		
REACH 3 RUX	216	142	181	179	174	163	152	156	148	194	132	95	78	57	36	20

Source: 5.3.5.3-4-Figure 3.4-1
REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

3.2.3　膵機能検査

急性 GVHD

C2301 試験の膵機能検査で，ベースライン後 Day 28 までに認められた膵リパーゼ及びアミラーゼの高値への悪化の大部分は RUX 群，BAT 群のいずれの群でも Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-4）。Grade 3 の高値に悪化した被験者の割合は群間で同程度であり，Grade 4 はいずれの群でも 1%未満と低かった。

データカットオフ 2 までに，RUX overall の被験者でベースライン後に認められた膵リパーゼ及びアミラーゼの高値への悪化の大部分は Grade 1 又は 2 であった（Table 3-4）。ベースライン後に Grade 3 の高値に悪化した被験者の割合は 10%未満であり，Grade 4 は 3%未満と低かった。

膵リパーゼの平均値は，Week 48 まで緩やかに低下した（Figure 3-9）。

慢性 GVHD

D2301 試験の膵機能検査で，ベースライン後 C7D1 までに認められた膵リパーゼ及びアミラーゼの高値への悪化の大部分は RUX 群，BAT 群のいずれの群でも Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-4）。Grade 3 の高値に悪化した被験者の割合は群間で同程度であり，Grade 4 はいずれの群でも 2%未満と低かった。

データカットオフまでに，RUX overall の被験者でベースライン後に認められた膵リパーゼ及びアミラーゼの高値への悪化の大部分は Grade 1 又は 2 であった（Table 3-4）。Grade 3 の高値に悪化した被験者の割合はいずれも 10%未満であり，Grade 4 は 3%未満と低かった。

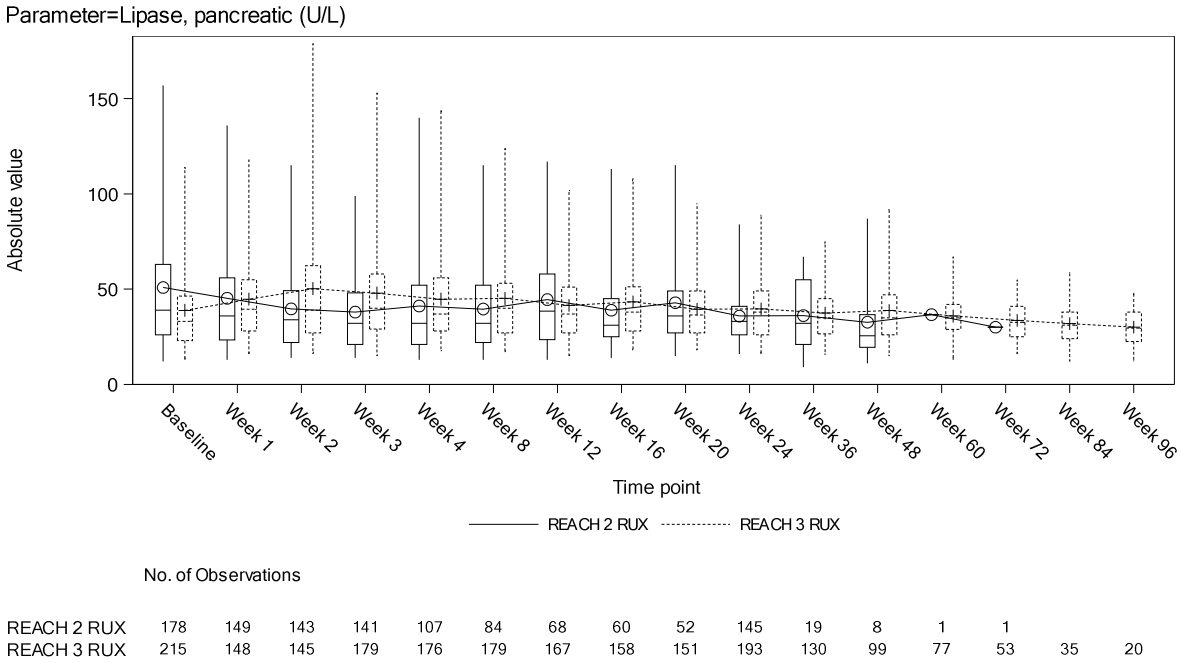
膵リパーゼの平均値は，Week 48 まで緩やかに低下した（Figure 3-9）。

Table 3-4 新たに発現又はベースラインに比べて悪化した膵機能検査値異常（C2301 試験及び D2301 試験，SAF）

		C2301 試験 RUX overall N = 201	D2301 試験 RUX overall N = 226
	Worsening from baseline to	n/m (%)	n/m (%)
膵リパーゼ高値	Grade 1	23/146 (15.8)	37/197 (18.8)
	Grade 2	17/164 (10.4)	21/212 (9.9)
	Grade 3	15/173 (8.7)	21/220 (9.5)
	Grade 4	4/183 (2.2)	1/223 (0.4)
	Any grade	59/183 (32.2)	80/223 (35.9)
アミラーゼ高値	Grade 1	26/142 (18.3)	42/191 (22.0)
	Grade 2	13/159 (8.2)	14/214 (6.5)
	Grade 3	14/166 (8.4)	9/216 (4.2)
	Grade 4	2/177 (1.1)	6/219 (2.7)
	Any grade	55/177 (31.1)	71/219 (32.4)

Source: 5.3.5.3-4-Table 3.4-2.2
n = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に Grade x に悪化した被験者数
m = 当該項目がベースラインで欠測又は Grade x 未満で，ベースライン後に少なくとも 1 回測定された被験者数
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

Figure 3-9　　膵リパーゼの推移（C2301 試験及び D2301 試験，SAF）



No. of Observations

REACH 2 RUX	178	149	143	141	107	84	68	60	52	145	19	8	1	1		
REACH 3 RUX	215	148	145	179	176	179	167	158	151	193	130	99	77	53	35	20

Source: 5.3.5.3-4-Figure 3.4-1
REACH 2= C2301 試験，REACH 3= D2301 試験
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの RUX overall の被験者の結果
箱：25～75 パーセンタイル，箱中の点：平均値，水平線：中央値，垂直線：10～90 パーセンタイル（この範囲外の値は示していない）

3.2.4　　その他の血液生化学的検査項目

急性 GVHD

C2301 試験でグルコースがベースライン後 Day 28 までに Grade 3 又は 4 の高値に悪化した被験者の割合は，RUX 群と BAT 群で大きな違いはなかった（Grade 3：RUX 群 8.8%，BAT 群 16.8%，Grade 4：RUX 群 2.0%，BAT 群 6.8%）（5.3.5.3-4-Table 3.4-4）。クレアチニンは，いずれの群でも Grade 4 及び 3 の高値への悪化は認められなかった。クレアチンキナーゼの Grade 3 又は 4 の高値への悪化はいずれの群でも 2%未満と低かった。電解質（ナトリウム，カリウム，マグネシウム，及びリン酸塩）が Grade 3 又は 4 に悪化した被験者の割合は群間で同程度であった。

データカットオフ 2 までに，RUX overall の被験者でベースライン後に認められたグルコース，クレアチニン，クレアチンキナーゼ，電解質の悪化の大部分は Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-2.2）。グルコースが Grade 3 又は 4 の高値に悪化した被験者の割合は，それぞれ 12.2%，2.1%であった。

慢性 GVHD

D2301 試験でグルコースがベースライン後 C7D1 までに Grade 3 に悪化した被験者の割合は，RUX 群と BAT 群で大きな違いはなく（9.8%，4.1%），Grade 4 はいずれの群も低かった（0.6%，

2.0%）（5.3.5.3-4-Table 3.4-4）。クレアチニン，クレアチンキナーゼの Grade 3 又は 4 の高値への悪化はいずれの群でも 2%未満と低かった。電解質が Grade 3 又は 4 に悪化した被験者の割合は群間で同程度であった。

データカットオフまでに，RUX overall の被験者でベースライン後に認められたグルコース，クレアチニン，クレアチンキナーゼ，電解質の悪化の大部分は Grade 1 又は 2 であった（5.3.5.3-4-Table 3.4-2.2）。グルコースが Grade 3 又は 4 の高値に悪化した被験者の割合は，それぞれ 7.9%, 0.5%であった。

4 バイタルサイン，身体的所見及び安全性に関する他の観察項目

急性 GVHD は C2301 試験のデータカットオフ 2 まで，慢性 GVHD は D2301 試験のデータカットオフまでのバイタルサインの結果を示す。異常の基準，解析手法は 1.1.3.2.4 項に示す。

4.1 バイタルサイン

4.1.1 急性 GVHD

収縮期血圧，拡張期血圧，脈拍，体温，及び体重のいずれも，臨床的に注目すべき異常が認められた被験者の割合は RUX 群と BAT 群で同程度であった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3-4.1）。

- 臨床的に注目すべき血圧上昇に該当した被験者の割合は各群 3%以下，血圧低下は各群 10%以下と低かった。
- 臨床的に注目すべき脈拍上昇に該当した被験者の割合はいずれの群でも約 30%であった（RUX 群 29.6%，BAT 群 29.3%，以下同順）。
- 臨床的に注目すべき体重変動に該当した被験者の割合は群間で同程度であり，いずれの群でも体重減少（26.3%，25.3%）が体重増加（17.8%，14.0%）より多かった。
- 臨床的に注目すべき体温上昇に該当した被験者の割合は各群 1%以下と低かった。

いずれの項目も，各評価時点のベースラインからの変化量の平均値は RUX 群，BAT 群ともに小さく，群間で大きな違いはなかった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3-4.2）。

4.1.2 慢性 GVHD

収縮期血圧，拡張期血圧，脈拍，体温，及び体重のほとんどの項目で，臨床的に注目すべき異常が認められた被験者の割合は RUX 群と BAT 群で同程度であった（5.3.5.1-2-D2301 試験-Table 14.3-4.2）。

- 臨床的に注目すべき収縮期血圧の上昇に該当した被験者の割合は各群 3%以下と低く，群間で同程度であった。
- 臨床的に注目すべき脈拍上昇に該当した被験者の割合は群間で同程度であった（RUX 群 23.0%，BAT 群 21.5%）。
- 臨床的に注目すべき体重増加に該当した被験者の割合は，RUX 群（30.3%）で BAT 群（16.5%）と比べて高かった。
- 臨床的に注目すべき体温上昇に該当した被験者はいなかった。

いずれの項目も，各評価時点のベースラインからの変化量の平均値は RUX 群，BAT 群ともに小さく，群間で大きな違いはなかった（5.3.5.1-2-D2301 試験-Table 14.3-4.4）。

5 特別な患者集団及び状況下における安全性

5.1 内因性要因

急性 GVHD は C2301 試験のデータカットオフ 2 までのデータ，慢性 GVHD は D2301 試験のデータカットオフまでのデータを対象に，Table 1-8 に示す要因別に RUX overall の被験者の安全性を評価した。日本人部分集団では，RUX 群，BAT 群，及び RUX overall の被験者の結果を示した。

5.1.1 日本人

5.1.1.1 急性 GVHD

5.1.1.1.1 被験者の内訳

日本人 30 名がランダム化され（RUX 群 9 名，BAT 群 21 名，以下同順），治験治療を実施した。データカットオフ 2 までに 25 名（7 名，18 名）が割り付けられた治験治療を中止し，主な中止理由は RUX 群では有害事象（4 名，0 名），BAT 群では効果不十分（0 名，9 名）であった。残りの 5 名は治験治療を完了した（2.7.3-Table 6-8）。

BAT 群で 6 名が RUX へクロスオーバーした。このうち 5 名がクロスオーバー後に投与を中止し，主な中止理由は有害事象（3 名）であった。残りの 1 名は継続中であった（5.3.5.3-1-Table 14.1-1.2j）。

治験治療が実施された 30 名が FAS 及び SAF に含まれた。

5.1.1.1.2 曝露の程度

データカットオフ 2 時点で，治験治療の曝露期間の中央値（最小値～最大値）は RUX 群が 72.0（14.0～335.0）日，BAT 群が 29.0（1.0～68.0）日であり，RUX 群で BAT 群と比べて 2 倍以上長かった。RUX 群の RUX の用量強度の中央値は Day 28 までが 19.2 mg/日，データカットオフ 2 までが 11.4 mg/日であった（5.3.5.3-1-Table 14.3-1.1j，Table 14.3-1.3.3j，5.3.5.3-7-Table 14.3-1.3.1j）。

BAT 群で 17 名に 1 種類のみの BAT が実施された。治療開始時の BAT で最も多かったものは MSC（11 名）であり，次いで抗胸腺細胞グロブリン（6 名），インフリキシマブ，MMF（各 2 名）であった。曝露期間が最も長かった BAT は MSC で，曝露期間の中央値（最小値～最大値）は 29.5（9.0～62.0）日であった（5.3.5.3-1-Table 14.3-1.2j，Table 14.3-1.3j）。

RUX crossover の被験者での RUX 曝露期間の中央値（最小値～最大値）は 38.0（8.0～259.0）日，RUX の用量強度の中央値は 16.2 mg/日であった（5.3.5.3-1-Table 14.3-1.5j，Table 14.3-1.6j）。

RUX overall の被験者（15 名）の RUX 曝露期間の中央値（最小値～最大値）は 9.0（1.1～47.9）週，総曝露期間は 3.7 人年であった（5.3.5.3-6-Table 1.2-1j）。

5.1.1.1.3 人口統計学的特性及びその他の特性

RUX 群及び BAT 群の人口統計学的特性及び疾患特性は FAS を対象に評価し，2.7.3-3.3.1.2.2 項に示した。日本人では FAS は SAF と同じ集団であった。

SAF の RUX overall の被験者の年齢の中央値は 58.0 歳であり，18 歳以上 65 歳以下が 13 名であった（5.3.5.3-6-Table 1.3-1j）。男性が 53.3%を占め，BMI の平均値は 19.5 kg/m^2 であった。

5.1.1.1.4 有害事象

日本人でのデータカットオフ 2 までの有害事象の発現状況を Table 5-1 に示す。

Table 5-1 急性 GVHD の有害事象の発現状況（C2301 試験，SAF，日本人，データカットオフ 2 まで）

	RUX N = 9 n (%)	BAT N = 21 n (%)	RUX overall N = 15 n (%)
曝露期間：中央値（最小値 - 最大値）	72.0 (14.0-335.0) 日	29.0 (1.0-68.0) 日	9.0 (1.1-47.9) 週
総曝露期間（人年）	2.5	1.9	3.7
有害事象	9 (100)	20 (95.2)	15 (100)
副作用	9 (100)	13 (61.9)	13 (86.7)
Grade 3 以上の有害事象	9 (100)	18 (85.7)	15 (100)
治験治療下の死亡	4 (44.4)	4 (19.0)	7 (46.7)
死亡に至った有害事象	3 (33.3)	3 (14.3)	6 (40.0)
重篤な有害事象	6 (66.7)	10 (47.6)	11 (73.3)
投与中止に至った有害事象	4 (44.4)	0	7 (46.7)
用量調節又は休薬に至った有害事象	8 (88.9)	2 (9.5)	11 (73.3)
治療を要した有害事象	9 (100)	20 (95.2)	15 (100)

Source: 5.3.5.3-6-Table 1.2-1j，Table 2.1-1j，Table 2.1-20j，5.3.5.3-1-Table 12-16aj，Table 14.3-1.1j，Table 14.3.1-2.2j
総曝露期間 = 全被験者の曝露期間の合計

比較的よくみられる有害事象

データカットオフ 2 までに有害事象は RUX 群 9 名全員（100%），BAT 群 21 名中 20 名（95.2%）に認められた。EAIR は RUX 群（6202.4）で BAT 群（4103.9）と比べて高かった（5.3.5.3-1-Table 14.3.1-1.23j）。SOC 別で，RUX 群で BAT 群と比べて多く認められた事象（発現率の差が 30%以上）は臨床検査（RUX 群 8 名，BAT 群 11 名，以下同順），胃腸障害（7 名，7 名），肝胆道系障害（4 名，1 名）であった（Table 7-14）。PT 別で，RUX 群で BAT 群と比べて多く認められた事象（発現率の差が 30%以上）は血小板減少症（4 名，2 名）であった。

副作用は RUX 群 9 名（100%），BAT 群 13 名（61.9%）に認められた（Table 7-16）。RUX 群で BAT 群と比べて多く認められた PT 別副作用は血小板減少症（4 名，0 名），血小板数減少（4 名，3 名）であった。

Grade 3 以上の有害事象は RUX 群 9 名（100%），BAT 群 18 名（85.7%）に認められ，RUX 群で BAT 群と比べて多く認められた PT 別事象（発現率の差が 30%以上）は血小板減少症（3 名，0 名）であった（Table 7-14）。

投与期間別の有害事象発現率（条件付き確率）の推移にはいずれの群でも特定の傾向は認められず，PT 別事象の発現率が投与期間の延長に伴って高くなる傾向はみられなかった（5.3.5.3-1-Table 14.3.1-1.22j，Table 14.3.1-1.33j）。

RUX overall の被験者では 15 名全員（100%）に有害事象が認められ，主な PT 別有害事象は貧血（7 名），血小板減少症，血小板数減少，白血球数減少（各 5 名）であった（5.3.5.3-6-Table 2.1-3j）。これらの事象は，副作用や Grade 3 以上の有害事象としても多く認められた（5.3.5.3-6-Table 2.1-4j）。全有害事象の発現率及び主な PT 別事象の発現率が投与期間の延長に伴って高くなる傾向はみられなかった（5.3.5.3-6-Table 2.1-23j）。

死亡

全体集団と同様に，治験治療下の死亡，死亡に至った有害事象をそれぞれ評価した。

治験治療下の死亡は RUX 群で 4 名（44.4%），BAT 群で 4 名（19.0%），RUX crossover の被験者で 3 名（50.0%）に認められた（Table 7-18）。死因は，RUX 群では急性 GVHD，敗血症，急性骨髄性白血病，腎機能障害（各 1 名），BAT 群では急性 GVHD（2 名），再発急性骨髄性白血病，急性肺損傷（各 1 名），RUX crossover の被験者ではアデノウイルス感染，特発性肺炎症候群，呼吸不全（各 1 名）であった（5.3.5.3-1-Table 14.3.1-2.2j，Table 14.3.1-2.3j）。RUX overall の被験者で日本人だけでみられた事象は急性骨髄性白血病，腎機能障害，アデノウイルス感染，特発性肺炎症候群であった（5.3.5.3-6-Table 2.1-20j）。

死亡に至った有害事象は RUX 群で 3 名（33.3%），BAT 群で 3 名（14.3%），RUX crossover の被験者で 3 名（50.0%）に認められた。PT 別事象はいずれも 1 名での発現であり，RUX 群では敗血症，腎機能障害，下部消化管出血，BAT 群では再発急性骨髄性白血病，急性肺損傷，肺水腫，RUX crossover の被験者ではアデノウイルス感染，特発性肺炎症候群，呼吸不全であった（5.3.5.1-1-C2301 試験 CSR2-Listing 14.3.2-2.2）。RUX overall の被験者で日本人だけでみられた事象は腎機能障害，下部消化管出血，特発性肺炎症候群，アデノウイルス感染であった。死亡に至った有害事象のうち敗血症，呼吸不全，アデノウイルス感染は RUX と他の急性 GVHD 治療薬の両方に関連するか，又は判別不可能と判断され，下部消化管出血は RUX のみに関連すると判断された。下部消化管出血が認められた被験者（被験者番号 [redacted]）の死因（CRF の死亡ページに記録された死亡の主因）は急性 GVHD であり，ステージ 3 の下部消化管病変を伴っていた（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-2.6，Listing 16.2.6-1.1，Listing 16.2.7-1.1）。

日本人 RUX 投与被験者で報告された死亡（死因，死亡に至った有害事象）は PT 別ではいずれも 1 名で認められ，原疾患，免疫抑制下の患者で想定される感染症，HSCT 後に予測される事象，又は重症な対象疾患の特性を反映するものであった。

重篤な有害事象

重篤な有害事象は RUX 群で 6 名（66.7%），BAT 群で 10 名（47.6%），RUX crossover の被験者で 5 名（83.3%）に認められた（Table 7-19，Table 7-20）。EAIR は，RUX 群（221.8）で BAT 群（322.9）と比べて低かった（5.3.5.3-1-Table 14.3.1-1.24j）。RUX overall の被験者で複数名に認められた PT 別事象は敗血症，呼吸不全，特発性肺炎症候群（各 2 名）であった（5.3.5.3-6-Table 2.1-5j）。敗血症及び呼吸不全は全体集団の RUX 投与被験者でも高頻度（敗血症 9.5%，呼吸不全 6.0%）に認められた（Table 2-24）。特発性肺炎症候群は日本人だけで認められたが，HSCT 後に予測される事象であった。その他に RUX 投与後に日本人だけでみられた事象は，肝機能異常，アデノウイルス感染，感染性腸炎，皮下血腫，可逆性後白質脳症症候群，急性肺損傷，ギラン・バレー症候群（各 1 名）であり， HSCT 後の免疫抑制下の易感染性患者で想定される感染症，又は重症な疾患であるステロイド抵抗性 GVHD の特性を反映するものであった。

その他の重要な有害事象

投与中止に至った有害事象は RUX 群で 4 名（44.4%），RUX crossover の被験者で 3 名（50.0%）に発現し，BAT 群では認められなかった。RUX overall の被験者で認められた PT 別事象は敗血症（2 名），血小板数減少，ギラン・バレー症候群，特発性肺炎症候群，アデノウイルス感染，呼吸不全（各 1 名）であった。これらの事象のうち，RUX のみと関連ありと判断された事象はなかった。RUX 投与後に日本人だけでみられた事象はギラン・バレー症候群，特発性肺炎症候群，アデノウイルス感染であった（5.3.5.3-1-Table 14.3.1-1.15j，Table 14.3.1-1.29j，5.3.5.1-1-C2301 試験 CSR2-Listing 16.2.7-1.1）。

用量調節又は休薬に至った有害事象は，RUX 群で 8 名（88.9%），BAT 群で 2 名（9.5%）に発現した。RUX 群で 2 名以上に認められた事象は血小板数減少（4 名），肝機能異常，血中クレアチニン増加（各 2 名）であった（5.3.5.3-1-Table 14.3.1-1.17j）。治療を要した有害事象は RUX 群で 9 名（100%），BAT 群で 20 名（95.2%）に発現した（5.3.5.3-1-Table 14.3.1-1.18j）。

器官別又は症候群別有害事象

臨床的に注目すべき有害事象の発現率を Table 7-21（RUX 群，BAT 群）及び Table 7-22（RUX crossover の被験者）に，詳細を以下に示す。なお，全体集団の RUX overall の被験者で認められた臨床的に注目すべき有害事象のうち，帯状疱疹，B 型肝炎の再活性化，その他の血球減少，挫傷，頭蓋内出血，悪性腫瘍，NMSC，めまいは日本人ではみられなかった。

感染症

感染症（結核を除く）は，RUX 群，BAT 群ともに被験者の大部分に認められた（全 Grade：RUX 群 8 名，BAT 群 18 名，以下同順；Grade 3 以上：6 名，10 名）。RUX 群で BAT 群と比べて多く認められた（発現率の差が 30%以上）PT 別事象はなかった（5.3.5.3-1-Table 14.3.1-1.20j）。RUX overall の被験者では，感染症（結核を除く）は 12 名（Grade 3 以上 9 名）に認められ，主な

PT 別事象は膀胱炎，サイトメガロウイルス感染（各 3 名）であった（5.3.5.3-6-Table 2.1-10j，Table 2.1-13.10j）。

死亡に至った事象は RUX 群で 1 名，RUX crossover の被験者で 1 名に認められ，BAT 群ではみられなかった。PT 別事象は敗血症，アデノウイルス感染（各 1 名）であり，RUX のみと関連ありと判断された事象はなかった（5.3.5.3-1-Table 14.3.1-1.20j，Table 14.3.1-1.31j）。

重篤な事象は RUX 群で 3 名，BAT 群で 2 名，RUX crossover の被験者で 2 名に認められた。RUX overall の被験者で認められた PT 別事象は敗血症（2 名），ギラン・バレー症候群，感染性腸炎，アデノウイルス感染（各 1 名）であり，RUX のみと関連ありと判断された事象はなかった（5.3.5.1-1-Listing 16.2.7-1.1）。死亡に至った上記のアデノウイルス感染を除き，いずれも加療により消失又は軽快した。

投与中止に至った事象は RUX 群で 3 名，RUX crossover の被験者で 1 名に認められ，BAT 群ではみられなかった。RUX overall の被験者で認められた PT 別事象は敗血症（2 名），ギラン・バレー症候群，アデノウイルス感染（各 1 名）であり，いずれも重篤であった。

その他の感染症カテゴリ（病原体別を除く）で，RUX 群で BAT 群と比べて発現率が特に高いものはなかった（Table 7-21）。RUX overall の被験者では，肺炎（3 名），日和見感染（2 名），サイトメガロウイルス感染／感染症（6 名），尿路感染（5 名），敗血症／敗血症性ショック（2 名）が認められた（5.3.5.3-6-Table 2.1-10j）。

血球減少

血球減少は，血小板減少症（全 Grade：RUX 群 8 名，BAT 群 8 名，以下同順；Grade 3 以上：7 名，6 名），赤血球減少症（全 Grade：5 名，6 名，Grade 3 以上：4 名，6 名），白血球減少症（全 Grade：7 名，8 名，Grade 3 以上：7 名，6 名）のいずれの事象も RUX 群で BAT 群と比べて高頻度に認められた。RUX overall の被験者では，血小板減少症は 10 名（Grade 3 以上 9 名），赤血球減少症は 7 名（Grade 3 以上 5 名），白血球減少症は 9 名（Grade 3 以上 9 名）に認められた（5.3.5.3-6-Table 2.1-10j）。

死亡に至った事象は認められなかった（5.3.5.3-1-Table 14.3.1-1.20j，Table 14.3.1-1.31j）。

重篤な事象は RUX 群，RUX crossover の被験者では認められず，BAT 群で血小板数減少，好中球数減少が各 1 名に認められた。

投与中止に至った事象は RUX 群で血小板数減少が 1 名に認められ，RUX crossover の被験者，BAT 群ではみられなかった。本事象は RUX と他の急性 GVHD 治療薬の両方に関連するか，又は判別不可能と判断され，最終報告時点で未消失であった（5.3.5.1-1-C2301 試験 CSR2-Listing 16.2.7-1.1）。

血液学的検査では，RUX 群，BAT 群ともに被験者の大部分でベースラインのヘモグロビン，リンパ球数，及び血小板数が低かった（5.3.5.3-1-Table 14.3-3.1ja，5.3.5.3-6-Table 3.3-1j）。ベースライン後の Grade 3 及び 4 の検査値異常のうち，RUX 群で BAT 群と比べて高頻度であったものは，Grade 3 の白血球数低値（5 名，3 名），Grade 4 の血小板数低値（8 名，10 名）であった。

RUX overall の被験者で認められたベースライン後の主な検査値異常は，リンパ球数低値（Grade 3：1 名，Grade 4：14 名），ヘモグロビン低値（Grade 3：12 名），血小板数低値（Grade 3：0 名，Grade 4：12 名），白血球数低値（Grade 3：5 名，Grade 4：4 名）であった（5.3.5.3-6-Table 3.3-1j）。

出血性事象

出血性事象は RUX 群で 4 名（Grade 3 以上 2 名），BAT 群で 6 名（Grade 3 以上 1 名）に認められ，群間で発現率に明らかな違いはなかった。PT 別で RUX 群で 2 名以上に発現した事象はなかった（5.3.5.3-1-Table 14.3.1-1.20j）。RUX overall の被験者では，出血性事象は 5 名（Grade 3 以上 2 名）に認められ，いずれの PT 別事象も 1 名での発現であった（5.3.5.3-6-Table 2.1-10j，Table 2.1-13.05j）。

死亡に至った事象は RUX 群で 1 名に認められ，BAT 群，RUX crossover の被験者ではみられなかった。PT 別事象は下部消化管出血で，RUX のみと関連ありと判断されたが，本被験者（被験者番号[redacted]）の死因は急性 GVHD であり，ステージ 3 の消化管病変を伴っていた。

重篤な出血性事象は RUX 群で 1 名，RUX crossover の被験者で 1 名に認められ，BAT 群ではみられなかった。PT 別事象は下部消化管出血（転帰死亡），皮下血腫（1 名）であった。皮下血腫は RUX と関連なしと判断された。

投与中止に至った事象はなかった。

その他の出血性事象カテゴリのうち，胃腸出血は RUX 群（3 名）で BAT 群（0 名）と比べて高頻度に認められた（Table 7-21）。RUX overall の被験者では，胃腸出血（3 名），挫傷，その他の出血性事象（各 1 名）のカテゴリで認められた（5.3.5.3-6-Table 2.1-10j）。

その他

その他の臨床的に注目すべき有害事象で RUX overall の被験者で認められたものは，トランスアミナーゼ上昇（3 名），脂質異常，高血圧，血栓塞栓症，骨折，体重増加（各 1 名）であった（5.3.5.3-6-Table 2.1-10j）。BAT 群と比べて明らかに多くみられた事象はなかった（Table 7-21）。重篤な事象又は RUX の投与中止に至った事象はなかった（5.3.5.3-6-Table 2.1-13.21j，Table 2.1-13.25j～Table 2.1-13.29j）。

5.1.1.1.5 臨床検査値

血液学的検査の要約は上記の血球減少の項に示す。

血液生化学的検査では，Grade 3 及び 4 の検査値異常のうち，RUX 群で BAT 群と比べて明らかに多くみられたものはなかった（5.3.5.3-1-Table 14.3-3.2ja）。RUX overall の被験者で認められた主な検査値異常は，アルブミン低値（Grade 3：10 名，ただしこのうち 6 名はベースラインでも Grade 3），GGT 高値（Grade 3：5 名，Grade 4：4 名），リン酸塩低値（Grade 3：6 名，Grade 4：1 名）であった（5.3.5.3-6-Table 3.4-1j）。

Hy's law に該当した被験者は，RUX 群で 1 名，BAT 群で 3 名にみられ，RUX crossover の被験者では認められなかった（5.3.5.3-1-Table 14.3-3.3.1ja，Table 14.3-3.8ja）。RUX 群で Hy's law に該当した 1 名（被験者番号 [redacted]）では，感染症を発現し抗生物質が併用されたことにより肝機能検査値が上昇した可能性が考えられた（5.3.5.1-1-C2301 試験 CSR2-12.4.2.1 項）。

5.1.1.1.6 バイタルサイン

バイタルサインの異常は，収縮期血圧低下（RUX 群 0 名，BAT 群 2 名，以下同順），拡張期血圧低下（1 名，0 名），脈拍上昇（2 名，8 名）が認められ，いずれも被験者の割合に群間で明らかな違いはなかった。体重の異常変動は，増加（4 名，5 名），減少（2 名，6 名）ともに割合は群間で同程度であった（5.3.5.3-1-Table 14.3-4.1j）。RUX crossover の被験者で 2 名以上に認められたバイタルサインの異常は脈拍上昇（3 名）であった（5.3.5.3-1-Table 14.3-4.3j）。

5.1.1.2 慢性 GVHD

5.1.1.2.1 被験者の内訳

日本人 37 名がランダム化され（RUX 群 22 名，BAT 群 15 名，以下同順），治験治療を実施した。C7D1 までに 20 名（11 名，9 名）が割り付けられた治験治療を中止し，主な中止理由は RUX 群では有害事象（8 名，3 名），BAT 群では有害事象，医師による判断（0 名，3 名）であった（2.7.3-Table 6-11）。

BAT 群で 2 名が RUX へクロスオーバーした。このうち 1 名がクロスオーバー後に投与を中止し，中止理由は有害事象であった。残りの 1 名は継続中であった（5.3.5.1-2-D2301 試験-Listing 16.2.3-2.1，Listing 16.2.5-1.1）。

治験治療が実施された 37 名が FAS 及び SAF に含まれた。

5.1.1.2.2 曝露の程度

C7D1 までの治験治療の曝露期間の中央値（最小値～最大値）は RUX 群が 25.6（3.0～25.6）週，BAT 群が 25.6（0.6～25.6）週であり，群間で同程度であった（5.3.5.3-2-Table 14.3-1.1j）。

データカットオフ時点で，曝露期間の中央値（最小値～最大値）は RUX 群で 44.4（3.0～112.1）週，BAT 群で 29.1（0.6～83.3）週であり，RUX 群で BAT 群と比べて長かった。総曝露期間は RUX 群（236.6 人月）で BAT 群（116.3 人月）と比べて長かった。RUX 群の RUX の用量強度の中央値は C7D1 までが 19.8 mg/日，データカットオフまでが 19.5 mg/日であった（5.3.5.3-2-Table 14.3-1.1j，Table 14.3-1.4j，Table 14.3-1.5j）。

BAT 群で 9 名に 1 種類のみの BAT が実施された。治療開始時の BAT で最も多かったものはイブルチニブ及び MMF（各 6 名）であり，次いでイマチニブ（2 名），リツキシマブ（1 名）であった。曝露期間が最も長かった BAT はイマチニブで，曝露期間の中央値（最小値～最大値）は 41.1（7.0～73.1）週であった（5.3.5.3-2-Table 14.3-1.2j，Table 14.3-1.3j）。

RUX crossover の被験者 2 名中 1 名での RUX の曝露期間は 65.4 週，もう 1 名では 15.7 週であった（5.3.5.3-2-Listing 16.2.5-1.1）。

RUX overall の被験者（24 名）の RUX 曝露期間の中央値（最小値～最大値）は 44.4（3.0～112.1）週，総曝露期間は 21.3 人年であった（5.3.5.3-6-Table 1.2-1j）。

5.1.1.2.3 人口統計学的特性及びその他の特性

RUX 群及び BAT 群の人口統計学的特性及び疾患特性は FAS を対象に評価し，2.7.3-3.3.2.2.2 項に示した。日本人では FAS は SAF と同じ集団であった。

SAF の RUX overall の被験者の年齢（CRF で収集した誕生年に基づく）の中央値は 46.5 歳であった。19 名が 18 歳以上 65 歳以下のカテゴリに含まれたが（5.3.5.3-6-Table 1.3-1j），19 名中 1 名（RUX 群，被験者番号 [redacted]）は実際はランダム化時点で 17 歳であった。性別は男性が 66.7%を占め，BMI の平均値は 18.2 kg/m^2 であった。

5.1.1.2.4 有害事象

日本人でのデータカットオフまでの有害事象の発現状況を Table 5-2 に示す。

Table 5-2 慢性 GVHD の有害事象の発現状況（D2301 試験，SAF，日本人，データカットオフまで）

	RUX N = 22 n (%)	BAT N = 15 n (%)	RUX overall N = 24 n (%)
曝露期間（週）：中央値（最小値 - 最大値）	44.4 (3.0-112.1)	29.1 (0.6-83.3)	44.4 (3.0-112.1)
総曝露期間	236.6 人月	116.3 人月	21.3 人年
有害事象	22 (100)	15 (100)	23 (95.8)
副作用	19 (86.4)	8 (53.3)	20 (83.3)
Grade 3 以上の有害事象	17 (77.3)	12 (80.0)	18 (75.0)
治験治療下の死亡	5 (22.7)	2 (13.3)	5 (20.8)
死亡に至った有害事象	5 (22.7)	2 (13.3)	5 (20.8)
重篤な有害事象	14 (63.6)	8 (53.3)	15 (62.5)
投与中止に至った有害事象	9 (40.9)	3 (20.0)	10 (41.7)
用量調節又は休薬に至った有害事象	8 (36.4)	3 (20.0)	9 (37.5)
治療を要した有害事象	21 (95.5)	14 (93.3)	22 (91.7)

Source: 5.3.5.3-6-Table 1.2-1j，Table 2.1-1j，Table 2.1-20j，5.3.5.3-2-Table 14.3-1.1j，Table 14.3.1-1.15j，Table 14.3.1-2.2j
総曝露期間 = 全被験者の曝露期間の合計

比較的よくみられた有害事象

データカットオフまでに有害事象は RUX 群 22 名全員（100%），BAT 群 15 名全員（100%）に認められた。EAIR は RUX 群（1265.4）で BAT 群（2263.9）と比べて高かった（5.3.5.3-2-Table 14.3.1-1.27j）。SOC 別で，RUX 群で BAT 群と比べて多く認められた事象（発現率の差が

30%以上）はなかった（Table 7-23）。PT 別で，RUX 群で BAT 群と比べて多く認められた事象（発現率の差が約 30%以上）は貧血（RUX 群 10 名，BAT 群 1 名）であった。

副作用は RUX 群 19 名（86.4%），BAT 群 8 名（53.3%）に認められた（Table 7-24）。RUX 群で BAT 群と比べて多く認められた PT 別副作用は貧血（9 名，0 名）であった。

Grade 3 以上の有害事象は RUX 群 17 名（77.3%），BAT 群 12 名（80.0%）に認められ，RUX 群で BAT 群と比べて明らかに多く認められた PT 別事象はなかった（Table 7-23）。

RUX overall の被験者では 23 名（95.8%）に有害事象が認められ，主な PT 別有害事象は貧血（11 名），肺炎，上咽頭炎（各 6 名），血小板数減少（5 名）であった（5.3.5.3-6-Table 2.1-3j）。主な副作用は貧血，血小板数減少であり（5.3.5.3-6-Table 2.1-4j），主な Grade 3 以上の有害事象は貧血，肺炎であった。全有害事象の発現率及び主な PT 別事象の発現率が投与期間の延長に伴って高くなる傾向はみられなかった（5.3.5.3-6-Table 2.1-23j）。

死亡

全体集団と同様に，治験治療下の死亡，死亡に至った有害事象をそれぞれ評価した。

治験治療下の死亡は RUX 群で 5 名（22.7%），BAT 群で 2 名（13.3%）に認められ，RUX crossover の被験者では認められなかった（Table 7-25）。いずれの死因も慢性 GVHD であった。

死亡に至った有害事象は RUX 群で 5 名（22.7%），BAT 群で 2 名（13.3%）に認められ，RUX crossover の被験者では認められなかった。PT 別事象は，RUX 群では肺炎（2 名），細菌性肺炎，敗血症，呼吸不全，イレウス（各 1 名），BAT 群では肺炎，多臓器機能不全症候群（各 1 名）であった（5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。RUX overall の被験者で日本人だけでみられた事象は細菌性肺炎，敗血症，呼吸不全，イレウス（各 1 名）であった。死亡に至った有害事象のうち肺炎（1 名），細菌性肺炎，敗血症，呼吸不全は RUX と他の慢性 GVHD 治療薬の両方に関連するか，又は判別不可能と判断された。RUX のみに関連すると判断された事象はなかった。

日本人 RUX 投与被験者で報告された死亡（死因，死亡に至った有害事象）は，いずれも免疫抑制下の患者で想定される感染症，HSCT 後に予測される事象，又は重症な対象疾患の特性を反映するものであった。

重篤な有害事象

重篤な有害事象は RUX 群で 14 名（63.6%），BAT 群で 8 名（53.3%），RUX crossover の被験者で 1 名（50.0%）に認められた（Table 7-26，5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。EAIR は，RUX 群（94.1）と BAT 群（93.5）で同程度であった（5.3.5.3-2-Table 14.3.1-1.28j）。RUX overall の被験者で複数名に認められた PT 別事象は肺炎（6 名），気胸（2 名）であり，いずれも全体集団の RUX 投与被験者でも認められた（5.3.5.3-6-Table 2.1-5j，Table 7-11）。

その他の重要な有害事象

投与中止に至った有害事象は RUX 群で 9 名（40.9%），BAT 群で 3 名（20.0%），RUX crossover の被験者で 1 名（50.0%）に発現した。RUX overall の被験者で認められた PT 別事象は，肺炎（4 名），イレウス，脳膿瘍，細菌性肺炎，敗血症，移植後リンパ増殖性障害，気胸，呼吸不全，血小板数減少（各 1 名）であった。これらの事象のうち，RUX のみと関連ありと判断された事象はなかった。RUX 投与後に日本人だけでみられた事象はイレウス，脳膿瘍，細菌性肺炎，移植後リンパ増殖性障害であった（5.3.5.3-2-Table 14.3.1-1.7j，5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。

用量調節又は休薬に至った有害事象は，RUX 群で 8 名（36.4%），BAT 群で 3 名（20.0%）に発現した。RUX 群で 2 名以上に認められた事象は貧血（2 名）であった（5.3.5.3-2-Table 14.3.1-1.22j）。治療を要した有害事象は RUX 群で 21 名（95.5%），BAT 群で 14 名（93.3%）に発現した。

器官別又は症候群別有害事象

RUX 群 BAT 群の臨床的に注目すべき有害事象の発現率を Table 7-27 に，詳細を以下に示す。なお，全体集団の RUX overall の被験者で認められた臨床的に注目すべき有害事象のうち，B 型肝炎の再活性化，その他の血球減少，胃腸出血，頭蓋内出血，悪性腫瘍，NMSC，めまいは日本人ではみられなかった。

感染症

感染症（結核を除く）は，RUX 群，BAT 群ともに被験者の大部分に認められた（全 Grade：RUX 群 19 名，BAT 群 12 名，以下同順；Grade 3 以上：11 名，5 名）。RUX 群で BAT 群と比べて多く認められた（発現率の差が 30%以上）PT 別事象はなかった（5.3.5.3-2-Table 14.3.1-1.25j）。RUX overall の被験者では，感染症（結核を除く）は 20 名（Grade 3 以上 11 名）に認められ，主な PT 別事象は肺炎，上咽頭炎（各 6 名），インフルエンザ（4 名）であった（5.3.5.3-6-Table 2.1-10j，Table 2.1-13.10j）。

死亡に至った事象は RUX 群で 4 名，BAT 群で 1 名に認められ，RUX crossover の被験者ではみられなかった。RUX 群で死亡に至った事象は肺炎（2 名），細菌性肺炎，敗血症（各 1 名）であり，RUX のみと関連ありと判断された事象はなかった（5.3.5.1-2-D2301 試験-Listing 16.2.7-1）。

重篤な事象は RUX 群で 11 名，BAT 群で 4 名に認められ，RUX crossover の被験者ではみられなかった。RUX 群で認められた PT 別事象は肺炎（6 名），脳膿瘍，サイトメガロウイルス感染，帯状疱疹，肺炎球菌感染，細菌性肺炎，移植後リンパ増殖性障害，腎盂腎炎，敗血症，尿路感染（各 1 名）であった。これらの事象のうち RUX のみと関連ありと判断されたものは帯状疱疹で，加療により消失又は軽快した。

投与中止に至った事象は RUX 群で 7 名，BAT 群で 1 名に認められ，RUX crossover の被験者ではみられなかった。RUX 群で認められた PT 別事象は肺炎（4 名），脳膿瘍，細菌性肺炎，移植後リンパ増殖性障害，敗血症（各 1 名）で，いずれも重篤であった。

その他の感染症カテゴリ（病原体別を除く）で，RUX 群で BAT 群と比べて発現率が特に高いものはなかった（Table 7-27）。RUX overall の被験者では，肺炎（8 名），日和見感染（1 名），サイトメガロウイルス感染／感染症（2 名），尿路感染（2 名），敗血症／敗血症性ショック（1 名），帯状疱疹（1 名）が認められた（5.3.5.3-6-Table 2.1-10j）。

血球減少

血球減少は，血小板減少症（全 Grade：RUX 群 8 名，BAT 群 3 名，以下同順；Grade 3 以上：7 名，3 名），赤血球減少症（全 Grade：10 名，1 名，Grade 3 以上：6 名，1 名）は RUX 群で BAT 群と比べて高頻度に認められ，白血球減少症（全 Grade：6 名，6 名，Grade 3 以上：6 名，4 名）は群間で大きな違いはなかった。RUX overall の被験者では，血小板減少症は 9 名（Grade 3 以上 8 名），赤血球減少症は 11 名（Grade 3 以上 7 名），白血球減少症は 7 名（Grade 3 以上 7 名）に認められた（5.3.5.3-6-Table 2.1-10j）。

死亡に至った事象は認められなかった。

重篤な事象は RUX 群，BAT 群では認められず，RUX crossover の被験者で血小板数減少が 1 名にみられた（5.3.5.3-2-Table 14.3.1-1.25j，5.3.5.3-6-Table 2.1-13.01j，Table 2.1-13.02j，Table 2.1-13.03j）。本事象は RUX と関連なしと判断され，最終報告時点で未消失であった（5.3.5.1-2-D2301-Listing 16.2.7-1）。

投与中止に至った事象は RUX 群ではみられず，BAT 群で白血球減少症が 1 名，RUX crossover の被験者で血小板数減少（重篤）が 1 名に認められた。

血液学的検査では，RUX 群，BAT 群ともに被験者の 4～6 割でベースラインのヘモグロビン及び血小板数が低かった（5.3.5.3-2-Table 14.3-3.1j）。ベースライン後の Grade 3 及び 4 の検査値異常の頻度はいずれの項目も群間で同程度であった。RUX overall の被験者で認められたベースライン後の主な検査値異常は，リンパ球数低値（Grade 3：9 名，Grade 4：2 名，以下同順），ヘモグロビン低値（6 名，該当なし），血小板数低値（1 名，8 名），白血球数低値，好中球数低値（各 3 名，2 名）であった（5.3.5.3-6-Table 3.3-1j）。

出血性事象

出血性事象は RUX 群で 3 名（Grade 3 以上 1 名），BAT 群で 6 名（Grade 3 以上 1 名）に認められ，群間で発現率に明らかな違いはなかった。PT 別で RUX 群で 2 名以上に発現した事象はなかった（5.3.5.3-2-Table 14.3.1-1.25j）。RUX overall の被験者では，出血性事象は 3 名（Grade 3 以上 1 名）に認められ，いずれの PT 別事象も 1 名での発現であった（5.3.5.3-6-Table 2.1-10j，Table 2.1-13.05j）。

死亡に至った事象は認められなかった。

重篤な出血性事象は RUX 群で 1 名に認められ，BAT 群，RUX crossover の被験者ではみられなかった。PT 別事象は脾臓出血で，RUX と関連なしと判断され，加療により軽快した。

投与中止に至った事象はなかった。

その他の出血性事象カテゴリで，RUX 群で BAT 群と比べて多くみられた事象はなかった（Table 7-27）。RUX overall の被験者では，挫傷（1 名），その他の出血性事象（2 名）のカテゴリで認められた（5.3.5.3-6-Table 2.1-10j）。

その他

その他の臨床的に注目すべき有害事象で RUX overall の被験者で認められたものは，トランスアミナーゼ上昇（4 名），脂質異常（5 名），高血圧（3 名），血栓塞栓症，骨折，体重増加（各 1 名）であった（5.3.5.3-6-Table 2.1-10j）。BAT 群と比べて明らかに多くみられた事象はなかった（Table 7-27）。重篤な事象又は RUX の投与中止に至った事象はなかった（5.3.5.3-6-Table 2.1-13.21j，Table 2.1-13.25j～Table 2.1-13.29j）。

5.1.1.2.5 臨床検査値

血液学的検査の要約は上記の血球減少の項に示す。

血液生化学的検査では，Grade 3 及び 4 の検査値異常のうち，RUX 群で BAT 群と比べて明らかに多くみられたものはなかった（5.3.5.3-2-Table 14.3-3.5j）。RUX overall の被験者で認められた主な検査値異常は，グルコース高値（Grade 3：4 名），GGT 高値［Grade 3：6 名，Grade 4：2 名（ただしこの 2 名はベースラインでも Grade 4）］であった（5.3.5.3-6-Table 3.4-1j）。

RUX 群，BAT 群で Hy's law に該当した被験者はいなかった（5.3.5.3-2-Table 14.3-3.6j）。

5.1.1.2.6 バイタルサイン

バイタルサインの異常は，収縮期血圧低下（RUX 群 1 名，BAT 群 0 名，以下同順），拡張期血圧上昇（2 名，1 名），拡張期血圧低下（0 名，1 名），脈拍上昇（9 名，4 名）が認められ，いずれも被験者の割合に群間で明らかな違いはなかった。体重の異常変動は，増加（7 名，3 名），減少（0 名，3 名）ともに割合に群間で明らかな違いはなかった（5.3.5.3-2-Table 14.3-4.2j）。

5.1.2 青少年

急性 GVHD

C2301 試験で青少年被験者（12 歳以上 18 歳未満）は 9 名（RUX 群 5 名，BAT 群 4 名）が SAF に含まれた。データカットオフ 2 までの RUX overall の青少年被験者 6 名の曝露期間の中央値（最小値～最大値）は 14.2（1.6～34.6）週，総曝露期間は 1.7 人年であった（5.3.5.3-4-Table 5.1-1.1.1）。

RUX overall の青少年被験者で，SOC 別の心臓障害，血管障害，免疫系障害は認められなかった（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-5.1）。PT 別有害事象，副作用，及び重篤な有害事象の発現状況は全体集団と同様であった。1 名が血液疾患の進行により死亡した（5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-5.2～Table 14.3.1-5.5）。骨関連の有害事象は 4 名に認められ，内訳は骨痛が 2 名，筋骨格痛，骨粗鬆症，骨粗鬆症性骨折が各 1 名であった。2 名中 1 名の骨痛と骨粗鬆症性骨折は同一被験者に発現し，いずれも重症度は Grade 3 で，RUX 投与に対する変更なく加療に

より軽快した。もう 1 名での骨痛及び筋骨格痛は Grade 1 であり，RUX 投与に対する変更や加療なく消失した。骨粗鬆症は Grade 2 で Day 106 に発現し，RUX 投与に対する変更なく加療により軽快した。いずれの事象も RUX との関連なしと判断された（5.3.5.1-1-C2301 試験 CSR2-Listing 16.2.7-1.1）。

慢性 GVHD

D2301 試験で青少年被験者は 11 名（RUX 群 4 名，BAT 群 7 名）が SAF に含まれた。データカットオフまでの RUX overall の青少年被験者 8 名の曝露期間の中央値（最小値～最大値）は 40.3（2.6～112.1）週，総曝露期間は 7.3 人年であった（5.3.5.3-4-Table 5.1-1.1.2）。

C7D1 までの RUX 群の青少年被験者で，SOC 別の免疫系障害は認められなかった（5.3.5.1-2-D2301 試験-Table 14.3.1-5.1）。PT 別有害事象の発現状況は全体集団と同様であった。副作用及び死亡は報告されなかった（5.3.5.1-2-D2301 試験-Table 14.3.1-5.2，Table 14.3.1-5.5）。骨折，その他の骨関連の有害事象は認められなかった。タナーステージ評価で特記すべき所見はなかった（5.3.5.1-2-D2301 試験-Listing 16.2.4-3.1）。

5.1.3 部分集団

年齢，性別，人種，地域

年齢，性別，人種，地域別のほとんどの部分集団で，急性 GVHD の C2301 試験のデータカットオフ 2 までの曝露期間の中央値は 8 週，慢性 GVHD の D2301 試験のデータカットオフまでの曝露期間の中央値は 40 週を超えた（5.3.5.3-4-Table 5.1-1.1.2，Table 5.1-1.2.2，Table 5.1-1.3.2，Table 5.1-1.4.2）。C2301 試験，D2301 試験のいずれの試験でも，一部の部分集団は他の部分集団と比べて被験者数が少なく，単純な比較は困難であるものの，有害事象発現率及び重篤な有害事象の発現率に一定の傾向はみられなかった（Table 5-3）。

ベースラインの肝機能障害の程度

肝臓は GVHD の重要な臓器の 1 つであり，ベースラインの肝機能障害の程度別に有害事象発現状況及び血液学的検査値を検討した。その結果，いずれの試験でも，有害事象の発現率や血液学的検査の異常低値の割合に，ベースラインの肝機能障害なしの集団とありの集団で特定の傾向はみられなかった。

急性 GVHD の C2301 試験の RUX overall の被験者で，ベースラインの肝機能障害の程度は，障害なしが 130 名，軽度が 21 名，中等度が 27 名，重度が 23 名（以下同順）であった。死亡に至った有害事象の発現率は，障害なし及び軽度の集団に比べ，中等度及び重度の集団で高かった（19.2%，19.0%，37.0%，39.1%）。重篤な有害事象の発現率（67.7%，76.2%，63.0%，78.3%），投与中止に至った有害事象の発現率（30.8%，19.0%，29.6%，30.4%）に，集団間で特定の傾向はみられなかった（5.3.5.3-4-Table 5.1-2.5.2）。臨床検査では，血小板数低値が Grade 4 へ悪化した被験者の割合は部分集団間で同程度であり（45.5%～57.9%），Grade 3 への悪化は，障害なし

で 29.2%，軽度で 42.9%，中等度で 42.9%，重度で 18.2%であった。好中球数低値の Grade 4 への悪化は，軽度（30.0%）以外の集団（18.5%～19.8%）で同程度であった。ヘモグロビン減少の Grade 3 への悪化は，障害なしで 53.1%，軽度で 52.6%，中等度で 40.0%，重度で 21.1%であった（5.3.5.3-4-Table 5.1-8.1.2）。

慢性 GVHD の D2301 試験の RUX overall の被験者で，ベースラインの肝機能障害の程度は，障害なしが 205 名と大部分を占め，軽度が 14 名，中等度が 4 名，重度が 3 名であった。肝機能障害なしの被験者数に比べて肝機能障害を有する被験者数が少なく比較は困難であったが，有害事象の発現率や血液学的検査の異常低値の割合に集団間で特定の傾向はみられなかった（5.3.5.3-4-Table 5.1-2.5.2，Table 5.1-8.1.2）。

ベースラインの肝機能障害の程度と RUX の薬物動態に関連は認められなかった（2.7.2-3.1.4 項）。

ベースラインの腎機能障害の程度

いずれの試験でも，ベースラインで末期腎不全であった被験者はいなかった。有害事象の発現率や血液学的検査の異常低値の割合に，ベースラインの腎機能障害なしの集団とありの集団で特定の傾向はみられなかった。

急性 GVHD の C2301 試験の RUX overall の被験者で，ベースラインの腎機能障害の程度は，障害なしが 137 名，軽度が 49 名，中等度が 15 名（以下同順）であり，重度はいなかった。死亡に至った有害事象の発現率（22.4%～26.7%），重篤な有害事象の発現率（68.6%～73.3%）はいずれも部分集団間で同程度であった。投与中止に至った有害事象の発現率は 28.5%，34.7%，20.0%であった（5.3.5.3-4-Table 5.1-2.6.2）。血小板数低値が Grade 4 へ悪化した被験者の割合は 50.0%，33.3%，76.9%であり，Grade 3 は 28.7%，46.9%，0%であった。好中球数低値の Grade 4 への悪化は，障害なし（20.0%）と軽度（26.5%）で同程度であり，中等度では 6.7%であった。Grade 3 は，各部分集団で同程度であった（14.3%～19.0%）。ヘモグロビン減少の Grade 3 への悪化は，障害なしで 44.9%であり，軽度（52.3%）と中等度（57.1%）で同程度であった（5.3.5.3-4-Table 5.1-8.2.1）。

慢性 GVHD の D2301 試験の RUX overall の被験者で，ベースラインの腎機能障害の程度は，障害なしが 117 名，軽度が 71 名，中等度が 35 名（以下同順）であり，重度が 2 名と少なかった。死亡に至った有害事象の発現率（8.5%，7.0%，5.7%），重篤な有害事象の発現率（41.9%，38.0%，42.9%）は部分集団間で同程度であった。投与中止に至った有害事象の発現率は 16.2%，22.5%，17.1%であった（5.3.5.3-4-Table 5.1-2.6.2）。血小板数低値及び好中球数低値の Grade 3 又は Grade 4 への悪化，ヘモグロビン低下の Grade 3 への悪化に該当した被験者の割合に，部分集団間で大きな違いはなかった（5.3.5.3-4-Table 5.1-8.2.2）。

ベースラインの腎機能障害の程度と RUX の薬物動態に関連は認められなかった（2.7.2-3.1.4 項）。

シクロスポリン併用

急性 GVHD の C2301 試験の RUX overall の被験者のうち，シクロスポリン併用あり（127 名）となし（74 名）の部分集団間で，有害事象の発現状況に違いはみられなかった（5.3.5.3-4-Table 5.1-2.7.1，Table 5.1-3.5.1，Table 5.1-4.5.1，Table 5.1-3.6.1，Table 5.1-4.6.1，Table 5.1-5.4.1，Table 5.1-6.4.1）。

慢性 GVHD の D2301 試験の RUX overall の被験者のうち，シクロスポリン併用あり（77 名）となし（149 名）の部分集団間で，有害事象の発現状況に違いはみられなかった（5.3.5.3-4-Table 5.1-2.7.2，Table 5.1-3.5.2，Table 5.1-4.5.2，Table 5.1-3.6.2，Table 5.1-4.6.2，Table 5.1-5.4.2，Table 5.1-6.4.2）。

ランダム化時の急性 GVHD の臓器障害発生部位（急性 GVHD のみ）

C2301 試験の RUX overall の被験者で，臓器障害発生部位の部分集団別に有害事象の発現状況を検討した結果，SOC 別で一般・全身障害および投与部位の状態の発現率は，臓器障害発生部位が肝臓である部分集団で他の集団に比べてやや低かった（下部消化管 46.6%，上部消化管 56.8%，皮膚 59.1%，肝臓 40.5%，以下同順）。また，胃腸障害の発現率は，臓器障害発生部位が上部消化管である部分集団で他の集団に比べて高かった（59.5%，75.7%，59.1%，61.9%）。その他の有害事象の発現状況に部分集団間で違いはみられなかった（5.3.5.3-4-Table 5.1-2.8，Table 5.1-3.7，Table 5.1-4.7，Table 5.1-5.5，Table 5.1-6.5）。

Table 5-3 部分集団別の有害事象及び重篤な有害事象（C2301 試験，271 試験，及び D2301 試験，SAF）

			C2301 試験 RUX overall		271 試験 RUX		D2301 試験 RUX overall	
要因		カテゴリー	N	n (%)	N	n (%)	N	n (%)
年齢	有害事象	12 歳以上 18 歳未満	6	6 (100)	0	0	8	6 (75.0)
		18 歳以上 65 歳以下	166	164 (98.8)	62	62 (100)	193	183 (94.8)
		65 歳超	29	28 (96.6)	9	9 (100)	25	25 (100)
	重篤な有害事象	12 歳以上 18 歳未満	6	4 (66.7)	0	0	8	6 (75.0)
		18 歳以上 65 歳以下	166	111 (66.9)	62	54 (87.1)	193	78 (40.4)
		65 歳超	29	24 (82.8)	9	5 (55.6)	25	10 (40.0)
性別	有害事象	男性	116	115 (99.1)	35	35 (100)	146	141 (96.6)
		女性	85	83 (97.6)	36	36 (100)	80	73 (91.3)
	重篤な有害事象	男性	116	78 (67.2)	35	28 (80.0)	146	60 (41.1)
		女性	85	61 (71.8)	36	31 (86.1)	80	34 (42.5)
人種	有害事象	White	141	140 (99.3)	66	66 (100)	170	159 (93.5)
		Asian	26	26 (100)	2	2 (100)	36	35 (97.2)
		その他	34	32 (94.1)	3	3 (100)	20	20 (100)
	重篤な有害事象	White	141	100 (70.9)	66	55 (83.3)	170	63 (37.1)
		Asian	26	15 (57.7)	2	2 (100)	36	20 (55.6)
		その他	34	24 (70.6)	3	2 (66.7)	20	11 (55.0)
地域	有害事象	アジア（日本以外）	10	10 (100)	0	0	8	8 (100)

要因		カテゴリー	C2301 試験 RUX overall N	C2301 試験 RUX overall n (%)	271 試験 RUX N	271 試験 RUX n (%)	D2301 試験 RUX overall N	D2301 試験 RUX overall n (%)
		日本	15	15 (100)	0	0	24	23 (95.8)
		その他	176	173 (98.3)	71	71 (100)	194	183 (94.3)
	重篤な有害事象	アジア（日本以外）	10	3 (30.0)	0	0	8	3 (37.5)
		日本	15	11 (73.3)	0	0	24	15 (62.5)
		その他	176	125 (71.0)	71	59 (83.1)	194	76 (39.2)
ベースラインの肝機能障害の程度	有害事象	正常	130	128 (98.5)	48	48 (100)	205	194 (94.6)
		軽度	21	21 (100)	4	4 (100)	14	13 (92.9)
		中等度	27	27 (100)	7	7 (100)	4	4 (100)
		重度	23	22 (95.7)	12	12 (100)	3	3 (100)
	重篤な有害事象	正常	130	88 (67.7)	48	38 (79.2)	205	85 (41.5)
		軽度	21	16 (76.2)	4	4 (100)	14	6 (42.9)
		中等度	27	17 (63.0)	7	6 (85.7)	4	1 (25.0)
		重度	23	18 (78.3)	12	11 (91.7)	3	2 (66.7)
ベースラインの腎機能障害の程度	有害事象	正常	137	136 (99.3)	50	50 (100)	117	110 (94.0)
		軽度	49	47 (95.9)	12	12 (100)	71	68 (95.8)
		中等度	15	15 (100)	9	9 (100)	35	33 (94.3)
		重度	0	0	0	0	2	2 (100)
		不明	0	0	0	0	1	1 (100)
	重篤な有害事象	正常	137	94 (68.6)	50	40 (80.0)	117	49 (41.9)
		軽度	49	34 (69.4)	12	10 (83.3)	71	27 (38.0)
		中等度	15	11 (73.3)	9	9 (100)	35	15 (42.9)
		重度	0	0	0	0	2	2 (100)
		不明	0	0	0	0	1	1 (100)
シクロスポリン併用	有害事象	あり	127	127 (100)	11	11 (100)	77	73 (94.8)
		なし	74	71 (95.9)	60	60 (100)	149	141 (94.6)
	重篤な有害事象	あり	127	87 (68.5)	11	10 (90.9)	77	29 (37.7)
		なし	74	52 (70.3)	60	49 (81.7)	149	65 (43.6)
ランダム化時の急性 GVHD の臓器障害発生部位（急性 GVHD のみ）	有害事象	肝臓	42	42 (100)	16	16 (100)	-	-
		下部消化管	131	129 (98.5)	51	51 (100)	-	-
		上部消化管	37	37 (100)	22	22 (100)	-	-
		皮膚	115	112 (97.4)	36	36 (100)	-	-
	重篤な有害事象	肝臓	42	29 (69.0)	16	15 (93.8)	-	-
		下部消化管	131	90 (68.7)	51	41 (80.4)	-	-
		上部消化管	37	22 (59.5)	22	20 (90.9)	-	-
		皮膚	115	79 (68.7)	36	31 (86.1)	-	-

Source: 5.3.5.3-4-Table 5.1-2.1.2, Table 5.1-2.2.2, Table 5.1-2.3.2, Table 5.1-2.4.2, Table 5.1-2.5.2, Table 5.1-2.6.2, Table 5.1-2.7.2, Table 5.1-2.8
C2301 試験はデータカットオフ 2 まで，D2301 試験はデータカットオフまでの結果

5.2 外因性要因

RUX の安全性及び忍容性に対する医療習慣又は生活習慣の差異等の外因性要因による影響を評価する解析は行っていない。

5.3 薬物相互作用

強い CYP3A4 阻害剤，中程度の CYP3A4 阻害剤並びに CYP3A4 と CYP2C9 の阻害剤（フルコナゾール）との併用により RUX のトラフ濃度の上昇が認められた（「2.7.2 臨床薬理試験」参照）。これらの薬剤との併用では，添付文書で注意喚起しているように，血中濃度の上昇や有害事象の発現に注意する必要がある。

5.4 妊娠及び授乳時の使用

ヒト胎児への潜在的リスクがあることから，妊娠可能な女性に対しては，RUX 投与期間中は適切な避妊を行うことを指導し，妊娠中又は妊娠している可能性のある女性は，RUX の使用を避ける必要がある。また，授乳期間中のルキソリチニブの使用も避ける必要がある。

5.5 過量投与

RUX の過量投与に対する解毒剤は知られていない。RUX 200 mg までの単回投与で忍容性が認められた。RUX 推奨用量を超える反復投与は白血球減少症，貧血，血小板減少症等の骨髄抑制のリスクが増加する危険性があり，適切な対症療法を行う必要がある。血液透析は，RUX の体内からの排出を促進しないと考えられる。

5.6 薬物乱用

RUX の薬物乱用の報告はこれまでになく，薬物乱用に関するリスクは知られていない。なお，薬物乱用に関する試験は実施していない。

5.7 離脱症状及び反跳現象

離脱症状及び反跳現象を評価する試験は実施していない。RUX を漸減せずに投与中止した場合，GVHD の症状や徴候が増加する可能性がある。患者の状態，併用療法，及び医師の臨床判断に基づき，適切な漸減方法を検討する必要がある。

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

RUX の自動車運転や機械操作に対する影響は検討していない。しかし，浮動性めまい，視力障害等を発現した患者は，症状が続く限り自動車運転や機械操作等の危険を伴う作業には従事させないように注意する必要がある。

6 市販後データ

6.1 進行中の試験

安全性評価に使用した C2301 試験，D2301 試験ともに，本承認申請時点で進行中である。

6.2 市販後の経験

本剤は，骨髄線維症の治療薬として 2011 年 11 月 16 日（国際誕生日）にライセンスパートナーである Incyte 社により米国で Jakafi の販売名で初めて承認され，2023 年 5 月現在，Novartis 社において世界 110 ヵ国以上で Jakavi の販売名で製造販売承認を取得している。GVHD に係る適応症については，61 ヵ国で急性 GVHD，59 ヵ国で慢性 GVHD の治療薬としてそれぞれ承認を取得している。一方，国内においては，ジャカビ錠の販売名で 2014 年 7 月に骨髄線維症，2015 年 9 月に真性多血症（既存治療が効果不十分又は不適当な場合に限る）を効能又は効果として承認されている。

2011 年 11 月 16 日以降，市販後の使用経験として定期的安全性最新報告（PSUR）が作成されており，安全性情報が評価されている。以下に直近 4 年間に関する複数の PSUR（2019 年 2 月 23 日～2023 年 2 月 22 日）の情報を示す。

6.2.1 推定患者数

1 日の標準投与量を 30 mg と仮定し，総販売量から推定すると，2023 年 2 月 22 日までに，約 317,838 人年に使用されたものと考える。

6.2.2 外国での医薬品安全性監視計画（Risk Management Plan）の概要

市販後の使用経験を踏まえ，最新の EU RMP Version 15.0 では，重要な特定されたリスク及び重要な潜在的リスクとして以下が定められている。

- 重要な特定されたリスク（Important identified risks）：重篤な感染症
- 重要な潜在的リスク（Important potential risks）：発達毒性

6.2.3 PSUR の要約

安全性の理由により規制当局又は製造業者が取った措置で，販売承認の取り下げ又は中止，販売承認更新の不可，販売の制限，臨床試験の中止，用法・用量の変更，対象患者の変更又は処方変更に至ったものはなかった。また，2011 年 11 月 16 日から 2023 年 2 月 22 日までに市販後で報告された副作用は，自発報告（文献を含む）123,634 件，試験からの報告（重篤）16,719 件であった。2020 年 5 月 12 日付で汎血球減少症を CCDS へ追記したが，それ以外には，新たな安全性の重点観察項目は特定されず，本剤の安全性プロファイル及びベネフィット／リスクプロファイルは良好であり変更はなかった。

2020 年 5 月 12 日付の CCDS への汎血球減少症の追記について，国内添付文書には 2021 年 1 月付で重大な副作用の骨髄抑制の項に汎血球減少症を追記した。

7 付録

Table 7-1 臨床的に注目すべき有害事象の定義

臨床的に注目すべき有害事象	定義
Bacterial infections	Bacterial infectious disorders (HLGT)
Bleeding (Haemorrhage)	Haemorrhages (SMQ) (narrow)
Bruising	Bruising (CMQ)
CMV infection_disease	CMV infection/disease (CMQ)
Dizziness	Dizziness (CMQ)
Elevated Transaminases (CT)	Elevated Transaminases (CMQ)
Erythropenia (Anemia)	Haematopoietic erythropenia (SMQ) (broad)
Fracture (CT)	Fractures (HLGT)
Fungal infections	Fungal infectious disorders (HLGT)
GI bleeding	GI bleeding (CMQ)
Growth Retardation	ADR Growth retardation (NMQ)
Hepatitis B reactivation	Hepatitis B reactivation (CMQ)
Herpes zoster	Herpes zoster (CMQ)
Hypertension	Hypertension (SMQ) (broad)
Infections excluding Tuberculosis	Infections excluding Tuberculosis (CMQ)
Infections with pathogen unspecified	Infections - pathogen unspecified (HLGT)
Intracranial haemorrhage	Intracranial haemorrhage (CMQ)
Leukopenia	Haematopoietic leukopenia (SMQ) (broad)
Lipid abnormalities	Dyslipidaemia (SMQ)
Long-term safety data, including secondary malignancies - Second Primary Malignancies	Malignant tumours (SMQ)
Non melanoma skin cancers	Non-melanoma skin cancer (NMSC) (including basal, squamous and Merkel cell carcinoma) (CMQ)
Opportunistic infections	Opportunistic infections (CMQ)
Other Cytopenias	Haematopoietic cytopenias affecting more than one type of blood cell (SMQ) (narrow)
Other haemorrhage events	Other haemorrhage events including epistaxis, post-procedural haemorrhage and hematuria (CMQ)
Other infections	Other Infections (CMQ)
Pneumonia	Pneumonia (CMQ)
Progressive multifocal leukoencephalopathy (CT)	Progressive multifocal leukoencephalopathy (risk definition) (CMQ)
Sepsis and septic shock	Sepsis and septic shock (CMQ)
Thrombocytopenia	Haematopoietic thrombocytopenia (SMQ) (broad)
Thromboembolic events	Embolic and thrombotic events (SMQ)
Tuberculosis	Tuberculosis (CMQ)
Urinary tract infections (UTI)	Urinary tract infections (UTI) (CMQ)
Viral infectinos	Viral infectious disorders (HLGT)
Weight gain	Weight gain (CMQ)

Source: 5.3.5.3-4-Listing 1
CMQ = customised MedDRA queries, NMQ = Novartis MedDRA queries, SMQ = standardised MedDRA queries
MedDRA version 23.0

Table 7-2 急性 GVHD の治験治療下の死亡（C2301 試験，SAF，データカットオフ 2 まで）

Category PT	RUX N = 152 n (%)	BAT N = 150 n (%)	RUX crossover N = 49 n (%)
曝露期間（日）：中央値（最小値 - 最大値）	63.0 (6.0-463.0)	29.0 (1.0-188.0)	61.0 (2.0-383.0)
総曝露期間（人年）	39.5	19.0	12.3
合計	43 (28.3)	36 (24.0)	19 (38.8)
死因：対象疾患	21 (13.8)	21 (14.0)	8 (16.3)
急性移植片対宿主病	21 (13.8)	21 (14.0)	8 (16.3)
死因：その他	22 (14.5)	15 (10.0)	11 (22.4)
敗血症	3 (2.0)	1 (0.7)	1 (2.0)
心停止	2 (1.3)	0	0
疾患進行	2 (1.3)	1 (0.7)	0
多臓器機能不全症候群	2 (1.3)	1 (0.7)	0
敗血症性ショック	2 (1.3)	2 (1.3)	0
急性骨髄性白血病	1 (0.7)	0	0
再発急性骨髄性白血病	1 (0.7)	1 (0.7)	0
状態悪化	1 (0.7)	0	0
全身健康状態異常	1 (0.7)	0	0
感染	1 (0.7)	0	0
肺障害	1 (0.7)	0	0
腎機能障害	1 (0.7)	0	0
呼吸障害	1 (0.7)	0	0
呼吸不全	1 (0.7)	1 (0.7)	2 (4.1)
気道感染	1 (0.7)	0	0
ウイルス感染	1 (0.7)	0	0
急性肺損傷	0	1 (0.7)	0
誤嚥	0	1 (0.7)	0
脳梗塞	0	1 (0.7)	0
易感染性宿主の感染	0	1 (0.7)	0
腸管虚血	0	1 (0.7)	0
多臓器障害	0	1 (0.7)	0
偽膜性大腸炎	0	1 (0.7)	0
腎不全	0	1 (0.7)	0
心肺不全	0	0	1 (2.0)
死亡	0	0	1 (2.0)
アデノウイルス感染	0	0	1 (2.0)
脳血管発作	0	0	1 (2.0)
昏睡	0	0	1 (2.0)
特発性肺炎症候群	0	0	1 (2.0)
肺臓炎	0	0	1 (2.0)
肺出血	0	0	1 (2.0)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.1，Table 14.3-1.5，Table 14.3.1-2.2，Table 14.3.1-2.3
RUX 群の発現率の降順
総曝露期間 = 全被験者の曝露期間の合計
MedDRA version 22.1

Table 7-3 急性 GVHD の死亡一覧（C2301 試験，SAF，データカットオフ 2 まで）

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
RUX 群					
AUS/[redacted]	5[redacted]/CA	81&	61	aGvHD	急性 GVHD
AUS/[redacted]	1[redacted]/CA	83&	69	aGvHD	急性 GVHD
AUS/[redacted]	6[redacted]/WH	78	9	aGvHD	急性 GVHD
AUS/[redacted]	3[redacted]/AS	315&	141	Rrespitory infection	気道感染
AUS/[redacted]	4[redacted]/OTH	18	1	aGvHD	急性 GVHD
AUS/[redacted]	5[redacted]/UN	39	9	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/CA	251&	223	Pneumonia	肺炎
DEU/[redacted]	4[redacted]/CA	244&	203	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/CA	162&	133	Sepsis with unknown focus	敗血症
DEU/[redacted]	6[redacted]/CA	57	4	multiple organ-system failure	多臓器機能不全症候群
DEU/[redacted]	5[redacted]/CA	153&	117	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/WH	17	10	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/CA	16	3	aGvHD	急性 GVHD
DEU/[redacted]	2[redacted]/CA	547&	435	Pulmonary sepsis	肺敗血症
DEU/[redacted]	2[redacted]/CA	493&	438	Multi-organ failure	多臓器機能不全症候群
DEU/[redacted]	7[redacted]/CA	617&	460	Multi-organ failure	多臓器機能不全症候群
DEU/[redacted]	6[redacted]/CA	64&	55	aGvHD	急性 GVHD
DEU/[redacted]	2[redacted]/CA	411&	382	ARDS	急性呼吸窮迫症候群
DEU/[redacted]	6[redacted]/CA	323&	303	Septic-toxic circulatory failure (no more info)	敗血症性ショック
DEU/[redacted]	6[redacted]/CA	135	4	aGvHD	急性 GVHD
DEU/[redacted]	5[redacted]/CA	39	19	aGvHD	急性 GVHD
DEU/[redacted]	5[redacted]/CA	77	28	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/CA	134&	105	ventricular fibrillation	心室細動
DEU/[redacted]	6[redacted]/CA	51	3	MODS	多臓器機能不全症候群
DEU/[redacted]	5[redacted]/CA	54	19	aGvHD	急性 GVHD
DEU/[redacted]	5[redacted]/CA	185&	170	aGvHD	急性 GVHD
DEU/[redacted]	1[redacted]/CA	174&	139	Fungal Infection of the Brain	中枢神経系真菌感染
ESP/[redacted]	2[redacted]/WH	153&	140	aGvHD	急性 GVHD
ESP/[redacted]	5[redacted]/CA	430&	325	disease relapse (MDS in October 2018)	骨髄異形成症候群
ESP/[redacted]	5[redacted]/CA	78&	56	aGvHD	急性 GVHD
ESP/[redacted]	5[redacted]/CA	19	6	respiratory infection	気道感染
ESP/[redacted]	2[redacted]/CA	174	30	underlyign disease progression	疾患進行
ESP/[redacted]	5[redacted]/CA	12	1	Septic shock	敗血症性ショック
ESP/[redacted]	5[redacted]/UN	33	13	aGvHD	急性 GVHD
ESP/[redacted]	5[redacted]/CA	107	10	aGvHD	急性 GVHD
ESP/[redacted]	6[redacted]/UN	15	10	Respiratory deterioration	呼吸障害
FRA/[redacted]	6[redacted]/CA	72&	51	hematology disease progression	血液障害

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
FRA/[redacted]	6[redacted]/UN	32	16	alteration of general state	全身健康状態異常
FRA/[redacted]	5[redacted]/UN	368&	356	alteration of general state	全身健康状態異常
FRA/[redacted]	5[redacted]/CA	43	31	Acute Myeloid Leukemia reapse	再発急性骨髄性白血病
FRA/[redacted]	5[redacted]/OTH	118&	106	pneumonitis	肺臓炎
FRA/[redacted]	3[redacted]/UN	56&	36	aGvHD	急性 GVHD
FRA/[redacted]	6[redacted]/CA	20	1	aGvHD	急性 GVHD
FRA/[redacted]	6[redacted]/CA	28	1	aGvHD	急性 GVHD
FRA/[redacted]	3[redacted]/CA	44	3	aGvHD	急性 GVHD
FRA/[redacted]	6[redacted]/UN	89	22	pneumopathy	肺障害
FRA/[redacted]	6[redacted]/OTH	248&	191	sepsis	敗血症
FRA/[redacted]	1[redacted]/UN	39	29	disease progression	疾患進行
FRA/[redacted]	1[redacted]/CA	230&	62	Respiratory faillure	呼吸不全
FRA/[redacted]	5[redacted]/UN	630&	555	Reason unknown	死亡
GBR/[redacted]	5[redacted]/CA	179&	117	aGvHD	急性 GVHD
GBR/[redacted]	5[redacted]/UN	16	4	aGvHD	急性 GVHD
GRC/[redacted]	4[redacted]/CA	29	12	infection	感染
ISR/[redacted]	6[redacted]/CA	207&	76	aGvHD	急性 GVHD
ISR/[redacted]	5[redacted]/WH	258&	252	aGvHD	急性 GVHD
ISR/[redacted]	6[redacted]/CA	14	2	aGvHD	急性 GVHD
ISR/[redacted]	5[redacted]/CA	33	22	aGvHD	急性 GVHD
ISR/[redacted]	5[redacted]/CA	79	13	aGvHD	急性 GVHD
ITA/[redacted]	6[redacted]/WH	11	1	aGvHD	急性 GVHD
ITA/[redacted]	4[redacted]/WH	338&	311	disease progression	疾患進行
ITA/[redacted]	5[redacted]/CA	21	13	aGvHD	急性 GVHD
ITA/[redacted]	6[redacted]/WH	199&	124	aGvHD	急性 GVHD
ITA/[redacted]	2[redacted]/WH	326&	298	disease progression	疾患進行
ITA/[redacted]	7[redacted]/CA	85	20	worsening of the clinical condition	状態悪化
ITA/[redacted]	6[redacted]/CA	14	1	Respiratory insufficiency	呼吸不全
ITA/[redacted]	3[redacted]/CA	430&	261	relapse of his acute lymphoblastic leukemia T	T 細胞型急性白血病
ITA/[redacted]	4[redacted]/CA	68&	33	AML progression	急性骨髄性白血病
ITA/[redacted]	5[redacted]/CA	100	2	cardiac arrest	心停止
ITA/[redacted]	3[redacted]/CA	50	6	virosys in definition	ウイルス感染
JPN/[redacted]	6[redacted]/AS	42	18	Acute renal dysfunction	腎機能障害
JPN/[redacted]	6[redacted]/AS	83	3	Sepsis	敗血症
JPN/[redacted]	6[redacted]/AS	79	8	aGvHD	急性 GVHD
JPN/[redacted]	5[redacted]/AS	48&	35	aGvHD	急性 GVHD
JPN/[redacted]	5[redacted]/AS	71	3	Due to Acute Myeloid leukemia.	急性骨髄性白血病
KOR/[redacted]	5[redacted]/AS	14	1	Cardiac arrest	心停止
RUS/[redacted]	3[redacted]/CA	38	6	sepsis	敗血症
SAU/[redacted]	4[redacted]/OTH	63&	32	aGvHD	急性 GVHD
TUR/[redacted]	2[redacted]/WH	47	6	septic shock	敗血症性ショック
TUR/[redacted]	6[redacted]/CA	137&	86	aGvHD	急性 GVHD
TUR/[redacted]	5[redacted]/CA	41	2	Sepsis	敗血症
TUR/[redacted]	2[redacted]/CA	182&	107	Multiorgan failure	多臓器機能不全症候群

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
TUR/[redacted]	5[redacted]/WH	102&	41	Glioblastoma multiforme	多形性神経膠芽細胞腫
BAT 群					
AUS/[redacted]	6[redacted]/CA	71	67	clostridium difficile pseudomembranous colitis	偽膜性大腸炎
AUS/[redacted]	7[redacted]/CA	308**	134	aGvHD	急性 GVHD
AUS/[redacted]	2[redacted]/CA	23*	3	Pneumonitis	肺臓炎
AUS/[redacted]	5[redacted]/WH	48**	33	Underlying disease: mantle cell lymphoma	マントル細胞リンパ腫
AUS/[redacted]	4[redacted]/CA	50*	9	aGvHD	急性 GVHD
AUS/[redacted]	6[redacted]/CA	23	7	aGvHD	急性 GVHD
AUS/[redacted]	4[redacted]/UN	225**	129	aGvHD	急性 GVHD
AUS/[redacted]	6[redacted]/WH	94&	66	Relapsed acute myeloid leukaemia	再発急性骨髄性白血病
AUS/[redacted]	5[redacted]/CA	15	15	aGvHD	急性 GVHD
AUS/[redacted]	3[redacted]/CA	15	5	aGvHD	急性 GVHD
CAN/[redacted]	5[redacted]/CA	8*	3	STROKE	脳血管発作
CAN/[redacted]	6[redacted]/CA	87	62	Event: respiratory failure Onset Date: [redacted] 20[redacted] Id: [redacted]	呼吸不全
CAN/[redacted]	6[redacted]/CA	21	5	aGvHD	急性 GVHD
CAN/[redacted]	6[redacted]/CA	22	8	aGvHD	急性 GVHD
CAN/[redacted]	5[redacted]/CA	61*	1	Respiratory failure	呼吸不全
CAN/[redacted]	2[redacted]/CA	21	15	aGvHD	急性 GVHD
CAN/[redacted]	6[redacted]/WH	202&	196	Chronic GVHD of the Liver	慢性肝移植片対宿主病
CAN/[redacted]	6[redacted]/CA	23*	12	unknown	死亡
CAN/[redacted]	6[redacted]/CA	27	21	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/CA	90	1	septic shock	敗血症性ショック
DEU/[redacted]	6[redacted]/CA	59*	25	aGvHD	急性 GVHD
DEU/[redacted]	6[redacted]/CA	8	1	Hypoximeia due to aspiration	誤嚥
DEU/[redacted]	5[redacted]/CA	38*	20	aGvHD	急性 GVHD
DEU/[redacted]	5[redacted]/CA	104&	83	Early recurrence of sAML	急性骨髄性白血病
DEU/[redacted]	7[redacted]/CA	134*	1	prolonged cardiopulmonary insufficiency	心肺不全
DEU/[redacted]	5[redacted]/CA	47	2	renal failure	腎不全
DEU/[redacted]	6[redacted]/CA	238**	32	Sepsis	敗血症
DEU/[redacted]	3[redacted]/CA	95&	50	septic shock	敗血症性ショック
DEU/[redacted]	2[redacted]/CA	27	13	uncontrolled infection due to several immunosuppresive	易感染性宿主の感染
ESP/[redacted]	6[redacted]/CA	120&	55	aGvHD	急性 GVHD
ESP/[redacted]	6[redacted]/CA	25	11	aGvHD	急性 GVHD
ESP/[redacted]	4[redacted]/CA	85*	6	pulmonary hemorrhage	肺出血
ESP/[redacted]	5[redacted]/CA	287&	243	underlying disease progression	疾患進行
ESP/[redacted]	4[redacted]/CA	390**	155	Acute respiratory distress syndrome	急性呼吸窮迫症候群
ESP/[redacted]	6[redacted]/CA	11	6	aGvHD	急性 GVHD
ESP/[redacted]	6[redacted]/CA	279&	190	aGvHD	急性 GVHD
ESP/[redacted]	2[redacted]/WH	624&	591	progression of the illness (AML)	急性骨髄性白血病

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
FRA/[redacted]	5[redacted]/UN	34	9	multi organ failure	多臓器機能不全症候群
FRA/[redacted]	3[redacted]/CA	276&	221	restrictive respiratory failure	呼吸不全
FRA/[redacted]	6[redacted]/CA	62	20	mesenteric ischemia	腸管虚血
FRA/[redacted]	4[redacted]/CA	196&	195	unknown	死亡
FRA/[redacted]	6[redacted]/UN	81&	61	acute leukemia relapse	白血病再発
FRA/[redacted]	6[redacted]/UN	49*	8	aGvHD	急性 GVHD
FRA/[redacted]	4[redacted]/UN	51*	12	SEPSIS	敗血症
FRA/[redacted]	5[redacted]/UN	7	7	aGvHD	急性 GVHD
FRA/[redacted]	7[redacted]/UN	47	12	multi-organs disorders	多臓器障害
FRA/[redacted]	5[redacted]/CA	76&	64	abscess of central nervous system	中枢神経系膿瘍
FRA/[redacted]	6[redacted]/CA	470**	444	Multi-organ failure	多臓器機能不全症候群
FRA/[redacted]	6[redacted]/WH	141	23	UNDERLYING DISEASE PROGRESSION	疾患進行
GBR/[redacted]	4[redacted]/CA	122*	11	aGvHD	急性 GVHD
GBR/[redacted]	6[redacted]/BL	16	1	aGvHD	急性 GVHD
ISR/[redacted]	2[redacted]/CA	12	6	aGvHD	急性 GVHD
ISR/[redacted]	4[redacted]/CA	24*	13	aGvHD	急性 GVHD
ISR/[redacted]	6[redacted]/CA	58	8	SEPSIS	敗血症
ISR/[redacted]	6[redacted]/CA	19	2	cerebral infarction	脳梗塞
ISR/[redacted]	6[redacted]/CA	62*	1	coma	昏睡
ITA/[redacted]	6[redacted]/CA	36	9	aGvHD	急性 GVHD
ITA/[redacted]	6[redacted]/CA	21	11	SEPTIC SHOCK	敗血症性ショック
ITA/[redacted]	6[redacted]/CA	108	31	aGvHD	急性 GVHD
ITA/[redacted]	7[redacted]/CA	43	30	aGvHD	急性 GVHD
ITA/[redacted]	4[redacted]/CA	84*	4	aGvHD	急性 GVHD
ITA/[redacted]	5[redacted]/CA	79*	16	aGvHD	急性 GVHD
ITA/[redacted]	6[redacted]/WH	107**	56	aGvHD	急性 GVHD
ITA/[redacted]	5[redacted]/CA	14	7	aGvHD	急性 GVHD
ITA/[redacted]	1[redacted]/WH	231**	214	aGvHD	急性 GVHD
JPN/[redacted]	4[redacted]/AS	303&	303	aGvHD	急性 GVHD
JPN/[redacted]	6[redacted]/AS	37	9	Acute lung injury	急性肺損傷
JPN/[redacted]	6[redacted]/AS	26	26	aGvHD	急性 GVHD
JPN/[redacted]	6[redacted]/AS	58	34	AML recurrence	再発急性骨髄性白血病
JPN/[redacted]	1[redacted]/AS	176&	121	Severe pneumonia	肺炎
JPN/[redacted]	5[redacted]/AS	136**	86	deterioration of general condition	全身健康状態悪化
JPN/[redacted]	6[redacted]/AS	31	4	aGvHD	急性 GVHD
JPN/[redacted]	5[redacted]/AS	115&	53	aGvHD	急性 GVHD
JPN/[redacted]	6[redacted]/AS	462&	436	Multiple organ failure	多臓器機能不全症候群
JPN/[redacted]	5[redacted]/AS	115&	100	sepsis	敗血症
JPN/[redacted]	6[redacted]/AS	23*	4	Idi0pathic pneumonia syndrome	特発性肺炎症候群
JPN/[redacted]	4[redacted]/AS	326**	319	Cytomegalovirus encephalitis	サイトメガロウイルス性脳炎
JPN/[redacted]	6[redacted]/AS	41*	11	respiratory failure	呼吸不全
JPN/[redacted]	5[redacted]/AS	47&	33	Acute respiratory failure	急性呼吸不全

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
JPN/[redacted]	6[redacted]/AS	56*	12	systemic adenovirus infection	アデノウイルス感染
NOR/[redacted]	3[redacted]/CA	157&	106	Residues of erythroleukemia	赤白血病
SAU/[redacted]	3[redacted]/CA	469&	329	aGvHD	急性 GVHD
SAU/[redacted]	5[redacted]/OTH	82	8	aGvHD	急性 GVHD
TUR/[redacted]	5[redacted]/OTH	26	4	aGvHD	急性 GVHD
TUR/[redacted]	3[redacted]/CA	26	1	aGvHD	急性 GVHD
TUR/[redacted]	2[redacted]/AS	124&	32	Disease relapse	疾患再発

Source: 5.3.5.1-1-C2301 試験 CSR2-Listing 14.3.2-1.1
M = 男性，F = 女性，AS = Asian，BL = Black or African American，CA = Caucasian，OTH = Other，UN = Unknown，WH = White
*：RUX へのクロスオーバー後の治験治療下の死亡。RUX 投与開始日からの日数を示す。
**：RUX へのクロスオーバー後の治験治療下よりも後の死亡。BAT 投与開始日からの日数を示す。
&：治験治療下よりも後の死亡
MedDRA version 22.1

Table 7-4　急性 GVHD の重篤な有害事象（いずれかの群で発現率 2%以上）（C2301 試験，SAF，データカットオフ 2 まで）

PT	RUX N = 152 n (%)	BAT N = 150 n (%)	RUX crossover N = 49 n (%)
曝露期間（日）：中央値（最小値 - 最大値）	63.0 (6.0-463.0)	61.0 (2.0-383.0)	29.0 (1.0-188.0)
総曝露期間（人年）	39.5	12.3	19.0
合計	101 (66.4)	80 (53.3)	38 (77.6)
敗血症	12 (7.9)	11 (7.3)	7 (14.3)
発熱	10 (6.6)	6 (4.0)	0
敗血症性ショック	10 (6.6)	8 (5.3)	3 (6.1)
下痢	8 (5.3)	3 (2.0)	0
肺炎	7 (4.6)	8 (5.3)	2 (4.1)
サイトメガロウイルス感染	6 (3.9)	8 (5.3)	3 (6.1)
呼吸不全	6 (3.9)	6 (4.0)	6 (12.2)
急性腎障害	3 (2.0)	5 (3.3)	2 (4.1)
血中ビリルビン増加	3 (2.0)	0	0
サイトメガロウイルス性大腸炎	3 (2.0)	0	0
発熱性好中球減少症	3 (2.0)	2 (1.3)	0
好中球減少症	3 (2.0)	3 (2.0)	0
汎血球減少症	3 (2.0)	0	1 (2.0)
シュードモナス性敗血症	3 (2.0)	0	0
呼吸窮迫	3 (2.0)	0	2 (4.1)
胃腸出血	2 (1.3)	1 (0.7)	2 (4.1)
血小板減少症	2 (1.3)	0	2 (4.1)
低カリウム血症	2 (1.3)	1 (0.7)	1 (2.0)
肺塞栓症	2 (1.3)	1 (0.7)	1 (2.0)
心不全	2 (1.3)	0	1 (2.0)
肺障害	2 (1.3)	0	1 (2.0)
多臓器機能不全症候群	2 (1.3)	3 (2.0)	0

PT	RUX N = 152 n (%)	BAT N = 150 n (%)	RUX crossover N = 49 n (%)
腎不全	2 (1.3)	3 (2.0)	0
イレウス	1 (0.7)	1 (0.7)	2 (4.1)
好中球数減少	1 (0.7)	1 (0.7)	1 (2.0)
菌血症	1 (0.7)	4 (2.7)	1 (2.0)
錯乱状態	1 (0.7)	3 (2.0)	1 (2.0)
医療機器関連感染	1 (0.7)	1 (0.7)	1 (2.0)
白血球数減少	1 (0.7)	1 (0.7)	1 (2.0)
昏睡	1 (0.7)	0	1 (2.0)
脳症	1 (0.7)	0	1 (2.0)
失神	1 (0.7)	0	1 (2.0)
特発性肺炎症候群	1 (0.7)	0	1 (2.0)
急性心筋梗塞	1 (0.7)	0	1 (2.0)
腸閉塞	1 (0.7)	0	1 (2.0)
状態悪化	1 (0.7)	0	1 (2.0)
転倒	1 (0.7)	0	1 (2.0)
腹痛	1 (0.7)	3 (2.0)	0
肺臓炎	0	0	2 (4.1)
血小板数減少	0	3 (2.0)	1 (2.0)
移植片対宿主病	0	3 (2.0)	1 (2.0)
意識レベルの低下	0	1 (0.7)	1 (2.0)
シュードモナス性菌血症	0	1 (0.7)	1 (2.0)
可逆性後白質脳症症候群	0	1 (0.7)	1 (2.0)
低血圧	0	1 (0.7)	1 (2.0)
肝機能異常	0	0	1 (2.0)
アデノウイルス感染	0	0	1 (2.0)
感染性腸炎	0	0	1 (2.0)
皮下血腫	0	0	1 (2.0)
大腸炎	0	0	1 (2.0)
急性膵炎	0	0	1 (2.0)
肝炎	0	0	1 (2.0)
アスペルギルス感染	0	0	1 (2.0)
カンピロバクター感染	0	0	1 (2.0)
クロストリジウム性敗血症	0	0	1 (2.0)
脳炎	0	0	1 (2.0)
腸球菌性菌血症	0	0	1 (2.0)
帯状疱疹	0	0	1 (2.0)
クレブシエラ性敗血症	0	0	1 (2.0)
真菌性下気道感染	0	0	1 (2.0)
腸球菌性髄膜炎	0	0	1 (2.0)
腹膜炎	0	0	1 (2.0)
レンサ球菌性肺炎	0	0	1 (2.0)

PT	RUX N = 152 n (%)	BAT N = 150 n (%)	RUX crossover N = 49 n (%)
股関節部骨折	0	0	1 (2.0)
肋骨骨折	0	0	1 (2.0)
サイトメガロウイルス検査陽性	0	0	1 (2.0)
トランスアミナーゼ上昇	0	0	1 (2.0)
骨痛	0	0	1 (2.0)
骨粗鬆症性骨折	0	0	1 (2.0)
中枢神経系リンパ腫	0	0	1 (2.0)
脳血管発作	0	0	1 (2.0)
舞踏病	0	0	1 (2.0)
痙攣発作	0	0	1 (2.0)
昏迷	0	0	1 (2.0)
低酸素症	0	0	1 (2.0)
肺出血	0	0	1 (2.0)
急性呼吸不全	0	3 (2.0)	0

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.1，Table 14.3-1.5，Table 14.3.1-1.13，Table 14.3.1-1.27
RUX 群の発現率の降順
総曝露期間 = 全被験者の曝露期間の合計
MedDRA version 22.1

Table 7-5　　急性 GVHD の重篤な有害事象の一覧（C2301 試験，SAF，データカットオフ 2 まで）

Listing 14.3.2-2.1 Serious adverse events (Safety set)

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 1 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/	2[redacted]	Yes/3	Bilirubin increased/	[redacted]	[redacted]	17	3	NO	999,1	2
[redacted]	CA		Blood bilirubin increased (血中ビリルビン増加)/	183	199				0	
			Investigations (臨床検査)							
		Yes/3	Deranged liver function tests/	[redacted]	[redacted]	17	4	NO	999,1	2
			Liver function test abnormal (肝機能検査異常)/	183	199				0	
			Investigations (臨床検査)							
AUS/	4[redacted]	Yes/	Gram Negative Sepsis/	[redacted]	[redacted]	8	4	YES, BOTH	5,10	2
[redacted]	CA	2,3,6	Bacterial sepsis (細菌性敗血症)/	37	44			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	Febrile Neutropenia/	[redacted]	[redacted]	2	3	YES, BOTH	5,10	2
			Febrile neutropenia (発熱性好中球減少症)/	36	37			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 2 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Blood and lymphatic system disorders					INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		
AUS/	5[redacted]	Yes/3	Acute Kidney Injury/	[redacted]	[redacted]	3	3	YES, OTHER	2,10	2
[redacted]	CA		Acute kidney injury (急性腎障害)/	80	82			STUDY		
			Renal and urinary disorders (腎および尿路障害)					TREATMENT		
								(NON-		
								INVESTIGATI		
								ONAL)		
		Yes/3	Generalised Muscle Pain/	[redacted]	[redacted]	5	3	NO	4,10	3
			Myalgia (筋肉痛)/	277	281					
			Musculoskeletal and connective tissue disorders							
			(筋骨格系および結合組織障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 3 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	5[redacted] CA	Yes/3	Parainfluenza/ Parainfluenzae virus infection (パラインフルエンザウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 22	[redacted] 25	4	2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2
		Yes/3	Febrile/ Pyrexia (発熱)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 22	[redacted] 23	2	2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2
		Yes/3	Respiratory Infection/	[redacted]	[redacted]	7	3	YES, OTHER	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 4 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory tract infection (気道感染)/ Infections and infestations (感染症および寄生虫症)	116	122			STUDY TREATMENT (NON-INVESTIGATIONAL)		
		Yes/6	Thrombocytopenia/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted]	[redacted]	4	4	YES, INVESTIGATIONAL TREATMENT	3	2
		Yes/3	Urinary Tract Infection/ Urinary tract infection (尿路感染)/ Infections and infestations (感染症および寄生虫症)	[redacted]	[redacted]	5	2	YES, OTHER STUDY TREATMENT (NON-	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 5 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 6 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	1[redacted] CA	Yes/3	enterobacter cloacae sepsis/ Enterobacter sepsis (エンテロバクター性敗血症) / Infections and infestations (感染症および寄生虫症)	[redacted] 14	Ongoing		3	NO	2,10	1
		Yes/2	Microangiopathy/ Microangiopathy (微小血管症)/ Vascular disorders (血管障害)	[redacted] 18	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	5,10	1
AUS/	6[redacted]	Yes/3	Non ST elevated myocardial infarction/	[redacted]	[redacted]	4	3	NO	4	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 7 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	WH		Acute myocardial infarction (急性心筋梗塞)/	41	44					
			Cardiac disorders (心臓障害)							
		Yes/2	Non ST elevated myocardial infarction/	[redacted]	[redacted]	3	4	NO	4,10	2
			Acute myocardial infarction (急性心筋梗塞)/	59	61					
			Cardiac disorders (心臓障害)							
		Yes/2	sepsis/	[redacted]	[redacted]	19	4	NO	2,10	2
			Sepsis (敗血症)/	5	23					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	sepsis/	[redacted]	[redacted]	1	5	NO	999	5
			Sepsis (敗血症)/	78	78					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 8 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	6[redacted] WH	Yes/2,3	septic shock/	[redacted]	[redacted]	3	4	NO	2	2
			Septic shock (敗血症性ショック)/	69	71					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	small bowel obstruction/	[redacted]	Ongoing		3	NO	2	1
			Small intestinal obstruction (小腸閉塞)/	41						
			Gastrointestinal disorders (胃腸障害)							
AUS/ [redacted]	3[redacted] AS	Yes/3	Diarrhoea/	[redacted]	[redacted]	29	3	NO	2	2
			Diarrhoea (下痢)/	23	51					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3,6	Hypokalemia/	[redacted]	[redacted]	14	4	NO	2,10	2
			Hypokalaemia (低カリウム血症)/	16	29					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 9 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Metabolism and nutrition disorders							
			(代謝および栄養障害)							
AUS/	4[redacted]	Yes/2	Sepsis/	[redacted]	[redacted]	2	4	YES, BOTH	2,10	1
[redacted]	OTH		Sepsis (敗血症)/	16	17			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	YES, BOTH	2,10	5
			Sepsis (敗血症)/	18	18			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 10 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	3[redacted] WH	Yes/3	Mucormycosis sinus infection/ Mucormycosis (ムコール症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 16	[redacted] 37	22	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	3
		Yes/3	Mucormycosis sinus infection/ Mucormycosis (ムコール症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 48	[redacted] 65	18	3	YES, BOTH AND/OR INDISTINGUISHABLE	5,10	4
AUT/ [redacted]	6[redacted] CA	Yes/3	Influenca Test B positive/ Influenza B virus test positive	[redacted] 114	[redacted] 125	12	2	NO	3,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 11 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(B型インフルエンザウイルス検査陽性)/							
			Investigations (臨床検査)							
		Yes/3	Fever/	[redacted]	[redacted]	16	1	NO	2,10	2
			Pyrexia (発熱)/	42	57					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
CAN/ [redacted]	6[redacted] CA	Yes/3	Lung Infection: RSV Pneumonia/	[redacted]	[redacted]	27	3	NO	999,10	2
			Pneumonia respiratory syncytial viral	62	88					
			(RSウイルス肺炎)/							
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 12 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	3[redacted] CA	Yes/3	HSV SKIN INFECTION/ Herpes simplex (単純ヘルペス)/ Infections and infestations (感染症および寄生虫症)	[redacted] 4	[redacted] 29	26	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	3
DEU/ [redacted]	7[redacted] CA	Yes/2	Stenosis of terminal ileum/ Ileal stenosis (回腸狭窄)/ Gastrointestinal disorders (胃腸障害)	[redacted] 6	Ongoing		4	NO	2,10	1
DEU/ [redacted]	6[redacted] CA	Yes/6	Viral infection Reactivation/ Viral infection (ウイルス感染)/	[redacted] 28	[redacted] 70&	43	3	YES, INVESTIGATI	5,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 13 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		
DEU/	6[redacted]	Yes/2,6	Bleeding of basal ganglia/	[redacted]	[redacted]	10	3	YES,	999,1	2
[redacted]	CA		Basal ganglia haemorrhage (大脳基底核出血)/	32	41			INVESTIGATI	0	
			Nervous system disorders (神経系障害)					ONAL		
								TREATMENT		
DEU/	6[redacted]	Yes/1	Multi organ-System failure/	[redacted]	[redacted]	1	5	NO	2	5
[redacted]	CA		Multiple organ dysfunction syndrome	57	57					
			(多臓器機能不全症候群)/							
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 14 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	adenoviral infection of bladder/ Cystitis viral (ウイルス性膀胱炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 29	[redacted] 86&	58	3	YES, INVESTIGATIONAL TREATMENT	5,10	2
DEU/ [redacted]	6[redacted] WH	Yes/2,3	Hemorrhage GI/ Gastrointestinal haemorrhage (胃腸出血)/ Gastrointestinal disorders (胃腸障害)	[redacted] 5	[redacted] 9	5	4	NO	2,10	2
		Yes/2,3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 13	[redacted] 16	4	4	NO	999,10	1
		Yes/1	Pneumonia/	[redacted]	[redacted]	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 15 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	17	17					
DEU/ [redacted]	6[redacted] CA	Yes/3	haemolysis/ Haemolysis (溶血)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 5	Ongoing		4	NO	2	1
DEU/ [redacted]	2[redacted] CA	Yes/2	respiratory insufficiency/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 8	[redacted] 13	6	4	YES, OTHER STUDY TREATMENT (NON-	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 16 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 17 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/3	Acute kidney injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 9	Ongoing		4	NO	2,10	1
		Yes/2	Respiratory insufficiency/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 11	Ongoing		4	NO	999,10	1
DEU/ [redacted]	6[redacted] CA	Yes/3	Sepsis due to infection right forearm/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 22	[redacted] 72&	51	3	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 18 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/6	CMV Colitis/ Cytomegalovirus colitis (サイトメガロウイルス性大腸炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 133	Ongoing		3	YES, BOTH AND/OR INDISTINGUISHABLE	5,10	1
		Yes/6	small intestinal ileus/ Ileus (イレウス)/ Gastrointestinal disorders (胃腸障害)	[redacted] 58	[redacted] 59	2	4	NO	4,10	2
		Yes/3	nausea/ Nausea (悪心)/ Gastrointestinal disorders (胃腸障害)	[redacted] 101	[redacted] 105	5	3	NO	2,10	3
		Yes/3	Fever/ Pyrexia (発熱)/	[redacted] 116	[redacted] 118	3	1	YES, BOTH AND/OR	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 19 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			General disorders and administration site conditions					INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 20 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/2	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 58	[redacted] 69	12	4	NO	4,10	2
		Yes/2	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 134	[redacted] 135	2	4	YES, BOTH AND/OR INDISTINGUISHABLE	5,10	1
		Yes/1	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 135	[redacted] 135	1	5	YES, BOTH AND/OR INDISTINGUISHABLE	5,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 21 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/2	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 22	[redacted] 38	17	4	YES, INVESTIGATIONAL TREATMENT	4,10	1
		Yes/1	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 39	[redacted] 39	1	5	YES, INVESTIGATIONAL TREATMENT	5,10	5
DEU/ [redacted]	4[redacted] CA	Yes/3	CMV Colitis/ Cytomegalovirus colitis (サイトメガロウイルス性大腸炎)/ Infections and infestations	[redacted] 86	[redacted] 174&	89	3	YES, OTHER STUDY TREATMENT (NON-	5,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 22 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)					INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 23 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	4[redacted] CA	Yes/3	diarrhea/ Diarrhoea (下痢)/ Gastrointestinal disorders (胃腸障害)	[redacted] 86	[redacted] 101	16	3	NO	2	2
		Yes/3	infection probably due to CMV colitis and GvHD/ Infection (感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 119	[redacted] 124	6	2	NO	999,10	2
		Yes/2,3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 151&	[redacted] 167&	17	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 24 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	Fever/ Pyrexia (発熱)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 61	[redacted] 72	12	1	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	2
DEU/ [redacted]	2[redacted] CA	Yes/3	Enteritis/ Enteritis (小腸炎)/ Gastrointestinal disorders (胃腸障害)	[redacted] 15	[redacted] 26	12	3	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	2
		Yes/2,3	Pneumonia/ Pneumonia (肺炎)/	[redacted] 60	[redacted] 64	5	4	YES, BOTH AND/OR	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 25 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 26 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/2	Sepsis/	[redacted]	[redacted]	1	4	NO	999,10	1
			Sepsis (敗血症)/	76	76					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	NO	999,10	5
			Sepsis (敗血症)/	77	77					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	Transplant associated thrombotic microangiopathy/	[redacted]	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATI	999,10	1
			Thrombotic microangiopathy (血栓性微小血管症)/	64						
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 27 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								ONAL)		
DEU/ [redacted]	6[redacted] CA	Yes/2	Atrial flutter/ Atrial flutter (心房粗動)/ Cardiac disorders (心臓障害)	[redacted] 44	[redacted] 46	3	4	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	2
		Yes/1	multiple organ failure/ Multiple organ dysfunction syndrome (多臓器機能不全症候群)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 51	[redacted] 51	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 28 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	Encephalopathy/	[redacted]	Ongoing		4	YES, BOTH	5,10	1
			Encephalopathy (脳症)/	36				AND/OR		
			Nervous system disorders (神経系障害)					INDISTINGUISHABLE		
		Yes/2	Septic shock with multiorgan Dysfunktion syndrome/	[redacted]	[redacted]	5	4	YES, BOTH	999,10	1
			Septic shock (敗血症性ショック)/	49	53			AND/OR		
			Infections and infestations					INDISTINGUISHABLE		
			(感染症および寄生虫症)							
		Yes/1	Septic shock with multiorgan dysfunction syndrome/	[redacted]	[redacted]	1	5	YES, BOTH	999,10	5
			Septic shock (敗血症性ショック)/	54	54			AND/OR		
			Infections and infestations					INDISTINGUISHABLE		
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 29 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	4[redacted] CA	Yes/3	CMV reactivation/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 28	[redacted] 36	9	3	NO	2,10	2
		Yes/3	Syncope/ Syncope (失神)/ Nervous system disorders (神経系障害)	[redacted] 7	[redacted] 7	1	2	NO	2	2
DEU/ [redacted]	5[redacted] CA	Yes/2,3	Acute renal failure/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 91	[redacted] 107	17	3	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 30 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	acute renal failure/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 156	[redacted] 163	8	3	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2
DEU/ [redacted]	5[redacted] CA	Yes/3	Progression of aGvHD/ Acute graft versus host disease (急性移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 10	[redacted] 149&	140	3	NO	2,10	2
DEU/ [redacted]	6[redacted] CA	Yes/3	CMV-Reactivation with Collitis/ Cytomegalovirus colitis (サイトメガロウイルス性大腸炎)/	[redacted] 15	[redacted] 70&	56	3	YES, BOTH AND/OR INDISTINGUI	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 31 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations					SHABLE		
			(感染症および寄生虫症)							
		Yes/3	Diarrhea/	[redacted]	[redacted]	4	3	NO	2,10	2
			Diarrhoea (下痢)/	15	18					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	Staphyloccoccus septicemia/	[redacted]	[redacted]	63	1	NO	2,10	2
			Staphylococcal sepsis (ブドウ球菌性敗血症)/	16	78&					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 32 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/3	confusion/ Confusional state (錯乱状態)/ Psychiatric disorders (精神障害)	[redacted] 25	[redacted] 36	12	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2	3
		Yes/3	Depression/ Depression (うつ病)/ Psychiatric disorders (精神障害)	[redacted] 25	[redacted] 36	12	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	3
		Yes/2	worsening of lower gastrointestinal hemorrhage/	[redacted]	[redacted]	2	4	YES,	5,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 33 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Lower gastrointestinal haemorrhage (下部消化管出血)	51	52			INVESTIGATI		
			/					ONAL		
			Gastrointestinal disorders (胃腸障害)					TREATMENT		
DEU/	1[redacted]	Yes/3	Bronchitis/	[redacted]	[redacted]	3	3	NO	999,1	2
[redacted]	CA		Bronchitis (気管支炎)/	63	65				0	
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	cough/	[redacted]	[redacted]	3	3	NO	999,1	2
			Cough (咳嗽)/	63	65				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 34 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	1[redacted] CA	Yes/3	Thrombocytopenia/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 32	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	4,10	1
DNK/ [redacted]	6[redacted] WH	Yes/6	pulmonary embolism/ Pulmonary embolism (肺塞栓症)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 9	Ongoing		3	YES, BOTH AND/OR INDISTINGUISHABLE	5,10	1
ESP/ [redacted]	2[redacted] WH	Yes/1	WORSENING OF GENERAL STATUS DUE TO PROGRESSION DISEASE/ General physical health deterioration (全身健康状態悪化)/	[redacted] 153&	[redacted] 153&	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 35 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/1	PROGRESSION DISEASE (GvHD)/	[redacted]	[redacted]	1	5	NO	999	5
			Graft versus host disease (移植片対宿主病)/	153&	153&					
			Immune system disorders (免疫系障害)							
ESP/	3[redacted]	Yes/3	fever/	[redacted]	[redacted]	12	3	NO	2,10	2
[redacted]	CA		Pyrexia (発熱)/	56	67					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
ESP/	5[redacted]	Yes/3	acute renal failure/	[redacted]	Ongoing		4	NO	999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 36 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	60&					0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 37 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ESP/	5[redacted]	Yes/2,3	ASPERGILOSIS PULMONARY/	[redacted]	[redacted]	47	4	NO		999,1	1
[redacted]	CA		Bronchopulmonary aspergillosis	31	77&					0	
			(気管支肺アスペルギルス症)/								
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/	ASPERGILOSIS PULMONARY/	[redacted]	[redacted]	1	5	NO		999	5
		1,2,3	Bronchopulmonary aspergillosis	78&	78&						
			(気管支肺アスペルギルス症)/								
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	ASPERGILOSIS CEREBRAL/	[redacted]	[redacted]	47	4	NO		999,1	1
			Cerebral aspergillosis (脳アスペルギルス症)/	31	77&					0	
			Infections and infestations								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 38 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
		Yes/	ASPERGILOSIS CEREBRAL/	[redacted]	[redacted]	1	5	NO	999	5
		1,2,3	Cerebral aspergillosis (脳アスペルギルス症)/	78&	78&					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/2,3	SEPTIC SHOCK OF ABDOMINAL FOCUS/	[redacted]	[redacted]	5	4	NO	999,10	2
			Septic shock (敗血症性ショック)/	38	42					
			Infections and infestations							
			(感染症および寄生虫症)							
ESP/ [redacted]	5[redacted] CA	Yes/2,3	respiratory infection by neumococo/	[redacted]	[redacted]	5	3	NO	4,10	1
			Respiratory tract infection bacterial	14	18					
			(細菌性気道感染)/							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 39 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 40 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/ [redacted]	5[redacted] CA	Yes/1,3	respiratory infection by neumococo/ Respiratory tract infection bacterial (細菌性気道感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 19	[redacted] 19	1	5	NO	5,10	5
		Yes/1	septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 19	[redacted] 19	1	5	NO	999	5
ESP/ [redacted]	4[redacted] WH	Yes/3	RESPIRATORY INFECCTION (CO-INFECTION PARA INFLUENZA TYP 3 AND ADENOVIRUS)/ Respiratory tract infection viral	[redacted] 74	[redacted] 84	11	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 41 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(ウイルス性気道感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							
ESP/	2[redacted]	Yes/3	Bacteraemia/	[redacted]	[redacted]	43	3	NO	2,10	2
[redacted]	CA		Bacteraemia (菌血症)/	62	104					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	VIRUS INFLUENZA B/	[redacted]	[redacted]	43	3	NO	2,10	2
			Influenza (インフルエンザ)/	62	104					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 42 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/ [redacted]	2[redacted] CA	Yes/3	PNEUMOCOCCI Pneumonia/ Pneumonia pneumococcal (肺炎球菌性肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 34	[redacted] 47	14	4	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2
ESP/ [redacted]	5[redacted] CA	Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 22	[redacted] 46	25	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	4,10	2
		Yes/3	Pneumonia/ Pneumonia (肺炎)/	[redacted] 79	[redacted] 98	20	2	YES, OTHER STUDY	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 43 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)					TREATMENT (NON-INVESTIGATIONAL)		
ESP/ [redacted]	5[redacted] CA	Yes/1	Septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 12	[redacted] 12	1	5	NO	2,10	5
ESP/ [redacted]	5[redacted] UN	Yes/6	Intestinal obstruction/ Intestinal obstruction (腸閉塞)/ Gastrointestinal disorders (胃腸障害)	[redacted] 21	[redacted] 22	2	3	NO	5,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 44 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/ [redacted]	5[redacted] CA	Yes/6	acute ischemic stroke/	[redacted]	[redacted]	2	4	NO	2,10	4
			Ischaemic stroke (虚血性脳卒中)/	55	56					
			Nervous system disorders (神経系障害)							
		Yes/2,3	SEPTIC SHOCK/	[redacted]	[redacted]	8	4	YES, BOTH	4,10	1
			Septic shock (敗血症性ショック)/	99	106			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/	SEPTIC SHOCK/	[redacted]	[redacted]	1	5	YES, BOTH	4	5
		1,2,3	Septic shock (敗血症性ショック)/	107	107			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
ESP/	6[redacted]	Yes/2	Respiratory deterioration/	[redacted]	[redacted]	1	4	NO	999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 45 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	UN		Respiratory disorder (呼吸障害)/	14	14				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/1	Respiratory deterioration/	[redacted]	[redacted]	1	5	NO	999,1	5
			Respiratory disorder (呼吸障害)/	15	15				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
FRA/	6[redacted]	Yes/1	alteration of general state/	[redacted]	[redacted]	1	5	NO	999	5
[redacted]	UN		General physical condition abnormal	32	32					
			(全身健康状態異常)/							
			Investigations (臨床検査)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 46 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/	6[redacted]	Yes/2	severe sepsis/	[redacted]	[redacted]	2	4	NO	999	2
[redacted]	UN		Sepsis (敗血症)/	30	31					
			Infections and infestations							
			(感染症および寄生虫症)							
FRA/	2[redacted]	Yes/3	suspicion of upper gastrointestinal GVHD/	[redacted]	[redacted]	13	3	NO	1	2
[redacted]	UN		Graft versus host disease in gastrointestinal tract	90	102					
			(消化管移植片対宿主病)/							
			Immune system disorders (免疫系障害)							
		Yes/6	neutropenia/	[redacted]	[redacted]	15	4	YES,	4	2
			Neutropenia (好中球減少症)/	76	90			INVESTIGATI		
			Blood and lymphatic system disorders					ONAL		
			(血液およびリンパ系障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 47 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	BACTERIAL PNEUMONIA/	[redacted]	[redacted]	9	3	NO	2,10	2
			Pneumonia bacterial (細菌性肺炎)/	118	126					
			Infections and infestations							
			(感染症および寄生虫症)							
FRA/ [redacted]	5[redacted] OTH	Yes/3,6	catheter related infection/	[redacted]	[redacted]	4	4	NO	999,10	2
			Device related infection (医療機器関連感染)/	30	33					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/6	Neutrophil count decreased/	[redacted]	[redacted]	3	4	YES,	4,10	3
			Neutrophil count decreased (好中球数減少)/	9	11			INVESTIGATIONAL TREATMENT		
			Investigations (臨床検査)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 48 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	5[redacted] OTH	Yes/6	Neutrophil count decreased/ Neutrophil count decreased (好中球数減少)/ Investigations (臨床検査)	[redacted] 14	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	5,10	1
		Yes/6	pancytopenia/ Pancytopenia (汎血球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 9	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	4,10	1
FRA/ [redacted]	6[redacted] CA	Yes/3	thromboembolic event/ Embolism (塞栓症)/ Vascular disorders (血管障害)	[redacted] 93	[redacted] 93	1	3	NO	5,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 49 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	3[redacted] UN	Yes/2,6	Sepsis by mucormycose/ Fungal sepsis (真菌性敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 44	Ongoing		4	NO	999,10	1
		Yes/2,6	HHV6 infection/ Human herpesvirus 6 infection (ヒトヘルペスウイルス６感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 37	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999,10	1
		Yes/2,6	microangiopathy/ Microangiopathy (微小血管症)/ Vascular disorders (血管障害)	[redacted] 24	[redacted] 45	22	3	NO	999	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 50 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	3[redacted] UN	Yes/3	mucor mycosis/ Mucormycosis (ムコール症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 44	Ongoing		2	NO	999,10	1
		Yes/3	pneumopathy klebsielle/ Pneumonia klebsiella (クレブシエラ菌性肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 21	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	5,10	1
		Yes/3	Sepsis at pseudomonas/ Pseudomonal sepsis (シュードモナス性敗血症)/ Infections and infestations	[redacted] 21	[redacted] 55&	35	3	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 51 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)								
		Yes/1	sepsis at pseudomonas/	[redacted]	[redacted]	1	5	NO		999	5
			Pseudomonal sepsis (シュードモナス性敗血症)/	56&	56&						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/2,6	pulmonary embolism/	[redacted]	Ongoing		3	NO		999	1
			Pulmonary embolism (肺塞栓症)/	26							
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
FRA/ [redacted]	6[redacted] CA	Yes/1,3	General condition alteration/	[redacted]	[redacted]	1	5	NO		5	5
			General physical condition abnormal	20	20						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 52 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(全身健康状態異常)/ Investigations (臨床検査)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 53 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/	6[redacted]	Yes/2	sepsis (pseudomonas aeruginosa)/	[redacted]	[redacted]	3	4	YES, BOTH	997,1	1
[redacted]	CA		Pseudomonal sepsis (シュードモナス性敗血症)/	17	19			AND/OR	0	
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/1	sepsis (pseudomonas aeruginosa)/	[redacted]	[redacted]	1	5	YES, BOTH	2	5
			Pseudomonal sepsis (シュードモナス性敗血症)/	20	20			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	respiratory distress/	[redacted]	Ongoing		4	NO	2,10	1
			Respiratory distress (呼吸窮迫)/	19						
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 54 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] CA	Yes/2	accute respiratory distress syndroma/ Acute respiratory distress syndrome (急性呼吸窮迫症候群)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 27	Ongoing		3	NO		997,10	1
		Yes/2	cardiac failure/ Cardiac failure (心不全)/ Cardiac disorders (心臓障害)	[redacted] 27	Ongoing		3	NO		997,10	1
		Yes/2	CMV infection/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 26	Ongoing		4	NO		997,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 55 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] CA	Yes/2	E.coli infection/ Escherichia infection (大腸菌感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 28	Ongoing		3	NO	997,10	1
		Yes/3	sepsis at e.coli/ Escherichia sepsis (大腸菌性敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 26	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	997,10	1
		Yes/3	flu/ Influenza (インフルエンザ)/ Infections and infestations	[redacted] 27	Ongoing		4	YES, OTHER STUDY TREATMENT	997,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 56 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		
		Yes/2	pancytopenia/	[redacted]	Ongoing		4	NO	997	1
			Pancytopenia (汎血球減少症)/	27						
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/2	petechia/	[redacted]	Ongoing		3	NO	997,10	1
			Petechiae (点状出血)/	27						
			Skin and subcutaneous tissue disorders							
			(皮膚および皮下組織障害)							
		Yes/1	sepsis/	[redacted]	[redacted]	1	5	NO	2	5
			Sepsis (敗血症)/	28	28					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 57 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 58 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/ [redacted]	3[redacted] CA	Yes/2	cardiac insufficiency/	[redacted]	Ongoing		4	NO		999	1
			Cardiac failure (心不全)/	43							
			Cardiac disorders (心臓障害)								
		Yes/2,3	coma/	[redacted]	Ongoing		4	NO		999,1	1
			Coma (昏睡)/	43						0	
			Nervous system disorders (神経系障害)								
		Yes/2	disseminated intravascular coagulation syndrome/	[redacted]	Ongoing		3	NO		999,1	1
			Disseminated intravascular coagulation	43						0	
			(播種性血管内凝固)/								
			Blood and lymphatic system disorders								
			(血液およびリンパ系障害)								
		Yes/3	cephalgia/	[redacted]	Ongoing		2	NO		5	1
			Headache (頭痛)/	41							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 59 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Nervous system disorders (神経系障害)							
		Yes/2	hepatic insufficiency/	[redacted]	Ongoing		4	NO	999	1
			Hepatic failure (肝不全)/	43						
			Hepatobiliary disorders (肝胆道系障害)							
		Yes/2	neutropenia/	[redacted]	Ongoing		4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2	1
			Neutropenia (好中球減少症)/	40						
			Blood and lymphatic system disorders (血液およびリンパ系障害)							
		Yes/2,3	sepsis (pseudomonas aeruginosa)/	[redacted]	[redacted]	1	4	NO	999,10	1
			Pseudomonal sepsis (シュードモナス性敗血症)/	43	43					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 60 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 61 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/	3[redacted]	Yes/1	sepsis (pseudomonas aeruginosa)/	[redacted]	[redacted]	1	5	NO	999	5
[redacted]	CA		Pseudomonal sepsis (シュードモナス性敗血症)/	44	44					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/2	renal insufficiency/	[redacted]	Ongoing		3	NO	999	1
			Renal failure (腎不全)/	43						
			Renal and urinary disorders (腎および尿路障害)							
		Yes/2	Acute respiratory distress/	[redacted]	Ongoing		4	NO	999	1
			Respiratory distress (呼吸窮迫)/	43						
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
FRA/	6[redacted]	Yes/3	Pneumopathy/	[redacted]	Ongoing		3	NO	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 62 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	UN		Lung disorder (肺障害)/	82						
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/1	pneumopathy/	[redacted]	[redacted]	1	5	NO	999	5
			Lung disorder (肺障害)/	89	89					
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
FRA/	2[redacted]	Yes/3	CMV infection/	[redacted]	[redacted]	53	3	NO	2,10	2
[redacted]	OTH		Cytomegalovirus infection	34	86					
			(サイトメガロウイルス感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 63 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	5[redacted] UN	Yes/3	fever/ Pyrexia (発熱)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 46	[redacted] 49	4	3	NO	2	2
FRA/ [redacted]	6[redacted] OTH	Yes/3	Bronchopulmonary Aspergillosis/ Bronchopulmonary aspergillosis (気管支肺アスペルギルス症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 20	[redacted] 104&	85	3	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	2
		Yes/3	Multiple fractures/ Multiple fractures (多発骨折)/ Injury, poisoning and procedural complications	[redacted] 20	[redacted] 41	22	3	YES, OTHER STUDY TREATMENT	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 64 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(傷害、中毒および処置合併症)					(NON-INVESTIGATIONAL)		
		Yes/2	LUNG INFECTION/	[redacted]	[redacted]	28	4	YES, BOTH	999,1	2
			Pneumonia (肺炎)/	77	104&			AND/OR	0	
			Infections and infestations					INDISTINGUISHABLE		
			(感染症および寄生虫症)							
		Yes/2,3	Sepsis/	[redacted]	[redacted]	12	4	NO	999,1	1
			Sepsis (敗血症)/	236&	247&				0	
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	NO	999,1	5
			Sepsis (敗血症)/	248&	248&				0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 65 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 66 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	2[redacted] OTH	Yes/6	Graft loss/ Graft loss (移植片機能損失)/ Injury, poisoning and procedural complications (傷害、中毒および処置合併症)	[redacted] 74	Ongoing		2	YES, INVESTIGATIONAL TREATMENT	5	1
		Yes/3	Lung condensation/ Lung disorder (肺障害)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 113	Ongoing		3	NO	999,10	1
FRA/ [redacted]	1[redacted] CA	Yes/6	neutropenia/ Neutropenia (好中球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 71	[redacted] 78	8	3	YES, INVESTIGATIONAL TREATMENT	2	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 67 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/6	neutropenia/	[redacted]	[redacted]	3	4	YES,	2	3
			Neutropenia (好中球減少症)/	78	80			INVESTIGATIONAL TREATMENT		
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/6	neutropenia/	[redacted]	[redacted]	20	3	YES,	2	2
			Neutropenia (好中球減少症)/	80	99			INVESTIGATIONAL TREATMENT		
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/6	White blood cells decrease/	[redacted]	[redacted]	8	3	YES,	2	2
			White blood cell count decreased (白血球数減少)/	71	78			INVESTIGATIONAL TREATMENT		
			Investigations (臨床検査)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 68 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	1[redacted] CA	Yes/3	Relapse of actute myeloid leukemia/ Acute myeloid leukaemia recurrent (再発急性骨髄性白血病)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] 204&	Ongoing		NO		999,10	1
		Yes/3	Dyspnea/ Dyspnoea (呼吸困難)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 204&	Ongoing		3	NO	999	1
		Yes/3	hypokaliemia/ Hypokalaemia (低カリウム血症)/	[redacted] 113	[redacted] 114	2	4	NO	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 69 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Metabolism and nutrition disorders							
			(代謝および栄養障害)							
		Yes/3	Pancytopenia/	[redacted]	Ongoing		4	NO	999,10	1
			Pancytopenia (汎血球減少症)/	204&						
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
FRA/	5[redacted]	Yes/2,3	ILEUM PERFORATION/	[redacted]	[redacted]	64	4	YES, BOTH	5,10	4
[redacted]	UN		Ileal perforation (回腸穿孔)/	77	140&			AND/OR		
			Gastrointestinal disorders (胃腸障害)					INDISTINGUI		
								SHABLE		
FRA/	5[redacted]	Yes/3	ANAL HEMORRHAGE/	[redacted]	[redacted]	9	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 70 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	UN		Anal haemorrhage (肛門出血)/ Gastrointestinal disorders (胃腸障害)	78	86					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 71 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	5[redacted] UN	Yes/3	VOMITING/ Vomiting (嘔吐)/ Gastrointestinal disorders (胃腸障害)	[redacted] 78	[redacted] 86	9	2	NO	2,10	2
GBR/ [redacted]	5[redacted] CA	Yes/3	Parainfluenza virus infection/ Parainfluenzae virus infection (パラインフルエンザウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 18	[redacted] 91	74	3	NO	2,10	2
GBR/ [redacted]	5[redacted] CA	Yes/3	Diarrhoea/ Diarrhoea (下痢)/ Gastrointestinal disorders (胃腸障害)	[redacted] 301	[redacted] 310	10	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 72 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GRC/ [redacted]	4[redacted] CA	Yes/2,3	intestinal hemorrage/ Intestinal haemorrhage (腸出血)/ Gastrointestinal disorders (胃腸障害)	[redacted] 22	[redacted] 22	1	4	YES, BOTH AND/OR INDISTINGUISHABLE	999,10	3
		Yes/2,3	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 25	[redacted] 28	4	4	NO	999,10	1
		Yes/ 1,2,3	respiratory INFECTION/ Respiratory tract infection (気道感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 29	[redacted] 29	1	5	NO	999,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 73 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
HKG/ [redacted]	3[redacted] AS	Yes/3	Fever (suspected due to seasonal flu)/ Pyrexia (発熱)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 185	[redacted] 188	4	2	NO	999,10	2
ISR/ [redacted]	6[redacted] CA	Yes/3	CMV reactivation/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 89	[redacted] 111	23	3	NO	2,10	3
ISR/ [redacted]	1[redacted] WH	Yes/3	Worsening of diarrhea/ Diarrhoea (下痢)/	[redacted] 15	[redacted] 20	6	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 74 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Gastrointestinal disorders (胃腸障害)							
ISR/	5[redacted]	Yes/3	high level of Bilirubin/	[redacted]	[redacted]	91	3	NO	2,10	2
[redacted]	CA		Blood bilirubin increased (血中ビリルビン増加)/	18	108					
			Investigations (臨床検査)							
		Yes/3	high level of bilirubin/	[redacted]	[redacted]	51	3	NO	2,10	2
			Blood bilirubin increased (血中ビリルビン増加)/	116	166					
			Investigations (臨床検査)							
		Yes/3	e.coli infection/	[redacted]	[redacted]	2	3	NO	2,10	2
			Escherichia infection (大腸菌感染)/	83	84					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 75 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ISR/	5[redacted]	Yes/3	upper respiratory tract infection/	[redacted]	[redacted]	5	3	YES,	2,10	2
[redacted]	CA		Upper respiratory tract infection (上気道感染)/	108	112			INVESTIGATI		
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		
ISR/	5[redacted]	Yes/3	rectal bleeding/	[redacted]	Ongoing		3	NO	2	1
[redacted]	CA		Rectal haemorrhage (直腸出血)/	60						
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	septic shock/	[redacted]	[redacted]	5	4	NO	999,1	1
			Septic shock (敗血症性ショック)/	74	78				0	
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	septic shock/	[redacted]	[redacted]	1	5	NO	999,1	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 76 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Septic shock (敗血症性ショック)/	79	79				0	
			Infections and infestations							
			(感染症および寄生虫症)							
ITA/	6[redacted]	Yes/1,2	sepsi/	[redacted]	[redacted]	1	5	NO	2,10	5
[redacted]	WH		Sepsis (敗血症)/	11	11					
			Infections and infestations							
			(感染症および寄生虫症)							
ITA/	4[redacted]	Yes/3	Bronchial fistula/	[redacted]	[redacted]	19	3	NO	999,1	2
[redacted]	WH		Bronchial fistula (気管支瘻)/	31	49				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 77 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/	5[redacted]	Yes/2	septic shock/	[redacted]	[redacted]	7	4	NO		2,10	1
[redacted]	CA		Septic shock (敗血症性ショック)/	14	20						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/1	septic shock/	[redacted]	[redacted]	1	5	NO		2,10	5
			Septic shock (敗血症性ショック)/	21	21						
			Infections and infestations								
			(感染症および寄生虫症)								
ITA/	6[redacted]	Yes/3	CMV RIACTIVATION/	[redacted]	[redacted]	7	3	NO		2,10	2
[redacted]	WH		Cytomegalovirus infection	5	11						
			(サイトメガロウイルス感染)/								
			Infections and infestations								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 78 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
		Yes/3	sepsi of staphilococcus aureus MRSA/	[redacted]	[redacted]	21	3	YES,	4,10	2
			Staphylococcal sepsis (ブドウ球菌性敗血症)/	65	85			INVESTIGATI		
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		
ITA/ [redacted]	7[redacted] CA	Yes/2,6	fever with BACTERIAL colonization/	[redacted]	Ongoing		3	NO	999,10	1
			Bacterial disease carrier (細菌性疾患キャリアー)	80					0	
			/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/6	PNEUMOCOCCUS Ag positivity (urine)/	[redacted]	[redacted]	8	2	NO	999,1	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 79 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Bacterial test positive (細菌検査陽性)/ Investigations (臨床検査)	76	83				0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 80 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	7[redacted]	Yes/1	worsening of the clinical condition/	[redacted]	[redacted]	1	5	NO	999	5
[redacted]	CA		Condition aggravated (状態悪化)/	85	85					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/3	CMV enteritis/	[redacted]	[redacted]	23	3	NO	999,10	2
			Cytomegalovirus enteritis	19	41					
			(サイトメガロウイルス性小腸炎)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	PNEUMOCYSTIS PNEUMONIA/	[redacted]	Ongoing		3	NO	999,10	1
			Pneumocystis jirovecii pneumonia	51						
			(ニューモシスチス・イロベチイ肺炎)/							
			Infections and infestations							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 81 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
		Yes/3	PNEUMONIA/	[redacted]	[redacted]	13	3	NO	2,10	2
			Pneumonia (肺炎)/	37	49					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/2,3	post-infection pneumonia/	[redacted]	[redacted]	4	3	NO	999,1	1
			Pneumonia (肺炎)/	69	72				0	
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/2,3	worsening of post-infection pneumonia/	[redacted]	Ongoing		4	NO	999,1	1
			Pneumonia (肺炎)/	73					0	
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 82 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/	7[redacted]	Yes/3	RENAL FAILURE/	[redacted]	[redacted]	19	2	NO		4,10	2
[redacted]	CA		Renal failure (腎不全)/	47	65						
			Renal and urinary disorders (腎および尿路障害)								
		Yes/2,3	respiratory failure/	[redacted]	[redacted]	4	3	NO		2,10	1
			Respiratory failure (呼吸不全)/	69	72						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
		Yes/2,3	worsening of respiratory failure/	[redacted]	Ongoing		4	NO		2,10	1
			Respiratory failure (呼吸不全)/	73							
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	SUSPECTED SEPTIC SHOCK/	[redacted]	[redacted]	4	4	NO		999,1	2
			Septic shock (敗血症性ショック)/	17	20					0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 83 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							
		Yes/2,3	URO-SEPSYS/ Urosepsis (尿路性敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 57	[redacted] 71	15	4	NO	999,10	2
ITA/ [redacted]	3[redacted] CA	Yes/6	Epileptic Crisis/ Epilepsy (てんかん)/ Nervous system disorders (神経系障害)	[redacted] 14	[redacted] 14	1	2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 84 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	6[redacted] CA	Yes/2	Respiratory insufficiency/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 13	[redacted] 13	1	4	NO	2,10	1
		Yes/1	Respiratory insufficiency/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 14	[redacted] 14	1	5	NO	2,10	5
ITA/ [redacted]	3[redacted] CA	Yes/3	bladder infection by polyoma virus BK/ Cystitis viral (ウイルス性膀胱炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 31	[redacted] 74	44	3	YES, OTHER STUDY TREATMENT (NON-	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 85 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								INVESTIGATIONAL)		
ITA/ [redacted]	4[redacted] CA	Yes/2,3	SIRS in neuropenia/ Systemic inflammatory response syndrome (全身性炎症反応症候群)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 40	[redacted] 49	10	4	NO	999,10	2
ITA/ [redacted]	5[redacted] CA	Yes/2	aortic valve insufficiency/ Aortic valve incompetence (大動脈弁閉鎖不全症)/ Cardiac disorders (心臓障害)	[redacted] 43	[redacted] 100	58	4	NO	2,10	1
		Yes/1	CCA (cardio circolatory arrest)/	[redacted]	[redacted]	1	5	NO	2	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 86 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Cardiac arrest (心停止)/ Cardiac disorders (心臓障害)	100	100					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 87 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	5[redacted]	Yes/3	worsening of diarroea/	[redacted]	[redacted]	58	3	NO	2,10	2
[redacted]	CA		Diarrhoea (下痢)/	30	87					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	endocarditis/	[redacted]	Ongoing		4	NO	2,10	1
			Endocarditis (心内膜炎)/	43						
			Infections and infestations							
			(感染症および寄生虫症)							
ITA/	4[redacted]	Yes/3	Diarrhoea/	[redacted]	[redacted]	29	3	NO	2,10	2
[redacted]	CA		Diarrhoea (下痢)/	142	170					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	pancitopenia/	[redacted]	[redacted]	20	3	YES, BOTH	2,10	2
			Pancytopenia (汎血球減少症)/	23	42			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 88 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Blood and lymphatic system disorders					INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		
		Yes/3	fever/	[redacted]	Ongoing		2	NO	999,1	3
			Pyrexia (発熱)/	353					0	
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/3	nausea with vomit/	[redacted]	[redacted]	9	3	NO	2,10	2
			Vomiting (嘔吐)/	79	87					
			Gastrointestinal disorders (胃腸障害)							
ITA/ [redacted]	3[redacted] CA	Yes/3	virosys in definition/	[redacted]	[redacted]	9	3	YES, BOTH	4,10	1
			Viral infection (ウイルス感染)/	41	49			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 89 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 90 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	3[redacted] CA	Yes/1	virosys in definition/ Viral infection (ウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 50	[redacted] 50	1	5	YES, BOTH AND/OR INDISTINGUISHABLE	999	5
ITA/ [redacted]	5[redacted] CA	Yes/3	diarroea/ Diarrhoea (下痢)/ Gastrointestinal disorders (胃腸障害)	[redacted] 25	[redacted] 44	20	3	NO	2,10	2
JPN/ [redacted]	6[redacted] AS	Yes/2	Acute lung injury/ Acute lung injury (急性肺損傷)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 28	[redacted] 39	12	4	YES, INVESTIGATIONAL TREATMENT	2,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 91 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/2	Acute lung injury/	[redacted]	Ongoing		3	YES,	999,10	1
			Acute lung injury (急性肺損傷)/	40				INVESTIGATIONAL		
			Respiratory, thoracic and mediastinal disorders					TREATMENT		
			(呼吸器、胸郭および縦隔障害)							
		Yes/2	Acute renal dysfunction/	[redacted]	[redacted]	10	4	YES, OTHER	2,10	1
			Renal impairment (腎機能障害)/	32	41			STUDY		
			Renal and urinary disorders (腎および尿路障害)					TREATMENT		
								(NON-INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 92 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	Yes/1	Acute renal dysfunction/ Renal impairment (腎機能障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 42	[redacted] 42	1	5	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999,10	5
JPN/ [redacted]	6[redacted] AS	Yes/6	Blood bilirubin increased/ Blood bilirubin increased (血中ビリルビン増加)/ Investigations (臨床検査)	[redacted] 43	Ongoing		4	NO	4,10	1
		Yes/2	Sepsis/ Sepsis (敗血症)/ Infections and infestations	[redacted] 76	[redacted] 82	7	4	YES, BOTH AND/OR INDISTINGUI	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 93 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)					SHABLE		
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	YES, BOTH	999,1	5
			Sepsis (敗血症)/	83	83			AND/OR	0	
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
JPN/	6[redacted]	Yes/2	Lower gastrointestinal hemorrhage/	[redacted]	[redacted]	15	4	YES,	2,10	1
[redacted]	AS		Lower gastrointestinal haemorrhage (下部消化管出血)	64	78			INVESTIGATI		
			/					ONAL		
			Gastrointestinal disorders (胃腸障害)					TREATMENT		
		Yes/1	Lower gastrointestinal hemorrhage/	[redacted]	[redacted]	1	5	YES,	999,1	5
			Lower gastrointestinal haemorrhage (下部消化管出血)	79	79			INVESTIGATI	0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 94 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			/					ONAL		
			Gastrointestinal disorders (胃腸障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 95 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	5[redacted]	Yes/2	idiopathic pneumonia syndrome/	[redacted]	[redacted]	6	4	YES, BOTH	999,1	1
[redacted]	AS		Idiopathic pneumonia syndrome (特発性肺炎症候群)/	42	47&			AND/OR	0	
			Respiratory, thoracic and mediastinal disorders					INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/1	idiopathic pneumonia syndrome/	[redacted]	[redacted]	1	5	YES, BOTH	999,1	5
			Idiopathic pneumonia syndrome (特発性肺炎症候群)/	48&	48&			AND/OR	0	
			Respiratory, thoracic and mediastinal disorders					INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/6	sepsis/	[redacted]	[redacted]	16	4	YES, BOTH	5,10	2
			Sepsis (敗血症)/	15	30			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 96 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	5[redacted] AS	Yes/2	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 80	Ongoing		4	NO	999,10	3
JPN/ [redacted]	6[redacted] AS	Yes/3	Guillain-Barre syndrome/ Guillain-Barre syndrome (ギラン・バレー症候群)/ Nervous system disorders (神経系障害)	[redacted] 155	[redacted] 183	29	3	YES, BOTH AND/OR INDISTINGUISHABLE	5,10	3
		Yes/6	Guillain-Barre syndrome/ Guillain-Barre syndrome (ギラン・バレー症候群)/ Nervous system disorders (神経系障害)	[redacted] 184	[redacted] 263&	80	2	YES, BOTH AND/OR INDISTINGUISHABLE	999	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 97 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	Yes/6	Guillain-Barre syndrome/ Guillain-Barre syndrome (ギラン・バレー症候群)/ Nervous system disorders (神経系障害)	[redacted] 264&	Ongoing		1	YES, BOTH AND/OR INDISTINGUISHABLE	999	1
KOR/ [redacted]	5[redacted] AS	Yes/2	Cardiac arrest/ Cardiac arrest (心停止)/ Cardiac disorders (心臓障害)	[redacted] 7	[redacted] 13	7	4	NO	2,10	1
		Yes/1	Cardiac arrest/ Cardiac arrest (心停止)/ Cardiac disorders (心臓障害)	[redacted] 14	[redacted] 14	1	5	NO	5,10	5
RUS/	3[redacted]	Yes/1	febrile neutropenia/	[redacted]	[redacted]	1	5	NO	2,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 98 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Febrile neutropenia (発熱性好中球減少症)/	38	38					
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/2	Headache, grade 3/	[redacted]	[redacted]	1	3	NO	2	4
			Headache (頭痛)/	9	9					
			Nervous system disorders (神経系障害)							
		Yes/2	febrile temperature/	[redacted]	[redacted]	3	4	NO	2,10	4
			Pyrexia (発熱)/	7	9					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/2	Sepsis/	[redacted]	[redacted]	30	3	NO	2,10	1
			Sepsis (敗血症)/	8	37					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 99 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 100 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
RUS/	3[redacted]	Yes/1	Sepsis/	[redacted]	[redacted]	1	5	NO	5,10	5
[redacted]	CA		Sepsis (敗血症)/	38	38					
			Infections and infestations							
			(感染症および寄生虫症)							
SAU/	4[redacted]	Yes/3	bone marrow suppression/	[redacted]	[redacted]	9	3	NO	999,1	2
[redacted]	OTH		Bone marrow failure (骨髄機能不全)/	36	44				0	
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/3	enterococcus faescium/	[redacted]	[redacted]	3	3	NO	999,1	2
			Enterococcal infection (腸球菌感染)/	50	52				0	
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 101 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/2,6	fall down/	[redacted]	[redacted]	1	3	NO	2	2
			Fall (転倒)/	29	29					
			Injury, poisoning and procedural complications							
			(傷害、中毒および処置合併症)							
		Yes/2	metabolic acidosis/	[redacted]	Ongoing		4	NO	999,1	1
			Metabolic acidosis (代謝性アシドーシス)/	61					0	
			Metabolism and nutrition disorders							
			(代謝および栄養障害)							
		Yes/1	multi organ failure/	[redacted]	[redacted]	1	5	NO	999	5
			Multiple organ dysfunction syndrome	63&	63&					
			(多臓器機能不全症候群)/							
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 102 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
SAU/	4[redacted]	Yes/3	klebsiella pneumonia/	[redacted]	Ongoing		3	NO		999,1	1
[redacted]	OTH		Pneumonia klebsiella (クレブシエラ菌性肺炎)/	61						0	
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/2	respiratory distress/	[redacted]	Ongoing		4	NO		999,1	1
			Respiratory distress (呼吸窮迫)/	62						0	
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
		Yes/1	septic shock/	[redacted]	[redacted]	1	5	NO		999	5
			Septic shock (敗血症性ショック)/	63&	63&						
			Infections and infestations								
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 103 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
TUR/ [redacted]	2[redacted] WH	Yes/2,3	GI Bleeding/ Gastrointestinal haemorrhage (胃腸出血)/ Gastrointestinal disorders (胃腸障害)	[redacted] 43	[redacted] 45	3	4	NO	4,10	2
		Yes/1	septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 47	[redacted] 47	1	5	NO	2	5
TUR/ [redacted]	5[redacted] CA	Yes/2	Gram Negative Sepsis/ Bacterial sepsis (細菌性敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 41	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 104 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
TUR/ [redacted]	5[redacted] CA	Yes/1	Gram Negative Sepsis/ Bacterial sepsis (細菌性敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 41	[redacted] 41	1	5	YES, INVESTIGATIONAL TREATMENT	5,10	5
		Yes/3	Dizziness Symptom/ Dizziness (浮動性めまい)/ Nervous system disorders (神経系障害)	[redacted] 19	[redacted] 41	23	2	NO	4	2
TUR/ [redacted]	2[redacted] CA	Yes/3	Cytomegalovirus infection/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 28	[redacted] 48	21	3	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 105 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	PSYCHIATRIC DISORDER/	[redacted]	[redacted]	23	3	YES, OTHER	2,10	2
			Mental disorder (精神障害)/	19	41			STUDY		
			Psychiatric disorders (精神障害)					TREATMENT		
								(NON-INVESTIGATIONAL)		
		Yes/3	FEVER/	[redacted]	[redacted]	2	3	NO	2,10	2
			Pyrexia (発熱)/	28	29					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
TUR/	3[redacted]	Yes/2	Epileptic Attack/	[redacted]	Ongoing		4	NO	2,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 106 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Epilepsy (てんかん)/ Nervous system disorders (神経系障害)	14						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 107 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
TUR/ [redacted]	3[redacted] CA	Yes/3	CMV related Diarrhea/ Viral diarrhoea (ウイルス性下痢)/ Infections and infestations (感染症および寄生虫症)	[redacted] 153	[redacted] 154	2	3	NO	2,10	3
TUR/ [redacted]	1[redacted] OTH	Yes/3	Febrile neutropenia/ Febrile neutropenia (発熱性好中球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 49	[redacted] 57	9	3	YES, INVESTIGATIONAL TREATMENT	4,10	2
TUR/ [redacted]	2[redacted] CA	Yes/3	Acute GvHD progression/ Acute graft versus host disease (急性移植片対宿主病)/	[redacted] 83	Ongoing		3	NO	999,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 108 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Immune system disorders (免疫系障害)							
TUR/ [redacted]	5[redacted] WH	Yes/3	glioblastoma multiforme/ Glioblastoma multiforme (多形性神経膠芽細胞腫)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] 62	Ongoing		3	NO	5,10	1
TWN/ [redacted]	3[redacted] AS	Yes/3	Abdominal pain/ Abdominal pain (腹痛)/ Gastrointestinal disorders (胃腸障害)	[redacted] 34	[redacted] 54	21	2	NO	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 109 of 238)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
TWN/ [redacted]	3[redacted] AS	Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 166	[redacted] 191	26	3	NO		2,10	2
		Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 193	[redacted] 205&	13	3	NO		999,10	2
		Yes/2,3	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 105	[redacted] 117	13	4	NO		4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 110 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
AUS/ [redacted]	3[redacted] CA	Yes/3	Scaedosporium prolificans lung infection/	[redacted]	[redacted]	9	3	NO		2,10	3
			Lower respiratory tract infection fungal	17*	25*						
			(真菌性下気道感染)/								
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	Pseudomonas bacteraemia/	[redacted]	[redacted]	9	3	NO		2,10	2
			Pseudomonal bacteraemia	17*	25*						
			(シュードモナス性菌血症)/								
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	Fever/	[redacted]	[redacted]	1	1	NO		2,10	2
			Pyrexia (発熱)/	43	43						
			General disorders and administration site conditions								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 111 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(一般・全身障害および投与部位の状態)							
		Yes/3	Serum Sickness/	[redacted]	[redacted]	8	3	YES,	2,10	2
			Serum sickness (血清病)/	21	28			INVESTIGATIONAL TREATMENT		
			Immune system disorders (免疫系障害)							
AUS/ [redacted]	6[redacted] CA	Yes/3,6	aspiration pneumonia/	[redacted]	Ongoing		3	NO	999,10	1
			Pneumonia aspiration (誤嚥性肺炎)/	55						
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Clostridium difficile pseudomembranous colitis/	[redacted]	[redacted]	3	4	NO	999,10	1
			Pseudomembranous colitis (偽膜性大腸炎)/	68	70					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 112 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 113 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
AUS/ [redacted]	6[redacted] CA	Yes/1	Clostridium difficile pseudomembranous colitis/	[redacted]	[redacted]	1	5	NO		999	5
			Pseudomembranous colitis (偽膜性大腸炎)/	71	71						
			Infections and infestations								
			(感染症および寄生虫症)								
AUS/ [redacted]	7[redacted] CA	Yes/3	Clostridium Difficile Sepsis/	[redacted]	[redacted]	6	2	NO		999,10	2
			Clostridial sepsis (クロストリジウム性敗血症)/	190*	195*						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	Sepsis/	[redacted]	[redacted]	3	3	NO		999,10	2
			Sepsis (敗血症)/	58	60						
			Infections and infestations								
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 114 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	2[redacted] CA	Yes/1,3	Pneumonitis/ Pneumonitis (肺臓炎)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 23*	[redacted] 23*	1	5	NO	999,10	5
		Yes/3	Respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 18*	Ongoing		4	NO	2,10	1
AUS/ [redacted]	6[redacted] CA	Yes/3	Intracerebral heamorrhage/ Cerebral haemorrhage (脳出血)/ Nervous system disorders (神経系障害)	[redacted] 20	[redacted] 21	2	4	NO	999,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 115 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
AUS/	6[redacted]	Yes/3	Staphylococcus Aureus Septicaemia/	[redacted]	[redacted]	12	2	NO		999,10	2
[redacted]	CA		Staphylococcal sepsis (ブドウ球菌性敗血症)/	7	18						
			Infections and infestations								
			(感染症および寄生虫症)								
AUS/	5[redacted]	Yes/6	non ST elevated Myocardial infarction/	[redacted]	[redacted]	7	3	NO		4	2
[redacted]	WH		Acute myocardial infarction (急性心筋梗塞)/	16*	22*						
			Cardiac disorders (心臓障害)								
		Yes/3	confusion by lymphoma brain/	[redacted]	[redacted]	27	4	NO		5,10	1
			Central nervous system lymphoma	21*	47&						
			(中枢神経系リンパ腫)/								
			Neoplasms benign, malignant and unspecified (incl cysts								
			and polyps)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 116 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(良性、悪性および詳細不明の新生物（嚢胞							
			およびポリープを含む）)							
		Yes/1	Relapsed mantle cell lymphoma/	[redacted]	[redacted]	1	5	NO	999	5
			Mantle cell lymphoma (マントル細胞リンパ腫)/	48&*	48&					
			Neoplasms benign, malignant and unspecified (incl cysts							
			and polyps)							
			(良性、悪性および詳細不明の新生物（嚢胞							
			およびポリープを含む）)							
		Yes/2	VRE meningitis/	[redacted]	Ongoing		4	NO	999,1	1
			Meningitis enterococcal (腸球菌性髄膜炎)/	38*					0	
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 117 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
AUS/ [redacted]	5[redacted] WH	Yes/2,3	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 16*	[redacted] 22*	7	4	NO		4,10	2
AUS/ [redacted]	4[redacted] CA	Yes/1,6	Death from progression of GVHD/ Graft versus host disease (移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 50*	[redacted] 50*	1	5	NO		999	5
AUS/ [redacted]	6[redacted] CA	Yes/1	Death from refractory acute gut GVHD/ Acute graft versus host disease in intestine (急性腸管移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 23	[redacted] 23	1	5	NO		999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 118 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/2,3	Dehydration/	[redacted]	[redacted]	3	4	NO	2,10	2
			Dehydration (脱水)/	1	3					
			Metabolism and nutrition disorders							
			(代謝および栄養障害)							
AUS/	4[redacted]	Yes/3	Hypotension/	[redacted]	[redacted]	6	3	NO	2,10	2
[redacted]	UN		Hypotension (低血圧)/	67*	72*					
			Vascular disorders (血管障害)							
AUS/	6[redacted]	Yes/3	Pneumonia/	[redacted]	[redacted]	5	3	YES, OTHER STUDY TREATMENT (NON-	999,10	2
[redacted]	WH		Pneumonia (肺炎)/	55	59					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 119 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 120 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
AUS/ [redacted]	5[redacted] CA	Yes/1	Progression of graft vs host disease/ Graft versus host disease (移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 15	[redacted] 15	1	5	NO		999,10	5
AUS/ [redacted]	3[redacted] CA	Yes/1	Progression of graft vs host disease/ Graft versus host disease (移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 15	[redacted] 15	1	5	NO		999	5
CAN/ [redacted]	5[redacted] CA	Yes/1	STROKE/ Cerebrovascular accident (脳血管発作)/ Nervous system disorders (神経系障害)	[redacted] 7*	[redacted] 8*	2	5	NO		5,10	5
CAN/	6[redacted]	Yes/3	diarrhea- c.diff positive/	[redacted]	Ongoing		3	NO		999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 121 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Clostridium difficile colitis	62					0	
			(クロストリジウム・ディフィシレ大腸炎)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	CMV reactivation by blood PCR only/	[redacted]	[redacted]	14	3	NO	999,1	2
			Cytomegalovirus infection	63	76				0	
			(サイトメガロウイルス感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3,6	metabolic acidosis/	[redacted]	Ongoing		4	NO	999,1	1
			Metabolic acidosis (代謝性アシドーシス)/	68					0	
			Metabolism and nutrition disorders							
			(代謝および栄養障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 122 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	Yes/3	Steroid induced myopathy/ Myopathy (ミオパチー)/ Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	[redacted] 21	[redacted] 31	11	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	5	3
		Yes/2,6	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 73	[redacted] 86	14	4	NO	999,10	1
		Yes/1	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders	[redacted] 87	[redacted] 87	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 123 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(呼吸器、胸郭および縦隔障害)							
		Yes/6	sepsis/	[redacted]	Ongoing		4	NO	999,10	1
			Sepsis (敗血症)/	69						
			Infections and infestations							
			(感染症および寄生虫症)							
CAN/ [redacted]	6[redacted] CA	Yes/2	pulmonary edema/	[redacted]	Ongoing		4	NO	999,10	1
			Pulmonary oedema (肺水腫)/	20						
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/ 1,2,6	respiratory failure/	[redacted]	[redacted]	2	5	NO	999,10	5
			Respiratory failure (呼吸不全)/	20	21					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 124 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 125 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/	6[redacted]	Yes/1	sepsis/	[redacted]	[redacted]	2	5	NO	999,10	5
[redacted]	CA		Sepsis (敗血症)/	20	21					
			Infections and infestations							
			(感染症および寄生虫症)							
CAN/	5[redacted]	Yes/2	Respiratory distress/	[redacted]	[redacted]	1	4	NO	2,10	1
[redacted]	CA		Respiratory distress (呼吸窮迫)/	60*	60*					
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/1	Respiratory Failure/	[redacted]	[redacted]	1	5	NO	5	5
			Respiratory failure (呼吸不全)/	61*	61*					
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 126 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	2[redacted] CA	Yes/2,3	Oliguric acute kidney injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 18	[redacted] 20	3	3	YES, INVESTIGATIONAL TREATMENT	2,10	1
		Yes/2,3	CMV Reactivation/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 18	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	999,10	997
		Yes/1,3	Hepatic Failure/ Hepatic failure (肝不全)/	[redacted] 21	[redacted] 21	1	5	YES, INVESTIGATI	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 127 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Hepatobiliary disorders (肝胆道系障害)					ONAL TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 128 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	2[redacted] CA	Yes/2,3	Severe liver insufficiency/ Hepatic failure (肝不全)/ Hepatobiliary disorders (肝胆道系障害)	[redacted] 18	[redacted] 20	3	4	YES, INVESTIGATIONAL TREATMENT	2	1
		Yes/2,3	Renal Failure/ Renal failure (腎不全)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 21	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	999	1
		Yes/2,3	Acute Tubular Necrosis/ Renal tubular necrosis (腎尿細管壊死)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 16	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 129 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
CAN/	6[redacted]	Yes/6	Rigors/	[redacted]	[redacted]	1	2	NO		999,1	2
[redacted]	WH		Chills (悪寒)/	120	120					0	
			General disorders and administration site conditions								
			(一般・全身障害および投与部位の状態)								
		Yes/	Hypoglycemia/	[redacted]	[redacted]	4	4	NO		999,1	2
		2,3,6	Hypoglycaemia (低血糖)/	104	107					0	
			Metabolism and nutrition disorders								
			(代謝および栄養障害)								
		Yes/3	Influenza Upper Respiratory Infection/	[redacted]	Ongoing		3	NO		999,1	3
			Influenza (インフルエンザ)/	120						0	
			Infections and infestations								
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 130 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
CAN/	6[redacted]	Yes/3	Infusion Related Reaction/	[redacted]	[redacted]	1	3	NO		999,1	2
[redacted]	WH		Infusion related reaction (注入に伴う反応)/	120	120					0	
			Injury, poisoning and procedural complications								
			(傷害、中毒および処置合併症)								
		Yes/3	Neutropenia/	[redacted]	[redacted]	4	3	NO		999,1	2
			Neutropenia (好中球減少症)/	104	107					0	
			Blood and lymphatic system disorders								
			(血液およびリンパ系障害)								
		Yes/3	Neutropenia/	[redacted]	[redacted]	3	4	NO		999,1	2
			Neutropenia (好中球減少症)/	120	122					0	
			Blood and lymphatic system disorders								
			(血液およびリンパ系障害)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 131 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	Yes/3	Acute Kidney Injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 27	[redacted] 30	4	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	4,10	2
		Yes/2	Acute Kidney injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 13*	[redacted] 22*	10	4	NO	2,10	1
		Yes/1	Acute kidney injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 23*	[redacted] 23*	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 132 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	Yes/3	Weakness/ Asthenia (無力症)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 27	[redacted] 32*	6	2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	4	2
		Yes/2	Choreiform movements/ Chorea (舞踏病)/ Nervous system disorders (神経系障害)	[redacted] 13*	Ongoing		4	NO	2,10	1
		Yes/3	Confusion/ Confusional state (錯乱状態)/ Psychiatric disorders (精神障害)	[redacted] 27	[redacted] 32*	6	2	YES, OTHER STUDY TREATMENT (NON-	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 133 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								INVESTIGATIONAL)		
		Yes/2	Decreased Level of Consciousness/ Depressed level of consciousness (意識レベルの低下)/ Nervous system disorders (神経系障害)	[redacted] 13*	Ongoing		4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
		Yes/2	Diffuse encephalopathy/ Encephalopathy (脳症)/ Nervous system disorders (神経系障害)	[redacted] 13*	[redacted] 22*	10	4	NO	2	1
		Yes/1	Diffuse encephalopathy/	[redacted]	[redacted]	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 134 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Encephalopathy (脳症)/	23*	23*					
			Nervous system disorders (神経系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 135 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	Yes/2	Vancomycin resistant E. faecium bacteremia/ Enterococcal bacteraemia (腸球菌性菌血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 13*	Ongoing		4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
		Yes/3	Hypoxia/ Hypoxia (低酸素症)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 6*	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
		Yes/3	Neutropenia/	[redacted]	[redacted]	6	4	NO	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 136 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Neutropenia (好中球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	27	32*					
		Yes/3	Pancytopenia/ Pancytopenia (汎血球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 11*	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	4,10	1
		Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 9*	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 137 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	Yes/2	Hypoxic Respiratory Failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 13*	[redacted] 22*	10	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
		Yes/1	Hypoxic Respiratory Failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 23*	[redacted] 23*	1	5	NO	999	5
		Yes/2	Septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations	[redacted] 13*	Ongoing		4	NO	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 138 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
CAN/ [redacted]	6[redacted] CA	Yes/6	ARDS acute respiratory distress syndrome/ Acute respiratory distress syndrome (急性呼吸窮迫症候群)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 20	Ongoing		4	YES, BOTH AND/OR INDISTINGUISHABLE	999,1 0	1
		Yes/2	left lower Lung lobe consolidation/ Lung consolidation (肺硬化)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 20	Ongoing		4	YES, BOTH AND/OR INDISTINGUISHABLE	999,1 0	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 139 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	Yes/1	multi-organ failure/ Multiple organ dysfunction syndrome (多臓器機能不全症候群)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 26	[redacted] 27	2	5	YES, BOTH AND/OR INDISTINGUISHABLE	999,1 0	5
		Yes/2	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 20	[redacted] 26	7	4	YES, BOTH AND/OR INDISTINGUISHABLE	999,1 0	1
		Yes/1	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 27	[redacted] 27	1	5	YES, BOTH AND/OR INDISTINGUISHABLE	999,1 0	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 140 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/6	Atrial fibrillation/ Atrial fibrillation (心房細動)/ Cardiac disorders (心臓障害)	[redacted] 1	[redacted] 6	6	3	YES, INVESTIGATIONAL TREATMENT	2,10	3
		Yes/6	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 46	[redacted] 59	14	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 141 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/2	pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 70	[redacted] 89	20	4	YES, INVESTIGATIONAL TREATMENT	2,10	1
		Yes/1	pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 90	[redacted] 90	1	5	YES, INVESTIGATIONAL TREATMENT	2	5
		Yes/ 1,2,3	Septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 90	[redacted] 90	1	5	YES, INVESTIGATIONAL TREATMENT	5,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 142 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	gut bleeding/ Gastrointestinal haemorrhage (胃腸出血)/ Gastrointestinal disorders (胃腸障害)	[redacted] 34*	[redacted] 35*	2	4	YES, INVESTIGATIONAL TREATMENT	5,10	2
DEU/ [redacted]	6[redacted] CA	Yes/1	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 59*	[redacted] 59*	1	5	NO	999	5
DEU/ [redacted]	6[redacted] CA	Yes/1	acute respiratory insufficiency/ Acute respiratory failure (急性呼吸不全)/	[redacted] 8	[redacted] 8	1	5	NO	5,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 143 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 144 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
DEU/	5[redacted]	Yes/1	Colitis/	[redacted]	[redacted]	1	5	NO		999	5
[redacted]	CA		Colitis (大腸炎)/	38*	38*						
			Gastrointestinal disorders (胃腸障害)								
		Yes/1	Peritonitis/	[redacted]	[redacted]	1	5	NO		999	5
			Peritonitis (腹膜炎)/	38*	38*						
			Infections and infestations								
			(感染症および寄生虫症)								
DEU/	7[redacted]	Yes/3	Gastrointestinal bleeding/	[redacted]	[redacted]	1	4	NO		2	2
[redacted]	CA		Gastrointestinal haemorrhage (胃腸出血)/	133*	133*						
			Gastrointestinal disorders (胃腸障害)								
DEU/	5[redacted]	Yes/3	aGvHD GI/	[redacted]	Ongoing		2	NO		999	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 145 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Graft versus host disease in gastrointestinal tract (消化管移植片対宿主病)/ Immune system disorders (免疫系障害)	-8						
DEU/ [redacted]	5[redacted] CA	Yes/3	Portinfection/ Device related infection (医療機器関連感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 20	[redacted] 45	26	3	NO	2,10	2
DEU/ [redacted]	5[redacted] CA	Yes/1,2	renal failure/ Renal failure (腎不全)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 47	[redacted] 47	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 146 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/3	Cardiac insufficiency/	[redacted]	Ongoing		3	NO		2	1
			Cardiac failure (心不全)/	146*							
			Cardiac disorders (心臓障害)								
		Yes/2	Sepsis/	[redacted]	[redacted]	1	4	NO		999	1
			Sepsis (敗血症)/	237*	237*						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	NO		999	5
			Sepsis (敗血症)/	238&*	238&						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	Syncope/	[redacted]	[redacted]	2	3	NO		2	2
			Syncope (失神)/	134*	135*						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 147 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Nervous system disorders (神経系障害)							
DEU/	3[redacted]	Yes/3	Respiratory Infection/	[redacted]	[redacted]	30	4	YES,	999,1	1
[redacted]	CA		Respiratory tract infection (気道感染)/	65	94&			INVESTIGATI	0	
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/1	septic shock/	[redacted]	[redacted]	1	5	YES,	999,1	5
			Septic shock (敗血症性ショック)/	95&	95&			INVESTIGATI	0	
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/3	Infection of upper airway with fever/	[redacted]	[redacted]	8	3	YES, BOTH	2,10	2
			Upper respiratory tract infection (上気道感染)/	21	28			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 148 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 149 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	1[redacted] OTH	Yes/3	abdominal pain/	[redacted]	[redacted]	13	2	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	3
			Abdominal pain (腹痛)/	67	79					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	intermitted diarrhea/	[redacted]	[redacted]	22	3	YES, BOTH AND/OR INDISTINGUISHABLE	2	2
			Diarrhoea (下痢)/	107	128					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	dizziness/	[redacted]	[redacted]	1	2	NO	2	2
			Dizziness (浮動性めまい)/	151	151					
			Nervous system disorders (神経系障害)							
		Yes/3	Hypertension/	[redacted]	[redacted]	1	1	NO	2	2
			Hypertension (高血圧)/	151	151					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Vascular disorders (血管障害)							
		Yes/3	fever/	[redacted]	[redacted]	1	3	YES, BOTH	2	2
			Pyrexia (発熱)/	67	67			AND/OR		
			General disorders and administration site conditions					INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
		Yes/3	fever/	[redacted]	[redacted]	2	3	YES, BOTH	2,10	2
			Pyrexia (発熱)/	107	108			AND/OR		
			General disorders and administration site conditions					INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
		Yes/3	fever/	[redacted]	[redacted]	1	2	YES, BOTH	2,10	2
			Pyrexia (発熱)/	151	151			AND/OR		
			General disorders and administration site conditions					INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 151 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	1[redacted] OTH	Yes/3	fever/	[redacted]	[redacted]	13	3	YES, BOTH	999,1	2
			Pyrexia (発熱)/	177	189			AND/OR	0	
			General disorders and administration site conditions					INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
		Yes/3	vomitting/	[redacted]	[redacted]	1	2	YES, BOTH	2	1
			Vomiting (嘔吐)/	107	107			AND/OR		
			Gastrointestinal disorders (胃腸障害)					INDISTINGUI		
								SHABLE		
		Yes/3	vomitting/	[redacted]	[redacted]	1	3	YES, BOTH	2,10	2
			Vomiting (嘔吐)/	108	108			AND/OR		
			Gastrointestinal disorders (胃腸障害)					INDISTINGUI		
								SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 152 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
DEU/	6[redacted]	Yes/3	confusion/	[redacted]	[redacted]	7	3	NO		2	2
[redacted]	CA		Confusional state (錯乱状態)/	47	53						
			Psychiatric disorders (精神障害)								
		Yes/3	worsening of fatigue/	[redacted]	[redacted]	5	3	NO		999	3
			Fatigue (疲労)/	68&*	72&						
			General disorders and administration site conditions								
			(一般・全身障害および投与部位の状態)								
		Yes/2	Ileus/	[redacted]	[redacted]	2	4	NO		2,10	2
			Ileus (イレウス)/	36	37						
			Gastrointestinal disorders (胃腸障害)								
		Yes/3	Tremor left hand/	[redacted]	[redacted]	5	2	NO		999	2
			Tremor (振戦)/	68&*	72&						
			Nervous system disorders (神経系障害)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 153 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	2[redacted] CA	Yes/1	Lung infection, pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 27	[redacted] 27	1	5	NO	999	5
		Yes/2	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 24	[redacted] 26	3	4	NO	999,10	1
DNK/ [redacted]	3[redacted] CA	Yes/3	Upper Respiratory Tract Infection/ Upper respiratory tract infection (上気道感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 93	[redacted] 100	8	3	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 154 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	Upper Respiratory Tract Infection/	[redacted]	[redacted]	5	3	YES, BOTH	2,10	3
			Upper respiratory tract infection (上気道感染)/	128	132			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	Upper respiratory infection/	[redacted]	[redacted]	5	3	YES, BOTH	2,10	3
			Upper respiratory tract infection (上気道感染)/	60	64			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
ESP/	6[redacted]	Yes/3	fever/	[redacted]	[redacted]	7	3	NO	999,1	2
[redacted]	CA		Pyrexia (発熱)/	67	73				0	
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 155 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ESP/	6[redacted]	Yes/3	SEVERE RESPIRATORY INSUFFICIENCY/	[redacted]	[redacted]	48	3	NO		999,10	2
[redacted]	CA		Respiratory failure (呼吸不全)/	73	120&						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	upper gastrointestinal bleeding/	[redacted]	[redacted]	31	3	NO		999,10	2
			Upper gastrointestinal haemorrhage (上部消化管出血)	90	120&						
			/								
			Gastrointestinal disorders (胃腸障害)								
ESP/	6[redacted]	Yes/2	respiratory insufficiency/	[redacted]	[redacted]	9	4	NO		5,10	1
[redacted]	CA		Respiratory failure (呼吸不全)/	16	24						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 156 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/1,3	respiratory insufficiency/	[redacted]	[redacted]	1	5	NO		999	5
			Respiratory failure (呼吸不全)/	25	25						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
ESP/ [redacted]	4[redacted] CA	Yes/3	diarrhea/	[redacted]	Ongoing		2	NO		2,10	1
			Diarrhoea (下痢)/	33							
			Gastrointestinal disorders (胃腸障害)								
		Yes/1	pulmonary hemorrhage/	[redacted]	[redacted]	1	5	NO		999	5
			Pulmonary haemorrhage (肺出血)/	85*	85*						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 157 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ESP/	5[redacted]	Yes/3	FEVER DUE TO INTERSTICIAL PNEUMNIA/	[redacted]	[redacted]	28	3	NO		999,10	2
[redacted]	CA		Interstitial lung disease (間質性肺疾患)/	51	78						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	FEVER due to BACTEREMIA P. AERUGINOSA/	[redacted]	[redacted]	5	3	NO		2,10	2
			Pseudomonal bacteraemia	18	22						
			(シュードモナス性菌血症)/								
			Infections and infestations								
			(感染症および寄生虫症)								
ESP/	2[redacted]	Yes/3	Anal abcess/	[redacted]	Ongoing		3	NO		999,10	3
[redacted]	CA		Anal abscess (肛門膿瘍)/	97							
			Infections and infestations								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 158 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
		Yes/3	LOWER Gastrointestinal Hemorrhage/	[redacted]	[redacted]	10	4	NO	2,10	2
			Lower gastrointestinal haemorrhage (下部消化管出血)	5	14					
			/							
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	Lower gastrointestinal bleeding/	[redacted]	[redacted]	2	3	NO	2,10	2
			Lower gastrointestinal haemorrhage (下部消化管出血)	55	56					
			/							
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	Perineal Ulcer/	[redacted]	[redacted]	15	3	NO	2,10	2
			Perineal ulceration (会陰潰瘍)/	28	42					
			Reproductive system and breast disorders							
			(生殖系および乳房障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 159 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/	2[redacted]	Yes/3	SEPSIS/	[redacted]	[redacted]	35	4	NO	2,10	2
[redacted]	CA		Sepsis (敗血症)/	58	92					
			Infections and infestations							
			(感染症および寄生虫症)							
ESP/	4[redacted]	Yes/3	Acute Kindney failure/	[redacted]	[redacted]	7	3	NO	2,10	2
[redacted]	CA		Acute kidney injury (急性腎障害)/	66	72					
			Renal and urinary disorders (腎および尿路障害)							
		Yes/3	Acute kidney failure/	[redacted]	[redacted]	4	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATI	2,10	2
			Acute kidney injury (急性腎障害)/	61	64					
			Renal and urinary disorders (腎および尿路障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 160 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								ONAL)		
		Yes/3	lower respiratory infection/	[redacted]	[redacted]	27	3	NO	2,10	2
			Lower respiratory tract infection (下気道感染)/	14	40					
			Infections and infestations							
			(感染症および寄生虫症)							
ESP/ [redacted]	4[redacted] WH	Yes/3	bacteremia/	[redacted]	[redacted]	6	2	NO	999,10	2
			Bacteraemia (菌血症)/	166	171					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	WORSENING OF CMV REACTIVATION/	[redacted]	[redacted]	17	3	NO	2,10	2
			Cytomegalovirus infection	25	41					
			(サイトメガロウイルス感染)/							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 161 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 162 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/ [redacted]	5[redacted] CA	Yes/3	INFECTION FOR REFRACTORY CMV/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 129	[redacted] 145	17	3	NO	4,10	2
		Yes/3	Reactivation of CMV refractory to Ganciclovir and Cidofovir/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 27*	[redacted] 65*	39	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2
ESP/ [redacted]	5[redacted]	Yes/3	acute renal failure/	[redacted]	[redacted]	5	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 163 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	WH		Acute kidney injury (急性腎障害)/	11*	15*					
			Renal and urinary disorders (腎および尿路障害)							
		Yes/3	hospitalization by Campylobacter Jejuni infection in feces/	[redacted]	[redacted]	12	2	NO	2,10	2
			Campylobacter infection (カンピロバクター感染)/	18*	29*					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	hospitalization by CMV test positive/	[redacted]	[redacted]	7	2	NO	2,10	2
			Cytomegalovirus test positive	29*	35*					
			(サイトメガロウイルス検査陽性)/							
			Investigations (臨床検査)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 164 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	5[redacted] UN	Yes/1	multi organ failure/ Multiple organ dysfunction syndrome (多臓器機能不全症候群)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 34	[redacted] 34	1	5	NO	999	5
FRA/ [redacted]	3[redacted] CA	Yes/3	cortico-induced diabetis/ Steroid diabetes (ステロイド糖尿病)/ Metabolism and nutrition disorders (代謝および栄養障害)	[redacted] 39&	Ongoing		2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 165 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	3[redacted] CA	Yes/2,3	epileptic seizures/	[redacted]	Ongoing		4	NO	2,10	1
			Epilepsy (てんかん)/	29						
			Nervous system disorders (神経系障害)							
		Yes/3	Posterior reversible encephalopathy syndrome/	[redacted]	[redacted]	11	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999,10	2
			Posterior reversible encephalopathy syndrome (可逆性後白質脳症症候群)/	75	85					
			Nervous system disorders (神経系障害)							
FRA/ [redacted]	6[redacted] CA	Yes/1	mesenteric ischemia/	[redacted]	[redacted]	1	5	NO	999,10	5
			Intestinal ischaemia (腸管虚血)/	62	62					
			Gastrointestinal disorders (胃腸障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 166 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] CA	Yes/3	pulmonary embolism/ Pulmonary embolism (肺塞栓症)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 59	Ongoing		3	NO	999,10	1
		Yes/3	SEPSIS/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 43	[redacted] 58	16	4	NO	5,10	2
FRA/ [redacted]	4[redacted] CA	Yes/3	psychomotor agitation/ Psychomotor hyperactivity (精神運動亢進)/ Nervous system disorders (神経系障害)	[redacted] 27	[redacted] 35&	9	4	YES, BOTH AND/OR INDISTINGUISHABLE	999,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 167 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] CA	Yes/3	diarrhea (related to aGVHD)/ Acute graft versus host disease in intestine (急性腸管移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 2	[redacted] 6	5	2	NO	999	2
		Yes/3	CMV REACTIVATION/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 2	[redacted] 44	43	3	NO	999,10	2
FRA/ [redacted]	5[redacted] UN	Yes/3	fall at home/ Fall (転倒)/	[redacted] 13*	[redacted] 56*	44	4	NO	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 168 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Injury, poisoning and procedural complications (傷害、中毒および処置合併症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 169 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/	5[redacted]	Yes/3	hip fracture/	[redacted]	[redacted]	44	4	NO		2,10	2
[redacted]	UN		Hip fracture (股関節部骨折)/	13*	56*						
			Injury, poisoning and procedural complications								
			(傷害、中毒および処置合併症)								
		Yes/3	pulmonary embolism/	[redacted]	[redacted]	15	2	NO		2,10	2
			Pulmonary embolism (肺塞栓症)/	13*	27*						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	broken rib/	[redacted]	[redacted]	44	4	NO		2,10	2
			Rib fracture (肋骨骨折)/	13*	56*						
			Injury, poisoning and procedural complications								
			(傷害、中毒および処置合併症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 170 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] UN	Yes/3	bacteremia/ Bacteraemia (菌血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 92	[redacted] 99	8	3	YES, INVESTIGATIONAL TREATMENT	999,10	2
		Yes/3	wORSENING OF Hypokaliema/ Hypokalaemia (低カリウム血症)/ Metabolism and nutrition disorders (代謝および栄養障害)	[redacted] 68	[redacted] 70	3	3	NO	999,10	2
FRA/ [redacted]	5[redacted] UN	Yes/3	aspergillosis/ Aspergillus infection (アスペルギルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 53*	[redacted] 56*	4	3	YES, INVESTIGATIONAL TREATMENT	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 171 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/	5[redacted]	Yes/6	bacille gram negativ bacteremia/	[redacted]	[redacted]	8	3	YES,	2,10	2
[redacted]	UN		Bacteraemia (菌血症)/	92*	99*			INVESTIGATIONAL TREATMENT		
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	confusion/	[redacted]	[redacted]	4	4	YES,	999	2
			Confusional state (錯乱状態)/	187*	190*			INVESTIGATIONAL TREATMENT		
			Psychiatric disorders (精神障害)							
		Yes/3	catheter infection/	[redacted]	[redacted]	3	3	YES,	999,10	2
			Device related infection (医療機器関連感染)/	187*	189*			INVESTIGATIONAL TREATMENT		
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	bowel obstruction/	[redacted]	[redacted]	5	3	YES,	999	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 172 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Intestinal obstruction (腸閉塞)/	186*	190*			INVESTIGATI		
			Gastrointestinal disorders (胃腸障害)					ONAL		
								TREATMENT		
		Yes/3	Acute pancreatitis/	[redacted]	Ongoing		4	NO	999	1
			Pancreatitis acute (急性膵炎)/	256&*						
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	acute pancreatitis/	[redacted]	[redacted]	10	4	NO	999,1	2
			Pancreatitis acute (急性膵炎)/	181*	190*				0	
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	respiratory distress/	[redacted]	[redacted]	13	4	YES,	999,1	2
			Respiratory distress (呼吸窮迫)/	190*	202*			INVESTIGATI	0	
			Respiratory, thoracic and mediastinal disorders					ONAL		
			(呼吸器、胸郭および縦隔障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 173 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	5[redacted] UN	Yes/3	Intermittent Thrombopenia/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 53*	[redacted] 91*	39	4	YES, INVESTIGATIONAL TREATMENT	2	2
		Yes/6	Thrombopenia/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 92*	[redacted] 98*	7	4	YES, BOTH AND/OR INDISTINGUISHABLE	3	2
FRA/ [redacted]	6[redacted] UN	Yes/3	Bacteriema/ Bacteraemia (菌血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 28	[redacted] 28	1	3	YES, INVESTIGATIONAL TREATMENT	999,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 174 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	acute leukemia relapse/ Leukaemia recurrent (白血病再発)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] 67	[redacted] 80&	14	4	NO		999	1
		Yes/1	acute leukemia relapse/ Leukaemia recurrent (白血病再発)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] 81&	[redacted] 81&	1	5	NO		999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 175 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] UN	Yes/3	hematuria/ Haematuria (血尿)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 120	[redacted] 128	9	3	YES, INVESTIGATIONAL TREATMENT	999	2
		Yes/3	renal failure/ Renal failure (腎不全)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 29	[redacted] 37	9	2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2	2
		Yes/3	BK VIRUS URINARY TRACT INFECTION/ Urinary tract infection viral (ウイルス性尿路感染)/	[redacted] 27	[redacted] 157	131	2	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 176 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations							
			(感染症および寄生虫症)							
FRA/	5[redacted]	Yes/3	acute hypoxemic respiratory failure/	[redacted]	[redacted]	5	3	NO	999,1	2
[redacted]	UN		Acute respiratory failure (急性呼吸不全)/	74	78				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Hypokaliema/	[redacted]	[redacted]	2	3	NO	2,10	2
			Hypokalaemia (低カリウム血症)/	59*	60*					
			Metabolism and nutrition disorders							
			(代謝および栄養障害)							
		Yes/3	Pneumopathy/	[redacted]	[redacted]	18	3	YES,	2,10	2
			Lung disorder (肺障害)/	27*	44*			INVESTIGATI		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders					ONAL		
			(呼吸器、胸郭および縦隔障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/	5[redacted]	Yes/2,3	Oxygen desaturation/	[redacted]	[redacted]	4	3	NO		999,1	2
[redacted]	UN		Oxygen saturation decreased (酸素飽和度低下)/	53	56					0	
			Investigations (臨床検査)								
		Yes/3	seizure/	[redacted]	[redacted]	2	3	NO		2	2
			Seizure (痙攣発作)/	59*	60*						
			Nervous system disorders (神経系障害)								
FRA/	6[redacted]	Yes/3	Ileus/	[redacted]	Ongoing		4	NO		4,10	1
[redacted]	UN		Ileus (イレウス)/	42*							
			Gastrointestinal disorders (胃腸障害)								
		Yes/1	septic shock/		[redacted]		5	NO		999	5
			Septic shock (敗血症性ショック)/		79*						
			Infections and infestations								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
FRA/ [redacted]	4[redacted] UN	Yes/2	SEPSIS/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 44*	[redacted] 50*	7	4	YES, INVESTIGATIONAL TREATMENT	999,10	1
		Yes/1	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 51*	[redacted] 51*	1	5	YES, INVESTIGATIONAL TREATMENT	999	5
FRA/ [redacted]	6[redacted] UN	Yes/3	hyperkaliemia/ Hyperkalaemia (高カリウム血症)/	[redacted] 34	[redacted] 35	2	2	NO	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 180 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Metabolism and nutrition disorders (代謝および栄養障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 181 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] UN	Yes/3	mononeuropathy of sciatic poplite externe (right foot reliever deficit (medical event)/ Mononeuropathy (単ニューロパチー)/ Nervous system disorders (神経系障害)	[redacted] 27	Ongoing		1	NO	2	1
FRA/ [redacted]	7[redacted] UN	Yes/2,3	sepsis severe at digestive point of call/ Intestinal sepsis (腸敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 45	Ongoing		4	NO	999,10	1
		Yes/1	multivisceral failure on serious infectious pneumonia/ Multiple organ dysfunction syndrome (多臓器機能不全症候群)/ General disorders and administration site conditions	[redacted] 47	[redacted] 47	1	5	NO	999,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 182 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(一般・全身障害および投与部位の状態)							
		Yes/2,3	serious infectious pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 45	Ongoing		4	NO	999,10	1
FRA/ [redacted]	6[redacted] CA	Yes/3	SEPSIS/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 40*	[redacted] 50*	11	4	NO	5,10	2
FRA/ [redacted]	1[redacted] UN	Yes/3,6	Cytolytic hepatitis/ Hepatitis (肝炎)/	[redacted] 21*	Ongoing		4	YES, BOTH AND/OR	4,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Hepatobiliary disorders (肝胆道系障害)					INDISTINGUISHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 184 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	1[redacted] UN	Yes/2	Thrombopenia [intermitent]/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 7*	[redacted] 93&	87	4	YES, INVESTIGATIONAL TREATMENT	5	2
FRA/ [redacted]	6[redacted] WH	Yes/4	state of agitation/ Agitation (激越)/ Psychiatric disorders (精神障害)	[redacted] 24	[redacted] 28	5	3	NO	2	2
		Yes/3	confusional state/ Confusional state (錯乱状態)/ Psychiatric disorders (精神障害)	[redacted] 7	Ongoing		3	NO	2	1
		Yes/3	Viral encephalitis [HHV6 related]/ Encephalitis viral (ウイルス性脳炎)/	[redacted] 9	[redacted] 66	58	4	NO	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	epileptic seizure/	[redacted]	[redacted]	5	3	NO	2	2
			Epilepsy (てんかん)/	24	28					
			Nervous system disorders (神経系障害)							
		Yes/1	SEVERE SEPSIS/	[redacted]	[redacted]	1	5	NO	999	5
			Sepsis (敗血症)/	141	141					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 186 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted]	Yes/3	planned hospitalization for profus condyloma/	[redacted]	[redacted]	2	2	NO	2	2
[redacted]	UN		Anogenital warts (肛門性器疣贅)/	2	3					
			Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
			(良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)							
		Yes/3	CMV INFECTION aggravation/	[redacted]	[redacted]	22	3	NO	2,10	2
			Cytomegalovirus infection	15	36					
			(サイトメガロウイルス感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	CMV infection aggravation/	[redacted]	[redacted]	21	3	NO	2,10	2
			Cytomegalovirus infection	11*	31*					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(サイトメガロウイルス感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	DIABETES/	[redacted]	[redacted]	26	3	YES, OTHER	2,10	2
			Diabetes mellitus (糖尿病)/	12	37			STUDY		
			Metabolism and nutrition disorders					TREATMENT		
			(代謝および栄養障害)					(NON-INVESTIGATIONAL)		
GBR/ [redacted]	4[redacted] CA	Yes/6	Neutraphil count decreased/	[redacted]	Ongoing		4	YES, BOTH	5	1
			Neutrophil count decreased (好中球数減少)/	107*				AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 188 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Investigations (臨床検査)					INDISTINGUISHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 189 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/ [redacted]	4[redacted] CA	Yes/6	Platelet count decreased/ Platelet count decreased (血小板数減少)/ Investigations (臨床検査)	[redacted] 114*	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	4,10	1
		Yes/6	White blood cell count decreased/ White blood cell count decreased (白血球数減少)/ Investigations (臨床検査)	[redacted] 107*	Ongoing		3	NO	2,10	1
GBR/ [redacted]	6[redacted] BL	Yes/3	GVHD/ Graft versus host disease (移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 3	[redacted] 15	13	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATI	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 190 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								ONAL)		
		Yes/1,3	worsening of GVHD/ Graft versus host disease (移植片対宿主病)/ Immune system disorders (免疫系障害)	[redacted] 16	[redacted] 16	1	5	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	5
HKG/ [redacted]	3[redacted] AS	Yes/3	Fever/ Pyrexia (発熱)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 26	[redacted] 55	30	1	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
HKG/ [redacted]	3[redacted] AS	Yes/3	maculopapular rash/ Rash maculo-papular (斑状丘疹状皮疹)/ Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)	[redacted] 27	[redacted] 55	29	1	NO		2,10	2
ISR/ [redacted]	2[redacted] CA	Yes/2	SEPTIC SHOCK/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 10	[redacted] 11	2	4	NO		5,10	1
		Yes/1,2	SEPTIC SHOCK/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 12	[redacted] 12	1	5	NO		999,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ISR/ [redacted]	4[redacted] CA	Yes/3	febrile neutropania/ Febrile neutropenia (発熱性好中球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 48	[redacted] 53	6	3	NO	2,10	2
		Yes/3	Gastroestinal tract bleeding/ Gastrointestinal haemorrhage (胃腸出血)/ Gastrointestinal disorders (胃腸障害)	[redacted] 51	[redacted] 58*	8	2	NO	5,10	2
		Yes/3	Fever/ Pyrexia (発熱)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 48	[redacted] 53	6	2	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ISR/ [redacted]	6[redacted] CA	Yes/3	worsening in CMV REACTIVATION/ Cytomegalovirus infection (サイトメガロウイルス感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 37	Ongoing		3	NO		2,10	1
		Yes/2,3	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 54	[redacted] 57	4	4	NO		2,10	1
		Yes/1	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 58	[redacted] 58	1	5	NO		2,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 194 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ISR/ [redacted]	4[redacted] CA	Yes/3	CMV reactivation/	[redacted]	[redacted]	29	3	NO	2,10	2
			Cytomegalovirus infection	13	41					
			(サイトメガロウイルス感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	intermittent neutropenia/	[redacted]	[redacted]	108	3	NO	2,10	2
			Neutropenia (好中球減少症)/	33	140					
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/3	pneumonia/	[redacted]	[redacted]	14	3	NO	2,10	2
			Pneumonia (肺炎)/	97	110					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 195 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 196 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ISR/ [redacted]	4[redacted] CA	Yes/3	septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 97	[redacted] 99	3	4	NO	2,10	2
ISR/ [redacted]	6[redacted] CA	Yes/2	cerebral infarction/ Cerebral infarction (脳梗塞)/ Nervous system disorders (神経系障害)	[redacted] 16	[redacted] 18	3	4	NO	2,10	1
		Yes/1	cerebral infarction/ Cerebral infarction (脳梗塞)/ Nervous system disorders (神経系障害)	[redacted] 19	[redacted] 19	1	5	NO	999,10	5
		Yes/3	pneumonia/ Pneumonia (肺炎)/	[redacted] 12	[redacted] 18	7	3	NO	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 197 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	pneumonia/	[redacted]	[redacted]	1	5	NO	999,1	5
			Pneumonia (肺炎)/	19	19				0	
			Infections and infestations							
			(感染症および寄生虫症)							
ISR/	6[redacted]	Yes/1	coma/	[redacted]	[redacted]	1	5	NO	2	5
[redacted]	CA		Coma (昏睡)/	62*	62*					
			Nervous system disorders (神経系障害)							
		Yes/3	stupor/	[redacted]	[redacted]	3	3	NO	2	1
			Stupor (昏迷)/	58*	60*					
			Nervous system disorders (神経系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 198 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ISR/ [redacted]	3[redacted] CA	Yes/3	anasarca/	[redacted]	[redacted]	15	3	NO		2,10	2
			Generalised oedema (全身性浮腫)/	85	99						
			General disorders and administration site conditions								
			(一般・全身障害および投与部位の状態)								
		Yes/3	septic shock/	[redacted]	[redacted]	20	3	NO		999,10	2
			Septic shock (敗血症性ショック)/	183	202&						
			Infections and infestations								
			(感染症および寄生虫症)								
ITA/ [redacted]	6[redacted] CA	Yes/1	Transplant-related mortality (TRM)/	[redacted]	[redacted]	1	5	NO		2,10	5
			Transplantation complication (移植合併症)/	36	36						
			Injury, poisoning and procedural complications								
			(傷害、中毒および処置合併症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 199 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	3[redacted] CA	Yes/3	Streptococcus pneumonia/ Pneumonia streptococcal (レンサ球菌性肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 94*	[redacted] 109*	16	3	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2
ITA/ [redacted]	6[redacted] CA	Yes/2	dyspnea/ Dyspnoea (呼吸困難)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 17	[redacted] 20	4	4	NO	999,10	1
		Yes/1	dyspnea/ Dyspnoea (呼吸困難)/	[redacted] 21	[redacted] 21	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 200 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 201 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	6[redacted]	Yes/2	pneumonia/	[redacted]	[redacted]	4	4	NO	999,10	1
[redacted]	CA		Pneumonia (肺炎)/	17	20					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	pneumonia/	[redacted]	[redacted]	1	5	NO	999,10	5
			Pneumonia (肺炎)/	21	21					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/2,3	septic shock/	[redacted]	[redacted]	4	4	YES, OTHER	999,10	1
			Septic shock (敗血症性ショック)/	17	20			STUDY		
			Infections and infestations					TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATI		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 202 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								ONAL)		
		Yes/1	septic shock/	[redacted]	[redacted]	1	5	YES, OTHER	999	5
			Septic shock (敗血症性ショック)/	21	21			STUDY		
			Infections and infestations					TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATI		
								ONAL)		
		Yes/2	STAPHILOCOCCUS AUREUS INFECTION/	[redacted]	[redacted]	4	4	NO	999,10	1
			Staphylococcal infection (ブドウ球菌感染)/	17	20					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/1	staphilococcus aureus infection/	[redacted]	[redacted]	1	5	NO	999,10	5
			Staphylococcal infection (ブドウ球菌感染)/	21	21					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 203 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 204 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/	6[redacted]	Yes/3	aGVHD flare/	[redacted]	[redacted]	17	4	NO		999,1	1
[redacted]	CA		Acute graft versus host disease	91	107					0	
			(急性移植片対宿主病)/								
			Immune system disorders (免疫系障害)								
		Yes/1	aGVHD flare/	[redacted]	[redacted]	1	5	NO		999,1	5
			Acute graft versus host disease	108	108					0	
			(急性移植片対宿主病)/								
			Immune system disorders (免疫系障害)								
		Yes/3	HEMORRHAGIC CYSTITIS/	[redacted]	[redacted]	22	2	NO		2,10	2
			Cystitis haemorrhagic (出血性膀胱炎)/	41	62						
			Renal and urinary disorders (腎および尿路障害)								
ITA/	7[redacted]	Yes/1	aGVDH WORSENIG/	[redacted]	[redacted]	35	5	NO		2,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 205 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Acute graft versus host disease (急性移植片対宿主病)/ Immune system disorders (免疫系障害)	9	43					
ITA/ [redacted]	4[redacted]	Yes/1	worsening of clinical condition/	[redacted]	[redacted]	1	5	NO	2	5
[redacted]	CA		Condition aggravated (状態悪化)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	84*	84*					
		Yes/3	sepsis by Klebsiella/	[redacted]	[redacted]	15	3	NO	2,10	2
			Klebsiella sepsis (クレブシエラ性敗血症)/ Infections and infestations (感染症および寄生虫症)	60*	74*					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 206 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/ [redacted]	4[redacted] CA	Yes/3,6	pneumonia right side/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 38*	[redacted] 48*	11	3	NO		4,10	2
		Yes/2,3	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 82*	[redacted] 83*	2	4	NO		5,10	4
		Yes/3	septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 48*	[redacted] 50*	3	3	NO		2,10	2
		Yes/2,3	septic shock/	[redacted]	[redacted]	7	4	NO		2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 207 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Septic shock (敗血症性ショック)/	78*	84*					
			Infections and infestations							
			(感染症および寄生虫症)							
ITA/	5[redacted]	Yes/3	pneumonitis/	[redacted]	[redacted]	22	3	NO	2,10	4
[redacted]	CA		Pneumonitis (肺臓炎)/	28*	49*					
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/2,3	pneumonitis/	[redacted]	[redacted]	15	2	YES,	2,10	2
			Pneumonitis (肺臓炎)/	62*	76*			INVESTIGATI		
			Respiratory, thoracic and mediastinal disorders					ONAL		
			(呼吸器、胸郭および縦隔障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 208 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	5[redacted]	Yes/1,2	WORSENING OF RESPIRATORY FAILURE/	[redacted]	[redacted]	1	5	YES,	4,10	5
[redacted]	CA		Respiratory failure (呼吸不全)/	79*	79*			INVESTIGATIONAL TREATMENT		
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/2,3	respiratory failure/	[redacted]	[redacted]	16	3	YES,	2,10	1
			Respiratory failure (呼吸不全)/	62*	77*			INVESTIGATIONAL TREATMENT		
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	SEPSIS/	[redacted]	[redacted]	2	3	NO	2,10	2
			Sepsis (敗血症)/	13	14					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3,6	sepsis/	[redacted]	[redacted]	17	4	NO	4,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 209 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	14*	30*					
		Yes/3	sepsis/	[redacted]	[redacted]	19	3	NO	2,10	2
			Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	31*	49*					
ITA/ [redacted]	6[redacted] WH	Yes/3	Encephalitis infection/ Encephalitis (脳炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 53*	[redacted] 107&	55	4	YES, INVESTIGATIONAL TREATMENT	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 210 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	6[redacted] WH	Yes/1	worsening of Encephalitis infection/ Encephalitis (脳炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 107&*	[redacted] 107&	1	5	YES, INVESTIGATIONAL TREATMENT	999	5
		Yes/3	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 39	[redacted] 56*	18	3	NO	2,10	2
		Yes/3	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 36*	[redacted] 40*	5	4	YES, INVESTIGATIONAL TREATMENT	2,10	2
		Yes/2	candidaemia/	[redacted]	[redacted]	5	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 211 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Systemic candida (全身性カンジダ)/	7	11					
			Infections and infestations							
			(感染症および寄生虫症)							
ITA/	5[redacted]	Yes/2	Respiratoy insufficiency/	[redacted]	[redacted]	5	4	NO	999,1	1
[redacted]	CA		Respiratory failure (呼吸不全)/	9	13				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/1	Respiratoy insufficiency/	[redacted]	[redacted]	1	5	NO	999,1	5
			Respiratory failure (呼吸不全)/	14	14				0	
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 212 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/	1[redacted]	Yes/3	Abdominal pain/	[redacted]	[redacted]	24	1	NO		999,1	2
[redacted]	WH		Abdominal pain (腹痛)/	90	113					0	
			Gastrointestinal disorders (胃腸障害)								
		Yes/3,4	bone pain/	[redacted]	Ongoing		3	NO		2,10	3
			Bone pain (骨痛)/	18*							
			Musculoskeletal and connective tissue disorders								
			(筋骨格系および結合組織障害)								
		Yes/6	CMV reactivation/	[redacted]	Ongoing		2	NO		2,10	3
			Cytomegalovirus infection	22*							
			(サイトメガロウイルス感染)/								
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	bloody diarrhoea/	[redacted]	[redacted]	37	3	NO		2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 213 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Diarrhoea haemorrhagic (血性下痢)/	155	191*					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	Clostridium Difficile Enteritis/	[redacted]	[redacted]	13	2	NO	999,1	2
			Gastroenteritis clostridial	90	102				0	
			(クロストリジウム菌性胃腸炎)/							
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	nausea/	[redacted]	[redacted]	13	3	NO	999,1	2
			Nausea (悪心)/	90	102				0	
			Gastrointestinal disorders (胃腸障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 214 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	1[redacted] WH	Yes/4	osteoporosis with vertebral fracture/ Osteoporotic fracture (骨粗鬆症性骨折)/ Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	[redacted] 22*	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	3
		Yes/2	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 94	[redacted] 96	3	4	NO	999,10	2
		Yes/3	Increase of transaminases/ Transaminases increased (トランスアミナーゼ上昇)/	[redacted] 18*	Ongoing		4	YES, INVESTIGATIONAL	5	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 215 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Investigations (臨床検査)					TREATMENT		
		Yes/3	vomiting/	[redacted]	[redacted]	13	3	NO	999,10	2
			Vomiting (嘔吐)/	90	102					
			Gastrointestinal disorders (胃腸障害)							
ITA/ [redacted]	1[redacted] CA	Yes/3	bacteremia/	[redacted]	[redacted]	5	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2
			Bacteraemia (菌血症)/	23	27					
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 216 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/ [redacted]	1[redacted] CA	Yes/3	herpes zoester infection/	[redacted]	[redacted]	13	3	NO		4,10	2
			Herpes zoster (帯状疱疹)/	126*	138*						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	septic shock/	[redacted]	[redacted]	17	4	NO		4,10	2
			Septic shock (敗血症性ショック)/	50*	66*						
			Infections and infestations								
			(感染症および寄生虫症)								
ITA/ [redacted]	5[redacted] CA	Yes/3	abdominal pains/	[redacted]	[redacted]	13	3	NO		999,10	2
			Abdominal pain (腹痛)/	27	39&						
			Gastrointestinal disorders (胃腸障害)								
		Yes/3	fever/	[redacted]	[redacted]	8	3	NO		999,1	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 217 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pyrexia (発熱)/	25	32				0	
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/3	TREMOR/	[redacted]	[redacted]	3	4	NO	999	2
			Tremor (振戦)/	27	29					
			Nervous system disorders (神経系障害)							
JPN/	4[redacted]	Yes/6	Neutrophil count decreased/	[redacted]	[redacted]	3	4	YES,	999,1	2
[redacted]	AS		Neutrophil count decreased (好中球数減少)/	9	11			INVESTIGATI	0	
			Investigations (臨床検査)					ONAL		
								TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 218 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	Yes/2	Acute lung injury/ Acute lung injury (急性肺損傷)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 35	[redacted] 36	2	4	NO	999,10	1
		Yes/1	Acute lung injury/ Acute lung injury (急性肺損傷)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 37	[redacted] 37	1	5	NO	999	5
JPN/ [redacted]	6[redacted] AS	Yes/2	Cytomegalovirus pneumonia/ Pneumonia cytomegaloviral (サイトメガロウイルス性肺炎)/ Infections and infestations	[redacted] 4	[redacted] 12	9	4	YES, INVESTIGATIONAL TREATMENT	999,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 219 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
JPN/ [redacted]	6[redacted] AS	Yes/1	AML recurrence/ Acute myeloid leukaemia recurrent (再発急性骨髄性白血病)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] 58	[redacted] 58	1	5	NO	999	5
		Yes/3	Platelet count decreased/ Platelet count decreased (血小板数減少)/ Investigations (臨床検査)	[redacted] 14	Ongoing		4	NO	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 220 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	5[redacted] AS	Yes/3	ileus/ Ileus (イレウス)/ Gastrointestinal disorders (胃腸障害)	[redacted] 74*	Ongoing		3	NO	999,10	1
JPN/ [redacted]	6[redacted] AS	Yes/1	Pulmonary edema/ Pulmonary oedema (肺水腫)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 31	[redacted] 31	1	5	NO	999,10	5
JPN/ [redacted]	4[redacted] AS	Yes/3	acute kidney injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] 51	[redacted] 60&	10	4	NO	999	1
		Yes/3	Generalized muscle weakness/	[redacted]	Ongoing		3	YES, OTHER	2	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 221 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Muscular weakness (筋力低下)/ Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	10				STUDY TREATMENT (NON-INVESTIGATIONAL)		
		Yes/3	thrombotic microangiopathy/ Thrombotic microangiopathy (血栓性微小血管症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted]	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 222 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	2[redacted]	Yes/3	Gastroenteritis/	[redacted]	[redacted]	17	3	YES, BOTH	999,1	2
[redacted]	AS		Gastroenteritis (胃腸炎)/	93	109			AND/OR	0	
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	gastroenteritis/	[redacted]	[redacted]	14	3	NO	999,1	2
			Gastroenteritis (胃腸炎)/	65	78				0	
			Infections and infestations							
			(感染症および寄生虫症)							
JPN/	5[redacted]	Yes/3	Acute kidney injury/	[redacted]	[redacted]	37	4	NO	2,10	3
[redacted]	AS		Acute kidney injury (急性腎障害)/	45	81					
			Renal and urinary disorders (腎および尿路障害)							
		Yes/3	Acute kidney injury/	[redacted]	[redacted]	19	3	NO	999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 223 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Acute kidney injury (急性腎障害)/	82	100&				0	
			Renal and urinary disorders (腎および尿路障害)							
		Yes/3	Acute kidney injury/	[redacted]	Ongoing		4	NO	999,1	1
			Acute kidney injury (急性腎障害)/	101&					0	
			Renal and urinary disorders (腎および尿路障害)							
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	YES, BOTH	999,1	5
			Sepsis (敗血症)/	115&	115&			AND/OR	0	
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
JPN/ [redacted]	3[redacted] AS	Yes/3	infectious enteritis/	[redacted]	[redacted]	51	3	NO	2,10	2
			Enteritis infectious (感染性腸炎)/	183*	233*					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 224 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 225 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	3[redacted] AS	Yes/3	Liver dysfunction/ Hepatic function abnormal (肝機能異常)/ Hepatobiliary disorders (肝胆道系障害)	[redacted] 310*	Ongoing		3	NO	2,10	1
		Yes/6	posterior reversible encephalopathy syndrome/ Posterior reversible encephalopathy syndrome (可逆性後白質脳症症候群)/ Nervous system disorders (神経系障害)	[redacted] 74*	[redacted] 127*	54	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2
		Yes/3	traumatic subcutaneous hematoma/ Subcutaneous haematoma (皮下血腫)/ Injury, poisoning and procedural complications (傷害、中毒および処置合併症)	[redacted] 257*	[redacted] 312*	56	2	NO	4,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 226 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	Yes/6	allergic reaction due to ATG/ Allergy to immunoglobulin therapy (免疫グロブリン療法アレルギー)/ Immune system disorders (免疫系障害)	[redacted] 1	[redacted] 2	2	2	YES, INVESTIGATIONAL TREATMENT	4,10	2
		Yes/1	idiopathic pneumonia syndrome/ Idiopathic pneumonia syndrome (特発性肺炎症候群)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 23*	[redacted] 23*	1	5	NO	999,10	5
JPN/ [redacted]	6[redacted] AS	Yes/2	respiratory failure/ Respiratory failure (呼吸不全)/	[redacted] 28*	[redacted] 40*	13	4	YES, BOTH AND/OR	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 227 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders					INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 228 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	Yes/1	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 41*	[redacted] 41*	1	5	YES, BOTH AND/OR INDISTINGUISHABLE	999,10	5
JPN/ [redacted]	5[redacted] AS	Yes/2	Acute respiratory failure/ Acute respiratory failure (急性呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 3	[redacted] 46&	44	4	NO	2,10	1
		Yes/1	Acute respiratory failure/ Acute respiratory failure (急性呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 47&	[redacted] 47&	1	5	NO	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 229 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	6[redacted]	Yes/6	systemic adenovirus infection/	[redacted]	[redacted]	12	3	YES, BOTH	3,10	1
[redacted]	AS		Adenovirus infection (アデノウイルス感染)/	34*	45*			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	systemic adenovirus infection/	[redacted]	[redacted]	10	4	YES, BOTH	5,10	1
			Adenovirus infection (アデノウイルス感染)/	46*	55*			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/1	systemic adenovirus infection/	[redacted]	[redacted]	1	5	YES, BOTH	999,10	5
			Adenovirus infection (アデノウイルス感染)/	56*	56*			AND/OR		
			Infections and infestations					INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 230 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
KOR/ [redacted]	3[redacted] AS	Yes/3	Rash maculo-papular/ Rash maculo-papular (斑状丘疹状皮疹)/ Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)	[redacted] 68	[redacted] 93	26	2	NO		2,10	2
NOR/ [redacted]	3[redacted] CA	Yes/3	stomach pain/ Abdominal pain upper (上腹部痛)/ Gastrointestinal disorders (胃腸障害)	[redacted] 45	Ongoing		1	NO		2,10	1
		Yes/3	Residues of erythroleukemia/ Erythroleukaemia (赤白血病)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞	[redacted] 71	Ongoing		1	NO		999,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 231 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			およびポリープを含む）)							
		Yes/3	HHV6 infection/	[redacted]	[redacted]	6	3	NO	2	2
			Human herpesvirus 6 infection	37	42					
			(ヒトヘルペスウイルス６感染)/							
			Infections and infestations							
			(感染症および寄生虫症)							
SAU/ [redacted]	3[redacted] CA	Yes/3	diarrhea/	[redacted]	[redacted]	6	4	NO	2,10	2
			Diarrhoea (下痢)/	15	20					
			Gastrointestinal disorders (胃腸障害)							
		Yes/3	hypotension/	[redacted]	[redacted]	3	3	NO	2,10	2
			Hypotension (低血圧)/	21	23					
			Vascular disorders (血管障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 232 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
SAU/	3[redacted]	Yes/2,3	decrease platelet/	[redacted]	[redacted]	12	4	NO		2,10	3
[redacted]	CA		Platelet count decreased (血小板数減少)/	9	20						
			Investigations (臨床検査)								
		Yes/2	septic shock/	[redacted]	[redacted]	3	4	NO		2,10	2
			Septic shock (敗血症性ショック)/	21	23						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	urine infection/	[redacted]	[redacted]	3	3	NO		2,10	2
			Urinary tract infection (尿路感染)/	21	23						
			Infections and infestations								
			(感染症および寄生虫症)								
SAU/	5[redacted]	Yes/1	cardiopulmonary arrest/	[redacted]	[redacted]	1	5	NO		999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 233 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	OTH		Cardio-respiratory arrest (心肺停止)/	82	82					
			Cardiac disorders (心臓障害)							
		Yes/2,3	decrease level of consciousness/	[redacted]	Ongoing		4	NO	999,1	1
			Depressed level of consciousness	81					0	
			(意識レベルの低下)/							
			Nervous system disorders (神経系障害)							
		Yes/3	febrile neutropenia/	[redacted]	[redacted]	2	4	NO	2,10	2
			Febrile neutropenia (発熱性好中球減少症)/	68	69					
			Blood and lymphatic system disorders							
			(血液およびリンパ系障害)							
		Yes/2,3	intracranial hemorrhage/	[redacted]	Ongoing		4	NO	999	1
			Haemorrhage intracranial (頭蓋内出血)/	81						
			Nervous system disorders (神経系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 234 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
SAU/ [redacted]	5[redacted]	Yes/3	leukopenia/	[redacted]	[redacted]	8	4	YES, BOTH	2,10	2
[redacted]	OTH		Leukopenia (白血球減少症)/	18	25			AND/OR		
			Blood and lymphatic system disorders					INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		
		Yes/3	decrease platelet/	[redacted]	Ongoing		4	YES, BOTH	5,10	1
			Platelet count decreased (血小板数減少)/	68				AND/OR		
			Investigations (臨床検査)					INDISTINGUI		
								SHABLE		
		Yes/3	septic shock/	[redacted]	[redacted]	7	4	NO	2,10	2
			Septic shock (敗血症性ショック)/	69	75					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	decrease WBC/	[redacted]	[redacted]	6	4	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 235 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			White blood cell count decreased (白血球数減少)/	68	73					
			Investigations (臨床検査)							
TUR/	5[redacted]	Yes/3	pneumonia/	[redacted]	[redacted]	17	3	NO	999,10	2
[redacted]	OTH		Pneumonia (肺炎)/	-9	8					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	pyelonephritis/	[redacted]	[redacted]	3	3	YES,	5,10	1
			Pyelonephritis (腎盂腎炎)/	23	25			INVESTIGATI		
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/1	pyelonephritis/	[redacted]	[redacted]	1	5	YES,	999	5
			Pyelonephritis (腎盂腎炎)/	26	26			INVESTIGATI		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 236 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations					ONAL		
			(感染症および寄生虫症)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 237 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
TUR/ [redacted]	3[redacted] CA	Yes/ 2,3,6	respiratory insufficiency/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 25	Ongoing		4	NO		2,10	1
		Yes/ 1,2,3	septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] 26	[redacted] 26	1	5	NO		2,10	5
TUR/ [redacted]	2[redacted] AS	Yes/3	Disease relapse/ Disease recurrence (疾患再発)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 94	[redacted] 123	30	4	NO		5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 238 of 238)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/1	Disease relapse/	[redacted]	[redacted]	1	5	NO		999	5
			Disease recurrence (疾患再発)/	124&	124&						
			General disorders and administration site conditions								
			(一般・全身障害および投与部位の状態)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Table 7-6 急性 GVHD の投与中止に至った有害事象の一覧（C2301 試験，SAF，データカットオフ 2 まで）

Listing 14.3.2-3.1 Adverse events leading to discontinuation **(**Safety Set**)**

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 1 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/	4[redacted]	Yes/	Gram Negative Sepsis/	[redacted]	[redacted]	8	4	YES, BOTH AND/	5,10	2
[redacted]	CA	2,3,6	Bacterial sepsis (細菌性敗血症)/	[redacted]	[redacted]			OR		
			Infections and infestations	37	44			INDISTINGUISH		
			(感染症および寄生虫症)					ABLE		
		Yes/3	Febrile Neutropenia/	[redacted]	[redacted]	2	3	YES, BOTH AND/	5,10	2
			Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]			OR		
			Blood and lymphatic system disorders	36	37			INDISTINGUISH		
			(血液およびリンパ系障害)					ABLE		
		No	Neutropenia/	[redacted]	[redacted]	6	4	YES, BOTH AND/	5,10	3
			Neutropenia (好中球減少症)/	[redacted]	[redacted]			OR		
			Blood and lymphatic system disorders	36	41			INDISTINGUISH		
			(血液およびリンパ系障害)					ABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 2 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	1[redacted] CA	No	altered cognitive state/ Cognitive disorder (認知障害)/ Nervous system disorders (神経系障害)	[redacted] 19	Ongoing		3	NO	5,10	1
		Yes/2	Microangiopathy/ Microangiopathy (微小血管症)/ Vascular disorders (血管障害)	[redacted] 18	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	5,10	1
AUS/ [redacted]	3[redacted] WH	Yes/3	Mucormycosis sinus infection/ Mucormycosis (ムコール症)/	[redacted]	[redacted]	18	3	YES, BOTH AND/ OR	5,10	4

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 3 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	48	65			INDISTINGUISH		
			(感染症および寄生虫症)					ABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 4 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/6	Viral infection Reactivation/	[redacted]	[redacted]	43	3	YES,	5,10	2
			Viral infection (ウイルス感染)/	[redacted]	[redacted]			INVESTIGATION		
			Infections and infestations	28	70&			AL TREATMENT		
			(感染症および寄生虫症)							
DEU/ [redacted]	4[redacted] CA	No	Anemia intermittent/	[redacted]	[redacted]	47	3	YES,	5,10	2
			Anaemia (貧血)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	1	47			AL TREATMENT		
			(血液およびリンパ系障害)							
		No	Leukopenia intermittent/	[redacted]	[redacted]	4	3	YES,	5	2
			Leukopenia (白血球減少症)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	42	45			AL TREATMENT		
			(血液およびリンパ系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 5 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	No	Anemia intermittent/	[redacted]	[redacted]	28	3	YES,	5,10	3
			Anaemia (貧血)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	2	29			AL TREATMENT		
			(血液およびリンパ系障害)							
		No	Leukopenia intermittent/	[redacted]	[redacted]	18	3	YES,	5,10	3
			Leukopenia (白血球減少症)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	14	31			AL TREATMENT		
			(血液およびリンパ系障害)							
		No	Thrombocytopenia/	[redacted]	[redacted]	30	4	YES,	5,10	3
			Thrombocytopenia (血小板減少症)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	-1	29			AL TREATMENT		
			(血液およびリンパ系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 6 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/	5[redacted]	Yes/3	adenoviral infection of bladder/	[redacted]	[redacted]	58	3	YES,	5,10	2
[redacted]	CA		Cystitis viral (ウイルス性膀胱炎)/	[redacted]	[redacted]			INVESTIGATION		
			Infections and infestations	29	86&			AL TREATMENT		
			(感染症および寄生虫症)							
DEU/	6[redacted]	Yes/6	CMV Colitis/	[redacted]	Ongoing		3	YES, BOTH AND/	5,10	1
[redacted]	CA		Cytomegalovirus colitis	[redacted]				OR		
			(サイトメガロウイルス性大腸炎)/	133				INDISTINGUISH		
			Infections and infestations					ABLE		
			(感染症および寄生虫症)							
		No	Neutropenia/	[redacted]	Ongoing		4	YES,	5	1
			Neutropenia (好中球減少症)/	[redacted]				INVESTIGATION		
			Blood and lymphatic system disorders	132				AL TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 7 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(血液およびリンパ系障害)							
		Yes/2	Sepsis/	[redacted]	[redacted]	2	4	YES, BOTH AND/	5,10	1
			Sepsis (敗血症)/	[redacted]	[redacted]			OR		
			Infections and infestations	134	135			INDISTINGUISH		
			(感染症および寄生虫症)					ABLE		
		Yes/1	Sepsis/	[redacted]	[redacted]	1	5	YES, BOTH AND/	5,10	5
			Sepsis (敗血症)/	[redacted]	[redacted]			OR		
			Infections and infestations	135	135			INDISTINGUISH		
			(感染症および寄生虫症)					ABLE		
DEU/ [redacted]	5[redacted] CA	Yes/1	Pneumonia/	[redacted]	[redacted]	1	5	YES,	5,10	5
			Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATION		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 8 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	39	39			AL TREATMENT		
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 9 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	4[redacted] CA	Yes/3	CMV Colitis/ Cytomegalovirus colitis (サイトメガロウイルス性大腸炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 86	[redacted] [redacted] 174&	89	3	YES, OTHER STUDY TREATMENT (NON- INVESTIGATION AL)	5,10	2
DEU/ [redacted]	5[redacted] CA	Yes/3	Encephalopathy/ Encephalopathy (脳症)/ Nervous system disorders (神経系障害)	[redacted] [redacted] 36	Ongoing		4	YES, BOTH AND/ OR INDISTINGUISH ABLE	5,10	1
DEU/	6[redacted]	No	Panzytopenia/	[redacted]	Ongoing		3	NO	5	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 10 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Pancytopenia (汎血球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 16						
DEU/ [redacted]	6[redacted] CA	Yes/2	worsening of lower gastrointestinal hemorrhage/ Lower gastrointestinal haemorrhage (下部消化管出血)/ Gastrointestinal disorders (胃腸障害)	[redacted] [redacted] 51	[redacted] [redacted] 52	2	4	YES, INVESTIGATIONAL TREATMENT	5,10	3
DNK/ [redacted]	6[redacted] WH	Yes/6	pulmonary embolism/ Pulmonary embolism (肺塞栓症)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 9	Ongoing		3	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 11 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ESP/ [redacted]	5[redacted] CA	No	Myelodisplasic syndrome Relapse/ Myelodysplastic syndrome (骨髄異形成症候群)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] [redacted] 91	Ongoing		2	NO		5,10	1
ESP/ [redacted]	5[redacted] CA	Yes/1,3	respiratory infection by neumococo/ Respiratory tract infection bacterial (細菌性気道感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 19	[redacted] [redacted] 19	1	5	NO		5,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 12 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/ [redacted]	5[redacted] CA	No	PLATELET COUNT DECREASED/ Platelet count decreased (血小板数減少)/ Investigations (臨床検査)	[redacted] [redacted] 99	[redacted] [redacted] 150&	52	4	YES, BOTH AND/ OR INDISTINGUISH ABLE	5	3
ESP/ [redacted]	5[redacted] UN	Yes/6	Intestinal obstruction/ Intestinal obstruction (腸閉塞)/ Gastrointestinal disorders (胃腸障害)	[redacted] [redacted] 21	[redacted] [redacted] 22	2	3	NO	5,10	2
FRA/ [redacted]	5[redacted] OTH	Yes/6	Neutrophil count decreased/ Neutrophil count decreased (好中球数減少)/ Investigations (臨床検査)	[redacted] [redacted] 14	Ongoing		4	YES, INVESTIGATION AL TREATMENT	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 13 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] CA	Yes/3	thromboembolic event/	[redacted]	[redacted]	1	3	NO	5,10	2
			Embolism (塞栓症)/	[redacted]	[redacted]					
			Vascular disorders (血管障害)	93	93					
FRA/ [redacted]	3[redacted] UN	No	anemia/	[redacted]	Ongoing		3	NO	5,10	1
			Anaemia (貧血)/	[redacted]						
			Blood and lymphatic system disorders	21						
			(血液およびリンパ系障害)							
		No	hypoxia/	[redacted]	Ongoing		3	NO	5,10	1
			Hypoxia (低酸素症)/	[redacted]						
			Respiratory, thoracic and mediastinal disorders	21						
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	pneumopathy klebsielle/	[redacted]	Ongoing		3	YES, OTHER	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 14 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonia klebsiella (クレブシエラ菌性肺炎)/	[redacted]				STUDY		
			Infections and infestations	21				TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		
		Yes/3	Sepsis at pseudomonas/	[redacted]	[redacted]	35	3	NO	5,10	1
			Pseudomonal sepsis (シュードモナス性敗血症)/	[redacted]	[redacted]					
			Infections and infestations	21	55&					
			(感染症および寄生虫症)							
		No	fever/	[redacted]	Ongoing		1	NO	5	1
			Pyrexia (発熱)/	[redacted]						
			General disorders and administration site conditions	21						
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 15 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/ [redacted]	3[redacted] UN	No	tachycardia/ Tachycardia (頻脈)/ Cardiac disorders (心臓障害)	[redacted] 21	Ongoing		3	NO		5	1
		No	thrombopenia/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 21	Ongoing		4	NO		5,10	1
FRA/ [redacted]	6[redacted] CA	Yes/1,3	General condition alteration/ General physical condition abnormal (全身健康状態異常)/ Investigations (臨床検査)	[redacted] 20	[redacted] 20	1	5	NO		5	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 16 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	3[redacted] CA	Yes/3	cephalgia/ Headache (頭痛)/ Nervous system disorders (神経系障害)	[redacted] [redacted] 41	Ongoing		2	NO	5	1
FRA/ [redacted]	6[redacted] UN	No	Hepatic cytolysys/ Hepatocellular injury (肝細胞損傷)/ Hepatobiliary disorders (肝胆道系障害)	[redacted] [redacted] 33	Ongoing		2	YES, INVESTIGATION AL TREATMENT	5	1
FRA/ [redacted]	2[redacted] OTH	Yes/6	Graft loss/ Graft loss (移植片機能損失)/ Injury, poisoning and procedural complications (傷害、中毒および処置合併症)	[redacted] [redacted] 74	Ongoing		2	YES, INVESTIGATION AL TREATMENT	5	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 17 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] UN	No	pancytopenia/ Pancytopenia (汎血球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 15	Ongoing		4	YES, INVESTIGATION AL TREATMENT	5,10	1
FRA/ [redacted]	5[redacted] UN	No	Diffuse large B cell Lymphoma/ Diffuse large B-cell lymphoma (びまん性大細胞型Ｂ細胞性リンパ腫)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] [redacted] 77	Ongoing		3	YES, BOTH AND/ OR INDISTINGUISH ABLE	5,10	1
		Yes/2,3	ILEUM PERFORATION/	[redacted]	[redacted]	64	4	YES, BOTH AND/	5,10	4

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 18 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Ileal perforation (回腸穿孔)/	[redacted]	[redacted]			OR		
			Gastrointestinal disorders (胃腸障害)	77	140&			INDISTINGUISHABLE		
GBR/ [redacted]	5[redacted] CA	No	Relapse of actue leukamia, diagnosis of myeloid sarcoma/	[redacted]	Ongoing		1	NO	5	1
			Leukaemia recurrent (白血病再発)/	[redacted]						
			Neoplasms benign, malignant and unspecified (incl cysts and polyps)	340						
			(良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)							
ISR/ [redacted]	6[redacted] CA	No	neutropenia/	[redacted]	[redacted]	9	4	NO	5	2
			Neutropenia (好中球減少症)/	[redacted]	[redacted]					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 19 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Blood and lymphatic system disorders	137	145					
			(血液およびリンパ系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 20 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	4[redacted] WH	No	thrombocytopenia/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 24	[redacted] [redacted] 58	35	4	YES, INVESTIGATION AL TREATMENT	5	2
ITA/ [redacted]	2[redacted] WH	No	TROMBOCITOPENIA/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 22	Ongoing		4	YES, BOTH AND/ OR INDISTINGUISH ABLE	5	1
ITA/ [redacted]	5[redacted] CA	No	NEUTROPENIA/ Neutropenia (好中球減少症)/ Blood and lymphatic system disorders	[redacted] [redacted] 70	[redacted] [redacted] 98	29	3	YES, BOTH AND/ OR INDISTINGUISH	5	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 21 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(血液およびリンパ系障害)					ABLE		
ITA/ [redacted]	4[redacted] CA	No	graft loss/ Graft loss (移植片機能損失)/ Injury, poisoning and procedural complications (傷害、中毒および処置合併症)	[redacted] [redacted] 33	Ongoing		3	NO	5	1
JPN/ [redacted]	6[redacted] AS	Yes/2	Sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 76	[redacted] [redacted] 82	7	4	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 22 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	No	Platelet count decreased/ Platelet count decreased (血小板数減少)/ Investigations (臨床検査)	[redacted] 68	[redacted] 73	6	2	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	1
JPN/ [redacted]	5[redacted] AS	Yes/6	sepsis/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 15	[redacted] 30	16	4	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	2
JPN/ [redacted]	6[redacted] AS	Yes/3	Guillain-Barre syndrome/ Guillain-Barre syndrome (ギラン・バレー症候群)/	[redacted] 155	[redacted] 183	29	3	YES, BOTH AND/ OR INDISTINGUISH	5,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 23 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Nervous system disorders (神経系障害)					ABLE		
KOR/ [redacted]	5[redacted] AS	Yes/1	Cardiac arrest/	[redacted]	[redacted]	1	5	NO	5,10	5
			Cardiac arrest (心停止)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	14	14					
RUS/ [redacted]	3[redacted] CA	No	dysphagia/	[redacted]	Ongoing		2	NO	5,10	1
			Dysphagia (嚥下障害)/	[redacted]						
			Gastrointestinal disorders (胃腸障害)	33						
		No	jejunal ulcer/	[redacted]	Ongoing		3	NO	5	1
			Jejunal ulcer (空腸潰瘍)/	[redacted]						
			Gastrointestinal disorders (胃腸障害)	34						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 24 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
RUS/ [redacted]	3[redacted] CA	Yes/1	Sepsis/	[redacted]	[redacted]	1	5	NO	5,10	5
			Sepsis (敗血症)/	[redacted]	[redacted]					
			Infections and infestations	38	38					
			(感染症および寄生虫症)							
		No	Jejunal hemorrhage/	[redacted]	Ongoing		3	NO	5	1
			Small intestinal haemorrhage (小腸出血)/	[redacted]						
			Gastrointestinal disorders (胃腸障害)	34						
TUR/ [redacted]	5[redacted] CA	Yes/2	Gram Negative Sepsis/	[redacted]	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	5,10	1
			Bacterial sepsis (細菌性敗血症)/	[redacted]						
			Infections and infestations	41						
			(感染症および寄生虫症)							
		Yes/1	Gram Negative Sepsis/	[redacted]	[redacted]	1	5	YES,	5,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 25 of 43)
Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Bacterial sepsis (細菌性敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 41	[redacted] 41			INVESTIGATIONAL TREATMENT		
TUR/ [redacted]	5[redacted] WH	Yes/3	glioblastoma multiforme/ Glioblastoma multiforme (多形性神経膠芽細胞腫)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] [redacted] 62	Ongoing		3	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 26 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/ [redacted]	2[redacted] CA	No	Neutropenia/ Neutropenia (好中球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 21*	[redacted] 22*	2	4	YES, INVESTIGATION AL TREATMENT	5,10	1
		No	THROMBOCYTOPENIA/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 15*	[redacted] 21*	7	3	YES, INVESTIGATION AL TREATMENT	5	1
AUS/ [redacted]	5[redacted] WH	Yes/3	confusion by lymphoma brain/ Central nervous system lymphoma (中枢神経系リンパ腫)/ Neoplasms benign, malignant and unspecified (incl cysts	[redacted] 21*	[redacted] 47&	27	4	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 27 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)							
CAN/ [redacted]	5[redacted] CA	Yes/1	STROKE/ Cerebrovascular accident (脳血管発作)/ Nervous system disorders (神経系障害)	[redacted] [redacted] 7*	[redacted] [redacted] 8*	2	5	NO	5,10	5
		No	THROMBOCYTOPENIA/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 7*	Ongoing		4	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 28 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/ [redacted]	6[redacted] CA	No	anemia/ Anaemia (貧血)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 26	[redacted] [redacted] 26	1	3	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	2
		No	hemolysis/ Haemolysis (溶血)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 21	Ongoing		3	YES, BOTH AND/ OR INDISTINGUISHABLE	5	1
		Yes/3	Steroid induced myopathy/ Myopathy (ミオパチー)/ Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	[redacted] [redacted] 21	[redacted] [redacted] 31	11	3	YES, OTHER STUDY TREATMENT (NON- INVESTIGATION	5	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 29 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								AL)		
CAN/ [redacted]	5[redacted] CA	Yes/1	Respiratory Failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted]	[redacted]	1	5	NO	5	5
DEU/ [redacted]	6[redacted] CA	Yes/ 1,2,3	Septic shock/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted]	[redacted]	1	5	YES, INVESTIGATION AL TREATMENT	5,10	5
DEU/	5[redacted]	Yes/3	gut bleeding/	[redacted]	[redacted]	2	4	YES,	5,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 30 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Gastrointestinal haemorrhage (胃腸出血)/	[redacted]	[redacted]			INVESTIGATION		
			Gastrointestinal disorders (胃腸障害)	34*	35*			AL TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 31 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	6[redacted] CA	Yes/1	acute respiratory insufficiency/	[redacted]	[redacted]	1	5	NO	5,10	5
			Acute respiratory failure (急性呼吸不全)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	8	8					
			(呼吸器、胸郭および縦隔障害)							
DEU/ [redacted]	6[redacted] CA	No	platelet Count reduced/	[redacted]	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	5,10	1
			Platelet count decreased (血小板数減少)/	[redacted]						
			Investigations (臨床検査)	40*						
ESP/ [redacted]	6[redacted] CA	Yes/2	respiratory insufficiency/	[redacted]	[redacted]	9	4	NO	5,10	1
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	16	24					
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 32 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/ [redacted]	6[redacted] CA	Yes/3	SEPSIS/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 43	[redacted] [redacted] 58	16	4	NO		5,10	2
FRA/ [redacted]	4[redacted] UN	No	pancytopenia/ Pancytopenia (汎血球減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 29*	Ongoing		3	NO		5	1
FRA/ [redacted]	5[redacted]	No	gastrointestinal bleeding/	[redacted]	[redacted]	7	3	NO		5,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 33 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	UN		Gastrointestinal haemorrhage (胃腸出血)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	23*	29*					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 34 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	5[redacted] UN	No	sub occlusion (intestinal)/	[redacted]	[redacted]	4	3	NO	5,10	2
			Intestinal obstruction (腸閉塞)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	23*	26*					
FRA/ [redacted]	6[redacted] UN	No	Thrombopenia/	[redacted]	[redacted]	35	4	YES,	5	3
			Thrombocytopenia (血小板減少症)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	43	77			AL TREATMENT		
			(血液およびリンパ系障害)							
		No	Thrombopenia/	[redacted]	[redacted]	6	3	YES,	5	3
			Thrombocytopenia (血小板減少症)/	[redacted]	[redacted]			INVESTIGATION		
			Blood and lymphatic system disorders	78	83&			AL TREATMENT		
			(血液およびリンパ系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

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Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 35 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/ [redacted]	7[redacted] UN	No	hepatic cytolysis/ Hepatocellular injury (肝細胞損傷)/ Hepatobiliary disorders (肝胆道系障害)	[redacted] [redacted] 43	Ongoing		3	NO	5	1
FRA/ [redacted]	6[redacted] CA	Yes/3	SEPSIS/ Sepsis (敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 40*	[redacted] [redacted] 50*	11	4	NO	5,10	2
FRA/ [redacted]	1[redacted] UN	Yes/2	Thrombopenia [intermitent]/ Thrombocytopenia (血小板減少症)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] [redacted] 7*	[redacted] [redacted] 93&	87	4	YES, INVESTIGATION AL TREATMENT	5	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 36 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/ [redacted]	4[redacted] CA	Yes/6	Neutraphil count decreased/ Neutrophil count decreased (好中球数減少)/ Investigations (臨床検査)	[redacted] [redacted] 107*	Ongoing		4	YES, BOTH AND/ OR INDISTINGUISHABLE	5	1
ISR/ [redacted]	2[redacted] CA	Yes/2	SEPTIC SHOCK/ Septic shock (敗血症性ショック)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 10	[redacted] [redacted] 11	2	4	NO	5,10	1
ISR/ [redacted]	4[redacted] CA	No	decreased blood count/ Full blood count decreased (全血球数減少)/ Investigations (臨床検査)	[redacted] [redacted] 12*	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	5	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 37 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/3	Gastroestinal tract bleeding/	[redacted]	[redacted]	8	2	NO		5,10	2
			Gastrointestinal haemorrhage (胃腸出血)/	[redacted]	[redacted]						
			Gastrointestinal disorders (胃腸障害)	51	58*						
ISR/ [redacted]	1[redacted] CA	No	EBV infection worsening/	[redacted]	[redacted]	1	2	NO		5	1
			Epstein-Barr virus infection	[redacted]	[redacted]						
			(エプスタイン・バーウイルス感染)/	1	1						
			Infections and infestations								
			(感染症および寄生虫症)								
		No	Worsening of Epstein?Barr virus infection/	[redacted]	Ongoing		3	NO		5,10	1
			Epstein-Barr virus infection	[redacted]							
			(エプスタイン・バーウイルス感染)/	2							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 38 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 39 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	5[redacted] WH	No	liver siderosis/ Hepatic siderosis (肝鉄症)/ Hepatobiliary disorders (肝胆道系障害)	[redacted] [redacted] 157	Ongoing		3	NO	5,10	1
ITA/ [redacted]	4[redacted] CA	Yes/2,3	respiratory failure/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] [redacted] 82*	[redacted] [redacted] 83*	2	4	NO	5,10	4
ITA/ [redacted]	6[redacted] WH	Yes/3	Encephalitis infection/ Encephalitis (脳炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 53*	[redacted] [redacted] 107&	55	4	YES, INVESTIGATION AL TREATMENT	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 40 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	1[redacted] WH	Yes/3	Increase of transaminases/ Transaminases increased (トランスアミナーゼ上昇)/ Investigations (臨床検査)	[redacted] [redacted] 18*	Ongoing		4	YES, INVESTIGATIONAL TREATMENT	5	3
JPN/ [redacted]	6[redacted] AS	No	idiopathic pneumonia syndrome/ Idiopathic pneumonia syndrome (特発性肺炎症候群)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] [redacted] 3*	[redacted] [redacted] 22*	20	3	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 41 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	6[redacted] AS	Yes/2	respiratory failure/	[redacted]	[redacted]	13	4	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	1
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	28*	40*					
JPN/ [redacted]	6[redacted] AS	Yes/2	systemic adenovirus infection/	[redacted]	[redacted]	10	4	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	1
			Adenovirus infection (アデノウイルス感染)/	[redacted]	[redacted]					
			Infections and infestations (感染症および寄生虫症)	46*	55*					
SAU/ [redacted]	5[redacted] OTH	Yes/3	decrease platelet/	[redacted]	Ongoing		4	YES, BOTH AND/ OR INDISTINGUISHABLE	5,10	1
			Platelet count decreased (血小板数減少)/	[redacted]						
			Investigations (臨床検査)	68						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 42 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
								ABLE		
TUR/ [redacted]	5[redacted] OTH	No	pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 23	Ongoing		4	YES, BOTH AND/ OR INDISTINGUISH ABLE	5,10	1
		Yes/3	pyelonephritis/ Pyelonephritis (腎盂腎炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 23	[redacted] 25	3	3	YES, INVESTIGATION AL TREATMENT	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.

CINC424C2301-Secondary CSR

Listing s14.3.2-3.1 Adverse events leading to discontinuation (Safety set) (Page 43 of 43)
Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
TUR/ [redacted]	2[redacted] AS	Yes/3	Disease relapse/	[redacted]	[redacted]	30	4	NO		5,10	1
			Disease recurrence (疾患再発)/	[redacted]	[redacted]						
			General disorders and administration site conditions	94	123						
			(一般・全身障害および投与部位の状態)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
* Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment; & Data collected during the post-treatment period.
MedDRA version 22.1, CTCAE version 4.03.
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Table 7-7　　急性 GVHD の死亡一覧（271 試験，SAF）

被験者番号	PT	発現日, 死亡日 (日目)	発現から死亡までの日数	RUX との関連	副腎皮質ステロイドとの関連
[redacted]	肺炎	5, 10	6	No	No
	ブドウ球菌性敗血症	5, 10	6	No	No
	呼吸不全	5, 10	6	No	No
[redacted]	敗血症	18, 63	46	No	Yes
[redacted]	肺感染	315, 331	17	No	No
[redacted]	急性移植片対宿主病	24, 52	29	No	No
[redacted]	静脈閉塞性肝疾患	2, 10	9	No	No
	医療機器関連感染	3, 10	8	No	Yes
	多臓器機能不全症候群	4, 10	7	No	Yes
[redacted]	無脈性電気活動	9, 9	1	No	No
[redacted]	腎尿細管壊死*	161, 165	5	No	Yes
[redacted]	真菌血症	22, 33	12	No	No
[redacted]	呼吸不全	28, 28	1	No	No
[redacted]	疾患進行*	37, 37	1	No	No
[redacted]	呼吸不全	141, 149	9	No	Yes
[redacted]	呼吸不全	242, 280	39	No	No
[redacted]	肝移植片対宿主病	23, 27	5	No	No
[redacted]	腹膜炎	10, 13	4	No	No
	多臓器機能不全症候群	13, 13	1	No	No
[redacted]	呼吸不全	39, 49	11	No	No
[redacted]	肝不全	21, 23	3	No	No
[redacted]	胃腸出血	42, 42	1	No	No
[redacted]	カンジダ感染	24, 41	18	No	Yes
[redacted]	消化管移植片対宿主病	8, 47	40	No	No
[redacted]	レジオネラ菌性肺炎	22, 30	9	No	Yes
[redacted]	肝不全	21, 23	3	No	No
	敗血症性ショック	21, 23	3	No	Yes
	ブドウ球菌性菌血症	21, 23	3	No	Yes
	急性腎障害	22, 23	2	No	No
[redacted]	呼吸不全	38, 38	1	No	No
[redacted]	下部消化管出血	19, 45	27	No	No
[redacted]	肺出血	50, 51	2	Yes	Yes
[redacted]	敗血症	41, 42	2	Yes	Yes
[redacted]	突然死	34, 34	1	No	No
[redacted]	疾患進行	48, 62	15	No	No
[redacted]	肝損傷	3, 16	14	No	No
[redacted]	心停止	93, 93	1	No	No

被験者番号	PT	発現日, 死亡日 (日目)	発現から死亡までの日数	RUX との関連	副腎皮質ステロイドとの関連
[redacted]	疾患進行	9, 14	6	No	No

Source: 5.3.5.2-1-271 試験-Listing 2.7.6
発現日 = 死亡に至った有害事象の発現日 – 初回投与日 + 1
死亡日 = 死亡した日 – 初回投与日 + 1
*：最終投与後 30 日より後の死亡
MedDRA version 19.1

Table 7-8 急性 GVHD の重篤な有害事象の一覧（271 試験，SAF）

被験者番号	PT	発現日, 消失日(日目)	持続期間 (日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
[redacted]	上室性頻脈	5, 6	2	4	No	No	Drug withdrawn	Concomitant medication was given	Recovered/resolved
	肺炎	5, 10	6	4	No	No	Drug withdrawn	Concomitant medication was given	Fatal
	ブドウ球菌性敗血症	5, 10	6	4	No	No	Drug withdrawn	Concomitant medication was given	Fatal
	呼吸不全	5, 10	6	4	No	No	Drug withdrawn	Concomitant medication was given/Procedure or non-drug therapy performed	Fatal
[redacted]	疼痛	18, 63	46	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	敗血症	18, 63	46	4	No	Yes	Drug withdrawn	Concomitant medication was given	Fatal
[redacted]	筋力低下	30, 46	17	3	No	Yes	Dose not changed	None	Recovered/resolved
	肺感染	121, 131	11	3	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
	肺感染	180, 224	45	3	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
	急性腎障害	236, 243	8	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	敗血症	245, 254	10	4	No	No	Dose not changed		Recovered/resolved
	肺感染	245, 271	27	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved with sequelae
	失神	259, 261	3	3	No	No	Dose not	Procedure or non-	Recovered/reso

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
							changed	drug therapy performed	lved
	上気道感染	269, 273	5	3	No	No	Dose not changed	None	Recovered/resolved
	発熱	291, 302	12	1	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	肺感染	315, 331	17	4	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Fatal
[redacted]	敗血症	22, 27	6	3	No	No	Drug withdrawn	Concomitant medication was given	Recovered/resolved
	急性移植片対宿主病	24, 52	29	4	No	No	Not applicable		Fatal
[redacted]	腸球菌感染	60, 73	14	3	Yes	Yes	Dose not changed	None	Recovered/resolved
	脳症	60, 99	40	3	Yes	Yes	Dose not changed	None	Recovered/resolved
	胆嚢炎	124, 160	37	3	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved with sequelae
	菌血症	132, 134	3	3	No	No	Dose not changed	None	Recovered/resolved
[redacted]	低ナトリウム血症	70, 73	4	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	頭痛	92, 93	2	3	No	No	Not applicable	None	Recovered/resolved
	肺感染	92, 202	111	3	Yes	No	Not applicable	Concomitant medication was given	Recovered/resolved
	大腸菌性尿路感染	93, 97	5	3	No	No	Not applicable	Concomitant medication was given	Recovered/resolved
	深部静脈血栓症	98, 154	57	2	No	No	Not applicable	Concomitant medication was given	Recovered/resolved
	深部静脈血栓症	103, 154	52	2	No	No	Not applicable	Concomitant medication was given	Recovered/resolved
[redacted]	細菌性肺炎	69, 103	35	3	No	No	Not applicable	Concomitant medication was given	Recovered/resolved
[redacted]	静脈閉塞性肝疾患	2, 10	9	4	No	No	Dose not changed	None	Fatal
	医療機器関連感染	3, 10	8	4	No	Yes	Dose reduced	Concomitant medication was given/Procedure or non-drug therapy performed	Fatal

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
	多臓器機能不全症候群	4, 10	7	4	No	Yes	Dose interrupted	None	Fatal
[redacted]	無脈性電気活動	9, 9	1	4	No	No	Drug withdrawn	Procedure or non-drug therapy performed	Fatal
	敗血症性ショック	9,		4	No	No	Dose interrupted	None	Not recovered/not resolved
[redacted]	敗血症	116, 119	4	3	Yes		Dose not changed	Concomitant medication was given	Recovered/resolved
	副鼻腔炎	116, 126	11	3	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	副鼻腔炎	177, 180	4	3	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	インフルエンザ	185, 189	5	3	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	肺炎	185, 189	5	3	Yes	No	Dose not changed	None	Recovered/resolved
	発熱	208, 210	3	3	Yes	No	Dose not changed	None	Recovered/resolved
	インフルエンザ	218, 220	3	2	Yes		Dose not changed	Concomitant medication was given	Recovered/resolved
	クレブシエラ性菌血症	230, 232	3	3	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	インフルエンザ	247, 248	2	3	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	インフルエンザ	252, 255	4	2	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	発熱	262, 263	2	1	Yes		Dose not changed	Concomitant medication was given	Recovered/resolved
	発熱	368, 370	3	3	Yes	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	貧血	46, 49	4	2	No	No	Dose interrupted	None	Recovered/resolved
	ブドウ球菌性菌血症	95, 99	5	3	Yes	No	Dose interrupted	Concomitant medication was given	Recovered/resolved
	錯乱状態	95, 114	20	3	Yes	No	Dose interrupted		Recovered/resolved
	血小板数減少	96, 118	23	4	Yes	No	Dose interrupted		Recovered/resolved
	筋力低下	96,		3	No	Yes	Dose not changed		Not recovered/not resolved
	自殺念慮	97, 99	3	2	No	No	Dose not changed	None	Recovered/resolved
	感染性小腸結	99, 114	16	3	Yes	No	Dose not	Concomitant	Recovered/reso

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
	腸炎						changed	medication was given	lved
	蜂巣炎*	152,		3	No	Yes	Not applicable	Concomitant medication was given	Not recovered/not resolved
	シュードモナス性菌血症*	152,		3	No	Yes	Not applicable	None	Not recovered/not resolved
	脳症*	152,		3	No	No	Not applicable	None	Not recovered/not resolved
	腎尿細管壊死*	161, 165	5	4	No	Yes	Not applicable	None	Fatal
[redacted]	失明	14,		2	No	No	Dose interrupted	Concomitant medication was given	Not recovered/not resolved
	真菌性眼内炎	21,		4	No	No	Dose interrupted	Concomitant medication was given	Not recovered/not resolved
	真菌血症	22, 33	12	4	No	No	Drug withdrawn	Concomitant medication was given	Fatal
	呼吸不全	28,		4	No	No	Drug withdrawn	Procedure or non-drug therapy performed	Not recovered/not resolved
[redacted]	膀胱炎	14, 39	26	2	No	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	呼吸不全	28, 28	1	4	No	No	Not applicable	None	Fatal
[redacted]	アラニンアミノトランスフェラーゼ増加	8, 32	25	2	Yes	Yes	Dose interrupted	None	Recovered/resolved
	アスパラギン酸アミノトランスフェラーゼ増加	8, 32	25	2	Yes	Yes	Dose interrupted	None	Recovered/resolved
	発熱	49, 49	1	1	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	疾患進行*	37, 37	1	4	No	No	Not applicable	None	Fatal
[redacted]	急性腎障害	153, 154	2	1	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	敗血症	153, 156	4	4	No	No	Dose not changed		Recovered/resolved
	インフルエンザ	153, 166	14	2	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	肺炎	352, 359	8	2	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	インフルエンザ様疾患	436, 450	15	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	小腸出血	35, 42	8	3	No	No	Not applicable	Concomitant medication was given/Procedure	Recovered/resolved

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
								or non-drug therapy performed	
[redacted]	菌血症	99, 174	76	4	Yes	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	腸壁気腫症	103, 221	119	4	Yes	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	成長障害	140,		3	No	Yes	Dose not changed		Not recovered/not resolved
	精神状態変化	140,		4	No	Yes	Dose not changed	None	Not recovered/not resolved
	下部消化管出血	145,		4	No	No	Dose not changed		Not recovered/not resolved
[redacted]	発熱	19, 19	1	1	No	Yes	Dose increased	Concomitant medication was given	Recovered/resolved
	腹痛	19, 20	2	3	No	No	Dose increased	None	Recovered/resolved
	下痢	19,		3	No	No	Dose increased	Concomitant medication was given	Not recovered/not resolved
	腸壁気腫症	41, 145	105	4	Yes	Yes	Drug withdrawn		Recovered/resolved
[redacted]	腸壁気腫症	15, 18	4	4	Yes	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	鼠径部痛	171, 171	1	3	No	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	骨壊死	279,		3	No	Yes	Dose not changed	Procedure or non-drug therapy performed	Not recovered/not resolved
	乳頭様甲状腺癌*	418, 418	1	3	Yes	No	Not applicable	Procedure or non-drug therapy performed	Recovered/resolved
[redacted]	貧血	95, 141	47	3	Yes	No	Drug withdrawn		Recovered/resolved
	血小板減少症	95, 141	47	4	Yes	Yes	Drug withdrawn		Recovered/resolved
	呼吸不全	141, 149	9	4	No	Yes	Not applicable	Concomitant medication was given	Fatal
[redacted]	発熱	32, 32	1	1	No	No	Dose not changed	None	Recovered/resolved
	腸壁気腫症	33, 90	58	4	Yes	Yes	Dose reduced	Concomitant medication was given	Recovered/resolved
	肺感染	33, 114	82	3	No	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	発熱	89, 89	1	2	Yes	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
	医療機器関連感染	89, 110	22	3	No	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	呼吸不全	183, 188	6	4	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	移行上皮癌	207,		3	No	Yes	Dose not changed	None	Not recovered/not resolved
	呼吸不全	242, 280	39	4	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Fatal
[redacted]	発熱	67, 67	1	1	Yes	Yes	Not applicable	Concomitant medication was given	Recovered/resolved
	肺感染	67, 69	3	3	Yes	Yes	Not applicable	Concomitant medication was given	Recovered/resolved
[redacted]	転倒	141, 156	16	3	No	No	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	下痢	205, 223	19	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	菌血症	209, 223	15	3	Yes	No	Dose reduced	Concomitant medication was given	Recovered/resolved
	気管支肺アスペルギルス症	209, 223	15	4	Yes	Yes	Dose reduced	Concomitant medication was given	Recovered/resolved with sequelae
	肺炎	209, 227	19	4	Yes	Yes	Dose reduced	Concomitant medication was given	Recovered/resolved
	肺感染	257, 260	4	3	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
	悪心	280, 281	2	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	疲労	280, 281	2	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	腸炎	293, 320	28	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	悪心	298, 302	5	3	No	No	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	嘔吐	298, 302	5	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	腸球菌性敗血	313, 320	8	3	No	No	Dose not changed	Concomitant medication was	Recovered/resolved

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
	症							given/Procedure or non-drug therapy performed	
[redacted]	肝移植片対宿主病	23, 27	5	4	No	No	Drug withdrawn	None	Fatal
[redacted]	嚥下障害	297, 298	2	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	歯痛	297, 298	2	2	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	唾液腺炎	297, 298	2	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	腹膜炎	10, 13	4	4	No	No	Drug withdrawn	Concomitant medication was given	Fatal
	多臓器機能不全症候群	13, 13	1	4	No	No	Drug withdrawn	None	Fatal
[redacted]	発熱	44, 44	1	1	No	No	Dose not changed	None	Recovered/resolved
	動悸	44, 45	2	1	No	No	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	シトロバクター感染	44, 46	3	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	血管確保合併症	39, 49	11	4	No	No	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	呼吸不全	39, 49	11	4	No	No	Dose interrupted	Concomitant medication was given	Fatal
[redacted]	ブドウ球菌感染	3, 6	4	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	上部消化管出血	39, 43	5	3	No	Yes	Not applicable	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
	胃炎	40, 43	4	3	No	No	Not applicable	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
	再発急性骨髄性白血病	48,		3	No	No	Not applicable	Concomitant medication was given	Not recovered/not resolved
[redacted]	肺炎	15,		3	No	No	Dose not changed	Concomitant medication was given	Not recovered/not resolved
	肝不全	21, 23	3	4	No	No	Drug withdrawn	Concomitant medication was given	Fatal

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
[redacted]	成長障害	32,		3	No	No	Dose not changed		Recovering/resolving
[redacted]	菌血症	8, 11	4	3	No	No	Dose not changed		Recovered/resolved
	精神状態変化	14, 20	7	3	No	No	Dose reduced		Recovered/resolved
	下痢	50, 54	5	3	No	No	Dose interrupted	None	Recovered/resolved
	悪心	50, 54	5	3	No	No	Dose interrupted	None	Recovered/resolved
	嘔吐	50, 54	5	3	No	No	Dose interrupted	None	Recovered/resolved
	上腹部痛	65, 69	5	3	No	No	Dose interrupted	None	Recovered/resolved
	下部消化管出血*	175, 181	7	3	No	No	Not applicable	Concomitant medication was given	Recovered/resolved
[redacted]	蜂巣炎	34,		4	No	No	Dose interrupted	Concomitant medication was given/Procedure or non-drug therapy performed	Not recovered/not resolved
	胃腸出血	42, 42	1	4	No	No	Dose not changed		Fatal
[redacted]	RS ウイルス感染	57, 71	15	2	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
[redacted]	肺塞栓症	21, 50	30	3	No	Yes	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	後腹膜血腫	27, 70	44	4	No	No	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	心筋梗塞	36, 36	1	3	No	No	Not applicable	None	Recovered/resolved
[redacted]	カンジダ感染	24, 41	18	4	No	Yes	Not applicable	Concomitant medication was given	Fatal
[redacted]	精神状態変化	19, 22	4	2	Yes	Yes	Drug withdrawn	Procedure or non-drug therapy performed	Recovered/resolved
	精神状態変化	26, 37	12	2	Yes	Yes	Dose reduced	Procedure or non-drug therapy performed	Recovered/resolved
[redacted]	消化管移植片対宿主病	8, 47	40	4	No	No	Dose not changed	Concomitant medication was given	Fatal
[redacted]	レジオネラ菌性肺炎	22, 30	9	4	No	Yes	Not applicable	Concomitant medication was given/Procedure or non-drug therapy performed	Fatal

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
[redacted]	肝不全	21, 23	3	4	No	No	Not applicable	Concomitant medication was given	Fatal
	敗血症性ショック	21, 23	3	4	No	Yes	Not applicable	Concomitant medication was given	Fatal
	ブドウ球菌性菌血症	21, 23	3	4	No	Yes	Not applicable	Concomitant medication was given	Fatal
	急性腎障害	22, 23	2	4	No	No	Not applicable	Procedure or non-drug therapy performed	Fatal
[redacted]	呼吸不全	38, 38	1	4	No	No	Not applicable	None	Fatal
[redacted]	真菌性肝感染	10,		3	No	Yes	Drug withdrawn	Concomitant medication was given/Procedure or non-drug therapy performed	Recovering/resolving
	背部痛	70, 74	5	3	No	No	Not applicable	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved with sequelae
[redacted]	敗血症	13, 27	15	4	Yes	No	Dose interrupted	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
	敗血症	39, 77	39	4	No	No	Drug withdrawn	Concomitant medication was given/Procedure or non-drug therapy performed	Recovered/resolved
[redacted]	下部消化管出血	19, 45	27	4	No	No	Drug withdrawn	Concomitant medication was given/Procedure or non-drug therapy performed	Fatal
[redacted]	眼の障害	12,		3	No	No	Dose interrupted	Concomitant medication was given/Procedure or non-drug therapy performed	Not recovered/not resolved
	肺出血	50, 51	2	4	Yes	Yes	Dose interrupted	Procedure or non-drug therapy performed	Fatal
[redacted]	敗血症	17, 32	16	4	No	Yes	Dose interrupted	Concomitant medication was given	Recovered/resolved
	頭痛	32, 39	8	3	No	No	Dose not changed	Concomitant medication was given/Procedure or non-drug therapy	Recovered/resolved

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
								performed	
	敗血症	52,		4	Yes	Yes	Drug withdrawn	Concomitant medication was given/Procedure or non-drug therapy performed	Not recovered/not resolved
[redacted]	股関節部骨折	29, 33	5	3	No	No	Dose interrupted	Procedure or non-drug therapy performed	Recovered/resolved
	敗血症	41, 42	2	4	Yes	Yes	Dose interrupted	Concomitant medication was given	Fatal
[redacted]	急性胆嚢炎	24,		4	No	No	Dose interrupted	Concomitant medication was given/Procedure or non-drug therapy performed	Not recovered/not resolved
[redacted]	敗血症	12,		4	No	No	Not applicable	Concomitant medication was given/Procedure or non-drug therapy performed	Not recovered/not resolved
	突然死	34, 34	1	4	No	No	Not applicable	None	Fatal
[redacted]	低血圧	60,		3	No	No	Dose interrupted	Concomitant medication was given/Procedure or non-drug therapy performed	Not recovered/not resolved
[redacted]	疾患進行	48, 62	15	4	No	No	Not applicable	None	Fatal
[redacted]	好中球数減少	15, 20	6	3	No	No	Dose interrupted	None	Recovered/resolved
	血小板数減少	15, 20	6	3	Yes	No	Dose interrupted	None	Recovered/resolved
	高血糖	15, 20	6	3	No	No	Dose interrupted	Concomitant medication was given	Recovered/resolved
[redacted]	急性腎障害	112,		4	Yes	No	Drug withdrawn		Not recovered/not resolved
[redacted]	敗血症性ショック	3, 3	1	4	No	Yes	Dose not changed	Concomitant medication was given	Recovered/resolved
	低血圧	3, 4	2	4	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	肝損傷	3, 16	14	4	No	No	Dose interrupted	None	Fatal
	低血圧	10, 10	1	4	No	No	Not applicable	None	Recovered/resolved
[redacted]	心筋梗塞	15, 58	44	3	No	No	Dose interrupted	Concomitant medication was given	Recovered/resolved
	低ナトリウム	84, 231	148	3	No	No	Dose not changed	Concomitant medication was	Recovered/resolved

被験者番号	PT	発現日, 消失日(日目)	持続期間(日)	Grade	RUX との関連	副腎皮質ステロイドとの関連	治験薬に対する処置	処置	転帰
	血症							given	
	サイトメガロウイルス血症	91, 132	42	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	尿路感染	95, 133	39	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
	低カリウム血症	97, 196	100	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	発熱	57, 63	7	3	No	No	Dose not changed	Concomitant medication was given	Recovered/resolved
[redacted]	交通事故	11, 33	23	3	No	No	Dose not changed	Procedure or non-drug therapy performed	Recovered/resolved
	心停止	93, 93	1	4	No	No	Dose interrupted	Concomitant medication was given	Fatal
[redacted]	疾患進行	9, 14	6	4	No	No	Not applicable	None	Fatal

Source: 5.3.5.2-1-271 試験-Listing 2.7.2
*：最終投与後 30 日より後に発現した有害事象
MedDRA version 19.1

Table 7-9 慢性 GVHD の治験治療下の死亡（D2301 試験，SAF，データカットオフまで）

Category PT	RUX N = 165 n (%)	BAT N = 158 n (%)	RUX crossover N = 61 n (%)
曝露期間（週）：中央値（最小値 - 最大値）	41.3 (0.7-127.3)	24.1 (0.6-108.4)	42.3 (2.6-98.7)
総曝露期間（人月）	1748.0	1061.8	593.5
合計	16 (9.7)	11 (7.0)	3 (4.9)
死因：対象疾患	14 (8.5)	7 (4.4)	2 (3.3)
慢性移植片対宿主病	14 (8.5)	7 (4.4)	2 (3.3)
死因：その他	2 (1.2)	4 (2.5)	1 (1.6)
全身健康状態悪化	1 (0.6)	0	0
シュードモナス性敗血症	1 (0.6)	0	0
肺炎	0	1 (0.6)	0
敗血症	0	1 (0.6)	0
全身性感染	0	1 (0.6)	0
呼吸不全	0	1 (0.6)	0
頭蓋内出血	0	0	1 (1.6)

Source: 5.3.5.1-2-D2301 試験-Table 14.3-1.1，Table 14.3-1.6，Table 14.3.1-2.2，Table 14.3.1-2.3
RUX 群の発現率の降順
総曝露期間 = 全被験者の曝露期間の合計
MedDRA version 23.0

Table 7-10　慢性 GVHD の死亡一覧（D2301 試験，SAF，データカットオフまで）

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
RUX 群					
AUS/[redacted]	3[redacted]/CA	334&	165	cGvHD	慢性 GVHD
AUS/[redacted]	2[redacted]/CA	230	1	Pseudomonas Sepsis	シュードモナス性敗血症
CZE/[redacted]	5[redacted]/CA	201&	88	cGvHD	慢性 GVHD
DEU/[redacted]	6[redacted]/CA	88	10	cGvHD	慢性 GVHD
DEU/[redacted]	5[redacted]/CA	630&	413	Underlying Malignancy	悪性新生物
ESP/[redacted]	3[redacted]/CA	291	15	cGvHD	慢性 GVHD
FRA/[redacted]	6[redacted]/UN	13	5	cGvHD	慢性 GVHD
GBR/[redacted]	7[redacted]/CA	240&	185	cGvHD	慢性 GVHD
GBR/[redacted]	7[redacted]/CA	185&	108	Type 1 Respiratory Failure	呼吸不全
IND/[redacted]	1[redacted]/AS	190&	49	Disease Relapse	疾患再発
IND/[redacted]	4[redacted]/AS	301	3	cGvHD	慢性 GVHD
ITA/[redacted]	1[redacted]/CA	133	15	cGvHD	慢性 GVHD
ITA/[redacted]	4[redacted]/CA	71	45	Worsening Of The General Conditions	全身健康状態悪化
JPN/[redacted]	6[redacted]/AS	51	11	cGvHD	慢性 GVHD
JPN/[redacted]	4[redacted]/AS	57	12	cGvHD	慢性 GVHD
JPN/[redacted]	5[redacted]/AS	29	9	cGvHD	慢性 GVHD
JPN/[redacted]	6[redacted]/AS	96&	34	cGvHD	慢性 GVHD
JPN/[redacted]	5[redacted]/AS	81	15	cGvHD	慢性 GVHD
JPN/[redacted]	4[redacted]/AS	666&	101	cGvHD	慢性 GVHD
JPN/[redacted]	3[redacted]/AS	28	5	cGvHD	慢性 GVHD
JPN/[redacted]	3[redacted]/AS	306&	165	Central Nervous System Infection	中枢神経系感染
JPN/[redacted]	5[redacted]/AS	352&	262	Unknown	死亡
NLD/[redacted]	6[redacted]/CA	339&	180	Relapse Of Myelopfibrosis	骨髄線維症
POL/[redacted]	4[redacted]/CA	178	26	cGvHD	慢性 GVHD
POL/[redacted]	6[redacted]/CA	62	26	cGvHD	慢性 GVHD
PRT/[redacted]	5[redacted]/CA	131&	117	cGvHD	慢性 GVHD
SAU/[redacted]	3[redacted]/OTH	436&	207	Relapsed Acute Myeloid Leukemia	急性骨髄性白血病
TUR/[redacted]	4[redacted]/CA	33	10	cGvHD	慢性 GVHD
TUR/[redacted]	2[redacted]/CA	99&	36	cGvHD	慢性 GVHD
USA/[redacted]	7[redacted]/NA	92	30	cGvHD	慢性 GVHD
USA/[redacted]	5[redacted]/OTH	193&	84	cGvHD	慢性 GVHD
BAT 群					
CZE/[redacted]	5[redacted]/CA	305&	111	Repeated Infection (Unknown)	感染
DEU/[redacted]	5[redacted]/CA	195&	54	Unknown	死亡
DEU/[redacted]	6[redacted]/CA	169&	78	Progression To Aml	急性骨髄性白血病
DEU/[redacted]	6[redacted]/CA	49	3	Severe Pneumonia	肺炎
DEU/[redacted]	4[redacted]/CA	208&	183	Recurrence Of The Underlying Disease	疾患再発
ESP/[redacted]	4[redacted]/CA	82*	5	cGvHD	慢性 GVHD
ESP/[redacted]	4[redacted]/CA	197&	140	Underlying Acute Myeloid Leukemia Relapse	再発急性骨髄性白血病
FRA/[redacted]	4[redacted]/OTH	123	17	Sepsis	敗血症

被験者番号	年齢/性別/人種	治験治療開始日から死亡日までの日数	最終投与日から死亡日までの日数	主な死因（医師記載）	PT
GRC[redacted]	4[redacted]/CA	90&	57	cGvHD	慢性 GVHD
GRC[redacted]	5[redacted]/CA	25	1	cGvHD	慢性 GVHD
GRC[redacted]	6[redacted]/CA	399&	309	cGvHD	慢性 GVHD
ISR[redacted]	5[redacted]/CA	192	6	cGvHD	慢性 GVHD
ISR[redacted]	6[redacted]/CA	30	15	cGvHD	慢性 GVHD
ISR[redacted]	5[redacted]/CA	681&	584	Sepsis	敗血症
ISR[redacted]	6[redacted]/CA	457**	293	Relapse Sezary Disease	皮膚 T 細胞性リンパ腫
ISR[redacted]	6[redacted]/CA	16	1	cGvHD	慢性 GVHD
ITA[redacted]	6[redacted]/CA	198	1	Respiratory Failure	呼吸不全
ITA[redacted]	4[redacted]/CA	148**	120	cGvHD	慢性 GVHD
JPN[redacted]	6[redacted]/AS	154	29	cGvHD	慢性 GVHD
JPN[redacted]	6[redacted]/AS	7	4	cGvHD	慢性 GVHD
JPN[redacted]	3[redacted]/AS	200&	144	Invasive Aspergillosis	アスペルギルス感染
NLD[redacted]	4[redacted]/CA	369&	348	Underlying Disease	疾患進行
POL[redacted]	2[redacted]/CA	59*	21	cGvHD	慢性 GVHD
USA[redacted]	5[redacted]/CA	137	7	cGvHD	慢性 GVHD
USA[redacted]	6[redacted]/CA	252&	51	cGvHD	慢性 GVHD
USA[redacted]	7[redacted]/CA	24	21	Infections And Infestations-Other, Systemic Infection	全身性感染
USA[redacted]	6[redacted]/CA	118*	3	Intracranial Hemorrhage	頭蓋内出血

Source: 5.3.5.1-2-D2301 試験-Listing 14.3.2-1.1
M = 男性，F = 女性，AS = Asian，BL = Black or African American，CA = Caucasian，NA = Native Hawaiian or other pacific islander，OTH = Other，UN = Unknown
*：RUX へのクロスオーバー後の治験治療下の死亡。RUX 投与開始日からの日数を示す。
**：RUX へのクロスオーバー後の治験治療下よりも後の死亡。BAT 投与開始日からの日数を示す。
&：治験治療下よりも後の死亡
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Table 7-11　慢性 GVHD の重篤な有害事象（いずれかの群で発現率 1%以上）（D2301 試験，SAF，データカットオフまで）

PT	RUX N = 165 n (%)	BAT N = 158 n (%)	RUX crossover N = 61 n (%)
曝露期間（週）：中央値（最小値 - 最大値）	41.3 (0.7-127.3)	24.1 (0.6-108.4)	42.3 (2.6-98.7)
総曝露期間（人月）	1748.0	1061.8	593.5
合計	72 (43.6)	63 (39.9)	22 (36.1)
肺炎	21 (12.7)	14 (8.9)	4 (6.6)
発熱	11 (6.7)	4 (2.5)	4 (6.6)
下気道感染	4 (2.4)	1 (0.6)	1 (1.6)
腹痛	3 (1.8)	0	1 (1.6)
背部痛	3 (1.8)	0	0
呼吸困難	3 (1.8)	3 (1.9)	2 (3.3)
発熱性好中球減少症	3 (1.8)	2 (1.3)	1 (1.6)
気胸	3 (1.8)	0	0
肺塞栓症	3 (1.8)	3 (1.9)	0
敗血症	3 (1.8)	1 (0.6)	0

PT	RUX N = 165 n (%)	BAT N = 158 n (%)	RUX crossover N = 61 n (%)
急性腎障害	2 (1.2)	3 (1.9)	0
気管支肺アスペルギルス症	2 (1.2)	4 (2.5)	0
サイトメガロウイルス感染再燃	2 (1.2)	1 (0.6)	0
食欲減退	2 (1.2)	1 (0.6)	0
脱水	2 (1.2)	0	0
真菌感染	2 (1.2)	0	0
帯状疱疹	2 (1.2)	0	1 (1.6)
低血圧	2 (1.2)	1 (0.6)	0
低酸素症	2 (1.2)	3 (1.9)	0
好中球減少症	2 (1.2)	0	0
呼吸不全	2 (1.2)	2 (1.3)	1 (1.6)
気道感染	2 (1.2)	0	2 (3.3)
失神	2 (1.2)	1 (0.6)	0
下痢	1 (0.6)	3 (1.9)	1 (1.6)
全身健康状態悪化	1 (0.6)	2 (1.3)	0
細菌性肺炎	1 (0.6)	2 (1.3)	0
サイトメガロウイルス性肺炎	1 (0.6)	2 (1.3)	0
敗血症性ショック	1 (0.6)	3 (1.9)	1 (1.6)
上気道感染	1 (0.6)	2 (1.3)	2 (3.3)
貧血	1 (0.6)	0	3 (4.9)
血小板数減少	1 (0.6)	0	1 (1.6)
血小板減少症	1 (0.6)	1 (0.6)	1 (1.6)
気管支炎	1 (0.6)	0	1 (1.6)
頭蓋内出血	1 (0.6)	0	1 (1.6)
大腸菌感染	0	2 (1.3)	0
胃腸出血	0	2 (1.3)	0
汎血球減少症	0	2 (1.3)	0
シュードモナス性肺炎	0	2 (1.3)	0
痙攣発作	0	2 (1.3)	0
嘔吐	0	2 (1.3)	1 (1.6)
潰瘍性角膜炎	0	0	2 (3.3)
脾臓障害	0	0	1 (1.6)
心嚢液貯留	0	1 (0.6)	1 (1.6)
悪心	0	1 (0.6)	1 (1.6)
疲労	0	1 (0.6)	1 (1.6)
高体温症	0	0	1 (1.6)
狭窄	0	0	1 (1.6)
腹壁感染	0	0	1 (1.6)
アスペルギルス感染	0	0	1 (1.6)
クロストリジウム・ディフィシレ感染	0	1 (0.6)	1 (1.6)
涙小管炎	0	0	1 (1.6)

PT	RUX N = 165 n (%)	BAT N = 158 n (%)	RUX crossover N = 61 n (%)
感染性小腸結腸炎	0	0	1 (1.6)
インフルエンザ	0	1 (0.6)	1 (1.6)
咽頭炎	0	0	1 (1.6)
副鼻腔炎	0	0	1 (1.6)
転倒	0	0	1 (1.6)
血中クレアチニン増加	0	0	1 (1.6)
骨壊死	0	1 (0.6)	1 (1.6)
カポジ肉腫	0	0	1 (1.6)
頭蓋内圧上昇	0	0	1 (1.6)
代謝性脳症	0	0	1 (1.6)
うつ病	0	1 (0.6)	1 (1.6)
高血圧	0	0	1 (1.6)

Source: 5.3.5.1-2-D2301 試験-Table 14.3-1.1，Table 14.3-1.6，Table 14.3.1-1.18，Table 14.3.1-1.35
RUX 群の発現率の降順
総曝露期間 = 全被験者の曝露期間の合計
MedDRA version 23.0

Table 7-12　　慢性 GVHD の重篤な有害事象の一覧（D2301 試験，SAF，データカットオフまで）

Listing 14.3.2-2.1 Serious adverse events (Safety set)

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 1 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/	3	Yes/3	Chest infection/			12	3	YES, BOTH	3,10	2
	CA		Lower respiratory tract infection (下気道感染)/					AND/OR		
			Infections and infestations	45	56			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
AUS/	2	Yes/3	Pulmomary Aspergillus/			8	3	NO	3,10	2
	CA		Bronchopulmonary aspergillosis							
			(気管支肺アスペルギルス症)/	34	41					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	Fungal Infection/		Ongoing		3	NO	2,10	1
			Fungal infection (真菌感染)/							
			Infections and infestations	224						
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 2 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	CHEST INFECTION/	[redacted]	[redacted]	22	2	NO	2,10	2
			Lower respiratory tract infection (下気道感染)/	[redacted]	[redacted]					
			Infections and infestations	173	194					
			(感染症および寄生虫症)							
		Yes/3	Chest Infection/	[redacted]	Ongoing		3	YES	2,10	1
			Lower respiratory tract infection (下気道感染)/	[redacted]						
			Infections and infestations	202						
			(感染症および寄生虫症)							
		Yes/3	Pseudomonas Sepsis/	[redacted]	[redacted]	24	3	NO	2,10	1
			Pseudomonal sepsis (シュードモナス性敗血症)/	[redacted]	[redacted]					
			Infections and infestations	202	225					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 3 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/	2[redacted]	Yes/	Pseudomonas Sepsis/	[redacted]	[redacted]	4	4	NO	3,10	1
[redacted]	CA	2,3	Pseudomonal sepsis (シュードモナス性敗血症)/	[redacted]	[redacted]					
			Infections and infestations	226	229					
			(感染症および寄生虫症)							
		Yes/1	Pseudomonas Sepsis/	[redacted]	[redacted]	1	5	NO	2	5
			Pseudomonal sepsis (シュードモナス性敗血症)/	[redacted]	[redacted]					
			Infections and infestations	230	230					
			(感染症および寄生虫症)							
AUT/	3[redacted]	Yes/3	respiratory infection/	[redacted]	[redacted]	2	2	NO	2,10	2
[redacted]	CA		Respiratory tract infection (気道感染)/	[redacted]	[redacted]					
			Infections and infestations	192	193					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 4 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
BEL/	6[redacted]	Yes/3	Cornea perforation/	[redacted]	[redacted]	2	4	NO		999,1	2
[redacted]	CA		Corneal perforation (角膜穿孔)/	[redacted]	[redacted]					0	
			Eye disorders (眼障害)	198	199						
BGR/	5[redacted]	Yes/3	Lung infection/	[redacted]	[redacted]	11	3	NO		4,10	4
[redacted]	CA		Pneumonia (肺炎)/	[redacted]	[redacted]						
			Infections and infestations	284	294						
			(感染症および寄生虫症)								
CAN/	6[redacted]	Yes/3	Pulmonary embolism/	[redacted]	[redacted]	3	3	NO		2,10	2
[redacted]	CA		Pulmonary embolism (肺塞栓症)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders	201	203						
			(呼吸器、胸郭および縦隔障害)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 5 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CAN/	6[redacted]	Yes/3	Syncope/	[redacted]	[redacted]	1	3	NO	2	2
[redacted]	CA		Syncope (失神)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	201	201					
DEU/	6[redacted]	Yes/3	Oral thrush/	[redacted]	[redacted]	4	2	NO	2,10	2
[redacted]	CA		Oral candidiasis (口腔カンジダ症)/	[redacted]	[redacted]					
			Infections and infestations	37	40					
			(感染症および寄生虫症)							
		Yes/3	pain syndrome of both legs/	[redacted]	[redacted]	3	3	NO	2,10	2
			Pain in extremity (四肢痛)/	[redacted]	[redacted]					
			Musculoskeletal and connective tissue disorders	63	65					
			(筋骨格系および結合組織障害)							
		Yes/3	Pneumonia/	[redacted]	[redacted]	11	4	YES, BOTH	5,10	1
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 6 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	77	87			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/1	Pneumonia/	[redacted]	[redacted]	1	5	YES, BOTH	5	5
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	88	88			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	systemic Infection unknown cause/	[redacted]	[redacted]	6	3	NO	2,10	2
			Systemic infection (全身性感染)/	[redacted]	[redacted]					
			Infections and infestations	49	54					
			(感染症および寄生虫症)							
DEU/ [redacted]	5[redacted] CA	Yes/3	Corneal erosion left eye/	[redacted]	[redacted]	2	3	NO	2,10	2
			Corneal erosion (角膜びらん)/	[redacted]	[redacted]					
			Eye disorders (眼障害)	212	213					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 7 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	acute kidney failure/	[redacted]	[redacted]	8	3	YES, OTHER	2,10	2
			Acute kidney injury (急性腎障害)/	[redacted]	[redacted]			STUDY		
			Renal and urinary disorders (腎および尿路障害)	100	107			TREATMENT (NON-INVESTIGATIONAL)		
		Yes/3	generalized epileptic seizure/	[redacted]	[redacted]	14	3	NO	2,10	2
			Epilepsy (てんかん)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	114	127					
		Yes/3	Pneumonia/	[redacted]	[redacted]	17	3	NO	4,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations (感染症および寄生虫症)	410	426					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 8 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/ [redacted]	5[redacted] CA	Yes/3	Basalioma nostril right/ Basal cell carcinoma (基底細胞癌)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] 139	[redacted] 147	9	3	NO	2,10	2
DNK/ [redacted]	1[redacted] CA	Yes/3	Anorexia/ Decreased appetite (食欲減退)/ Metabolism and nutrition disorders (代謝および栄養障害)	[redacted] 180	Ongoing		3	NO	2,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 9 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/	4[redacted]	Yes/3	Confusion/	[redacted]	[redacted]	4	1	NO	5,10	2
[redacted]	CA		Confusional state (錯乱状態)/	[redacted]	[redacted]					
			Psychiatric disorders (精神障害)	258	261					
ESP/	5[redacted]	Yes/3	anal abcess worsening/	[redacted]	[redacted]	14	3	NO	2,10	2
[redacted]	CA		Anal abscess (肛門膿瘍)/	[redacted]	[redacted]					
			Infections and infestations	448	461					
			(感染症および寄生虫症)							
		Yes/3	diarrhea/	[redacted]	[redacted]	2	3	NO	2,10	2
			Diarrhoea (下痢)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	349	350					
		Yes/3	fever/	[redacted]	[redacted]	6	3	NO	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	335	340					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 10 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(一般・全身障害および投与部位の状態)							
		Yes/3	respiratory infection/	[redacted]	[redacted]	3	3	NO	2	2
			Respiratory tract infection (気道感染)/	[redacted]	[redacted]					
			Infections and infestations	145	147					
			(感染症および寄生虫症)							
		Yes/3	sepsis/	[redacted]	[redacted]	12	4	NO	2,10	2
			Sepsis (敗血症)/	[redacted]	[redacted]					
			Infections and infestations	427	438					
			(感染症および寄生虫症)							
ESP/ [redacted]	5[redacted] CA	Yes/3	Upper Respiratory Tract Infection/	[redacted]	[redacted]	8	1	NO	2,10	2
			Upper respiratory tract infection (上気道感染)/	[redacted]	[redacted]					
			Infections and infestations	37	44					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 11 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/	2[redacted]	Yes/3	Pneumothorax/	[redacted]	[redacted]	47	3	NO	2,10	2
[redacted]	CA		Pneumothorax (気胸)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	25	71					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	FEVER/	[redacted]	[redacted]	5	3	NO	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	164	168					
			(一般・全身障害および投与部位の状態)							
ESP/	3[redacted]	Yes/3	Fungal infection/	[redacted]	[redacted]	23	3	NO	4,10	3
[redacted]	CA		Fungal infection (真菌感染)/	[redacted]	[redacted]					
			Infections and infestations	114	136					
			(感染症および寄生虫症)							
		Yes/3	RESPIRATORY INFECTION BY Klebsiella pneumoniae/	[redacted]	[redacted]	11	4	NO	999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 12 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory tract infection bacterial	[redacted]	[redacted]				0	
			(細菌性気道感染)/	280	290					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/	RESPIRATORY INFECTION BY Klebsiella pneumoniae/	[redacted]	[redacted]	1	5	NO	999,1	5
		1,3	Respiratory tract infection bacterial	[redacted]	[redacted]				0	
			(細菌性気道感染)/	291	291					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	RESPIRATORY INFECTION BY Stenotrophomonas maltophilia/	[redacted]	[redacted]	11	4	NO	999,1	1
			Respiratory tract infection bacterial	[redacted]	[redacted]				0	
			(細菌性気道感染)/	280	290					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 13 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ESP/	3[redacted]	Yes/	RESPIRATORY INFECTION BY Stenotrophomonas maltophilia/	[redacted]	[redacted]	1	5	NO	999,1	5
[redacted]	CA	1,3	Respiratory tract infection bacterial	[redacted]	[redacted]				0	
			(細菌性気道感染)/	291	291					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	RESPIRATORY INFECTION BY ASPERGILLUS FUMIGATUS/	[redacted]	[redacted]	11	4	NO	2,10	1
			Respiratory tract infection fungal (真菌性気道感染)	[redacted]	[redacted]					
			/	280	290					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/	RESPIRATORY INFECTION BY ASPERGILLUS FUMIGATUS/	[redacted]	[redacted]	1	5	NO	2,10	5
		1,3	Respiratory tract infection fungal (真菌性気道感染)	[redacted]	[redacted]					
			/	291	291					
			Infections and infestations							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 14 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
		Yes/3	RESPIRATORY INFECTION BY CITOMEGALOVIRUS/	[redacted]	[redacted]	11	4	NO	999,1	1
			Respiratory tract infection viral	[redacted]	[redacted]				0	
			(ウイルス性気道感染)/	280	290					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/	RESPIRATORY INFECTION BY CITOMEGALOVIRUS/	[redacted]	[redacted]	1	5	NO	999,1	5
		1,3	Respiratory tract infection viral	[redacted]	[redacted]				0	
			(ウイルス性気道感染)/	291	291					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 15 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
FRA/	6[redacted]	Yes/2	pulmonary embolism with intensive care transfer/	[redacted]	[redacted]	6	3	NO	2,10	2
[redacted]	UN		Pulmonary embolism (肺塞栓症)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	13	18					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Vertebral compaction/	[redacted]	Ongoing		3	NO	2	1
			Spinal cord compression (脊髄圧迫)/	[redacted]						
			Nervous system disorders (神経系障害)	109						
FRA/	6[redacted]	Yes/3	dehydration/	[redacted]	[redacted]	9	3	NO	2	2
[redacted]	CA		Dehydration (脱水)/	[redacted]	[redacted]					
			Metabolism and nutrition disorders	9	17					
			(代謝および栄養障害)							
		Yes/3	Gastric and duodenum ulcers/	[redacted]	[redacted]	8	3	NO	2	2
			Gastrointestinal ulcer (胃腸潰瘍)/	[redacted]	[redacted]					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 16 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Gastrointestinal disorders (胃腸障害)	10	17					
		Yes/3	Gastric and duodenum ulcers/	[redacted]	[redacted]	30	3	NO	2	2
			Gastrointestinal ulcer (胃腸潰瘍)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	22	51					
		Yes/3	hypotension/	[redacted]	[redacted]	28	3	NO	2,10	2
			Hypotension (低血圧)/	[redacted]	[redacted]					
			Vascular disorders (血管障害)	9	36					
		Yes/6	leuconeutropenia/	[redacted]	[redacted]	5	4	YES,	4	3
			Leukopenia (白血球減少症)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	25	29			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
		Yes/3	Melena/	[redacted]	[redacted]	9	3	NO	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 17 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Melaena (メレナ)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	9	17					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 18 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (days)	Grade	Relat. study drug	Action taken	Out-come
FRA/	6[redacted]	Yes/3	melena/	[redacted]	[redacted]	6	3	NO	2	2
[redacted]	CA		Melaena (メレナ)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	22	27					
FRA/	6[redacted]	Yes/2	Lyell syndrome/	[redacted]	[redacted]	4	4	NO	5,10	1
[redacted]	UN		Toxic epidermal necrolysis	[redacted]	[redacted]					
			(中毒性表皮壊死融解症)/	9	12					
			Skin and subcutaneous tissue disorders							
			(皮膚および皮下組織障害)							
		Yes/1	Lyell syndrome/	[redacted]	[redacted]	1	5	NO	999,1	5
			Toxic epidermal necrolysis	[redacted]	[redacted]				0	
			(中毒性表皮壊死融解症)/	13	13					
			Skin and subcutaneous tissue disorders							
			(皮膚および皮下組織障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 19 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/	2[redacted]	Yes/3	Abdominal Pain/	[redacted]	[redacted]	16	3	YES	2	2
[redacted]	CA		Abdominal pain (腹痛)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	302	317					
		Yes/6	ALT increase/	[redacted]	[redacted]	12	4	YES	4	2
			Alanine aminotransferase increased	[redacted]	[redacted]					
			(アラニンアミノトランスフェラーゼ増加)/	29	40					
			Investigations (臨床検査)							
		Yes/3	Bacterial Translocation/	[redacted]	[redacted]	11	3	NO	2,10	2
			Bacterial translocation	[redacted]	[redacted]					
			(バクテリアルトランスロケーション)/	254	264					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 20 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/	2[redacted]	Yes/3	COUGH/	[redacted]	[redacted]	122	2	NO	2,10	2
[redacted]	CA		Cough (咳嗽)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	-16#	106					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	cough/	[redacted]	[redacted]	6	3	YES,	2	2
			Cough (咳嗽)/	[redacted]	[redacted]			INVESTIGATI		
			Respiratory, thoracic and mediastinal disorders	200	205			ONAL		
			(呼吸器、胸郭および縦隔障害)					TREATMENT		
		Yes/3	Dyspnea/	[redacted]	[redacted]	66	2	YES	2	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	41	106					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Enterococcus faecium infection/	[redacted]	[redacted]	5	3	YES	2,10	2
			Enterococcal infection (腸球菌感染)/	[redacted]	[redacted]					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 21 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	247	251					
			(感染症および寄生虫症)							
		Yes/2	GGT Increase/	[redacted]	[redacted]	1	4	YES	4	2
			Gamma-glutamyltransferase increased	[redacted]	[redacted]					
			(γ－グルタミルトランスフェラーゼ増加)/	29	29					
			Investigations (臨床検査)							
		Yes/3	Hypotension/	[redacted]	[redacted]	9	3	NO	2,10	2
			Hypotension (低血圧)/	[redacted]	[redacted]					
			Vascular disorders (血管障害)	161	169					
		Yes/3	Lower respiratory tract infection/	[redacted]	[redacted]	65	3	YES	2,10	2
			Lower respiratory tract infection (下気道感染)/	[redacted]	[redacted]					
			Infections and infestations	42	106					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 22 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/	2[redacted]	Yes/3	Pleuritic Pain/	[redacted]	[redacted]	66	2	YES	2	2
[redacted]	CA		Pleuritic pain (胸膜痛)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	41	106					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	FEVER/	[redacted]	[redacted]	6	3	YES,	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]			INVESTIGATI		
			General disorders and administration site conditions	200	205			ONAL		
			(一般・全身障害および投与部位の状態)					TREATMENT		
		Yes/3	Fever/	[redacted]	[redacted]	66	1	YES	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	41	106					
			(一般・全身障害および投与部位の状態)							
		Yes/3	Fever/	[redacted]	[redacted]	5	1	YES	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 23 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			General disorders and administration site conditions	124	128					
			(一般・全身障害および投与部位の状態)							
		Yes/3	Fever/	[redacted]	[redacted]	9	2	NO	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	161	169					
			(一般・全身障害および投与部位の状態)							
		Yes/3	Fever/	[redacted]	[redacted]	1	3	YES,	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]			INVESTIGATI		
			General disorders and administration site conditions	184	184			ONAL		
			(一般・全身障害および投与部位の状態)					TREATMENT		
		Yes/3	Fever/	[redacted]	[redacted]	8	3	YES,	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]			INVESTIGATI		
			General disorders and administration site conditions	190	197			ONAL		
			(一般・全身障害および投与部位の状態)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 24 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/	2[redacted]	Yes/3	Fever/	[redacted]	[redacted]	1	1	YES	2,10	2
[redacted]	CA		Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	247	247					
			(一般・全身障害および投与部位の状態)							
GBR/	6[redacted]	Yes/3	Infusion Related Reaction/	[redacted]	Ongoing		3	NO	999,1	3
[redacted]	OTH		Infusion related reaction (注入に伴う反応)/	[redacted]					0	
			Injury, poisoning and procedural complications	169&						
			(傷害、中毒および処置合併症)							
		Yes/3	Syncopal Episode/	[redacted]	[redacted]	5	3	NO	999,1	2
			Syncope (失神)/	[redacted]	[redacted]				0	
			Nervous system disorders (神経系障害)	148&	152&					
		Yes/3	orthostatic collapse/	[redacted]	[redacted]	7	3	NO	999	2
			Syncope (失神)/	[redacted]	[redacted]					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 25 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Nervous system disorders (神経系障害)	159&	165&					
GBR/	4[redacted]	Yes/3	Fever/	[redacted]	[redacted]	4	1	NO	2,10	2
[redacted]	CA		Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	152	155					
			(一般・全身障害および投与部位の状態)							
GBR/	5[redacted]	Yes/3	Fever/	[redacted]	[redacted]	20	2	NO	2,10	2
[redacted]	CA		Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	66	85					
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 26 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (days)	Grade	Relat. study drug	Action taken	Out-come
GBR/ [redacted]	7[redacted] CA	Yes/6	Viral Meningitus/ Meningitis viral (ウイルス性髄膜炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 52	Ongoing		3	NO	5,10	1
		Yes/3	Vaginal Inflammation/ Vulvovaginal inflammation (外陰腟の炎症)/ Reproductive system and breast disorders (生殖系および乳房障害)	[redacted] 22	Ongoing		3	NO	2,10	1
GBR/ [redacted]	7[redacted] CA	Yes/3	adenovirus reactivation/ Adenovirus reactivation (アデノウイルス再活性化)/ Infections and infestations (感染症および寄生虫症)	[redacted] 74	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	2,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 27 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	bronchial infection/	[redacted]	Ongoing		3	NO	999,10	1
			Bronchitis (気管支炎)/	[redacted]						
			Infections and infestations	102						
			(感染症および寄生虫症)							
		Yes/3	CMV Reactivation/	[redacted]	[redacted]	33	2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
			Cytomegalovirus infection reactivation	[redacted]	[redacted]					
			(サイトメガロウイルス感染再燃)/	11	43					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 28 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GBR/ [redacted]	7[redacted] CA	Yes/3	CMV Reactivation/ Cytomegalovirus infection reactivation (サイトメガロウイルス感染再燃)/ Infections and infestations (感染症および寄生虫症)	[redacted] 61	Ongoing		3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
		Yes/3	Dehydration/ Dehydration (脱水)/ Metabolism and nutrition disorders (代謝および栄養障害)	[redacted] 50	[redacted] 53	4	3	NO	2,10	2
		Yes/3	mycobacterium chimera infection/ Mycobacterial infection (マイコバクテリア感染)/ Infections and infestations (感染症および寄生虫症)	20[redacted]	Ongoing		3	YES, INVESTIGATIONAL TREATMENT	2	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 29 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/	Lung infection/	[redacted]	[redacted]	57	5	NO	999,1	5
		1,3	Pneumonia (肺炎)/	[redacted]	[redacted]				0	
			Infections and infestations	129&	185&					
			(感染症および寄生虫症)							
GRC/	3[redacted]	Yes/3	hemorrhage at Hickman catheter puncture site/	[redacted]	[redacted]	3	2	NO	4	2
[redacted]	CA		Catheter site haemorrhage	[redacted]	[redacted]					
			(カテーテル留置部位出血)/	5	7					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/3	febrile gingivostomatitis/	[redacted]	[redacted]	18	3	YES, BOTH	999,1	2
			Stomatitis (口内炎)/	[redacted]	[redacted]			AND/OR	0	
			Gastrointestinal disorders (胃腸障害)	30	47			INDISTINGUI		
								SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 30 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
IND/	1[redacted]	Yes/3	Lung Infection/	[redacted]	[redacted]	6	3	YES,	2,10	3
[redacted]	AS		Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	31	36			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/3	Lung Infection/	[redacted]	[redacted]	4	3	YES,	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	44	47			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/3	Fever/	[redacted]	[redacted]	4	1	YES, BOTH	4	2
			Pyrexia (発熱)/	[redacted]	[redacted]			AND/OR		
			General disorders and administration site conditions	72	75			INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
IND/	3[redacted]	Yes/3	diabetic keto acidosis/	[redacted]	[redacted]	3	2	NO	999,1	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 31 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	AS		Diabetic ketoacidosis (糖尿病性ケトアシドーシス)/ Metabolism and nutrition disorders (代謝および栄養障害)	[redacted] -8#	[redacted] -6#				0	
IND/ [redacted]	3[redacted] AS	Yes/3	Lower respiratory Tract Infection/ Lower respiratory tract infection (下気道感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 39	[redacted] 44	6	2	YES, INVESTIGATIONAL TREATMENT	3,10	2
IND/ [redacted]	4[redacted] AS	Yes/3	Intracranial Bleed/ Haemorrhage intracranial (頭蓋内出血)/ Nervous system disorders (神経系障害)	[redacted] 300	[redacted] 301	2	3	YES, INVESTIGATIONAL TREATMENT	4,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 32 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
IND/	4[redacted]	Yes/1	Intracranial Bleed/	[redacted]	[redacted]	1	5	YES,	5,10	5
[redacted]	AS		Haemorrhage intracranial (頭蓋内出血)/	[redacted]	[redacted]			INVESTIGATI		
			Nervous system disorders (神経系障害)	301	301			ONAL		
								TREATMENT		
		Yes/3	Lung Infection/	[redacted]	[redacted]	7	3	YES, BOTH	3,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	286	292			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	Thrombocytopenia/	[redacted]	Ongoing		4	YES	5,10	1
			Thrombocytopenia (血小板減少症)/	[redacted]						
			Blood and lymphatic system disorders	300						
			(血液およびリンパ系障害)							
ISR/	5[redacted]	Yes/3	Cryptococcal meningitis/	[redacted]	[redacted]	8	3	YES,	3,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 33 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Meningitis cryptococcal (クリプトコッカス性髄膜炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 718	[redacted] 725			INVESTIGATIONAL TREATMENT		
ISR/ [redacted]	5[redacted] CA	Yes/3	anorexia/ Decreased appetite (食欲減退)/ Metabolism and nutrition disorders (代謝および栄養障害)	[redacted] 94	Ongoing		3	NO	2,10	1
ITA/ [redacted]	2[redacted] CA	Yes/2	RESPIRATORY INSUFFICIENCY/ Respiratory failure (呼吸不全)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 8	[redacted] 15	8	4	NO	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 34 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	5[redacted]	Yes/3	Hypoxia/	[redacted]	[redacted]	14	3	YES, BOTH	5,10	2
[redacted]	CA		Hypoxia (低酸素症)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	236	249			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/3	Pulmonary edema/	[redacted]	[redacted]	35	2	YES, BOTH	2,10	2
			Pulmonary oedema (肺水腫)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	5	39			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
ITA/	2[redacted]	Yes/3	sepsis/	[redacted]	[redacted]	16	3	YES, BOTH	3,10	2
[redacted]	CA		Sepsis (敗血症)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	77	92			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 35 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	4[redacted] CA	Yes/3	erysipelas/	[redacted]	[redacted]	12	3	NO	2,10	2
			Erysipelas (丹毒)/	[redacted]	[redacted]					
			Infections and infestations	158	169					
			(感染症および寄生虫症)							
ITA/ [redacted]	2[redacted] CA	Yes/3	suspect bacteraemia/	[redacted]	[redacted]	28	3	YES, BOTH	4,10	2
			Bacteraemia (菌血症)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	92	119			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	CMV reactivation/	[redacted]	[redacted]	26	3	NO	2,10	2
			Cytomegalovirus infection reactivation	[redacted]	[redacted]					
			(サイトメガロウイルス感染再燃)/	19	44					
			Infections and infestations							
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 36 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	2[redacted]	Yes/3	CMV reactivation/	[redacted]	[redacted]	16	3	NO	2,10	2
[redacted]	CA		Cytomegalovirus infection reactivation	[redacted]	[redacted]					
			(サイトメガロウイルス感染再燃)/	69	84					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/6	Measles infection/	[redacted]	[redacted]	4	4	NO	999	2
			Measles (麻疹)/	[redacted]	[redacted]					
			Infections and infestations	156&	159&					
			(感染症および寄生虫症)							
ITA/	5[redacted]	Yes/	septic shock/	[redacted]	[redacted]	36	4	YES, BOTH	5,10	2
[redacted]	CA	2,3	Septic shock (敗血症性ショック)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	21	56&			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 37 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	1[redacted]	Yes/	acute respiratory distress syndrome/	[redacted]	[redacted]	4	5	NO	999,1	5
[redacted]	CA	1,3	Acute respiratory distress syndrome	[redacted]	[redacted]				0	
			(急性呼吸窮迫症候群)/	130	133					
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	herpes zoester infection/	[redacted]	Ongoing		3	NO	4,10	1
			Herpes zoster (帯状疱疹)/	[redacted]						
			Infections and infestations	102						
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 38 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	4[redacted]	Yes/1	WORSENING OF THE GENERAL CONDITIONS/	[redacted]	[redacted]	1	5	NO	5	5
[redacted]	CA		General physical health deterioration	[redacted]	[redacted]					
			(全身健康状態悪化)/	71&	71&					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/3	HEMATEMESIS/	[redacted]	[redacted]	6	3	NO	2,10	2
			Haematemesis (吐血)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	61&	66&					
		Yes/3	acute pancreatitis/	[redacted]	Ongoing		2	NO	2,10	1
			Pancreatitis acute (急性膵炎)/	[redacted]						
			Gastrointestinal disorders (胃腸障害)	28						
		Yes/3	PNEUMOCYSTIS PNEUMONIA/	[redacted]	Ongoing		3	NO	2,10	3
			Pneumocystis jirovecii pneumonia	[redacted]						
			(ニューモシスチス・イロベチイ肺炎)/	37						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 39 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	unknown origin fever/	[redacted]	[redacted]	4	2	NO	4,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	27	30					
			(一般・全身障害および投与部位の状態)							
JPN/ [redacted]	6[redacted] AS	Yes/2	Bacterial pulmonary infection/	[redacted]	[redacted]	10	4	YES, BOTH AND/OR	5,10	1
			Pneumonia bacterial (細菌性肺炎)/	[redacted]	[redacted]					
			Infections and infestations	41	50			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 40 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	6[redacted]	Yes/1	Bacterial pulmonary infection/	[redacted]	[redacted]	1	5	YES, BOTH	999	5
[redacted]	AS		Pneumonia bacterial (細菌性肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	51	51			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
JPN/	5[redacted]	Yes/3	Pneumococcal infection/	[redacted]	[redacted]	16	3	YES, BOTH	2,10	3
[redacted]	AS		Pneumococcal infection (肺炎球菌感染)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	214	229			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	Urinary infection/	[redacted]	[redacted]	12	3	YES, BOTH	2,10	3
			Urinary tract infection (尿路感染)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	52	63			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 41 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	4[redacted]	Yes/3	Decline of Activities of daily living/	[redacted]	Ongoing		3	YES, BOTH	2	1
[redacted]	AS		Loss of personal independence in daily activities	[redacted]				AND/OR		
			(日常活動における個人の自立の喪失)/	15				INDISTINGUI		
			Social circumstances (社会環境)					SHABLE		
		Yes/1	SEPSIS/	[redacted]	[redacted]	1	5	YES, BOTH	999,1	5
			Sepsis (敗血症)/	[redacted]	[redacted]			AND/OR	0	
			Infections and infestations	57	57			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	Sepsis/	[redacted]	[redacted]	18	4	YES, BOTH	5,10	1
			Sepsis (敗血症)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	39	56			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 42 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	2[redacted]	Yes/3	upper respiratory inflammation/	[redacted]	[redacted]	17	3	YES, BOTH	2,10	2
[redacted]	AS		Upper respiratory tract inflammation (上気道の炎症)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	365	381			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
JPN/	2[redacted]	Yes/3	pyelonephritis/	[redacted]	[redacted]	29	3	YES, BOTH	3,10	2
[redacted]	AS		Pyelonephritis (腎盂腎炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	419	447			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
JPN/	5[redacted]	Yes/3	pneumonia/	[redacted]	[redacted]	2	3	YES, BOTH	3,10	1
[redacted]	AS		Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	21	22			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 43 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	pneumonia/	[redacted]	[redacted]	2	3	YES,	3,10	1
			Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	21	22			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/2	pneumonia/	[redacted]	[redacted]	6	4	YES, BOTH	5	1
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	23	28			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/	pneumonia/	[redacted]	[redacted]	6	4	YES, BOTH	5,10	1
		2,3	Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	23	28			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 44 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	5	Yes/1	pneumonia/	[redacted]	[redacted]	1	5	YES,	999	5
[redacted]	AS		Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	29	29			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/1	pneumonia/	[redacted]	[redacted]	1	5	YES, BOTH	999	5
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	29	29			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	respiratory failure/	[redacted]	[redacted]	7	4	YES, BOTH	5,10	1
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	22	28			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/1	respiratory failure/	[redacted]	[redacted]	1	5	YES, BOTH	999	5
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders	29	29			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
JPN/	6[redacted]	Yes/3	Right Pneumothorax/	[redacted]	[redacted]	16	3	NO	3,10	2
[redacted]	AS		Pneumothorax (気胸)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	29	44					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Right Pneumothorax/	[redacted]	Ongoing		3	NO	5,10	1
			Pneumothorax (気胸)/	[redacted]						
			Respiratory, thoracic and mediastinal disorders	63						
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 46 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	5[redacted] AS	Yes/2	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 80	[redacted] 80	1	4	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	1
		Yes/1	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 81	[redacted] 81	1	5	NO	2	5
		Yes/2	posttransplantation lymphoproliferative disease/ Post transplant lymphoproliferative disorder (移植後リンパ増殖性障害)/ Neoplasms benign, malignant and unspecified (incl cysts	[redacted] 67	Ongoing		3	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 47 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			and polyps) (良性、悪性および詳細不明の新生物（嚢胞 およびポリープを含む）)							
JPN/ [redacted]	4[redacted] AS	Yes/3	Abdominal pain/ Abdominal pain (腹痛)/ Gastrointestinal disorders (胃腸障害)	[redacted] [redacted] 536	Ongoing	2	NO		2,10	1
		Yes/3	Dyspnoea/ Dyspnoea (呼吸困難)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] [redacted] 504	Ongoing	2	NO		2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 48 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	4[redacted]	Yes/3	Hypoxia/	[redacted]	Ongoing		2	NO	2,10	1
[redacted]	AS		Hypoxia (低酸素症)/	[redacted]						
			Respiratory, thoracic and mediastinal disorders	287						
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Pneumonia/	[redacted]	[redacted]	32	3	NO	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	443	474					
			(感染症および寄生虫症)							
		Yes/3	Pneumothorax/	[redacted]	[redacted]	13	2	NO	2,10	2
			Pneumothorax (気胸)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	473	485					
			(呼吸器、胸郭および縦隔障害)							
JPN/	3[redacted]	Yes/3	Small intestine ileus/	[redacted]	[redacted]	3	3	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 49 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	AS		Ileus (イレウス)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	25	27					
		Yes/1	Small intestine ileus/	[redacted]	[redacted]	1	5	NO	999,1	5
			Ileus (イレウス)/	[redacted]	[redacted]				0	
			Gastrointestinal disorders (胃腸障害)	28	28					
JPN/	3[redacted]	Yes/2	Brain abscess/	[redacted]	[redacted]	22	4	YES, BOTH	5,10	3
[redacted]	AS		Brain abscess (脳膿瘍)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	146	167			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	Brain abscess/	[redacted]	[redacted]	21	3	YES, BOTH	999,1	3
			Brain abscess (脳膿瘍)/	[redacted]	[redacted]			AND/OR	0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 50 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	168	188&			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 51 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	3[redacted]	Yes/2	Brain abscess/	[redacted]	[redacted]	66	2	YES, BOTH	999,1	2
[redacted]	AS		Brain abscess (脳膿瘍)/	[redacted]	[redacted]			AND/OR	0	
			Infections and infestations	189&	254&			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	Cytomegalovirus infection/	[redacted]	[redacted]	29	3	YES, BOTH	2,10	2
			Cytomegalovirus infection	[redacted]	[redacted]			AND/OR		
			(サイトメガロウイルス感染)/	22	50			INDISTINGUI		
			Infections and infestations					SHABLE		
			(感染症および寄生虫症)							
		Yes/2	Pneumonia/	[redacted]	Ongoing		2	YES, BOTH	999,1	1
			Pneumonia (肺炎)/	[redacted]				AND/OR	0	
			Infections and infestations	189&				INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	pneumonia/	[redacted]	[redacted]	22	4	YES, BOTH	5,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 52 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	146	167			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/2	pneumonia/	[redacted]	[redacted]	21	3	YES, BOTH	999,1	3
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR	0	
			Infections and infestations	168	188&			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
JPN/ [redacted]	5[redacted] AS	Yes/3	worsening of back pain/	[redacted]	[redacted]	79	3	NO	2,10	2
			Back pain (背部痛)/	[redacted]	[redacted]					
			Musculoskeletal and connective tissue disorders	31	109&					
			(筋骨格系および結合組織障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 53 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	5[redacted]	Yes/3	lung infection/	[redacted]	[redacted]	210	3	NO	5,10	2
[redacted]	AS		Pneumonia (肺炎)/	[redacted]						
			Infections and infestations	33	242&					
			(感染症および寄生虫症)							
		Yes/3	bleeding from splenic artery/	[redacted]	Ongoing		3	NO	999,1	3
			Splenic haemorrhage (脾臓出血)/	[redacted]					0	
			Blood and lymphatic system disorders	59						
			(血液およびリンパ系障害)							
JPN/	5[redacted]	Yes/3	worsening of lung infection/	[redacted]	Ongoing		3	NO	5,10	3
[redacted]	AS		Pneumonia (肺炎)/	[redacted]						
			Infections and infestations	91						
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 54 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	1[redacted]	Yes/3	Herpes zoster/	[redacted]	[redacted]	15	3	YES,	2,10	2
[redacted]	AS		Herpes zoster (帯状疱疹)/	[redacted]	[redacted]			INVESTIGATIONAL		
			Infections and infestations	251	265					
			(感染症および寄生虫症)					TREATMENT		
NLD/	4[redacted]	Yes/3	lung infection/	[redacted]	[redacted]	14	3	NO	4,10	2
[redacted]	CA		Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	262	275					
			(感染症および寄生虫症)							
POL/	4[redacted]	Yes/3	anemia/	[redacted]	[redacted]	4	3	YES,	3,10	2
[redacted]	CA		Anaemia (貧血)/	[redacted]	[redacted]			INVESTIGATIONAL		
			Blood and lymphatic system disorders	91	94					
			(血液およびリンパ系障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 55 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
POL/ [redacted]	4[redacted]	Yes/3	anemia/	[redacted]	[redacted]	2	3	YES,	3,10	3
[redacted]	CA		Anaemia (貧血)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	148	149			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
		Yes/	anemia/	[redacted]	[redacted]	1	3	YES,	999	3
		3,4	Anaemia (貧血)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	177	177			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
		Yes/3	Cryptogenic Organizing Pneumonia (COP) related to chronic	[redacted]	[redacted]	6	3	NO	999,1	1
			graft-vesrsus-host disease/	[redacted]	[redacted]				0	
			Organising pneumonia (器質化肺炎)/	173	178					
			Respiratory, thoracic and mediastinal disorders							
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 56 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
POL/	6[redacted]	Yes/	Weakness/	[redacted]	Ongoing		4	YES, BOTH	4	1
[redacted]	CA	3,6	Asthenia (無力症)/	[redacted]				AND/OR		
			General disorders and administration site conditions	29				INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
		Yes/	dyspnoea/	[redacted]	Ongoing		4	YES, BOTH	4	1
		3,6	Dyspnoea (呼吸困難)/	[redacted]				AND/OR		
			Respiratory, thoracic and mediastinal disorders	29				INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/	Pneumonia/	[redacted]	[redacted]	33	3	YES, BOTH	5,10	4
		3,6	Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	29	61			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
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Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
POL/	6[redacted]	Yes/	Pneumonia/	[redacted]	[redacted]	1	5	YES, BOTH	999	5
[redacted]	CA	1,2,	Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
		3,4,	Infections and infestations	62	62			INDISTINGUI		
		6	(感染症および寄生虫症)					SHABLE		
		Yes/	Tachypnoea/	[redacted]	Ongoing		4	YES, BOTH	4	1
		3,6	Tachypnoea (頻呼吸)/	[redacted]				AND/OR		
			Respiratory, thoracic and mediastinal disorders	29				INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
PRT/	5[redacted]	Yes/3	FEBRILE NEUTROPENIA/	[redacted]	[redacted]	5	4	NO	4,10	2
[redacted]	CA		Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]					
			Blood and lymphatic system disorders	15	19					
			(血液およびリンパ系障害)							
		Yes/3	Pneumonitis/	[redacted]	Ongoing		4	NO	999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 58 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonitis (肺臓炎)/	[redacted]					0	
			Respiratory, thoracic and mediastinal disorders	22						
			(呼吸器、胸郭および縦隔障害)							
SAU/	3[redacted]	Yes/3	semi-unconsciousness/	20[redacted]	[redacted]		3	NO	2	2
[redacted]	OTH		Depressed level of consciousness		[redacted]					
			(意識レベルの低下)/		93					
			Nervous system disorders (神経系障害)							
		Yes/3	anasarca/	[redacted]	[redacted]	54	3	YES, OTHER	2,10	2
			Generalised oedema (全身性浮腫)/	[redacted]	[redacted]			STUDY		
			General disorders and administration site conditions	26	79			TREATMENT		
			(一般・全身障害および投与部位の状態)					(NON-INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 59 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
SAU/ [redacted]	3[redacted] OTH	Yes/3	anasarca/	[redacted]	[redacted]	7	3	YES, OTHER	2,10	2
			Generalised oedema (全身性浮腫)/	[redacted]	[redacted]			STUDY		
			General disorders and administration site conditions	91	97			TREATMENT		
			(一般・全身障害および投与部位の状態)					(NON-INVESTIGATIONAL)		
		Yes/3	lower limb edema/	[redacted]	[redacted]	4	3	NO	2,10	2
			Oedema peripheral (末梢性浮腫)/	[redacted]	[redacted]					
			General disorders and administration site conditions	26	29					
			(一般・全身障害および投与部位の状態)							
		Yes/3	multilevel compression fractures of lumbar spine/	[redacted]	Ongoing		3	NO	2,10	1
			Spinal compression fracture (脊椎圧迫骨折)/	[redacted]						
			Injury, poisoning and procedural complications	26						
			(傷害、中毒および処置合併症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 60 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
SAU/	1[redacted]	Yes/2	neutropenia/	[redacted]	[redacted]	8	4	NO	4,10	2
[redacted]	OTH		Neutropenia (好中球減少症)/	[redacted]	[redacted]					
			Blood and lymphatic system disorders	281	288					
			(血液およびリンパ系障害)							
SAU/	3[redacted]	Yes/2	neutropenia/	[redacted]	[redacted]	7	4	YES, BOTH	4,10	3
[redacted]	OTH		Neutropenia (好中球減少症)/	[redacted]	[redacted]			AND/OR		
			Blood and lymphatic system disorders	230	236			INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		
		Yes/2	neutropenia/	[redacted]	[redacted]	32	4	NO	999,1	2
			Neutropenia (好中球減少症)/	[redacted]	[redacted]				0	
			Blood and lymphatic system disorders	243	274&					
			(血液およびリンパ系障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 61 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
SAU/ [redacted]	3[redacted] OTH	Yes/2	decrease platelet/	[redacted]	[redacted]	7	3	NO	999,10	1
			Platelet count decreased (血小板数減少)/	[redacted]	[redacted]					
			Investigations (臨床検査)	230	236					
		Yes/2	decrease platelet/	[redacted]	[redacted]	26	4	NO	999,10	2
			Platelet count decreased (血小板数減少)/	[redacted]	[redacted]					
			Investigations (臨床検査)	237	262&					
		Yes/3	pneumonia/	[redacted]	[redacted]	12	3	NO	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	184	195					
			(感染症および寄生虫症)							
		Yes/3	fever/	[redacted]	[redacted]	4	1	NO	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	184	187					
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 62 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/2	decrease WBC/	[redacted]	[redacted]	15	4	NO	999	2
			White blood cell count decreased (白血球数減少)/	[redacted]	[redacted]					
			Investigations (臨床検査)	247	261&					
SAU/	4[redacted]	Yes/3	pneumonia/	[redacted]	[redacted]	5	3	YES, BOTH	2,10	2
[redacted]	OTH		Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	22	26			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	pneumonia/	[redacted]	[redacted]	8	3	NO	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	35	42					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 63 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
SAU/	4[redacted]	Yes/3	pneumonia/	[redacted]	[redacted]	8	3	NO	2,10	2
[redacted]	OTH		Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	89	96					
			(感染症および寄生虫症)							
		Yes/3	pneumonia/	[redacted]	[redacted]	15	3	NO	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	268	282					
			(感染症および寄生虫症)							
		Yes/3	tracheitis/	[redacted]	[redacted]	5	3	NO	2,10	2
			Tracheitis (気管炎)/	[redacted]	[redacted]					
			Infections and infestations	22	26					
			(感染症および寄生虫症)							
TUR/	5[redacted]	Yes/3	Headache/	[redacted]	[redacted]	5	3	NO	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 64 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	AS		Headache (頭痛)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	32	36					
TUR/	6[redacted]	Yes/3	Fever/	[redacted]	[redacted]	3	3	YES, BOTH	4,10	2
[redacted]	AS		Pyrexia (発熱)/	[redacted]	[redacted]			AND/OR		
			General disorders and administration site conditions	33	35			INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
TUR/	5[redacted]	Yes/3	pneumonia/	[redacted]	[redacted]	5	3	YES,	4,10	2
[redacted]	CA		Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	40	44			ONAL		
			(感染症および寄生虫症)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 65 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
TUR/ [redacted]	5[redacted] CA	Yes/3	pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 106	[redacted] 115	10	2	YES, INVESTIGATIONAL TREATMENT	5,10	3
TUR/ [redacted]	4[redacted] CA	Yes/2	Pulmoner aspergillozis/ Bronchopulmonary aspergillosis (気管支肺アスペルギルス症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 29	[redacted] 33	5	3	YES, INVESTIGATIONAL TREATMENT	4,10	1
		Yes/1	Pulmoner aspergillozis/ Bronchopulmonary aspergillosis (気管支肺アスペルギルス症)/ Infections and infestations	[redacted] 33	[redacted] 33	1	5	YES, INVESTIGATIONAL TREATMENT	4,10	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 66 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
		Yes/3	Febrile neutropenia/	[redacted]	[redacted]	6	3	YES,	4,10	3
			Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	24	29			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
TUR/ [redacted]	2[redacted] CA	Yes/3	Acute kidney injur/	[redacted]	[redacted]	6	3	YES,	5,10	2
			Acute kidney injury (急性腎障害)/	[redacted]	[redacted]			INVESTIGATI		
			Renal and urinary disorders (腎および尿路障害)	64	69			ONAL		
								TREATMENT		
		Yes/3	Febrile Neutropenia/	[redacted]	[redacted]	6	3	YES,	4,10	2
			Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	35	40			ONAL		
			(血液およびリンパ系障害)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 67 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
TUR/	2[redacted]	Yes/3	Febrile neutropenia/	[redacted]	[redacted]	9	3	YES,	4,10	2
[redacted]	CA		Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	7	15			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
		Yes/2	multilobar pneumonia/	[redacted]	[redacted]	33	3	YES,	999,1	1
			Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI	0	
			Infections and infestations	66	98&			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/1	multilobar pneumonia/	[redacted]	[redacted]	1	5	YES,	2	5
			Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	99&	99&			ONAL		
			(感染症および寄生虫症)					TREATMENT		
USA/	4[redacted]	Yes/3	Back Pain/	[redacted]	[redacted]	1	2	YES,	2	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 68 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Back pain (背部痛)/	[redacted]	[redacted]			INVESTIGATI		
			Musculoskeletal and connective tissue disorders	38	38			ONAL		
			(筋骨格系および結合組織障害)					TREATMENT		
		Yes/3	Pneumonia/	[redacted]	[redacted]	6	1	YES, BOTH	5,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	49	54			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	Fever/	[redacted]	[redacted]	3	3	YES,	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]			INVESTIGATI		
			General disorders and administration site conditions	38	40			ONAL		
			(一般・全身障害および投与部位の状態)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 69 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	4[redacted]	Yes/3	Pyrexia/	[redacted]	[redacted]	6	1	YES, BOTH	5	2
[redacted]	CA		Pyrexia (発熱)/	[redacted]	[redacted]			AND/OR		
			General disorders and administration site conditions	49	54			INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
USA/	7[redacted]	Yes/3	Atrial flutter/	[redacted]	Ongoing		3	YES,	5,10	3
[redacted]	NA		Atrial flutter (心房粗動)/	[redacted]				INVESTIGATI		
			Cardiac disorders (心臓障害)	61				ONAL		
								TREATMENT		
		Yes/3	Generalized muscle weakness/	[redacted]	Ongoing		3	YES,	2	3
			Muscular weakness (筋力低下)/	[redacted]				INVESTIGATI		
			Musculoskeletal and connective tissue disorders	61				ONAL		
			(筋骨格系および結合組織障害)					TREATMENT		
		Yes/1	LUNG INFECTION/	[redacted]	[redacted]	1	5	YES,	999,1	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 70 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonia (肺炎)/	[redacted]	[redacted]			INVESTIGATI	0	
			Infections and infestations	92	92			ONAL		
			(感染症および寄生虫症)					TREATMENT		
USA/	5[redacted]	Yes/3	Congestive Heart Failure/	[redacted]	Ongoing		3	NO	999	1
[redacted]	CA		Cardiac failure congestive (うっ血性心不全)/	[redacted]						
			Cardiac disorders (心臓障害)	194						
		Yes/3	E. coli Septic Shock/	[redacted]	Ongoing		3	NO	5,10	1
			Escherichia sepsis (大腸菌性敗血症)/	[redacted]						
			Infections and infestations	192						
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 71 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	5[redacted] CA	Yes/3	multi-organ failure/ Multiple organ dysfunction syndrome (多臓器機能不全症候群)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] 192	Ongoing		3	NO	5,10	1
		Yes/3	(Multifocal) Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 192	Ongoing		3	NO	5,10	1
		Yes/3	CMV Pneumonia/ Pneumonia cytomegaloviral (サイトメガロウイルス性肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 22	[redacted] [redacted] 83	62	2	NO	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 72 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	5[redacted]	Yes/3	NSTEMI/	[redacted]	[redacted]	3	3	NO	3,10	2
[redacted]	CA		Acute myocardial infarction (急性心筋梗塞)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	-1#	2					
		Yes/3	Chest pain - cardiac/	[redacted]	[redacted]	15	3	NO	5,10	2
			Angina pectoris (狭心症)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	-1#	14					
USA/	6[redacted]	Yes/3	Back pain/	[redacted]	[redacted]	5	3	YES, BOTH	4,10	2
[redacted]	CA		Back pain (背部痛)/	[redacted]	[redacted]			AND/OR		
			Musculoskeletal and connective tissue disorders	231	235			INDISTINGUI		
			(筋骨格系および結合組織障害)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 73 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	6[redacted]	Yes/3	Lung infection (pneumonia)/	[redacted]	[redacted]	13	3	YES, BOTH	4,10	2
[redacted]	CA		Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	360	372			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	pneumonia/	[redacted]	[redacted]	3	3	NO	999	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	652	654					
			(感染症および寄生虫症)							
		Yes/3	Fever/	[redacted]	[redacted]	2	2	YES, BOTH	4,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]			AND/OR		
			General disorders and administration site conditions	231	232			INDISTINGUI		
			(一般・全身障害および投与部位の状態)					SHABLE		
USA/	4[redacted]	Yes/3	ABDOMINAL PAIN/	[redacted]	[redacted]	35	3	YES,	2,10	3

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 74 of 151)

Treatment: Ruxolitinib 10 mg BID

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	NA		Abdominal pain (腹痛)/	[redacted]	[redacted]			INVESTIGATI		
			Gastrointestinal disorders (胃腸障害)	22	56			ONAL		
								TREATMENT		
USA/	5[redacted]	Yes/	bilateral lower extremity DVT/	[redacted]	[redacted]	4	2	NO	2,10	4
[redacted]	OTH	2,3	Deep vein thrombosis (深部静脈血栓症)/	[redacted]	[redacted]					
			Vascular disorders (血管障害)	87	90					
		Yes/	pulmonary embolism/	[redacted]	[redacted]	6	3	NO	2,10	4
		2,3	Pulmonary embolism (肺塞栓症)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	85	90					
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 75 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
AUS/	6[redacted]	Yes/3	NON ST ELEVATION MYOCARDIAL INFARCT (NSTEMI)/	[redacted]	[redacted]	49	3	NO		999,1	2
[redacted]	CA		Acute myocardial infarction (急性心筋梗塞)/	[redacted]	[redacted]					0	
			Cardiac disorders (心臓障害)	26	74						
		Yes/3	Pulmonary Embolus/	[redacted]	[redacted]	9	3	NO		999,1	2
			Pulmonary embolism (肺塞栓症)/	[redacted]	[redacted]					0	
			Respiratory, thoracic and mediastinal disorders	77	85						
			(呼吸器、胸郭および縦隔障害)								
AUS/	6[redacted]	Yes/3	Febrile Neutropenia/	[redacted]	[redacted]	6	1	NO		2,10	2
[redacted]	CA		Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]						
			Blood and lymphatic system disorders	109*	114*						
			(血液およびリンパ系障害)								
		Yes/3	febrile neutropenia/	[redacted]	[redacted]	12	4	NO		2,10	2
			Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 76 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Blood and lymphatic system disorders	41*	52*					
			(血液およびリンパ系障害)							
		Yes/3	Hypoxia/	[redacted]	[redacted]	15	3	NO	2	2
			Hypoxia (低酸素症)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	10	24					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Lower Respiratory Tract Infection/	[redacted]	[redacted]	11	3	YES	2,10	2
			Lower respiratory tract infection (下気道感染)/	[redacted]	[redacted]					
			Infections and infestations	62*	72*					
			(感染症および寄生虫症)							
		Yes/3	PNEUMONIA/	[redacted]	[redacted]	10	2	NO	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	66	75					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 77 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUS/	6[redacted]	Yes/3	Respiratory Tract Infection/	[redacted]	[redacted]	13	3	YES	2,10	2
[redacted]	CA		Respiratory tract infection (気道感染)/	[redacted]	[redacted]					
			Infections and infestations	75*	87*					
			(感染症および寄生虫症)							
AUT/	3[redacted]	Yes/3	Increased Creatinine/	[redacted]	[redacted]	4	3	YES,	2,10	3
[redacted]	CA		Blood creatinine increased	[redacted]	[redacted]			INVESTIGATI		
			(血中クレアチニン増加)/	27*	30*			ONAL		
			Investigations (臨床検査)					TREATMENT		
		Yes/3	Increased Creatinine/	[redacted]	[redacted]	23	2	YES,	5,10	3
			Blood creatinine increased	[redacted]	[redacted]			INVESTIGATI		
			(血中クレアチニン増加)/	31*	53*			ONAL		
			Investigations (臨床検査)					TREATMENT		
		Yes/3	Increased Creatinine/	[redacted]	[redacted]	5	1	YES, BOTH	999,1	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 78 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Blood creatinine increased	[redacted]	[redacted]			AND/OR	0	
			(血中クレアチニン増加)/	54*	58*			INDISTINGUI		
			Investigations (臨床検査)					SHABLE		
		Yes/3	Increased Creatinine/	[redacted]	[redacted]	5	2	YES, BOTH	999,1	3
			Blood creatinine increased	[redacted]	[redacted]			AND/OR	0	
			(血中クレアチニン増加)/	59*	63&			INDISTINGUI		
			Investigations (臨床検査)					SHABLE		
		Yes/3	Stomach flu/	[redacted]	[redacted]	4	3	NO	999	2
			Gastroenteritis viral (ウイルス性胃腸炎)/	[redacted]	[redacted]					
			Infections and infestations	148	151					
			(感染症および寄生虫症)							
		Yes/3	Nausea/	[redacted]	[redacted]	4	3	NO	999	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 79 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Nausea (悪心)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	148	151					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 80 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
AUT/	3	Yes/3	Pneumatosis colonflexur right/			4	1	NO	999	2
	CA		Pneumatosis intestinalis (腸壁気腫症)/							
			Gastrointestinal disorders (胃腸障害)	148	151					
		Yes/3	Thrombocytopenia/			28	4	YES,	5,10	3
			Thrombocytopenia (血小板減少症)/					INVESTIGATI		
			Blood and lymphatic system disorders	31*	58*			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
AUT/	6	Yes/3	Reduced general condition/		Ongoing		3	NO	5	1
	CA		General physical health deterioration							
			(全身健康状態悪化)/	17						
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 81 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
BEL/ [redacted]	7[redacted] CA	Yes/3	absces upper arm/	[redacted]	[redacted]	12	3	NO		999,1	2
			Abscess limb (四肢膿瘍)/	[redacted]	[redacted]					0	
			Infections and infestations	106	117						
			(感染症および寄生虫症)								
		Yes/3	Anorexia/	[redacted]	[redacted]	8	2	NO		999	2
			Decreased appetite (食欲減退)/	[redacted]	[redacted]						
			Metabolism and nutrition disorders	204	211						
			(代謝および栄養障害)								
		Yes/3	e. coli infection/	[redacted]	[redacted]	5	3	NO		2,10	2
			Escherichia infection (大腸菌感染)/	[redacted]	[redacted]						
			Infections and infestations	99	103						
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 82 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
BEL/	7[redacted]	Yes/3	general decline in health/	[redacted]	[redacted]	3	3	NO		999	2
[redacted]	CA		General physical health deterioration	[redacted]	[redacted]						
			(全身健康状態悪化)/	237	239						
			General disorders and administration site conditions								
			(一般・全身障害および投与部位の状態)								
		Yes/3	hematuria/	[redacted]	[redacted]	11	3	NO		999	2
			Haematuria (血尿)/	[redacted]	[redacted]						
			Renal and urinary disorders (腎および尿路障害)	241	251						
		Yes/3	hypotension/	[redacted]	[redacted]	11	3	NO		999	2
			Hypotension (低血圧)/	[redacted]	[redacted]						
			Vascular disorders (血管障害)	241	251						
		Yes/3	Urinary retention/	[redacted]	[redacted]	4	2	NO		999,1	2
			Urinary retention (尿閉)/	[redacted]	[redacted]					0	
			Renal and urinary disorders (腎および尿路障害)	266	269						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 83 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/3	urosepsis/	[redacted]	[redacted]	12	3	NO		999,10	2
			Urosepsis (尿路性敗血症)/	[redacted]	[redacted]						
			Infections and infestations	240	251						
			(感染症および寄生虫症)								
CAN/ [redacted]	6[redacted] CA	Yes/3	Lung Infection: Pneumonia/	[redacted]	[redacted]	4	3	NO		999,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]						
			Infections and infestations	-6#	-3#						
			(感染症および寄生虫症)								
CHE/ [redacted]	6[redacted] CA	Yes/3	Abdominal pain/	[redacted]	[redacted]	15	2	NO		2,10	2
			Abdominal pain (腹痛)/	[redacted]	[redacted]						
			Gastrointestinal disorders (胃腸障害)	414*	428*						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 84 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CHE/ [redacted]	6[redacted] CA	Yes/3	Anemia/	[redacted]	Ongoing		2	YES, BOTH	2	3
			Anaemia (貧血)/	[redacted]				AND/OR		
			Blood and lymphatic system disorders	85*				INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		
		Yes/3	Bronchial infection/	[redacted]	[redacted]	31	3	YES, BOTH	2,10	2
			Bronchitis (気管支炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	159*	189*			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	Depression/	[redacted]	[redacted]	71	2	NO	2,10	2
			Depression (うつ病)/	[redacted]	[redacted]					
			Psychiatric disorders (精神障害)	7*	77*					
		Yes/3	Diarrhea/	[redacted]	[redacted]	3	1	NO	2	2
			Diarrhoea (下痢)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	84*	86*					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 85 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
CZE/ [redacted]	5[redacted] CA	Yes/3	INFECTION DEMONSTRATED BY FEBRILIA AND SHIVER/	[redacted]	[redacted]	52	3	NO	5,10	2
			Febrile infection (熱性感染症)/	[redacted]	[redacted]					
			Infections and infestations	182	233&					
			(感染症および寄生虫症)							
		Yes/3	Pneumococcal infection/	[redacted]	[redacted]	35	4	NO	4,10	2
			Pneumococcal infection (肺炎球菌感染)/	[redacted]	[redacted]					
			Infections and infestations	84	118					
			(感染症および寄生虫症)							
DEU/ [redacted]	6[redacted] CA	Yes/3	Diarrhea/	[redacted]	[redacted]	5	3	NO	2,10	3
			Diarrhoea (下痢)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	429	433					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 86 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
DEU/	6[redacted]	Yes/3	Laryngeal edema/	[redacted]	[redacted]	3	3	NO		2,10	2
[redacted]	CA		Laryngeal oedema (喉頭浮腫)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders	628	630						
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	syncope/	[redacted]	[redacted]	3	3	NO		2	2
			Syncope (失神)/	[redacted]	[redacted]						
			Nervous system disorders (神経系障害)	545	547						
DEU/	6[redacted]	Yes/3	coxarthrosis/	[redacted]	[redacted]	23	2	NO		2,10	2
[redacted]	CA		Osteoarthritis (変形性関節症)/	[redacted]	[redacted]						
			Musculoskeletal and connective tissue disorders	382	404						
			(筋骨格系および結合組織障害)								
DEU/	5[redacted]	Yes/3	cytomegaly pneumonia/	[redacted]	[redacted]	12	3	NO		2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 87 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Pneumonia cytomegaloviral (サイトメガロウイルス性肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 129	[redacted] 140					
DEU/ [redacted]	6[redacted] CA	Yes/3	Unclear Tumor in the lungs/ Lung neoplasm (肺新生物)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	[redacted] [redacted] 103	Ongoing		3	NO	999	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 88 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/	6[redacted]	Yes/3	suspected gastrointestinal bleeding/	[redacted]	[redacted]	2	3	YES, BOTH	2,10	2
[redacted]	CA		Gastrointestinal haemorrhage (胃腸出血)/	[redacted]	[redacted]			AND/OR		
			Gastrointestinal disorders (胃腸障害)	35	36			INDISTINGUI		
								SHABLE		
		Yes/2	severe pneunomia on both sides/	[redacted]	[redacted]	2	4	YES, BOTH	2,10	1
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	47	48			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/1	severe pneunomia on both sides/	[redacted]	[redacted]	1	5	YES, BOTH	999,1	5
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR	0	
			Infections and infestations	49	49			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
DEU/	5[redacted]	Yes/3	perfusion deficit (fingers)/	[redacted]	[redacted]	12	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 89 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Poor peripheral circulation (末梢循環不良)/	[redacted]	[redacted]					
			Vascular disorders (血管障害)	44	55					
DEU/	5[redacted]	Yes/3	Respiratory Infection/	[redacted]	[redacted]	5	3	YES,	3,10	2
[redacted]	CA		Respiratory tract infection (気道感染)/	[redacted]	[redacted]			INVESTIGATIONAL		
			Infections and infestations	179*	183*			TREATMENT		
			(感染症および寄生虫症)							
DEU/	3[redacted]	Yes/3	Pneumonia/	[redacted]	[redacted]	5	3	YES, OTHER	2,10	2
[redacted]	CA		Pneumonia (肺炎)/	[redacted]	[redacted]			STUDY		
			Infections and infestations	76	80			TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 90 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
DEU/ [redacted]	7[redacted] CA	Yes/3	Kolon Infection/	[redacted]	[redacted]	5	3	NO		2,10	2
			Large intestine infection (大腸感染)/	[redacted]	[redacted]						
			Infections and infestations	46	50						
			(感染症および寄生虫症)								
		Yes/3	Pneumonia/	[redacted]	[redacted]	7	3	NO		2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]						
			Infections and infestations	22	28						
			(感染症および寄生虫症)								
		Yes/3	Virusinfection upper respiratory/	[redacted]	[redacted]	3	2	NO		2	2
			Viral upper respiratory tract infection	[redacted]	[redacted]						
			(ウイルス性上気道感染)/	268	270						
			Infections and infestations								
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 91 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/	5[redacted]	Yes/3	Myocardial infarction/	[redacted]	[redacted]	1	3	NO	4,10	2
[redacted]	CA		Myocardial infarction (心筋梗塞)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	139	139					
DEU/	2[redacted]	Yes/	Seizure/	[redacted]	[redacted]	1	2	NO	999,1	2
[redacted]	CA	2,3	Seizure (痙攣発作)/	[redacted]	[redacted]				0	
			Nervous system disorders (神経系障害)	21	21					
		Yes/3	Thrombotic microangiopathy/	[redacted]	[redacted]	47	3	NO	999,1	4
			Thrombotic microangiopathy (血栓性微小血管症)/	[redacted]	[redacted]				0	
			Blood and lymphatic system disorders (血液およびリンパ系障害)	14	60&					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 92 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
DEU/	6[redacted]	Yes/	atypical hemolytic uremic syndrome/	[redacted]	[redacted]	41	4	YES, OTHER	5,10	2
[redacted]	CA	2,3	Atypical haemolytic uraemic syndrome	[redacted]	[redacted]			STUDY		
			(非定型溶血性尿毒症症候群)/	5	45			TREATMENT		
			Blood and lymphatic system disorders					(NON-INVESTIGATIONAL)		
			(血液およびリンパ系障害)							
		Yes/3	hyperglycemia/	[redacted]	[redacted]	5	3	YES, OTHER	999,10	2
			Hyperglycaemia (高血糖)/	[redacted]	[redacted]			STUDY		
			Metabolism and nutrition disorders	-2#	3			TREATMENT		
			(代謝および栄養障害)					(NON-INVESTIGATIONAL)		
DEU/	4[redacted]	Yes/3	Gastritis/	[redacted]	[redacted]	10	3	NO	999,1	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
[redacted]	CA		Gastritis (胃炎)/	[redacted]	[redacted]				0	
			Gastrointestinal disorders (胃腸障害)	60	69					
		Yes/3	Vomiting/	[redacted]	[redacted]	3	1	NO	999,1	2
			Vomiting (嘔吐)/	[redacted]	[redacted]				0	
			Gastrointestinal disorders (胃腸障害)	89	91					
ESP/	4[redacted]	Yes/1	uncontrolled apergillosis/	[redacted]	[redacted]	1	5	NO	999	5
[redacted]	CA		Aspergillus infection (アスペルギルス感染)/	[redacted]	[redacted]					
			Infections and infestations	82*	82*					
			(感染症および寄生虫症)							
		Yes/3	uncontrolled aspergillosis/	[redacted]	[redacted]	5	4	NO	5	1
			Aspergillus infection (アスペルギルス感染)/	[redacted]	[redacted]					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	78*	82*					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ESP/ [redacted]	4[redacted] CA	Yes/3	INTESTINAL OBSTRUCTION/	[redacted]	[redacted]	15	3	NO		4,10	2
			Intestinal obstruction (腸閉塞)/	[redacted]	[redacted]						
			Gastrointestinal disorders (胃腸障害)	26	40						
		Yes/3	pancitopenia/	[redacted]	[redacted]	20	4	NO		4,10	2
			Pancytopenia (汎血球減少症)/	[redacted]	[redacted]						
			Blood and lymphatic system disorders	135	154						
			(血液およびリンパ系障害)								
		Yes/3	FEVER worsening/	[redacted]	[redacted]	4	3	NO		2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]						
			General disorders and administration site conditions	96	99						
			(一般・全身障害および投与部位の状態)								
		Yes/3	fever worsening(hospitalizaion requiered)/	[redacted]	[redacted]	6	2	NO		2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]						
			General disorders and administration site conditions	22*	27*						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
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Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(一般・全身障害および投与部位の状態)							
ESP/	6[redacted]	Yes/3	Pain in central venous catheter/	[redacted]	[redacted]	9	3	NO	999,1	2
[redacted]	CA		Catheter site pain (カテーテル留置部位疼痛)/	[redacted]	[redacted]				0	
			General disorders and administration site conditions	134	142					
			(一般・全身障害および投与部位の状態)							
		Yes/3	Infection due to Disseminated Herpes Zoster/	[redacted]	[redacted]	5	3	NO	999,1	2
			Herpes zoster disseminated (播種性帯状疱疹)/	[redacted]	[redacted]				0	
			Infections and infestations	-30#	-26#					
			(感染症および寄生虫症)							
		Yes/3	Pneumonia in right lobe/	[redacted]	[redacted]	6	3	NO	4,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	86*	91*					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/	6[redacted]	Yes/3	Clostridium difficile infection/	[redacted]	[redacted]	38	3	NO		2,10	2
[redacted]	UN		Clostridium difficile infection	[redacted]	[redacted]						
			(クロストリジウム・ディフィシレ感染)/	104	141						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	profuse diarrhea/	[redacted]	[redacted]	8	3	NO		999,1	2
			Diarrhoea (下痢)/	[redacted]	[redacted]					0	
			Gastrointestinal disorders (胃腸障害)	100	107						
		Yes/3	aphagia/	[redacted]	[redacted]	9	3	NO		999,1	2
			Dysphagia (嚥下障害)/	[redacted]	[redacted]					0	
			Gastrointestinal disorders (胃腸障害)	-2#	7						
		Yes/3	bleeding in the digestive tract/	[redacted]	[redacted]	6	3	NO		999,1	2
			Gastrointestinal haemorrhage (胃腸出血)/	[redacted]	[redacted]					0	
			Gastrointestinal disorders (胃腸障害)	28	33						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
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Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/3	Peri-vesicular liver abscess/	[redacted]	[redacted]	43	3	NO		999,10	2
			Liver abscess (肝膿瘍)/	[redacted]	[redacted]						
			Infections and infestations	62	104						
			(感染症および寄生虫症)								
FRA/ [redacted]	2[redacted] UN	Yes/3	Intracranial hypertension/	[redacted]	Ongoing		4	NO		2,10	1
			Intracranial pressure increased (頭蓋内圧上昇)/	[redacted]							
			Nervous system disorders (神経系障害)	15*							
		Yes/3	Venous left lateral sinus stenosis/	[redacted]	Ongoing		3	NO		2	1
			Stenosis (狭窄)/	[redacted]							
			General disorders and administration site conditions	17*							
			(一般・全身障害および投与部位の状態)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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treatment. MedDRA version 23.0, CTCAE version 4.03.

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Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
FRA/	2[redacted]	Yes/3	depression/	[redacted]	[redacted]	3	3	NO		999,1	2
[redacted]	UN		Depression (うつ病)/	[redacted]	[redacted]					0	
			Psychiatric disorders (精神障害)	181	183						
		Yes/3	Obliterating bronchiolitis/	[redacted]	[redacted]	11	3	NO		2,10	2
			Obliterative bronchiolitis (閉塞性細気管支炎)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	82	92						
FRA/	4[redacted]	Yes/	cardiogenic shock/	[redacted]	[redacted]	14	4	NO		999,1	1
[redacted]	OTH	2,3	Cardiogenic shock (心原性ショック)/	[redacted]	[redacted]					0	
			Cardiac disorders (心臓障害)	109	122						
		Yes/	cardiogenic shock/	[redacted]	[redacted]	1	5	NO		999,1	5
		1,2,	Cardiogenic shock (心原性ショック)/	[redacted]	[redacted]					0	
		3	Cardiac disorders (心臓障害)	123	123						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 100 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/	septic shock to staphylococcus aureus/	[redacted]	[redacted]	17	5	YES,	5,10	5
		1,3	Septic shock (敗血症性ショック)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	107	123			ONAL		
			(感染症および寄生虫症)					TREATMENT		
GBR/	4[redacted]	Yes/3	Abdominal Pain/	[redacted]	[redacted]	14	3	NO	999,1	2
[redacted]	CA		Abdominal pain (腹痛)/	[redacted]	[redacted]				0	
			Gastrointestinal disorders (胃腸障害)	-4#	10					
GBR/	2[redacted]	Yes/3	Fever/	[redacted]	[redacted]	4	2	NO	999,1	2
[redacted]	CA		Pyrexia (発熱)/	[redacted]	[redacted]				0	
			General disorders and administration site conditions	298&	301&					
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 101 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
GBR/	5[redacted]	Yes/3	Upper respiratory tract infection/	[redacted]	[redacted]	148	3	NO		2	2
[redacted]	OTH		Upper respiratory tract infection (上気道感染)/	[redacted]	[redacted]						
			Infections and infestations	106	253*						
			(感染症および寄生虫症)								
GBR/	5[redacted]	Yes/3	Keratoconjunctivitis/	[redacted]	[redacted]	7	3	NO		2,10	2
[redacted]	CA		Keratitis (角膜炎)/	[redacted]	[redacted]						
			Eye disorders (眼障害)	99	105						
		Yes/3	Lower respiratory Chest Infection/	[redacted]	[redacted]	5	3	NO		2,10	2
			Lower respiratory tract infection (下気道感染)/	[redacted]	[redacted]						
			Infections and infestations	283	287						
			(感染症および寄生虫症)								
		Yes/3	Lung Infection/	[redacted]	[redacted]	8	3	NO		999,1	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					0	

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 102 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	263	270					
			(感染症および寄生虫症)							
GRC/	6[redacted]	Yes/3	diarrhea/	[redacted]	[redacted]	14	3	YES,	3,10	2
[redacted]	CA		Diarrhoea (下痢)/	[redacted]	[redacted]			INVESTIGATI		
			Gastrointestinal disorders (胃腸障害)	67	80			ONAL		
								TREATMENT		
		Yes/3	abdominal pain, nephrolithiasis, hospitalization/	[redacted]	[redacted]	4	3	NO	2,10	2
			Nephrolithiasis (腎結石症)/	[redacted]	[redacted]					
			Renal and urinary disorders (腎および尿路障害)	27	30					
		Yes/3	pancytopenia/	[redacted]	[redacted]	10	3	YES, BOTH	3,10	2
			Pancytopenia (汎血球減少症)/	[redacted]	[redacted]			AND/OR		
			Blood and lymphatic system disorders	71	80			INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 103 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
GRC/	6[redacted]	Yes/3	Fever, hospitalization/	[redacted]	[redacted]	12	3	YES,	3,10	2
[redacted]	CA		Pyrexia (発熱)/	[redacted]	[redacted]			INVESTIGATI		
			General disorders and administration site conditions	10	21			ONAL		
			(一般・全身障害および投与部位の状態)					TREATMENT		
ISR/	5[redacted]	Yes/3	lung infection-aspergillosis/	[redacted]	[redacted]	9	2	NO	2,10	2
[redacted]	CA		Bronchopulmonary aspergillosis	[redacted]	[redacted]					
			(気管支肺アスペルギルス症)/	21	29					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	Deep Vein Thrombosis/	[redacted]	Ongoing		3	NO	2,10	1
			Deep vein thrombosis (深部静脈血栓症)/	[redacted]						
			Vascular disorders (血管障害)	153						
		Yes/3	DYSPNEA/	[redacted]	[redacted]	10	3	NO	2	2

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Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 104 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	77	86					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	pseudomonas pneumonia/	[redacted]	[redacted]	9	3	NO	2,10	2
			Pneumonia pseudomonal (シュードモナス性肺炎)/	[redacted]	[redacted]					
			Infections and infestations	111	119					
			(感染症および寄生虫症)							
		Yes/3	respiratory failure/	[redacted]	[redacted]	4	3	NO	2,10	1
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	188	191					
			(呼吸器、胸郭および縦隔障害)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 105 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ISR/ [redacted]	5[redacted] CA	Yes/1	respiratory failure/	[redacted]	[redacted]	1	5	NO		999	5
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders	192	192						
			(呼吸器、胸郭および縦隔障害)								
ISR/ [redacted]	6[redacted] CA	Yes/3	corneal ulcer/	[redacted]	[redacted]	27	3	NO		2,10	2
			Ulcerative keratitis (潰瘍性角膜炎)/	[redacted]	[redacted]						
			Eye disorders (眼障害)	258*	284*						
ISR/ [redacted]	6[redacted] CA	Yes/1	acute respiratory distress syndrome/	[redacted]	[redacted]	1	5	NO		999	5
			Acute respiratory distress syndrome	[redacted]	[redacted]						
			(急性呼吸窮迫症候群)/	30	30						
			Respiratory, thoracic and mediastinal disorders								
			(呼吸器、胸郭および縦隔障害)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 106 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/2	pneumonia/	[redacted]	[redacted]	2	4	NO		999,10	1
			Pneumonia (肺炎)/	[redacted]	[redacted]						
			Infections and infestations	28	29						
			(感染症および寄生虫症)								
		Yes/1	pneumonia/	[redacted]	[redacted]	1	5	NO		999	5
			Pneumonia (肺炎)/	[redacted]	[redacted]						
			Infections and infestations	30	30						
			(感染症および寄生虫症)								
		Yes/3	fever/	[redacted]	[redacted]	2	2	NO		4	2
			Pyrexia (発熱)/	[redacted]	[redacted]						
			General disorders and administration site conditions	17	18						
			(一般・全身障害および投与部位の状態)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 107 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ISR/	6[redacted]	Yes/2	thrombocytopenia/	[redacted]	Ongoing		4	NO	999,10	1
[redacted]	CA		Thrombocytopenia (血小板減少症)/	[redacted]						
			Blood and lymphatic system disorders	19						
			(血液およびリンパ系障害)							
ISR/	7[redacted]	Yes/3	neutropenic fever/	[redacted]	[redacted]	6	3	NO	4,10	2
[redacted]	CA		Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]					
			Blood and lymphatic system disorders	44	49					
			(血液およびリンパ系障害)							
ISR/	4[redacted]	Yes/3	HUMAN METAPNEUMOVIRUS/	[redacted]	[redacted]	8	3	NO	2	2
[redacted]	CA		Metapneumovirus infection	[redacted]	[redacted]					
			(メタニューモウイルス感染)/	64	71					
			Infections and infestations							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 108 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)								
		Yes/3	somnolence/	[redacted]	Ongoing		3	NO		2	1
			Somnolence (傾眠)/	[redacted]							
			Nervous system disorders (神経系障害)	64							
		Yes/3	DVT superior vena cava/	[redacted]	Ongoing		3	NO		999,1	1
			Vena cava thrombosis (大静脈血栓症)/	[redacted]						0	
			Vascular disorders (血管障害)	81							
ISR/ [redacted]	6[redacted] CA	Yes/3	suspected pulmonary aspergillosis/	[redacted]	[redacted]	11	3	NO		2,10	2
			Bronchopulmonary aspergillosis	[redacted]	[redacted]						
			(気管支肺アスペルギルス症)/	149	159						
			Infections and infestations								
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 109 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ISR/ [redacted]	6[redacted] CA	Yes/3	shortness of breath/	[redacted]	[redacted]	2	3	NO		2,10	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders	87*	88*						
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	shortness of breath/	[redacted]	[redacted]	3	2	NO		2,10	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders	93*	95*						
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	shortness of breath/	[redacted]	[redacted]	3	2	NO		2,10	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]						
			Respiratory, thoracic and mediastinal disorders	128*	130*						
			(呼吸器、胸郭および縦隔障害)								
		Yes/3	worsening HYPERTENSION/	[redacted]	[redacted]	3	3	NO		2,10	2
			Hypertension (高血圧)/	[redacted]	[redacted]						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 110 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Vascular disorders (血管障害)	128*	130*					
		Yes/3	Upper respiratory infection/	[redacted]	[redacted]	17	3	NO	999,1	2
			Upper respiratory tract infection (上気道感染)/	[redacted]	[redacted]				0	
			Infections and infestations	186*	202&					
			(感染症および寄生虫症)							
		Yes/3	upper respiratory tract infection/	[redacted]	[redacted]	11	3	NO	2,10	2
			Upper respiratory tract infection (上気道感染)/	[redacted]	[redacted]					
			Infections and infestations	149	159					
			(感染症および寄生虫症)							
ISR/ [redacted]	6[redacted] CA	Yes/ 2,3, 4	septic shock/	[redacted]	[redacted]	2	4	NO	2,10	1
			Septic shock (敗血症性ショック)/	[redacted]	[redacted]					
			Infections and infestations	14	15					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 111 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ISR/ [redacted]	6[redacted] CA	Yes/1	septic shock/	[redacted]	[redacted]	1	5	NO		999,10	5
			Septic shock (敗血症性ショック)/	[redacted]	[redacted]						
			Infections and infestations	16	16						
			(感染症および寄生虫症)								
ITA/ [redacted]	2[redacted] CA	Yes/3	Trigeminal Zooster/	[redacted]	[redacted]	21	3	NO		4,10	2
			Herpes zoster (帯状疱疹)/	[redacted]	[redacted]						
			Infections and infestations	453*	473*						
			(感染症および寄生虫症)								
ITA/ [redacted]	1[redacted] CA	Yes/3	Infection Lacrimal canaliculi to left eye/	[redacted]	[redacted]	3	2	NO		2,10	2
			Dacryocanaliculitis (涙小管炎)/	[redacted]	[redacted]						
			Infections and infestations	221*	223*						
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 112 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
		Yes/3	Fever/	[redacted]	[redacted]	6	2	NO		2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]						
			General disorders and administration site conditions	30*	35*						
			(一般・全身障害および投与部位の状態)								
		Yes/3	Sinusitis/	[redacted]	[redacted]	21	3	NO		4,10	2
			Sinusitis (副鼻腔炎)/	[redacted]	[redacted]						
			Infections and infestations	31*	51*						
			(感染症および寄生虫症)								
		Yes/3	Sinusitis/	[redacted]	[redacted]	9	2	NO		2,10	2
			Sinusitis (副鼻腔炎)/	[redacted]	[redacted]						
			Infections and infestations	166*	174*						
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 113 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	1[redacted] CA	Yes/3	Perforated corneal ulcer left eye/ Ulcerative keratitis (潰瘍性角膜炎)/ Eye disorders (眼障害)	[redacted] 293*	[redacted] 296*	4	3	NO	999,10	2
ITA/ [redacted]	2[redacted] CA	Yes/3	HERPETIC GENGIVO-STOMATITIS/ Oral herpes (口腔ヘルペス)/ Infections and infestations (感染症および寄生虫症)	[redacted] 125	[redacted] 139	15	3	NO	4,10	2
ITA/ [redacted]	1[redacted] CA	Yes/6	Kaposi Sarcoma/ Kaposi's sarcoma (カポジ肉腫)/ Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞	[redacted] 17*	Ongoing		2	YES, OTHER STUDY TREATMENT (NON-INVESTIGATI	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 114 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			およびポリープを含む))					ONAL)		
ITA/ [redacted]	4[redacted] CA	Yes/3	pancreatitis/ Pancreatitis (膵炎)/ Gastrointestinal disorders (胃腸障害)	[redacted] 109	[redacted] 116	8	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999	3
ITA/ [redacted]	7[redacted] CA	Yes/3	CVC related sepsis/ Device related sepsis (医療機器関連敗血症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 157	[redacted] 162	6	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 115 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	6[redacted]	Yes/3	neutropenic fever/	[redacted]	[redacted]	9	4	YES, BOTH	999,1	2
[redacted]	CA		Febrile neutropenia (発熱性好中球減少症)/	[redacted]	[redacted]			AND/OR	0	
			Blood and lymphatic system disorders	49&	57&			INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		
ITA/	6[redacted]	Yes/3	febrile syndrome with positivity per E coli ESBL+/	[redacted]	[redacted]	9	3	NO	2,10	2
[redacted]	CA		Escherichia infection (大腸菌感染)/	[redacted]	[redacted]					
			Infections and infestations	31	39					
			(感染症および寄生虫症)							
		Yes/3	febrile syndrome with positivity to influenza a/	[redacted]	[redacted]	9	3	NO	2,10	2
			Influenza (インフルエンザ)/	[redacted]	[redacted]					
			Infections and infestations	31	39					
			(感染症および寄生虫症)							
		Yes/3	pneumoniae/	[redacted]	Ongoing		3	NO	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 116 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonia (肺炎)/	[redacted]						
			Infections and infestations	141						
			(感染症および寄生虫症)							
		Yes/1	respiratory failure/	[redacted]	[redacted]	1	5	NO	5	5
			Respiratory failure (呼吸不全)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	198	198					
			(呼吸器、胸郭および縦隔障害)							
ITA/	5[redacted]	Yes/3	hepigastralgies/	[redacted]	[redacted]	22	3	NO	2,10	2
[redacted]	CA		Abdominal pain upper (上腹部痛)/	[redacted]	[redacted]					
			Gastrointestinal disorders (胃腸障害)	70	91					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 117 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade		Relat. study drug	Action taken	Out-come
ITA/	5[redacted]	Yes/3	cmv REACTIVATION/	[redacted]	[redacted]	28	2	NO		2,10	2
[redacted]	CA		Cytomegalovirus infection reactivation	[redacted]	[redacted]						
			(サイトメガロウイルス感染再燃)/	64	91						
			Infections and infestations								
			(感染症および寄生虫症)								
		Yes/3	vomit/	[redacted]	[redacted]	19	3	NO		2,10	2
			Vomiting (嘔吐)/	[redacted]	[redacted]						
			Gastrointestinal disorders (胃腸障害)	19	37						
ITA/	4[redacted]	Yes/3	SEPSI/	[redacted]	[redacted]	13	1	NO		2,10	2
[redacted]	CA		Sepsis (敗血症)/	[redacted]	[redacted]						
			Infections and infestations	14	26						
			(感染症および寄生虫症)								

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 118 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	2[redacted] CA	Yes/6	Nonmicrobiologicallydefined infections Pneumonia notrequiring mechanicalventilation/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 10	[redacted] 15	6	2	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2
		Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 33	Ongoing		3	NO	2,10	2
ITA/ [redacted]	4[redacted] CA	Yes/3	HYPOXIA/ Hypoxia (低酸素症)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 31	Ongoing		3	YES	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 119 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/	4[redacted]	Yes/3	ASPERGILLOSI PNEUMONIA/	[redacted]	Ongoing		3	NO	2,10	1
[redacted]	CA		Bronchopulmonary aspergillosis	[redacted]						
			(気管支肺アスペルギルス症)/	85						
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	BILATERAL PNEUMONIA/	[redacted]	Ongoing		3	NO	2,10	1
			Pneumonia (肺炎)/	[redacted]						
			Infections and infestations	24*						
			(感染症および寄生虫症)							
		Yes/3	STENOTROPHOMONAS MALTOPHILIA PNEUMONIA/	[redacted]	[redacted]	105	3	YES, BOTH	2,10	4
			Pneumonia bacterial (細菌性肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	57	161			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	CMV PNEUMONIA/	[redacted]	[redacted]	77	3	NO	2,10	4

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 120 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Pneumonia cytomegaloviral	[redacted]	[redacted]					
			(サイトメガロウイルス性肺炎)/	85	161					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	PNEMOCOCCUS PNEUMONIA/	[redacted]	[redacted]	55	3	NO	999,10	4
			Pneumonia pneumococcal (肺炎球菌性肺炎)/	[redacted]	[redacted]					
			Infections and infestations	-13#	42					
			(感染症および寄生虫症)							
		Yes/3	PSEUDOMONAS AERUGINOSA MDR PNEUMONIA/	[redacted]	[redacted]	25	3	NO	2,10	4
			Pneumonia pseudomonal (シュードモナス性肺炎)/	[redacted]	[redacted]					
			Infections and infestations	137	161					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 121 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
ITA/ [redacted]	4[redacted] CA	Yes/3	SEPSI FROM PSEUDOMONAS AERUGIOSA/	[redacted]	[redacted]	10	3	YES, BOTH	2,10	2
			Pseudomonal sepsis (シュードモナス性敗血症)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	129	138			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
		Yes/3	NOCARDIA SPP PNEUMONIA/	[redacted]	[redacted]	77	3	NO	2,10	4
			Pulmonary nocardiosis (肺ノカルジア症)/	[redacted]	[redacted]					
			Infections and infestations	85	161					
			(感染症および寄生虫症)							
		Yes/3	FEVER OF UNKNOW ORIGIN/	[redacted]	[redacted]	5	3	NO	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]					
			General disorders and administration site conditions	1*	5*					
			(一般・全身障害および投与部位の状態)							
		Yes/2	SEPTIC SHOCK/	[redacted]	[redacted]	9	4	YES, BOTH	5,10	2
			Septic shock (敗血症性ショック)/	[redacted]	[redacted]			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 122 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations (感染症および寄生虫症)	29*	37*			INDISTINGUISHABLE		
JOR/ [redacted]	3[redacted] CA	Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted]	[redacted]-	4	3	NO	2,10	3
				[redacted]	[redacted]					
				110*	113*					
JOR/ [redacted]	4[redacted] CA	Yes/3	Relative adrenal Insufficiency/ Adrenal insufficiency (副腎機能不全)/ Endocrine disorders (内分泌障害)	[redacted]	[redacted]	8	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	3
				[redacted]	[redacted]					
				202	209					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 123 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JOR/ [redacted]	4[redacted] CA	Yes/3	(Wound infection)Left leg medial malleolus area/ Wound infection (創傷感染)/ Infections and infestations (感染症および寄生虫症)	[redacted] 202	[redacted] 209	8	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	3
JPN/ [redacted]	6[redacted] AS	Yes/2	lung infection/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 123	[redacted] 153	31	4	YES, INVESTIGATIONAL TREATMENT	5,10	1
		Yes/1	lung infection/ Pneumonia (肺炎)/ Infections and infestations	[redacted] 154	[redacted] 154	1	5	YES, INVESTIGATIONAL	999	5

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 124 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)					TREATMENT		
JPN/ [redacted]	6[redacted] AS	Yes/3	heart failure/	[redacted]	Ongoing		3	NO	2,10	1
			Cardiac failure (心不全)/	[redacted]						
			Cardiac disorders (心臓障害)	55						
		Yes/3	pneumonia/	[redacted]	[redacted]	15	3	YES, BOTH	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	49	63			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
JPN/ [redacted]	6[redacted] AS	Yes/3	Severe aortic incompetence/	[redacted]	[redacted]	103	3	NO	2	3
			Aortic valve incompetence (大動脈弁閉鎖不全症)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	212	314&					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 125 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	6[redacted]	Yes/3	Pneumonitis/	[redacted]	[redacted]	64	2	YES, BOTH	2,10	3
[redacted]	AS		Pneumonitis (肺臓炎)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	58	121			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/3	Pneumonitis/	[redacted]	[redacted]	12	2	YES, BOTH	2,10	1
			Pneumonitis (肺臓炎)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	211	222			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/3	Pneumonitis/	[redacted]	[redacted]	2	4	YES, BOTH	2,10	1
			Pneumonitis (肺臓炎)/	[redacted]	[redacted]			AND/OR		
			Respiratory, thoracic and mediastinal disorders	223	224			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/3	Pneumonitis/	[redacted]	[redacted]	14	3	YES, BOTH	2,10	3
			Pneumonitis (肺臓炎)/	[redacted]	[redacted]			AND/OR		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 126 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Respiratory, thoracic and mediastinal disorders	225	238			INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
		Yes/3	Pneumonitis/	[redacted]	Ongoing		1	YES, BOTH	2,10	3
			Pneumonitis (肺臓炎)/	[redacted]				AND/OR		
			Respiratory, thoracic and mediastinal disorders	239				INDISTINGUI		
			(呼吸器、胸郭および縦隔障害)					SHABLE		
JPN/ [redacted]	3[redacted] AS	Yes/3	Peripheval neuropathy/	[redacted]	[redacted]	17	3	YES, BOTH	2	3
			Neuropathy peripheral (末梢性ニューロパチー)/	[redacted]	[redacted]			AND/OR		
			Nervous system disorders (神経系障害)	111	127			INDISTINGUI		
								SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 127 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/	6	Yes/3	pneumonia/			14	3	YES, OTHER	2,10	2
	AS		Pneumonia (肺炎)/					STUDY		
			Infections and infestations	176	189			TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		
JPN/	6	Yes/2	Multi-organ failure/			2	4	NO	5,10	1
	AS		Multiple organ dysfunction syndrome							
			(多臓器機能不全症候群)/	5	6					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
		Yes/1	Multi-organ failure/			1	5	NO	999,10	5
			Multiple organ dysfunction syndrome							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 128 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(多臓器機能不全症候群)/	7	7					
			General disorders and administration site conditions							
			(一般・全身障害および投与部位の状態)							
JPN/	3[redacted]	Yes/3	invasive aspergillosis/	[redacted]	[redacted]	11	3	YES,	999,1	1
[redacted]	AS		Aspergillus infection (アスペルギルス感染)/	[redacted]	[redacted]			INVESTIGATI	0	
			Infections and infestations	189&	199&			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/1	invasive aspergillosis/	[redacted]	[redacted]	1	5	YES,	999,1	5
			Aspergillus infection (アスペルギルス感染)/	[redacted]	[redacted]			INVESTIGATI	0	
			Infections and infestations	200&	200&			ONAL		
			(感染症および寄生虫症)					TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 129 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
JPN/ [redacted]	3[redacted] AS	Yes/3	Interstitial lung disease/ Interstitial lung disease (間質性肺疾患)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] [redacted] 58	[redacted] [redacted] 117&	60	2	YES, INVESTIGATIONAL TREATMENT	999,10	2
JPN/ [redacted]	2[redacted] AS	Yes/3	Pneumonia/ Pneumonia (肺炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] [redacted] 137	[redacted] [redacted] 145	9	1	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2
JPN/ [redacted]	3[redacted] AS	Yes/3	PLT decreaced/ Platelet count decreased (血小板数減少)/	[redacted] [redacted]	Ongoing		4	NO	5,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 130 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Investigations (臨床検査)	479*						
NLD/ [redacted]	4[redacted] CA	Yes/3	Dyspneu/	[redacted]	[redacted]	28	3	NO	999,10	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	198&	225&					
			(呼吸器、胸郭および縦隔障害)							
POL/ [redacted]	2[redacted] CA	Yes/3	pneumonia/	[redacted]	[redacted]	12	3	NO	2,10	2
			Pneumonia (肺炎)/	[redacted]	[redacted]					
			Infections and infestations	27*	38*					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 131 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
POL/	2[redacted]	Yes/	respiratory failure/	[redacted]	[redacted]	20	4	NO	999,10	4
[redacted]	CA	2,3,	Respiratory failure (呼吸不全)/	[redacted]	[redacted]					
		4	Respiratory, thoracic and mediastinal disorders	40*	59*					
			(呼吸器、胸郭および縦隔障害)							
RUS/	4[redacted]	Yes/3	anemia/	[redacted]	[redacted]	35	3	YES,	3,10	2
[redacted]	CA		Anaemia (貧血)/	[redacted]	[redacted]			INVESTIGATI		
			Blood and lymphatic system disorders	19*	53*			ONAL		
			(血液およびリンパ系障害)					TREATMENT		
		Yes/3	Enterocolitis infectious/	[redacted]	[redacted]	91	3	NO	2,10	2
			Enterocolitis infectious (感染性小腸結腸炎)/	[redacted]	[redacted]					
			Infections and infestations	4*	94*					
			(感染症および寄生虫症)							
		Yes/3	left femoral avascular necrosis/	[redacted]	[redacted]	8	3	NO	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 132 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Osteonecrosis (骨壊死)/	[redacted]	[redacted]					
			Musculoskeletal and connective tissue disorders	446*	453*					
			(筋骨格系および結合組織障害)							
		Yes/3	right femoral avascular necrosis/	[redacted]	[redacted]	16	3	NO	2	2
			Osteonecrosis (骨壊死)/	[redacted]	[redacted]					
			Musculoskeletal and connective tissue disorders	289*	304*					
			(筋骨格系および結合組織障害)							
		Yes/3	pharyngitis/	[redacted]	[redacted]	35	3	NO	2,10	2
			Pharyngitis (咽頭炎)/	[redacted]	[redacted]					
			Infections and infestations	19*	53*					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 133 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
RUS/ [redacted]	4[redacted] CA	Yes/2	spleen disorder/ Spleen disorder (脾臓障害)/ Blood and lymphatic system disorders (血液およびリンパ系障害)	[redacted] 33*	[redacted] 53*	21	4	YES, BOTH AND/OR INDISTINGUISHABLE	4,10	2
RUS/ [redacted]	3[redacted] CA	Yes/3	pulmonary venous embolism/ Pulmonary embolism (肺塞栓症)/ Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)	[redacted] 86	[redacted] 106	21	3	YES	5,10	2
TUR/ [redacted]	2[redacted] CA	Yes/3	Acute Gastroenteritis/ Gastroenteritis (胃腸炎)/ Infections and infestations (感染症および寄生虫症)	[redacted] 26	[redacted] 37	12	1	YES, INVESTIGATIONAL TREATMENT	4,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 134 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	5[redacted]	Yes/3	AGITATION/	[redacted]	[redacted]	4	4	NO	2,10	2
[redacted]	CA		Agitation (激越)/	[redacted]	[redacted]					
			Psychiatric disorders (精神障害)	3	6					
		Yes/3	ACUTE ENCELPHALOPATHY/	[redacted]	[redacted]	4	4	NO	2,10	2
			Encephalopathy (脳症)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	3	6					
		Yes/3	Enterocolitis/	[redacted]	[redacted]	34	3	NO	999,1	2
			Enterocolitis (腸炎)/	[redacted]	[redacted]				0	
			Gastrointestinal disorders (胃腸障害)	149	182					
		Yes/3	SEIZURE/	[redacted]	[redacted]	4	3	NO	2	2
			Seizure (痙攣発作)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	3	6					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 135 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	6[redacted] CA	Yes/3	Acute kidney injury/ Acute kidney injury (急性腎障害)/ Renal and urinary disorders (腎および尿路障害)	[redacted] [redacted] 122	[redacted] [redacted] 127	6	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	999	2
		Yes/3	Anasarca/ Generalised oedema (全身性浮腫)/ General disorders and administration site conditions (一般・全身障害および投与部位の状態)	[redacted] [redacted] 121	[redacted] [redacted] 143	23	3	YES, INVESTIGATIONAL TREATMENT	999,10	4
USA/ [redacted]	5[redacted] CA	Yes/2	Gram Negative Bacilli Sepsis/ Bacterial sepsis (細菌性敗血症)/ Infections and infestations	[redacted] [redacted] 59	Ongoing		3	YES, OTHER STUDY TREATMENT	2,10	1

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 136 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		
		Yes/3	Aspergillus Pneumonia/ Bronchopulmonary aspergillosis (気管支肺アスペルギルス症)/ Infections and infestations (感染症および寄生虫症)	[redacted] 12	[redacted] 19	8	3	YES, OTHER STUDY TREATMENT (NON-INVESTIGATIONAL)	2,10	2

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 137 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	5[redacted]	Yes/	E-coli bacteremia/	[redacted]	[redacted]	28	3	YES, OTHER	2,10	4
[redacted]	CA	2,3	Escherichia bacteraemia (大腸菌性菌血症)/	[redacted]	[redacted]			STUDY		
			Infections and infestations	59	86			TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		
		Yes/3	Esophagitis/	[redacted]	[redacted]	28	3	YES, OTHER	3	4
			Oesophagitis (食道炎)/	[redacted]	[redacted]			STUDY		
			Gastrointestinal disorders (胃腸障害)	59	86			TREATMENT		
								(NON-INVESTIGATIONAL)		
		Yes/	Cavitary Pneumonia/	[redacted]	[redacted]	28	3	YES, OTHER	2	4
		2,3	Pneumonia (肺炎)/	[redacted]	[redacted]			STUDY		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 138 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Infections and infestations	59	86			TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		
		Yes/3	Enterococcus faecialis pneumonia/	[redacted]	[redacted]	22	3	YES, OTHER	999,10	3
			Pneumonia bacterial (細菌性肺炎)/	[redacted]	[redacted]			STUDY		
			Infections and infestations	30	51			TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 139 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	6[redacted] AS	Yes/3	HYPERKALEMIA/	[redacted]	[redacted]	1	3	NO	4,10	3
			Hyperkalaemia (高カリウム血症)/	[redacted]	[redacted]					
			Metabolism and nutrition disorders	44	44					
			(代謝および栄養障害)							
		Yes/3	HYPOXIA/	[redacted]	[redacted]	13	3	NO	4,10	1
			Hypoxia (低酸素症)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	116	128					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	TACHYCARDIA/	[redacted]	[redacted]	13	3	NO	4,10	2
			Tachycardia (頻脈)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	116	128					
USA/ [redacted]	5[redacted] CA	Yes/3	acute kidney injury/	[redacted]	Ongoing		3	YES, INVESTIGATI	4	1
			Acute kidney injury (急性腎障害)/	[redacted]						

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 140 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			Renal and urinary disorders (腎および尿路障害)	131				ONAL TREATMENT		
		Yes/3	atrial flutter/	[redacted]	[redacted]	4	3	YES,	2,10	3
			Atrial flutter (心房粗動)/	[redacted]	[redacted]			INVESTIGATI		
			Cardiac disorders (心臓障害)	86	89			ONAL TREATMENT		
		Yes/3	Fatigue/	[redacted]	Ongoing		3	NO	2	1
			Fatigue (疲労)/	[redacted]						
			General disorders and administration site conditions (一般・全身障害および投与部位の状態)	79						
		Yes/3	hypoglycemia/	[redacted]	[redacted]	1	3	NO	4,10	2
			Hypoglycaemia (低血糖)/	[redacted]	[redacted]					
			Metabolism and nutrition disorders (代謝および栄養障害)	131	131					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 141 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	5[redacted] CA	Yes/3	Infection (other)/	[redacted]	[redacted]	11	3	NO	2,10	2
			Infection (感染)/	[redacted]	[redacted]					
			Infections and infestations	97	107					
			(感染症および寄生虫症)							
		Yes/3	oral dysesthesia/	[redacted]	Ongoing		2	NO	2,10	1
			Oral dysaesthesia (口腔知覚不全)/	[redacted]						
			Gastrointestinal disorders (胃腸障害)	79						
		Yes/3	worsening avascular necrosis/	[redacted]	[redacted]-	5	2	NO	2	2
			Osteonecrosis (骨壊死)/	[redacted]	[redacted]					
			Musculoskeletal and connective tissue disorders	79	83					
			(筋骨格系および結合組織障害)							
		Yes/	septic shock/	[redacted]	[redacted]	6	4	YES, BOTH	4,10	1
		2,3	Septic shock (敗血症性ショック)/	[redacted]	[redacted]			AND/OR		
			Infections and infestations	131	136			INDISTINGUI		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 142 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)					SHABLE		
		Yes/1	septic shock/	[redacted]	[redacted]	1	5	YES,	4,10	5
			Septic shock (敗血症性ショック)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	137	137			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/	SKIN INFECTION/	[redacted]	[redacted]	17	3	YES, BOTH	4,10	3
		3,4,	Skin infection (皮膚感染)/	[redacted]	[redacted]			AND/OR		
		6	Infections and infestations	42	58			INDISTINGUI		
			(感染症および寄生虫症)					SHABLE		
USA/	3[redacted]	Yes/3	bronchial infection/	[redacted]	[redacted]	10	3	NO	999,1	4
[redacted]	CA		Bronchitis (気管支炎)/	[redacted]	[redacted]				0	
			Infections and infestations	-18#	-9#					
			(感染症および寄生虫症)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 143 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	3[redacted]	Yes/3	Dyspnea/	[redacted]	[redacted]	5	3	NO	999,1	4
[redacted]	CA		Dyspnoea (呼吸困難)/	[redacted]	[redacted]				0	
			Respiratory, thoracic and mediastinal disorders	-18#	-14#					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Influenza A/	[redacted]	[redacted]	4	3	YES,	2,10	2
			Influenza (インフルエンザ)/	[redacted]	[redacted]			INVESTIGATI		
			Infections and infestations	505*	508*			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/3	nausea/	[redacted]	[redacted]	4	3	YES,	2,10	3
			Nausea (悪心)/	[redacted]	[redacted]			INVESTIGATI		
			Gastrointestinal disorders (胃腸障害)	106*	109*			ONAL		
								TREATMENT		
		Yes/3	fever/	[redacted]	[redacted]	2	1	YES,	2,10	2
			Pyrexia (発熱)/	[redacted]	[redacted]			INVESTIGATI		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 144 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			General disorders and administration site conditions	106*	107*			ONAL		
			(一般・全身障害および投与部位の状態)					TREATMENT		
		Yes/3	upper respiratory infection/	[redacted]	[redacted]	9	3	YES,	999,1	2
			Upper respiratory tract infection (上気道感染)/	[redacted]	[redacted]			INVESTIGATI	0	
			Infections and infestations	293*	301*			ONAL		
			(感染症および寄生虫症)					TREATMENT		
		Yes/3	vomiting/	[redacted]	[redacted]	4	3	YES,	2,10	2
			Vomiting (嘔吐)/	[redacted]	[redacted]			INVESTIGATI		
			Gastrointestinal disorders (胃腸障害)	106*	109*			ONAL		
								TREATMENT		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 145 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	7[redacted] CA	Yes/3	Atelectasis (right lung)/	[redacted]	Ongoing		3	NO	2	1
			Atelectasis (無気肺)/	[redacted]						
			Respiratory, thoracic and mediastinal disorders	6						
			(呼吸器、胸郭および縦隔障害)							
		Yes/	Colonic perforation/	[redacted]	Ongoing		4	NO	2,10	1
		2,3,	Large intestine perforation (大腸穿孔)/	[redacted]						
		4	Gastrointestinal disorders (胃腸障害)	6						
		Yes/3	thromboembolic event (left lung)/	[redacted]	Ongoing		3	NO	2	1
			Pulmonary embolism (肺塞栓症)/	[redacted]						
			Respiratory, thoracic and mediastinal disorders	6						
			(呼吸器、胸郭および縦隔障害)							
		Yes/1	Infections and Infestations-Other, Systemic Infection/	[redacted]	[redacted]	1	5	NO	2,10	5
			Systemic infection (全身性感染)/	[redacted]	[redacted]					
			Infections and infestations	24	24					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 146 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
			(感染症および寄生虫症)							
USA/ [redacted]	6[redacted] CA	Yes/3	Abdominal wall infection/	[redacted]	Ongoing		3	NO	2,10	1
			Abdominal wall infection (腹壁感染)/	[redacted]						
			Infections and infestations	65*						
			(感染症および寄生虫症)							
USA/ [redacted]	6[redacted] CA	Yes/3	traumatic fall/	[redacted]	[redacted]	3	4	NO	4,10	1
			Fall (転倒)/	[redacted]	[redacted]					
			Injury, poisoning and procedural complications	116*	118*					
			(傷害、中毒および処置合併症)							
		Yes/	intracranial hemorrhage/	[redacted]	[redacted]	2	4	NO	4,10	1
		2,3	Haemorrhage intracranial (頭蓋内出血)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	116*	117*					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 147 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	6[redacted]	Yes/1	intracranial hemorrhage/	[redacted]	[redacted]	1	5	NO	5,10	5
[redacted]	CA		Haemorrhage intracranial (頭蓋内出血)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	118*	118*					
		Yes/3	metabolic encephalopathy/	[redacted]	[redacted]	2	3	NO	3,10	2
			Metabolic encephalopathy (代謝性脳症)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	55*	56*					
USA/	7[redacted]	Yes/3	ACUTE KIDNEY INJURY/	[redacted]	[redacted]	8	3	NO	999,1	4
[redacted]	CA		Acute kidney injury (急性腎障害)/	[redacted]	[redacted]				0	
			Renal and urinary disorders (腎および尿路障害)	164	171*					
		Yes/3	ANEMIA/	[redacted]	[redacted]	5	3	YES, BOTH	2	3
			Anaemia (貧血)/	[redacted]	[redacted]			AND/OR		
			Blood and lymphatic system disorders	111*	115*			INDISTINGUI		
			(血液およびリンパ系障害)					SHABLE		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover
treatment. MedDRA version 23.0, CTCAE version 4.03.
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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 148 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/6	DYSPNEA/	[redacted]	[redacted]	18	3	YES, OTHER	999,10	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]			STUDY		
			Respiratory, thoracic and mediastinal disorders	157	174*			TREATMENT		
			(呼吸器、胸郭および縦隔障害)					(NON-INVESTIGATIONAL)		
		Yes/3	INCREASED SHORTNESS OF BREATH/	[redacted]	[redacted]	6	3	NO	2	2
			Dyspnoea (呼吸困難)/	[redacted]	[redacted]					
			Respiratory, thoracic and mediastinal disorders	110*	115*					
			(呼吸器、胸郭および縦隔障害)							
		Yes/3	Increased Fatigue/	[redacted]	[redacted]	11	3	YES,	2	2
			Fatigue (疲労)/	[redacted]	[redacted]			INVESTIGATIONAL		
			General disorders and administration site conditions	110*	120*			TREATMENT		
			(一般・全身障害および投与部位の状態)							

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability,
5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn,
10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae,
5=Fatal, 997=Unknown.
# Data collected during the pre-treatment period. & More than 30 days after last study treatment.
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treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 149 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/ [redacted]	7[redacted] CA	Yes/3	HYPERTHERMIA/	[redacted]	[redacted]	1	2	NO	4,10	2
			Hyperthermia (高体温症)/	[redacted]	[redacted]					
			General disorders and administration site conditions	24*	24*					
			(一般・全身障害および投与部位の状態)							
		Yes/6	PERICARDIAL EFFUSION/	[redacted]	[redacted]	12	3	NO	999,10	3
			Pericardial effusion (心嚢液貯留)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	157	168					
		Yes/3	PERICARDIAL EFFUSION/	[redacted]	[redacted]	4	4	YES, BOTH AND/OR INDISTINGUISHABLE	2,10	3
			Pericardial effusion (心嚢液貯留)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	111*	114*					
		Yes/6	PERICARDITIS/	[redacted]	[redacted]	12	3	NO	999,10	3
			Pericarditis (心膜炎)/	[redacted]	[redacted]					
			Cardiac disorders (心臓障害)	157	168					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 150 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
		Yes/3	WORSENING PLEURAL EFFUSIONS/	[redacted]	[redacted]	7	3	YES, OTHER	999,10	3
			Pleural effusion (胸水)/	[redacted]	[redacted]			STUDY		
			Respiratory, thoracic and mediastinal disorders	157	163			TREATMENT		
			(呼吸器、胸郭および縦隔障害)					(NON-INVESTIGATIONAL)		
		Yes/3	LUNG INFECTION/	[redacted]	[redacted]	20	3	YES, OTHER	999,10	3
			Pneumonia (肺炎)/	[redacted]	[redacted]			STUDY		
			Infections and infestations	157	176*			TREATMENT		
			(感染症および寄生虫症)					(NON-INVESTIGATIONAL)		

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

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Listing s14.3.2-2.1 Serious adverse events (Safety set) (Page 151 of 151)

Treatment: Best available therapy

Country/ Subject identifier	Age/ Sex/ Race	SAE/ Criteria	REPORTED / Preferred term / System organ class	Start date/ Study day	End date/ Study day	Dur. (dys)	Grade	Relat. study drug	Action taken	Out-come
USA/	1[redacted]	Yes/3	CLOSTRIDIUM DIFFICILE INFECTIONS - STOOL/	[redacted]	[redacted]	16	2	NO	2,10	2
[redacted]	CA		Clostridium difficile infection	[redacted]	[redacted]					
			(クロストリジウム・ディフィシレ感染)/	7*	22*					
			Infections and infestations							
			(感染症および寄生虫症)							
		Yes/3	BILATERAL UPPER ARM NEUROPATHIC PAIN/	[redacted]	[redacted]	3	3	NO	2,10	2
			Neuralgia (神経痛)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	127	129					
		Yes/	TRANSIENT ISCHEMIC ATTACK/	[redacted]	[redacted]	2	2	NO	2,10	2
		3,6	Transient ischaemic attack (一過性脳虚血発作)/	[redacted]	[redacted]					
			Nervous system disorders (神経系障害)	115	116					

Seriousness criteria: 1=Death, 2=Life threatening, 3=Requires or prolongs hospitalization, 4=Significant disability, 5=Congenital anomaly or birth defect, 6=Other medically important serious event.
Action taken: 1=Dose increased, 2=Dose not changed, 3=Dose reduced, 4=Drug interrupted, 5=Drug withdrawn, 10=Concomitant medication or non-drug therapy 997=Unknown, 999=Not applicable.
Outcome: 1=Not recovered/not resolved, 2=Recovered/resolved, 3=Recovering/resolving, 4=Recovered/resolved with sequelae, 5=Fatal, 997=Unknown.
Data collected during the pre-treatment period. & More than 30 days after last study treatment.
*Study day for data collected on or after crossover treatment start date is with respect to the first dose of crossover treatment. MedDRA version 23.0, CTCAE version 4.03.

Table 7-13　慢性 GVHD の投与中止に至った有害事象の一覧（D2301 試験，SAF，データカットオフまで）

被験者番号	年齢/性別/人種	重篤性	PT	発現日(日目)	消失日(日目)	持続期間(日)	Grade	関連	処置	転帰
RUX 群										
CZE/[redacted]	5[redacted]/CA	No	腎不全	112			3	Yes, 治験治療	5,10	1
DEU/[redacted]	6[redacted]/CA	Yes/3	肺炎	77	87	11	4	Yes, 両方又は判別不可能	5,10	1
		Yes/1	肺炎	88	88	1	5	Yes, 両方又は判別不可能	5	5
DNK/[redacted]	6[redacted]/CA	No	クッシング様症状	64			1	No	5	1
ESP/[redacted]	4[redacted]/CA	Yes/3	錯乱状態	258	261	4	1	No	5,10	2
ESP/[redacted]	2[redacted]/CA	No	気胸	91			2	No	5	3
FRA/[redacted]	6[redacted]/UN	Yes/2	中毒性表皮壊死融解症	9	12	4	4	No	5,10	1
GBR/[redacted]	3[redacted]/CA	No	貧血	366	409&	44	2	Yes, 両方又は判別不可能	5,10	3
		No	貧血	409&	429&	21	1	Yes, 両方又は判別不可能	5,10	2
GBR/[redacted]	6[redacted]/OTH	No	好中球減少症	57	151&	95	2	Yes, 両方又は判別不可能	5,10	2
GBR/[redacted]	7[redacted]/CA	Yes/6	ウイルス性髄膜炎	52			3	No	5,10	1
GBR/[redacted]	7[redacted]/CA	No	好中球数減少	79	85	7	4	Yes, 治験治療	5	3
		No	好中球数減少	77	78	2	3	Yes, 治験治療	5	1
IND/[redacted]	4[redacted]/AS	Yes/1	頭蓋内出血	301	301	1	5	Yes, 治験治療	5,10	5
		Yes/2	血小板減少症	300			4	Yes	5,10	1
ITA/[redacted]	5[redacted]/CA	Yes/3	低酸素症	236	249	14	3	Yes, 両方又は判別不可能	5,10	2
ITA/[redacted]	5[redacted]/CA	Yes/2,3	敗血症性ショック	21	56&	36	4	Yes, 両方又は判別不可能	5,10	2
ITA/[redacted]	4[redacted]/CA	Yes/1	全身健康状態悪化	71&	71&	1	5	No	5	5
ITA/[redacted]	4[redacted]/CA	No	高アミラーゼ血症	224	236	13	4	Yes, 両方又は判別不可能	5,10	1
		No	高アミラーゼ血症	237			3	Yes, 両方又は判別不可能	5,10	3
JPN/[redacted]	6[redacted]/AS	Yes/2	細菌性肺炎	41	50	10	4	Yes, 両方又は判別不可能	5,10	1
JPN/[redacted]	4[redacted]/AS	Yes/2	敗血症	39	56	18	4	Yes, 両方又は判別不可能	5,10	1
JPN/[redacted]	5[redacted]/AS	Yes/2	肺炎	23	28	6	4	Yes, 両方又は判別不可能	5	1
		Yes/2,3	肺炎	23	28	6	4	Yes, 両方又は判別不可能	5,10	1
		Yes/2	呼吸不全	22	28	7	4	Yes, 両方又は判別不可能	5,10	1
JPN/[redacted]	6[redacted]/AS	Yes/3	気胸	63			3	No	5,10	1
JPN/[redacted]	5[redacted]/AS	Yes/2	移植後リンパ増殖性障害	67			3	No	5,10	1
JPN/[redacted]	3[redacted]/AS	Yes/3	イレウス	25	27	3	3	No	5,10	1
JPN/[redacted]	3[redacted]/AS	Yes/2	脳膿瘍	146	167	22	4	Yes, 両方又は判別不可能	5,10	3
		Yes/2	肺炎	146	167	22	4	Yes, 両方又は判別不可能	5,10	3
JPN/[redacted]	5[redacted]/AS	Yes/3	肺炎	33	242&	210	3	No	5,10	2
JPN/[redacted]	5[redacted]/AS	Yes/3	肺炎	91			3	No	5,10	3
NLD/[redacted]	4[redacted]/CA	No	皮膚のつっぱり感	477			3	Yes, 治験治療	5	1
POL/[redacted]	6[redacted]/CA	Yes/3,6	肺炎	29	61	33	3	Yes, 両方又は判別不可能	5,10	4
TUR/[redacted]	3[redacted]/CA	No	体温上昇	122			1	Yes, 治験治療	5,10	1
TUR/[redacted]	5[redacted]/CA	No	貧血	84	115	32	2	Yes, 治験治療	5,10	2
		Yes/3	肺炎	106	115	10	2	Yes, 治験治療	5,10	3
TUR/[redacted]	2[redacted]/CA	Yes/3	急性腎障害	64	69	6	3	Yes, 治験治療	5,10	2
USA/[redacted]	4[redacted]/CA	Yes/3	肺炎	49	54	6	1	Yes, 両方又は判別不可能	5,10	2

被験者番号	年齢/性別/人種	重篤性	PT	発現日(日目)	消失日(日目)	持続期間(日)	Grade	関連	処置	転帰
		Yes/3	発熱	49	54	6	1	Yes, 両方又は判別不可能	5	2
USA/[redacted]	7[redacted]/NA	Yes/3	心房粗動	61			3	Yes, 治験治療	5,10	3
USA/[redacted]	5[redacted]/CA	Yes/3	肺炎	192			3	No	5,10	1
		Yes/3	大腸菌性敗血症	192			3	No	5,10	1
		Yes/3	多臓器機能不全症候群	192			3	No	5,10	1
USA/[redacted]	6[redacted]/CA	No	血栓症	23			2	No	5,10	3
USA/[redacted]	5[redacted]/OTH	No	アラニンアミノトランスフェラーゼ増加	110	119	10	3	Yes, 治験治療	5	4
BAT 群										
AUT/[redacted]	3[redacted]/CA	Yes/3	血中クレアチニン増加	31*	53*	23	2	Yes, 治験治療	5,10	3
		Yes/3	血小板減少症	31*	58*	28	4	Yes, 治験治療	5,10	3
AUT/[redacted]	6[redacted]/CA	No	貧血	17			2	No	5	1
		Yes/3	全身健康状態悪化	17			3	No	5	1
		No	血栓性微小血管症	19			3	Yes, 治験治療	5,10	1
CAN/[redacted]	6[redacted]/CA	No	血小板数減少	19	26	8	4	Yes, 他の急性 GVHD 治療薬	5	2
CZE/[redacted]	5[redacted]/CA	Yes/3	熱性感染症	182	233&	52	3	No	5,10	2
DEU/[redacted]	6[redacted]/CA	No	肺炎	5	13	9	3	Yes, 治験治療	5,10	2
		No	微小血管症	5	45	41	3	Yes, 両方又は判別不可能	5,10	4
		Yes/2,3	非定型溶血性尿毒症症候群	5	45	41	4	Yes, 他の急性 GVHD 治療薬	5,10	2
		No	血小板減少症	5	55	51	2	Yes, 他の急性 GVHD 治療薬	5,10	2
ESP/[redacted]	4[redacted]/CA	Yes/3	アスペルギルス感染	78*	82*	5	4	No	5	1
ESP/[redacted]	5[redacted]/CA	No	下痢	46	50	5	2	Yes, 他の急性 GVHD 治療薬	5,10	2
FRA/[redacted]	4[redacted]/OTH	Yes/1,3	敗血症性ショック	107	123	17	5	Yes, 治験治療	5,10	5
ISR/[redacted]	6[redacted]/CA	No	好中球減少症	17	17	1	3	No	5,10	1
ITA/[redacted]	1[redacted]/CA	Yes/6	カポジ肉腫	17*			2	Yes, 他の急性 GVHD 治療薬	5,10	1
ITA/[redacted]	4[redacted]/CA	No	嘔吐	25	26	2	2	Yes, 他の急性 GVHD 治療薬	5	2
ITA/[redacted]	6[redacted]/CA	Yes/1	呼吸不全	198	198	1	5	No	5	5
ITA/[redacted]	4[redacted]/CA	Yes/2	敗血症性ショック	29*	37*	9	4	Yes, 両方又は判別不可能	5,10	2
JOR/[redacted]	3[redacted]/CA	No	アラニンアミノトランスフェラーゼ増加	1*	10*	10	1	Yes, 治験治療	5	2
JPN/[redacted]	6[redacted]/AS	Yes/2	肺炎	123	153	31	4	Yes, 治験治療	5,10	1
JPN/[redacted]	6[redacted]/AS	Yes/2	多臓器機能不全症候群	5	6	2	4	No	5,10	1
JPN/[redacted]	3[redacted]/AS	Yes/3	血小板数減少	479*			4	No	5,10	1
		No	白血球数減少	100	183*	84	2	Yes, 治験治療	5	2
RUS/[redacted]	3[redacted]/CA	Yes/3	肺塞栓症	86	106	21	3	Yes	5,10	2
USA/[redacted]	6[redacted]/CA	No	急性腎障害	393			2	Yes, 治験治療	5	3
USA/[redacted]	6[redacted]/CA	Yes/1	頭蓋内出血	118*	118*	1	5	No	5,10	5

Source: 5.3.5.1-2-D2301 試験-Listing 16.2.7-1
M = 男性，F = 女性，AS = Asian，CA = Caucasian，NA = Native Hawaiian or other pacific islander，OTH = Other，UN = Unknown
重篤性（Yes）：1 = Death，2 = Life threatening，3 = Requires or prolongs hospitalization，4 = Significant disability，5 = Congenital anomaly or birth defect，6 = Other medically important serious event.
処置：1 = Dose increased，2 = Dose not changed，3 = Dose reduced，4 = Drug interrupted，5 = Drug withdrawn，10 = Concomitant medication or non-drug therapy，997 = Unknown，999 = Not applicable.
転帰：1 = Not recovered/not resolved，2 = Recovered/resolved，3 = Recovering/resolving，4 = Recovered/resolved with sequelae，5 = Fatal，997 = Unknown.
*：RUX へのクロスオーバー後に発現した事象。RUX 投与開始日からの日数を示す。
&：治験治療の最終投与後 30 日より後に発現した事象
MedDRA version 23.0

Table 7-14 急性 GVHD の SOC 別 PT 別の有害事象（C2301 試験，SAF，日本人，データカットオフ 2 まで）

	RUX N=9		BAT N=21	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Number of subjects with at least one event	9 (100)	9 (100)	20 (95.2)	18 (85.7)
Blood and lymphatic system disorders (血液およびリンパ系障害)	7 (77.8)	5 (55.6)	11 (52.4)	8 (38.1)
Anaemia (貧血)	5 (55.6)	4 (44.4)	6 (28.6)	6 (28.6)
Thrombocytopenia (血小板減少症)	4 (44.4)	3 (33.3)	2 (9.5)	0
Leukopenia (白血球減少症)	1 (11.1)	1 (11.1)	0	0
Neutropenia (好中球減少症)	1 (11.1)	1 (11.1)	2 (9.5)	1 (4.8)
Thrombotic microangiopathy (血栓性微小血管症)	1 (11.1)	1 (11.1)	2 (9.5)	1 (4.8)
Hypoglobulinaemia (低グロブリン血症)	0	0	1 (4.8)	0
Nephrogenic anaemia (腎性貧血)	0	0	1 (4.8)	1 (4.8)
Cardiac disorders (心臓障害)	1 (11.1)	1 (11.1)	1 (4.8)	0
Cardiovascular insufficiency (心血管不全)	1 (11.1)	1 (11.1)	0	0
Cardiac dysfunction (心機能障害)	0	0	1 (4.8)	0
Endocrine disorders (内分泌障害)	1 (11.1)	0	2 (9.5)	0
Hypoparathyroidism (副甲状腺機能低下症)	1 (11.1)	0	0	0
Hypothyroidism (甲状腺機能低下症)	0	0	2 (9.5)	0
Eye disorders (眼障害)	2 (22.2)	0	2 (9.5)	0
Dry eye (ドライアイ)	2 (22.2)	0	0	0
Cataract (白内障)	0	0	1 (4.8)	0
Conjunctival haemorrhage (結膜出血)	0	0	1 (4.8)	0
Gastrointestinal disorders (胃腸障害)	7 (77.8)	1 (11.1)	7 (33.3)	1 (4.8)
Constipation (便秘)	3 (33.3)	0	2 (9.5)	0
Nausea (悪心)	3 (33.3)	0	2 (9.5)	1 (4.8)
Abdominal distension (腹部膨満)	2 (22.2)	0	0	0
Vomiting (嘔吐)	2 (22.2)	0	2 (9.5)	0
Abdominal pain upper (上腹部痛)	1 (11.1)	0	0	0
Anal haemorrhage (肛門出血)	1 (11.1)	0	0	0
Gastrointestinal haemorrhage (胃腸出血)	1 (11.1)	0	0	0

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Lower gastrointestinal haemorrhage (下部消化管出血)	1 (11.1)	1 (11.1)	0	0
Stomatitis (口内炎)	1 (11.1)	0	1 (4.8)	0
Abdominal pain (腹痛)	0	0	1 (4.8)	0
Ascites (腹水)	0	0	1 (4.8)	0
Proctalgia (肛門周囲痛)	0	0	1 (4.8)	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)	4 (44.4)	1 (11.1)	9 (42.9)	1 (4.8)
Malaise (倦怠感)	2 (22.2)	0	0	0
Oedema peripheral (末梢性浮腫)	2 (22.2)	0	5 (23.8)	0
Fatigue (疲労)	1 (11.1)	1 (11.1)	0	0
Oedema (浮腫)	1 (11.1)	0	0	0
Pain (疼痛)	1 (11.1)	0	1 (4.8)	0
Pyrexia (発熱)	1 (11.1)	0	2 (9.5)	0
Generalised oedema (全身性浮腫)	0	0	2 (9.5)	1 (4.8)
Injection site reaction (注射部位反応)	0	0	1 (4.8)	0
Medical device site erosion (医療機器使用部位びらん)	0	0	1 (4.8)	0
Hepatobiliary disorders (肝胆道系障害)	4 (44.4)	3 (33.3)	1 (4.8)	0
Hepatic function abnormal (肝機能異常)	2 (22.2)	2 (22.2)	1 (4.8)	0
Hepatotoxicity (肝毒性)	1 (11.1)	0	0	0
Liver disorder (肝障害)	1 (11.1)	1 (11.1)	0	0
Immune system disorders (免疫系障害)	0	0	2 (9.5)	0
Allergy to immunoglobulin therapy (免疫グロブリン療法アレルギー)	0	0	1 (4.8)	0
Hypogammaglobulinaemia (低γグロブリン血症)	0	0	1 (4.8)	0
Infections and infestations (感染症および寄生虫症)	7 (77.8)	5 (55.6)	18 (85.7)	10 (47.6)
Cytomegalovirus infection (サイトメガロウイルス感染)	3 (33.3)	1 (11.1)	2 (9.5)	2 (9.5)
Candida infection (カンジダ感染)	2 (22.2)	2 (22.2)	0	0
Enterococcal infection (腸球菌感染)	2 (22.2)	1 (11.1)	0	0
Pneumonia (肺炎)	2 (22.2)	2 (22.2)	1 (4.8)	1 (4.8)
Sepsis (敗血症)	2 (22.2)	2 (22.2)	2 (9.5)	2 (9.5)
Bacteraemia (菌血症)	1 (11.1)	1 (11.1)	2 (9.5)	1 (4.8)
Bacterial infection (細菌感染)	1 (11.1)	0	3 (14.3)	2 (9.5)
Bronchopulmonary aspergillosis (気管支肺アスペルギルス症)	1 (11.1)	1 (11.1)	0	0
Clostridium difficile infection (クロストリジウム・ディフィシレ感染)	1 (11.1)	1 (11.1)	0	0
Conjunctivitis (結膜炎)	1 (11.1)	0	2 (9.5)	0
Cystitis (膀胱炎)	1 (11.1)	0	1 (4.8)	0
Device related infection (医療機器関連感染)	1 (11.1)	1 (11.1)	1 (4.8)	1 (4.8)

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Epstein-Barr virus infection (エプスタイン・バーウイルス感染)	1 (11.1)	0	2 (9.5)	1 (4.8)
Infection (感染)	1 (11.1)	0	0	0
Penile infection (陰茎感染)	1 (11.1)	0	0	0
Septic embolus (敗血症性塞栓)	1 (11.1)	1 (11.1)	0	0
Urinary tract infection (尿路感染)	1 (11.1)	1 (11.1)	0	0
Cellulitis (蜂巣炎)	0	0	1 (4.8)	1 (4.8)
Conjunctivitis bacterial (細菌性結膜炎)	0	0	1 (4.8)	0
Cytomegalovirus viraemia (サイトメガロウイルス血症)	0	0	1 (4.8)	0
Fungal infection (真菌感染)	0	0	1 (4.8)	0
Gastroenteritis (胃腸炎)	0	0	1 (4.8)	1 (4.8)
Gingivitis (歯肉炎)	0	0	1 (4.8)	0
Herpes zoster (帯状疱疹)	0	0	1 (4.8)	0
Large intestine infection (大腸感染)	0	0	1 (4.8)	0
Meningoencephalitis herpetic (ヘルペス性髄膜脳炎)	0	0	1 (4.8)	1 (4.8)
Meningomyelitis herpes (ヘルペス性髄膜脊髄炎)	0	0	1 (4.8)	0
Oral candidiasis (口腔カンジダ症)	0	0	1 (4.8)	0
Pathogen resistance (病原体耐性)	0	0	1 (4.8)	0
Pneumonia cytomegaloviral (サイトメガロウイルス性肺炎)	0	0	1 (4.8)	1 (4.8)
Pseudomonas infection (シュードモナス感染)	0	0	1 (4.8)	0
Respiratory syncytial virus infection (RS ウイルス感染)	0	0	1 (4.8)	0
Staphylococcal bacteraemia (ブドウ球菌性菌血症)	0	0	1 (4.8)	1 (4.8)
Injury, poisoning and procedural complications (傷害，中毒および処置合併症)	2 (22.2)	1 (11.1)	5 (23.8)	2 (9.5)
Compression fracture (圧迫骨折)	1 (11.1)	0	0	0
Mouth injury (口腔内損傷)	1 (11.1)	0	0	0
Procedural haemorrhage (処置による出血)	1 (11.1)	1 (11.1)	0	0
Contusion (挫傷)	0	0	1 (4.8)	0
Graft loss (移植片機能損失)	0	0	1 (4.8)	1 (4.8)
Procedural pain (処置による疼痛)	0	0	1 (4.8)	0
Sedation complication (鎮静合併症)	0	0	1 (4.8)	0
Spinal compression fracture (脊椎圧迫骨折)	0	0	1 (4.8)	0
Transplantation complication (移植合併症)	0	0	1 (4.8)	1 (4.8)
Investigations (臨床検査)	8 (88.9)	7 (77.8)	11 (52.4)	10 (47.6)
Platelet count decreased (血小板数減少)	4 (44.4)	4 (44.4)	6 (28.6)	6 (28.6)
White blood cell count decreased (白血球数減少)	4 (44.4)	4 (44.4)	6 (28.6)	5 (23.8)
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)	3 (33.3)	2 (22.2)	1 (4.8)	1 (4.8)
Neutrophil count decreased (好中球数減少)	3 (33.3)	3 (33.3)	4 (19.0)	4 (19.0)

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増	2 (22.2)	1 (11.1)	1 (4.8)	1 (4.8)
Blood alkaline phosphatase increased (血中アルカリホスファターゼ増加)	2 (22.2)	2 (22.2)	1 (4.8)	1 (4.8)
Blood creatinine increased (血中クレアチニン増加)	2 (22.2)	0	3 (14.3)	0
Cytomegalovirus test positive (サイトメガロウイルス検査陽性)	2 (22.2)	0	2 (9.5)	0
Amylase increased (アミラーゼ増加)	1 (11.1)	1 (11.1)	0	0
Aspergillus test positive (アスペルギルス検査陽性)	1 (11.1)	0	0	0
Blood beta-D-glucan increased (血中 β-D-グルカン増加)	1 (11.1)	0	0	0
Blood bilirubin increased (血中ビリルビン増加)	1 (11.1)	1 (11.1)	1 (4.8)	0
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)	1 (11.1)	0	0	0
Blood fibrinogen decreased (血中フィブリノゲン減少)	1 (11.1)	1 (11.1)	0	0
Gamma-glutamyltransferase increased (γ-グルタミルトランスフェラーゼ増加)	1 (11.1)	1 (11.1)	2 (9.5)	1 (4.8)
Lipase increased (リパーゼ増加)	1 (11.1)	0	0	0
Weight increased (体重増加)	1 (11.1)	0	1 (4.8)	1 (4.8)
Blood lactate dehydrogenase increased (血中乳酸脱水素酵素増加)	0	0	1 (4.8)	0
Blood pressure decreased (血圧低下)	0	0	1 (4.8)	1 (4.8)
Metabolism and nutrition disorders (代謝および栄養障害)	8 (88.9)	5 (55.6)	13 (61.9)	9 (42.9)
Decreased appetite (食欲減退)	1 (11.1)	0	0	0
Dyslipidaemia (脂質異常症)	1 (11.1)	0	0	0
Hyperglycaemia (高血糖)	1 (11.1)	1 (11.1)	1 (4.8)	1 (4.8)
Hyperkalaemia (高カリウム血症)	1 (11.1)	1 (11.1)	0	0
Hypernatraemia (高ナトリウム血症)	1 (11.1)	1 (11.1)	1 (4.8)	1 (4.8)
Hypoalbuminaemia (低アルブミン血症)	1 (11.1)	1 (11.1)	5 (23.8)	3 (14.3)
Hypocalcaemia (低カルシウム血症)	1 (11.1)	1 (11.1)	3 (14.3)	2 (9.5)
Hypoglycaemia (低血糖)	1 (11.1)	0	2 (9.5)	0
Hypokalaemia (低カリウム血症)	1 (11.1)	1 (11.1)	5 (23.8)	2 (9.5)
Hypophosphataemia (低リン酸血症)	1 (11.1)	1 (11.1)	2 (9.5)	2 (9.5)
Steroid diabetes (ステロイド糖尿病)	1 (11.1)	1 (11.1)	2 (9.5)	0
Acidosis (アシドーシス)	0	0	1 (4.8)	1 (4.8)
Dehydration (脱水)	0	0	3 (14.3)	1 (4.8)
Fluid retention (体液貯留)	0	0	1 (4.8)	0
Hyperamylasaemia (高アミラーゼ血症)	0	0	1 (4.8)	0
Hyperlipasaemia (高リパーゼ血症)	0	0	1 (4.8)	1 (4.8)
Hyperuricaemia (高尿酸血症)	0	0	1 (4.8)	0
Hypomagnesaemia (低マグネシウム血症)	0	0	3 (14.3)	0

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Hyponatraemia (低ナトリウム血症)	0	0	1 (4.8)	1 (4.8)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	0	0	4 (19.0)	2 (9.5)
Arthralgia (関節痛)	0	0	1 (4.8)	0
Back pain (背部痛)	0	0	1 (4.8)	1 (4.8)
Muscular weakness (筋力低下)	0	0	1 (4.8)	1 (4.8)
Myalgia (筋肉痛)	0	0	1 (4.8)	0
Pain in extremity (四肢痛)	0	0	1 (4.8)	1 (4.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	0	0	1 (4.8)	1 (4.8)
Acute myeloid leukaemia recurrent (再発急性骨髄性白血病)	0	0	1 (4.8)	1 (4.8)
Nervous system disorders (神経系障害)	4 (44.4)	1 (11.1)	4 (19.0)	1 (4.8)
Dysgeusia (味覚不全)	1 (11.1)	0	0	0
Guillain-Barre syndrome (ギラン・バレー症候群)	1 (11.1)	1 (11.1)	0	0
Somnolence (傾眠)	1 (11.1)	0	0	0
Tremor (振戦)	1 (11.1)	0	0	0
Amnesia (健忘)	0	0	1 (4.8)	0
Cognitive disorder (認知障害)	0	0	1 (4.8)	0
Loss of consciousness (意識消失)	0	0	1 (4.8)	1 (4.8)
Neuralgia (神経痛)	0	0	1 (4.8)	0
Psychiatric disorders (精神障害)	2 (22.2)	0	5 (23.8)	2 (9.5)
Insomnia (不眠症)	2 (22.2)	0	3 (14.3)	0
Confusional state (錯乱状態)	0	0	1 (4.8)	1 (4.8)
Delirium (譫妄)	0	0	1 (4.8)	1 (4.8)
Renal and urinary disorders (腎および尿路障害)	3 (33.3)	1 (11.1)	5 (23.8)	4 (19.0)
Acute kidney injury (急性腎障害)	2 (22.2)	0	3 (14.3)	3 (14.3)
Renal impairment (腎機能障害)	1 (11.1)	1 (11.1)	1 (4.8)	0
Cystitis haemorrhagic (出血性膀胱炎)	0	0	2 (9.5)	1 (4.8)
Reproductive system and breast disorders (生殖系および乳房障害)	1 (11.1)	0	0	0
Scrotum erosion (陰嚢びらん)	1 (11.1)	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器，胸郭および縦隔障害)	3 (33.3)	3 (33.3)	9 (42.9)	3 (14.3)
Idiopathic pneumonia syndrome (特発性肺炎症候群)	2 (22.2)	2 (22.2)	0	0
Acute lung injury (急性肺損傷)	1 (11.1)	1 (11.1)	1 (4.8)	1 (4.8)
Respiratory failure (呼吸不全)	1 (11.1)	1 (11.1)	0	0
Acute respiratory failure (急性呼吸不全)	0	0	1 (4.8)	1 (4.8)
Epistaxis (鼻出血)	0	0	2 (9.5)	0

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Hypoxia (低酸素症)	0	0	2 (9.5)	0
Pleural effusion (胸水)	0	0	4 (19.0)	2 (9.5)
Pneumothorax (気胸)	0	0	1 (4.8)	0
Pulmonary oedema (肺水腫)	0	0	1 (4.8)	1 (4.8)
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)	4 (44.4)	0	5 (23.8)	0
Pruritus (そう痒症)	2 (22.2)	0	1 (4.8)	0
Decubitus ulcer (褥瘡性潰瘍)	1 (11.1)	0	0	0
Skin erosion (皮膚びらん)	1 (11.1)	0	1 (4.8)	0
Epidermolysis (表皮融解)	0	0	1 (4.8)	0
Rash (発疹)	0	0	1 (4.8)	0
Urticaria (蕁麻疹)	0	0	1 (4.8)	0
Vascular disorders (血管障害)	2 (22.2)	1 (11.1)	6 (28.6)	2 (9.5)
Hypertension (高血圧)	1 (11.1)	0	3 (14.3)	2 (9.5)
Hypotension (低血圧)	1 (11.1)	1 (11.1)	2 (9.5)	0
Hot flush (ほてり)	0	0	1 (4.8)	0
Phlebitis (静脈炎)	0	0	1 (4.8)	0

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-5.16
MedDRA version 22.1
SOC はアルファベット順，PT は SOC 内の RUX 群の All grades の発現率の降順
Region=Japan のデータを示した。

Table 7-15 急性 GVHD の SOC 別 PT 別の有害事象（C2301 試験，SAF，日本人，RUX crossover の被験者，データカットオフ 2 まで）

	RUX N=6	
Primary system organ class	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)
Number of subjects with at least one event	6 (100)	6 (100)
Blood and lymphatic system disorders (血液およびリンパ系障害)	2 (33.3)	1 (16.7)
Anaemia (貧血)	2 (33.3)	1 (16.7)
Thrombocytopenia (血小板減少症)	1 (16.7)	1 (16.7)
Cardiac disorders (心臓障害)	1 (16.7)	1 (16.7)
Cardiac failure (心不全)	1 (16.7)	1 (16.7)
Gastrointestinal disorders (胃腸障害)	2 (33.3)	1 (16.7)
Abdominal pain (腹痛)	1 (16.7)	0
Enteritis (小腸炎)	1 (16.7)	0
Ileus (イレウス)	1 (16.7)	1 (16.7)
Vomiting (嘔吐)	1 (16.7)	0

Primary system organ class Preferred term	RUX N=6 All grades n (%)	 Grade ≥ 3 n (%)
General disorders and administration site conditions (一般・全身障害および投与部位の状態)	2 (33.3)	0
Pyrexia (発熱)	2 (33.3)	0
Hepatobiliary disorders (肝胆道系障害)	1 (16.7)	1 (16.7)
Hepatic function abnormal (肝機能異常)	1 (16.7)	1 (16.7)
Infections and infestations (感染症および寄生虫症)	4 (66.7)	3 (50.0)
Cystitis (膀胱炎)	2 (33.3)	1 (16.7)
Enteritis infectious (感染性腸炎)	2 (33.3)	1 (16.7)
Adenovirus infection (アデノウイルス感染)	1 (16.7)	1 (16.7)
Conjunctivitis (結膜炎)	1 (16.7)	1 (16.7)
Cytomegalovirus enteritis (サイトメガロウイルス性小腸炎)	1 (16.7)	1 (16.7)
Epstein-Barr virus infection (エプスタイン・バーウイルス感染)	1 (16.7)	1 (16.7)
Otitis media (中耳炎)	1 (16.7)	0
Pyelonephritis (腎盂腎炎)	1 (16.7)	0
Injury, poisoning and procedural complications (傷害，中毒および処置合併症)	2 (33.3)	0
Subcutaneous haematoma (皮下血腫)	1 (16.7)	0
Traumatic haematoma (外傷性血腫)	1 (16.7)	0
Wound complication (創合併症)	1 (16.7)	0
Investigations (臨床検査)	4 (66.7)	4 (66.7)
Amylase increased (アミラーゼ増加)	1 (16.7)	1 (16.7)
C-reactive protein increased (C-反応性蛋白増加)	1 (16.7)	1 (16.7)
Lipase increased (リパーゼ増加)	1 (16.7)	1 (16.7)
Neutrophil count decreased (好中球数減少)	1 (16.7)	1 (16.7)
Platelet count decreased (血小板数減少)	1 (16.7)	1 (16.7)
White blood cell count decreased (白血球数減少)	1 (16.7)	1 (16.7)
Metabolism and nutrition disorders (代謝および栄養障害)	5 (83.3)	3 (50.0)
Hypokalaemia (低カリウム血症)	2 (33.3)	0
Hyperglycaemia (高血糖)	1 (16.7)	1 (16.7)
Hyperuricaemia (高尿酸血症)	1 (16.7)	0
Hypoalbuminaemia (低アルブミン血症)	1 (16.7)	1 (16.7)
Hypocalcaemia (低カルシウム血症)	1 (16.7)	1 (16.7)
Hypophosphataemia (低リン酸血症)	1 (16.7)	1 (16.7)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	2 (33.3)	0
Arthralgia (関節痛)	1 (16.7)	0
Back pain (背部痛)	1 (16.7)	0

	RUX N=6	
Primary system organ class	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)
Nervous system disorders (神経系障害)	1 (16.7)	1 (16.7)
Posterior reversible encephalopathy syndrome (可逆性後白質脳症症候群)	1 (16.7)	1 (16.7)
Reversible cerebral vasoconstriction syndrome (可逆性脳血管収縮症候群)	1 (16.7)	1 (16.7)
Psychiatric disorders (精神障害)	1 (16.7)	1 (16.7)
Delirium (譫妄)	1 (16.7)	1 (16.7)
Insomnia (不眠症)	1 (16.7)	0
Respiratory, thoracic and mediastinal disorders (呼吸器，胸郭および縦隔障害)	2 (33.3)	2 (33.3)
Idiopathic pneumonia syndrome (特発性肺炎症候群)	1 (16.7)	1 (16.7)
Respiratory failure (呼吸不全)	1 (16.7)	1 (16.7)
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)	2 (33.3)	0
Purpura (紫斑)	1 (16.7)	0
Skin disorder (皮膚障害)	1 (16.7)	0

Source: 5.3.5.3-1-Table 14.3.1-1.25j
MedDRA version 22.1
SOC はアルファベット順，PT は SOC 内の All grades の発現率の降順

Table 7-16 急性 GVHD の SOC 別 PT 別の副作用（C2301 試験，SAF，日本人，データカットオフ 2 まで）

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Number of subjects with at least one event	9 (100)	9 (100)	13 (61.9)	10 (47.6)
Blood and lymphatic system disorders (血液およびリンパ系障害)	5 (55.6)	3 (33.3)	1 (4.8)	1 (4.8)
Thrombocytopenia (血小板減少症)	4 (44.4)	2 (22.2)	0	0
Anaemia (貧血)	3 (33.3)	2 (22.2)	1 (4.8)	1 (4.8)
Neutropenia (好中球減少症)	1 (11.1)	1 (11.1)	0	0
Gastrointestinal disorders (胃腸障害)	2 (22.2)	1 (11.1)	1 (4.8)	0
Gastrointestinal haemorrhage (胃腸出血)	1 (11.1)	0	0	0
Lower gastrointestinal haemorrhage (下部消化管出血)	1 (11.1)	1 (11.1)	0	0
Constipation (便秘)	0	0	1 (4.8)	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)	1 (11.1)	0	1 (4.8)	0
Oedema peripheral (末梢性浮腫)	1 (11.1)	0	1 (4.8)	0
Hepatobiliary disorders (肝胆道系障害)	3 (33.3)	2 (22.2)	0	0

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Hepatic function abnormal (肝機能異常)	1 (11.1)	1 (11.1)	0	0
Hepatotoxicity (肝毒性)	1 (11.1)	0	0	0
Liver disorder (肝障害)	1 (11.1)	1 (11.1)	0	0
Immune system disorders (免疫系障害)	0	0	2 (9.5)	0
Allergy to immunoglobulin therapy (免疫グロブリン療法アレルギー)	0	0	1 (4.8)	0
Hypogammaglobulinaemia (低γグロブリン血症)	0	0	1 (4.8)	0
Infections and infestations (感染症および寄生虫症)	4 (44.4)	3 (33.3)	7 (33.3)	4 (19.0)
Sepsis (敗血症)	2 (22.2)	2 (22.2)	1 (4.8)	1 (4.8)
Bacteraemia (菌血症)	1 (11.1)	1 (11.1)	1 (4.8)	0
Bronchopulmonary aspergillosis (気管支肺アスペルギルス症)	1 (11.1)	1 (11.1)	0	0
Clostridium difficile infection (クロストリジウム・ディフィシレ感染)	1 (11.1)	1 (11.1)	0	0
Cytomegalovirus infection (サイトメガロウイルス感染)	1 (11.1)	0	1 (4.8)	1 (4.8)
Device related infection (医療機器関連感染)	1 (11.1)	1 (11.1)	0	0
Epstein-Barr virus infection (エプスタイン・バーウイルス感染)	1 (11.1)	0	0	0
Pneumonia (肺炎)	1 (11.1)	1 (11.1)	0	0
Urinary tract infection (尿路感染)	1 (11.1)	1 (11.1)	0	0
Bacterial infection (細菌感染)	0	0	1 (4.8)	0
Fungal infection (真菌感染)	0	0	1 (4.8)	0
Gastroenteritis (胃腸炎)	0	0	1 (4.8)	1 (4.8)
Herpes zoster (帯状疱疹)	0	0	1 (4.8)	0
Large intestine infection (大腸感染)	0	0	1 (4.8)	0
Oral candidiasis (口腔カンジダ症)	0	0	1 (4.8)	0
Pneumonia cytomegaloviral (サイトメガロウイルス性肺炎)	0	0	1 (4.8)	1 (4.8)
Staphylococcal bacteraemia (ブドウ球菌性菌血症)	0	0	1 (4.8)	1 (4.8)
Injury, poisoning and procedural complications (傷害，中毒および処置合併症)	1 (11.1)	0	0	0
Compression fracture (圧迫骨折)	1 (11.1)	0	0	0
Investigations (臨床検査)	7 (77.8)	5 (55.6)	7 (33.3)	6 (28.6)
Platelet count decreased (血小板数減少)	4 (44.4)	4 (44.4)	3 (14.3)	3 (14.3)
White blood cell count decreased (白血球数減少)	4 (44.4)	4 (44.4)	5 (23.8)	4 (19.0)
Neutrophil count decreased (好中球数減少)	3 (33.3)	3 (33.3)	2 (9.5)	2 (9.5)
Blood creatinine increased (血中クレアチニン増加)	2 (22.2)	0	2 (9.5)	0
Cytomegalovirus test positive (サイトメガロウイルス検査陽性)	2 (22.2)	0	2 (9.5)	0
Aspergillus test positive (アスペルギルス検査陽性)	1 (11.1)	0	0	0
Blood beta-D-glucan increased (血中 β-D-グルカン増加)	1 (11.1)	0	0	0

	RUX N=9		BAT N=21	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Weight increased (体重増加)	1 (11.1)	0	0	0
Metabolism and nutrition disorders (代謝および栄養障害)	0	0	2 (9.5)	0
Dehydration (脱水)	0	0	1 (4.8)	0
Hyperuricaemia (高尿酸血症)	0	0	1 (4.8)	0
Hypoalbuminaemia (低アルブミン血症)	0	0	1 (4.8)	0
Nervous system disorders (神経系障害)	2 (22.2)	1 (11.1)	1 (4.8)	0
Dysgeusia (味覚不全)	1 (11.1)	0	0	0
Guillain-Barre syndrome (ギラン・バレー症候群)	1 (11.1)	1 (11.1)	0	0
Neuralgia (神経痛)	0	0	1 (4.8)	0
Renal and urinary disorders (腎および尿路障害)	1 (11.1)	1 (11.1)	0	0
Renal impairment (腎機能障害)	1 (11.1)	1 (11.1)	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器，胸郭および縦隔障害)	2 (22.2)	2 (22.2)	0	0
Acute lung injury (急性肺損傷)	1 (11.1)	1 (11.1)	0	0
Idiopathic pneumonia syndrome (特発性肺炎症候群)	1 (11.1)	1 (11.1)	0	0

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-5.17
MedDRA version 22.1
SOC はアルファベット順，PT は SOC 内の RUX 群の All grades の発現率の降順
Region=Japan のデータを示した。

Table 7-17 急性 GVHD の SOC 別 PT 別の副作用（C2301 試験，SAF，日本人，RUX crossover の被験者，データカットオフ 2 まで）

	RUX N=6	
Primary system organ class	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)
Number of subjects with at least one event	4 (66.7)	3 (50.0)
Blood and lymphatic system disorders (血液およびリンパ系障害)	1 (16.7)	0
Anaemia (貧血)	1 (16.7)	0
Infections and infestations (感染症および寄生虫症)	2 (33.3)	1 (16.7)
Adenovirus infection (アデノウイルス感染)	1 (16.7)	1 (16.7)
Cystitis (膀胱炎)	1 (16.7)	1 (16.7)
Pyelonephritis (腎盂腎炎)	1 (16.7)	0
Investigations (臨床検査)	2 (33.3)	2 (33.3)
Neutrophil count decreased (好中球数減少)	1 (16.7)	1 (16.7)
White blood cell count decreased (白血球数減少)	1 (16.7)	1 (16.7)
Respiratory, thoracic and mediastinal disorders (呼吸器，胸郭および縦隔障害)	1 (16.7)	1 (16.7)
Respiratory failure (呼吸不全)	1 (16.7)	1 (16.7)

Source: 5.3.5.3-1-Table 14.3.1-1.26j
MedDRA version 22.1
SOC はアルファベット順

Table 7-18　急性 GVHD の治験治療下の死亡（C2301 試験，SAF，全体／日本人，データカットオフ 2 まで）

	全体			日本人		
Category PT	RUX N = 152 n (%)	BAT N = 150 n (%)	RUX crossover N = 49 n (%)	RUX N = 9 n (%)	BAT N = 21 n (%)	RUX crossover N = 6 n (%)
曝露期間（日）：中央値（最小値 - 最大値）	63.0 (6.0-463.0)	29.0 (1.0-188.0)	61.0 (2.0-383.0)	72.0 (14.0-335.0)	29.0 (1.0-68.0)	38.0 (8.0-259.0)
総曝露期間（人年）	39.5	19.0	12.3	2.5	1.9	1.1
合計	43 (28.3)	36 (24.0)	19 (38.8)	4 (44.4)	4 (19.0)	3 (50.0)
死因：対象疾患	21 (13.8)	21 (14.0)	8 (16.3)	1 (11.1)	2 (9.5)	0
急性移植片対宿主病	21 (13.8)	21 (14.0)	8 (16.3)	1 (11.1)	2 (9.5)	0
死因：その他	22 (14.5)	15 (10.0)	11 (22.4)	3 (33.3)	2 (9.5)	3 (50.0)
敗血症	3 (2.0)	1 (0.7)	1 (2.0)	1 (11.1)	0	0
心停止	2 (1.3)	0	0	0		0
疾患進行	2 (1.3)	1 (0.7)	0	0	0	0
多臓器機能不全症候群	2 (1.3)	1 (0.7)	0	0	0	0
敗血症性ショック	2 (1.3)	2 (1.3)	0	0	0	0
急性骨髄性白血病	1 (0.7)	0	0	1 (11.1)	0	0
再発急性骨髄性白血病	1 (0.7)	1 (0.7)	0	0	1 (4.8)	0
状態悪化	1 (0.7)	0	0	0	0	0
全身健康状態異常	1 (0.7)	0	0	0	0	0
感染	1 (0.7)	0	0	0	0	0
肺障害	1 (0.7)	0	0	0	0	0
腎機能障害	1 (0.7)	0	0	1 (11.1)	0	0
呼吸障害	1 (0.7)	0	0	0	0	0
呼吸不全	1 (0.7)	1 (0.7)	2 (4.1)	0	0	1 (16.7)
気道感染	1 (0.7)	0	0	0	0	0
ウイルス感染	1 (0.7)	0	0	0	0	0
急性肺損傷	0	1 (0.7)	0	0	1 (4.8)	0
誤嚥	0	1 (0.7)	0	0	0	0
脳梗塞	0	1 (0.7)	0	0	0	0
易感染性宿主の感染	0	1 (0.7)	0	0	0	0
腸管虚血	0	1 (0.7)	0	0	0	0
多臓器障害	0	1 (0.7)	0	0	0	0
偽膜性大腸炎	0	1 (0.7)	0	0	0	0
腎不全	0	1 (0.7)	0	0	0	0
心肺不全	0	0	1 (2.0)	0	0	0
死亡	0	0	1 (2.0)	0	0	0
アデノウイルス感染	0	0	1 (2.0)	0	0	1 (16.7)

Category PT	全体 RUX N = 152 n (%)	全体 BAT N = 150 n (%)	全体 RUX crossover N = 49 n (%)	日本人 RUX N = 9 n (%)	日本人 BAT N = 21 n (%)	日本人 RUX crossover N = 6 n (%)
脳血管発作	0	0	1 (2.0)	0	0	0
昏睡	0	0	1 (2.0)	0	0	0
特発性肺炎症候群	0	0	1 (2.0)	0	0	1 (16.7)
肺臓炎	0	0	1 (2.0)	0	0	0
肺出血	0	0	1 (2.0)	0	0	0

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3-1.1，Table 14.3-1.5，Table 14.3.1-2.2，Table 14.3.1-2.3，5.3.5.3-1-Table 14.3-1.1j，Table 14.3-1.5j，Table 14.3.1-2.2j，Table 14.3.1-2.3j
全体集団の RUX 群の発現率の降順
総曝露期間 = 全被験者の曝露期間の合計
MedDRA version 22.1

Table 7-19　急性 GVHD の重篤な有害事象（C2301 試験，SAF，日本人，データカットオフ 2 まで）

PT	RUX N=9 n (%)	BAT N=21 n (%)
合計	6 (66.7)	10 (47.6)
敗血症	2 (22.2)	0
下部消化管出血	1 (11.1)	0
血中ビリルビン増加	1 (11.1)	0
急性肺損傷	1 (11.1)	1 (4.8)
ギラン・バレー症候群	1 (11.1)	0
腎機能障害	1 (11.1)	0
特発性肺炎症候群	1 (11.1)	0
呼吸不全	1 (11.1)	0
急性腎障害	0	2 (9.5)
血栓性微小血管症	0	1 (4.8)
免疫グロブリン療法アレルギー	0	1 (4.8)
胃腸炎	0	1 (4.8)
サイトメガロウイルス性肺炎	0	1 (4.8)
好中球数減少	0	1 (4.8)
血小板数減少	0	1 (4.8)
筋力低下	0	1 (4.8)
再発急性骨髄性白血病	0	1 (4.8)
急性呼吸不全	0	1 (4.8)
肺水腫	0	1 (4.8)

Source: 5.3.5.1-1-C2301 試験 CSR2-Table 14.3.1-5.18
MedDRA version 22.1
RUX 群の発現率の降順
Region=Japan のデータを示した。

Table 7-20 急性 GVHD の重篤な有害事象（C2301 試験，SAF，日本人，RUX crossover の被験者，データカットオフ 2 まで）

PT	RUX crossover N=6 n (%)
合計	5 (83.3)
イレウス	1 (16.7)
肝機能異常	1 (16.7)
アデノウイルス感染	1 (16.7)
感染性腸炎	1 (16.7)
皮下血腫	1 (16.7)
可逆性後白質脳症症候群	1 (16.7)
特発性肺炎症候群	1 (16.7)
呼吸不全	1 (16.7)

Source: 5.3.5.3-1-Table 14.3.1-1.27j
MedDRA version 22.1

Table 7-21 急性 GVHD の臨床的に注目すべき有害事象の要約（C2301 試験，SAF，日本人，データカットオフ 2 まで）

	RUX N=9		BAT N=21	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
感染症				
感染症（結核を除く）	8 (88.9)	6 (66.7)	18 (85.7)	10 (47.6)
肺炎	2 (22.2)	2 (22.2)	2 (9.5)	2 (9.5)
日和見感染	1 (11.1)	1 (11.1)	4 (19.0)	2 (9.5)
サイトメガロウイルス感染／感染症	5 (55.6)	1 (11.1)	6 (28.6)	3 (14.3)
尿路感染	2 (22.2)	1 (11.1)	1 (4.8)	0
敗血症／敗血症性ショック	2 (22.2)	2 (22.2)	2 (9.5)	2 (9.5)
帯状疱疹	0	0	1 (4.8)	0
その他の感染	6 (66.7)	3 (33.3)	15 (71.4)	7 (33.3)
血球減少				
血小板減少症	8 (88.9)	7 (77.8)	8 (38.1)	6 (28.6)
赤血球減少症	5 (55.6)	4 (44.4)	6 (28.6)	6 (28.6)
白血球減少症	7 (77.8)	7 (77.8)	8 (38.1)	6 (28.6)
出血性事象				
出血性事象	4 (44.4)	2 (22.2)	6 (28.6)	1 (4.8)
胃腸出血	3 (33.3)	1 (11.1)	0	0
挫傷	0	0	1 (4.8)	0
その他の出血性事象	1 (11.1)	1 (11.1)	5 (23.8)	1 (4.8)
その他				
トランスアミナーゼ上昇	3 (33.3)	2 (22.2)	1 (4.8)	1 (4.8)

	RUX N=9		BAT N=21	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
脂質異常	1 (11.1)	0	0	0
高血圧	1 (11.1)	0	3 (14.3)	2 (9.5)
血栓塞栓症	1 (11.1)	1 (11.1)	2 (9.5)	1 (4.8)
悪性腫瘍	0	0	1 (4.8)	1 (4.8)
骨折	1 (11.1)	0	1 (4.8)	0
体重増加	1 (11.1)	0	1 (4.8)	1 (4.8)

Source: 5.3.5.3-1-Table 14.3.1-1.19j
MedDRA version 22.1

Table 7-22 急性 GVHD の臨床的に注目すべき有害事象の要約（C2301 試験，SAF，日本人，RUX crossover の被験者，データカットオフ 2 まで）

	RUX crossover N=6	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)
感染症		
感染症（結核を除く）	4 (66.7)	3 (50.0)
肺炎	1 (16.7)	1 (16.7)
日和見感染	1 (16.7)	1 (16.7)
サイトメガロウイルス感染／感染症	1 (16.7)	1 (16.7)
尿路感染	3 (50.0)	1 (16.7)
その他の感染	4 (66.7)	3 (50.0)
血球減少		
血小板減少症	2 (33.3)	2 (33.3)
赤血球減少症	2 (33.3)	1 (16.7)
白血球減少症	2 (33.3)	2 (33.3)
出血性事象		
出血性事象	1 (16.7)	0
挫傷	1 (16.7)	0

Source: 5.3.5.3-1-Table 14.3.1-1.30j
MedDRA version 22.1

Table 7-23 慢性 GVHD の SOC 別 PT 別の有害事象（D2301 試験，SAF，日本人，データカットオフまで）

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Number of subjects with at least one event	22 (100)	17 (77.3)	15 (100)	12 (80.0)
Blood and lymphatic system disorders (血液およびリンパ系障害)	10 (45.5)	7 (31.8)	4 (26.7)	3 (20.0)
Anaemia (貧血)	10 (45.5)	6 (27.3)	1 (6.7)	1 (6.7)
Thrombocytopenia (血小板減少症)	4 (18.2)	4 (18.2)	1 (6.7)	1 (6.7)
Febrile neutropenia (発熱性好中球減少症)	1 (4.5)	1 (4.5)	2 (13.3)	2 (13.3)
Hypoglobulinaemia (低グロブリン血症)	1 (4.5)	0	0	0
Leukopenia (白血球減少症)	1 (4.5)	1 (4.5)	0	0
Lymphopenia (リンパ球減少症)	1 (4.5)	1 (4.5)	2 (13.3)	1 (6.7)
Neutropenia (好中球減少症)	1 (4.5)	1 (4.5)	1 (6.7)	0
Splenic haemorrhage (脾臓出血)	1 (4.5)	1 (4.5)	0	0
Cardiac disorders (心臓障害)	0	0	3 (20.0)	3 (20.0)
Aortic valve incompetence (大動脈弁閉鎖不全症)	0	0	1 (6.7)	1 (6.7)
Cardiac failure (心不全)	0	0	1 (6.7)	1 (6.7)
Cardiac failure congestive (うっ血性心不全)	0	0	1 (6.7)	1 (6.7)
Pericardial effusion (心嚢液貯留)	0	0	1 (6.7)	1 (6.7)
Supraventricular tachycardia (上室性頻脈)	0	0	1 (6.7)	0
Eye disorders (眼障害)	5 (22.7)	0	3 (20.0)	0
Dry eye (ドライアイ)	3 (13.6)	0	0	0
Glaucoma (緑内障)	1 (4.5)	0	0	0
Keratitis (角膜炎)	1 (4.5)	0	0	0
Cataract (白内障)	0	0	1 (6.7)	0
Conjunctival haemorrhage (結膜出血)	0	0	1 (6.7)	0
Iritis (虹彩炎)	0	0	1 (6.7)	0
Punctate keratitis (点状角膜炎)	0	0	1 (6.7)	0
Gastrointestinal disorders (胃腸障害)	9 (40.9)	1 (4.5)	8 (53.3)	2 (13.3)
Constipation (便秘)	3 (13.6)	0	0	0
Nausea (悪心)	3 (13.6)	0	2 (13.3)	0
Haemorrhoids (痔核)	2 (9.1)	0	0	0
Abdominal pain (腹痛)	1 (4.5)	0	1 (6.7)	0
Diarrhoea (下痢)	1 (4.5)	0	3 (20.0)	0
Ileus (イレウス)	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
Lip dry (口唇乾燥)	1 (4.5)	0	0	0
Toothache (歯痛)	1 (4.5)	0	0	0
Abdominal discomfort (腹部不快感)	0	0	1 (6.7)	0
Abdominal pain upper (上腹部痛)	0	0	1 (6.7)	0

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Ascites (腹水)	0	0	1 (6.7)	0
Enterocolitis (腸炎)	0	0	1 (6.7)	0
Stomatitis (口内炎)	0	0	1 (6.7)	1 (6.7)
Vomiting (嘔吐)	0	0	1 (6.7)	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)	6 (27.3)	0	5 (33.3)	1 (6.7)
Pyrexia (発熱)	4 (18.2)	0	2 (13.3)	0
Oedema peripheral (末梢性浮腫)	3 (13.6)	0	1 (6.7)	0
Oedema (浮腫)	1 (4.5)	0	0	0
Multiple organ dysfunction syndrome (多臓器機能不全症候群)	0	0	1 (6.7)	1 (6.7)
Non-cardiac chest pain (非心臓性胸痛)	0	0	2 (13.3)	0
Hepatobiliary disorders (肝胆道系障害)	3 (13.6)	0	2 (13.3)	1 (6.7)
Hepatic function abnormal (肝機能異常)	1 (4.5)	0	1 (6.7)	0
Hyperbilirubinaemia (高ビリルビン血症)	1 (4.5)	0	0	0
Liver disorder (肝障害)	1 (4.5)	0	0	0
Hepatobiliary disease (肝胆道系疾患)	0	0	1 (6.7)	1 (6.7)
Immune system disorders (免疫系障害)	2 (9.1)	1 (4.5)	2 (13.3)	0
Hypogammaglobulinaemia (低γグロブリン血症)	2 (9.1)	1 (4.5)	2 (13.3)	0
Infections and infestations (感染症および寄生虫症)	19 (86.4)	11 (50.0)	12 (80.0)	5 (33.3)
Pneumonia (肺炎)	6 (27.3)	6 (27.3)	4 (26.7)	3 (20.0)
Nasopharyngitis (上咽頭炎)	5 (22.7)	0	4 (26.7)	0
Influenza (インフルエンザ)	4 (18.2)	0	1 (6.7)	0
Upper respiratory tract infection (上気道感染)	3 (13.6)	0	0	0
Conjunctivitis (結膜炎)	2 (9.1)	0	1 (6.7)	0
Pharyngitis (咽頭炎)	2 (9.1)	0	0	0
Adenovirus infection (アデノウイルス感染)	1 (4.5)	1 (4.5)	0	0
Aspergillus infection (アスペルギルス感染)	1 (4.5)	0	0	0
BK virus infection (BK ウイルス感染)	1 (4.5)	0	0	0
Brain abscess (脳膿瘍)	1 (4.5)	1 (4.5)	0	0
Bronchitis (気管支炎)	1 (4.5)	0	0	0
Bursitis infective (感染性滑液包炎)	1 (4.5)	0	0	0
Cystitis (膀胱炎)	1 (4.5)	0	1 (6.7)	0
Cytomegalovirus infection (サイトメガロウイルス感染)	1 (4.5)	1 (4.5)	1 (6.7)	0
Enteritis infectious (感染性腸炎)	1 (4.5)	0	0	0
Gingivitis (歯肉炎)	1 (4.5)	0	0	0
Herpes zoster (帯状疱疹)	1 (4.5)	1 (4.5)	0	0
Meningitis (髄膜炎)	1 (4.5)	1 (4.5)	0	0
Nail bed infection bacterial (細菌性爪床感染)	1 (4.5)	0	0	0

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Oral herpes (口腔ヘルペス)	1 (4.5)	0	0	0
Pneumococcal infection (肺炎球菌感染)	1 (4.5)	1 (4.5)	0	0
Pneumonia bacterial (細菌性肺炎)	1 (4.5)	1 (4.5)	0	0
Pneumonia fungal (真菌性肺炎)	1 (4.5)	0	0	0
Pyelonephritis (腎盂腎炎)	1 (4.5)	1 (4.5)	0	0
Sepsis (敗血症)	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
Skin infection (皮膚感染)	1 (4.5)	0	0	0
Urinary tract infection (尿路感染)	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
Varicella (水痘)	1 (4.5)	0	1 (6.7)	1 (6.7)
Wound infection (創傷感染)	1 (4.5)	0	0	0
Abscess limb (四肢膿瘍)	0	0	1 (6.7)	0
Bacteraemia (菌血症)	0	0	1 (6.7)	0
Cellulitis (蜂巣炎)	0	0	1 (6.7)	0
Cystitis viral (ウイルス性膀胱炎)	0	0	3 (20.0)	0
Cytomegalovirus viraemia (サイトメガロウイルス血症)	0	0	1 (6.7)	1 (6.7)
Otitis media (中耳炎)	0	0	1 (6.7)	1 (6.7)
Injury, poisoning and procedural complications (傷害，中毒および処置合併症)	4 (18.2)	0	1 (6.7)	0
Clavicle fracture (鎖骨骨折)	1 (4.5)	0	0	0
Skin abrasion (皮膚擦過傷)	1 (4.5)	0	0	0
Subcutaneous haematoma (皮下血腫)	1 (4.5)	0	0	0
Tendon rupture (腱断裂)	1 (4.5)	0	0	0
Contusion (挫傷)	0	0	1 (6.7)	0
Fractured sacrum (仙骨骨折)	0	0	1 (6.7)	0
Investigations (臨床検査)	11 (50.0)	7 (31.8)	8 (53.3)	6 (40.0)
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)	4 (18.2)	1 (4.5)	0	0
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)	4 (18.2)	1 (4.5)	0	0
Platelet count decreased (血小板数減少)	4 (18.2)	3 (13.6)	2 (13.3)	2 (13.3)
Gamma-glutamyltransferase increased (γ-グルタミルトランスフェラーゼ増加)	3 (13.6)	2 (9.1)	1 (6.7)	1 (6.7)
Blood bilirubin increased (血中ビリルビン増加)	2 (9.1)	1 (4.5)	0	0
Blood creatinine increased (血中クレアチニン増加)	2 (9.1)	0	0	0
Lymphocyte count decreased (リンパ球数減少)	2 (9.1)	2 (9.1)	1 (6.7)	1 (6.7)
Neutrophil count decreased (好中球数減少)	2 (9.1)	2 (9.1)	1 (6.7)	1 (6.7)
Blood alkaline phosphatase increased (血中アルカリホスファターゼ増加)	1 (4.5)	0	1 (6.7)	1 (6.7)
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)	1 (4.5)	0	0	0

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Blood lactate dehydrogenase increased (血中乳酸脱水素酵素増加)	1 (4.5)	0	0	0
Cytomegalovirus test positive (サイトメガロウイルス検査陽性)	1 (4.5)	0	0	0
Weight decreased (体重減少)	1 (4.5)	0	1 (6.7)	0
Weight increased (体重増加)	1 (4.5)	0	0	0
White blood cell count decreased (白血球数減少)	1 (4.5)	1 (4.5)	2 (13.3)	1 (6.7)
Amylase increased (アミラーゼ増加)	0	0	1 (6.7)	0
Blood cholesterol increased (血中コレステロール増加)	0	0	1 (6.7)	1 (6.7)
Blood urine (尿中血)	0	0	1 (6.7)	0
Lipase increased (リパーゼ増加)	0	0	1 (6.7)	1 (6.7)
Metabolism and nutrition disorders (代謝および栄養障害)	14 (63.6)	5 (22.7)	11 (73.3)	3 (20.0)
Dehydration (脱水)	3 (13.6)	0	2 (13.3)	0
Hyperuricaemia (高尿酸血症)	3 (13.6)	0	0	0
Hypokalaemia (低カリウム血症)	3 (13.6)	0	3 (20.0)	2 (13.3)
Hypercholesterolaemia (高コレステロール血症)	2 (9.1)	1 (4.5)	0	0
Hyperlipidaemia (高脂血症)	2 (9.1)	1 (4.5)	2 (13.3)	1 (6.7)
Hypocalcaemia (低カルシウム血症)	2 (9.1)	0	0	0
Hypomagnesaemia (低マグネシウム血症)	2 (9.1)	0	1 (6.7)	0
Decreased appetite (食欲減退)	1 (4.5)	1 (4.5)	1 (6.7)	0
Diabetes mellitus (糖尿病)	1 (4.5)	0	0	0
Folate deficiency (葉酸欠乏)	1 (4.5)	0	0	0
Hyperglycaemia (高血糖)	1 (4.5)	0	0	0
Hyperkalaemia (高カリウム血症)	1 (4.5)	1 (4.5)	1 (6.7)	0
Hypermagnesaemia (高マグネシウム血症)	1 (4.5)	1 (4.5)	0	0
Hypertriglyceridaemia (高トリグリセリド血症)	1 (4.5)	0	0	0
Hypoalbuminaemia (低アルブミン血症)	1 (4.5)	0	2 (13.3)	1 (6.7)
Hypozincaemia (低亜鉛血症)	1 (4.5)	0	0	0
Steroid diabetes (ステロイド糖尿病)	1 (4.5)	1 (4.5)	0	0
Hyperferritinaemia (高フェリチン血症)	0	0	1 (6.7)	0
Hypoglycaemia (低血糖)	0	0	2 (13.3)	0
Hyponatraemia (低ナトリウム血症)	0	0	1 (6.7)	0
Hypophosphataemia (低リン酸血症)	0	0	2 (13.3)	1 (6.7)
Malnutrition (栄養障害)	0	0	1 (6.7)	0
Vitamin B1 deficiency (ビタミン B1 欠乏)	0	0	1 (6.7)	0
Zinc deficiency (亜鉛欠乏)	0	0	1 (6.7)	0
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)	8 (36.4)	1 (4.5)	4 (26.7)	0
Back pain (背部痛)	2 (9.1)	1 (4.5)	1 (6.7)	0

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Myalgia (筋肉痛)	2 (9.1)	0	0	0
Muscular weakness (筋力低下)	1 (4.5)	0	0	0
Musculoskeletal chest pain (筋骨格系胸痛)	1 (4.5)	0	0	0
Osteoporosis (骨粗鬆症)	1 (4.5)	0	0	0
Pain in extremity (四肢痛)	1 (4.5)	0	0	0
Arthralgia (関節痛)	0	0	1 (6.7)	0
Muscle fatigue (筋肉疲労)	0	0	1 (6.7)	0
Muscle spasms (筋痙縮)	0	0	1 (6.7)	0
Myopathy (ミオパチー)	0	0	1 (6.7)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）)	1 (4.5)	1 (4.5)	3 (20.0)	1 (6.7)
Post transplant lymphoproliferative disorder (移植後リンパ増殖性障害)	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
Fibroma (線維腫)	0	0	1 (6.7)	0
Oral neoplasm benign (口腔の良性新生物)	0	0	1 (6.7)	0
Nervous system disorders (神経系障害)	7 (31.8)	2 (9.1)	4 (26.7)	1 (6.7)
Headache (頭痛)	3 (13.6)	0	3 (20.0)	0
Brain oedema (脳浮腫)	1 (4.5)	1 (4.5)	0	0
Cerebral infarction (脳梗塞)	1 (4.5)	0	0	0
Presyncope (失神寸前の状態)	1 (4.5)	1 (4.5)	0	0
Sciatica (坐骨神経痛)	1 (4.5)	0	0	0
Neuropathy peripheral (末梢性ニューロパチー)	0	0	1 (6.7)	1 (6.7)
Psychiatric disorders (精神障害)	5 (22.7)	0	4 (26.7)	0
Insomnia (不眠症)	3 (13.6)	0	1 (6.7)	0
Delirium (譫妄)	2 (9.1)	0	1 (6.7)	0
Anxiety disorder (不安障害)	1 (4.5)	0	0	0
Depression (うつ病)	1 (4.5)	0	0	0
Confusional state (錯乱状態)	0	0	1 (6.7)	0
Depressive symptom (抑うつ症状)	0	0	1 (6.7)	0
Renal and urinary disorders (腎および尿路障害)	1 (4.5)	1 (4.5)	0	0
Renal failure (腎不全)	1 (4.5)	1 (4.5)	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器，胸郭および縦隔障害)	9 (40.9)	4 (18.2)	7 (46.7)	1 (6.7)
Pneumothorax (気胸)	3 (13.6)	1 (4.5)	0	0
Dyspnoea (呼吸困難)	2 (9.1)	1 (4.5)	0	0
Rhinorrhoea (鼻漏)	2 (9.1)	0	1 (6.7)	0
Upper respiratory tract inflammation (上気道の炎症)	2 (9.1)	1 (4.5)	0	0
Cough (咳嗽)	1 (4.5)	0	1 (6.7)	0

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Emphysema (肺気腫)	1 (4.5)	0	0	0
Epistaxis (鼻出血)	1 (4.5)	0	2 (13.3)	0
Hypoxia (低酸素症)	1 (4.5)	0	1 (6.7)	0
Respiratory failure (呼吸不全)	1 (4.5)	1 (4.5)	0	0
Interstitial lung disease (間質性肺疾患)	0	0	1 (6.7)	0
Pleural effusion (胸水)	0	0	1 (6.7)	0
Pleurisy (胸膜炎)	0	0	1 (6.7)	0
Pneumonitis (肺臓炎)	0	0	1 (6.7)	1 (6.7)
Pulmonary haemorrhage (肺出血)	0	0	1 (6.7)	1 (6.7)
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)	5 (22.7)	0	3 (20.0)	0
Dry skin (皮膚乾燥)	2 (9.1)	0	0	0
Alopecia (脱毛症)	1 (4.5)	0	0	0
Dermal cyst (皮膚嚢腫)	1 (4.5)	0	0	0
Dermatitis allergic (アレルギー性皮膚炎)	1 (4.5)	0	0	0
Epidermolysis (表皮融解)	1 (4.5)	0	0	0
Acne (ざ瘡)	0	0	2 (13.3)	0
Blister (水疱)	0	0	1 (6.7)	0
Dermatitis (皮膚炎)	0	0	1 (6.7)	0
Ingrowing nail (嵌入爪)	0	0	1 (6.7)	0
Skin haemorrhage (皮膚出血)	0	0	1 (6.7)	0
Social circumstances (社会環境)	1 (4.5)	1 (4.5)	0	0
Loss of personal independence in daily activities (日常活動における個人の自立の喪失)	1 (4.5)	1 (4.5)	0	0
Vascular disorders (血管障害)	4 (18.2)	1 (4.5)	1 (6.7)	1 (6.7)
Hypertension (高血圧)	3 (13.6)	1 (4.5)	1 (6.7)	1 (6.7)
Hypotension (低血圧)	1 (4.5)	0	0	0

Source: 5.3.5.3-2-D2301 試験-Table 14.3.1-1.16j
MedDRA version 23.0
SOC はアルファベット順，PT は SOC 内の RUX 群の All grades の発現率の降順

Table 7-24 慢性 GVHD の SOC 別 PT 別の副作用（D2301 試験，SAF，日本人，データカットオフまで）

	RUX N=22		BAT N=15	
Primary system organ class Preferred term	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
Number of subjects with at least one event	19 (86.4)	12 (54.5)	8 (53.3)	5 (33.3)
Blood and lymphatic system disorders (血液およびリンパ系障害)	9 (40.9)	6 (27.3)	0	0

	RUX N=22		BAT N=15	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Anaemia (貧血)	9 (40.9)	5 (22.7)	0	0
Thrombocytopenia (血小板減少症)	3 (13.6)	3 (13.6)	0	0
Febrile neutropenia (発熱性好中球減少症)	1 (4.5)	1 (4.5)	0	0
Leukopenia (白血球減少症)	1 (4.5)	1 (4.5)	0	0
Neutropenia (好中球減少症)	1 (4.5)	1 (4.5)	0	0
Eye disorders (眼障害)	1 (4.5)	0	0	0
Keratitis (角膜炎)	1 (4.5)	0	0	0
Gastrointestinal disorders (胃腸障害)	0	0	2 (13.3)	1 (6.7)
Ileus (イレウス)	0	0	1 (6.7)	1 (6.7)
Vomiting (嘔吐)	0	0	1 (6.7)	0
Hepatobiliary disorders (肝胆道系障害)	2 (9.1)	0	0	0
Hepatic function abnormal (肝機能異常)	1 (4.5)	0	0	0
Liver disorder (肝障害)	1 (4.5)	0	0	0
Immune system disorders (免疫系障害)	1 (4.5)	1 (4.5)	1 (6.7)	0
Hypogammaglobulinaemia (低γグロブリン血症)	1 (4.5)	1 (4.5)	1 (6.7)	0
Infections and infestations (感染症および寄生虫症)	13 (59.1)	7 (31.8)	5 (33.3)	3 (20.0)
Pneumonia (肺炎)	2 (9.1)	2 (9.1)	2 (13.3)	2 (13.3)
Adenovirus infection (アデノウイルス感染)	1 (4.5)	1 (4.5)	0	0
Brain abscess (脳膿瘍)	1 (4.5)	1 (4.5)	0	0
Cystitis (膀胱炎)	1 (4.5)	0	0	0
Cytomegalovirus infection (サイトメガロウイルス感染)	1 (4.5)	1 (4.5)	0	0
Gingivitis (歯肉炎)	1 (4.5)	0	0	0
Herpes zoster (帯状疱疹)	1 (4.5)	1 (4.5)	0	0
Meningitis (髄膜炎)	1 (4.5)	1 (4.5)	0	0
Nail bed infection bacterial (細菌性爪床感染)	1 (4.5)	0	0	0
Nasopharyngitis (上咽頭炎)	1 (4.5)	0	0	0
Oral herpes (口腔ヘルペス)	1 (4.5)	0	0	0
Pneumococcal infection (肺炎球菌感染)	1 (4.5)	1 (4.5)	0	0
Pneumonia bacterial (細菌性肺炎)	1 (4.5)	1 (4.5)	0	0
Pneumonia fungal (真菌性肺炎)	1 (4.5)	0	0	0
Pyelonephritis (腎盂腎炎)	1 (4.5)	1 (4.5)	0	0
Sepsis (敗血症)	1 (4.5)	1 (4.5)	0	0
Upper respiratory tract infection (上気道感染)	1 (4.5)	0	0	0
Urinary tract infection (尿路感染)	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
Varicella (水痘)	1 (4.5)	0	1 (6.7)	1 (6.7)
Cystitis viral (ウイルス性膀胱炎)	0	0	3 (20.0)	0
Cytomegalovirus viraemia (サイトメガロウイルス血症)	0	0	1 (6.7)	1 (6.7)
Investigations (臨床検査)	9 (40.9)	4 (18.2)	1 (6.7)	0
Platelet count decreased (血小板数減少)	4 (18.2)	3 (13.6)	0	0

	RUX N=22		BAT N=15	
Primary system organ class	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Preferred term	n (%)	n (%)	n (%)	n (%)
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)	3 (13.6)	1 (4.5)	0	0
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)	3 (13.6)	0	0	0
Blood bilirubin increased (血中ビリルビン増加)	1 (4.5)	0	0	0
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)	1 (4.5)	0	0	0
Blood lactate dehydrogenase increased (血中乳酸脱水素酵素増加)	1 (4.5)	0	0	0
Cytomegalovirus test positive (サイトメガロウイルス検査陽性)	1 (4.5)	0	0	0
Gamma-glutamyltransferase increased (γ-グルタミルトランスフェラーゼ増加)	1 (4.5)	0	0	0
Neutrophil count decreased (好中球数減少)	1 (4.5)	1 (4.5)	0	0
White blood cell count decreased (白血球数減少)	1 (4.5)	1 (4.5)	1 (6.7)	0
Nervous system disorders (神経系障害)	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
Brain oedema (脳浮腫)	1 (4.5)	1 (4.5)	0	0
Neuropathy peripheral (末梢性ニューロパチー)	0	0	1 (6.7)	1 (6.7)
Respiratory, thoracic and mediastinal disorders (呼吸器，胸郭および縦隔障害)	2 (9.1)	2 (9.1)	2 (13.3)	1 (6.7)
Respiratory failure (呼吸不全)	1 (4.5)	1 (4.5)	0	0
Upper respiratory tract inflammation (上気道の炎症)	1 (4.5)	1 (4.5)	0	0
Interstitial lung disease (間質性肺疾患)	0	0	1 (6.7)	0
Pleurisy (胸膜炎)	0	0	1 (6.7)	0
Pneumonitis (肺臓炎)	0	0	1 (6.7)	1 (6.7)
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)	1 (4.5)	0	0	0
Alopecia (脱毛症)	1 (4.5)	0	0	0
Social circumstances (社会環境)	1 (4.5)	1 (4.5)	0	0
Loss of personal independence in daily activities (日常活動における個人の自立の喪失)	1 (4.5)	1 (4.5)	0	0

Source: 5.3.5.3-2-D2301 試験-Table 14.3.1-1.17j
MedDRA version 23.0
SOC はアルファベット順，PT は SOC 内の RUX 群の All grades の発現率の降順

Table 7-25　慢性 GVHD の治験治療下の死亡（D2301 試験，SAF，全体／日本人，データカットオフまで）

Category PT	全体 RUX N = 165 n (%)	全体 BAT N = 158 n (%)	全体 RUX crossover N = 61 n (%)	日本人 RUX N = 22 n (%)	日本人 BAT N = 15 n (%)	日本人 RUX crossover N = 2 n (%)
曝露期間（週）： 中央値（最小値 - 最大値）	41.3 (0.7-127.3)	24.1 (0.6-108.4)	42.3 (2.6-98.7)	44.4 (3.0-112.1)	29.1 (0.6-83.3)	NA
総曝露期間（人月）	1748.0	1061.8	593.5	236.6	116.3	NA
合計	16 (9.7)	11 (7.0)	3 (4.9)	5 (22.7)	2 (13.3)	0
死因：対象疾患	14 (8.5)	7 (4.4)	2 (3.3)	5 (22.7)	2 (13.3)	0
慢性移植片対宿主病	14 (8.5)	7 (4.4)	2 (3.3)	5 (22.7)	2 (13.3)	0
死因：その他	2 (1.2)	4 (2.5)	1 (1.6)	0	0	0
全身健康状態悪化	1 (0.6)	0	0	0	0	0
シュードモナス性敗血症	1 (0.6)	0	0	0	0	0
肺炎	0	1 (0.6)	0	0	0	0
敗血症	0	1 (0.6)	0	0	0	0
全身性感染	0	1 (0.6)	0	0	0	0
呼吸不全	0	1 (0.6)	0	0	0	0
頭蓋内出血	0		1 (1.6)	0	0	0

Source: 5.3.5.1-2-D2301 試験-Table 14.3-1.1，Table 14.3-1.6，Table 14.3.1-2.2，Table 14.3.1-2.3，Listing 14.3.2-1.1，5.3.5.3-2-Table 14.3-1.1j，Table 14.3.1-2.2j
全体集団の RUX 群の発現率の降順
総曝露期間 = 全被験者の曝露期間の合計
NA = not analyzed.
MedDRA version 23.0

Table 7-26　慢性 GVHD の重篤な有害事象（D2301 試験，SAF，日本人，データカットオフまで）

	RUX N=22 n (%)	BAT N=15 n (%)
合計	14 (63.6)	8 (53.3)
肺炎	6 (27.3)	4 (26.7)
気胸	2 (9.1)	0
脾臓出血	1 (4.5)	0
腹痛	1 (4.5)	0
イレウス	1 (4.5)	0
脳膿瘍	1 (4.5)	0
サイトメガロウイルス感染	1 (4.5)	0
帯状疱疹	1 (4.5)	0
肺炎球菌感染	1 (4.5)	0
細菌性肺炎	1 (4.5)	0

	RUX N=22 n (%)	BAT N=15 n (%)
腎盂腎炎	1 (4.5)	0
敗血症	1 (4.5)	0
尿路感染	1 (4.5)	0
背部痛	1 (4.5)	0
移植後リンパ増殖性障害	1 (4.5)	0
呼吸困難	1 (4.5)	0
低酸素症	1 (4.5)	0
呼吸不全	1 (4.5)	0
上気道の炎症	1 (4.5)	0
日常活動における個人の自立の喪失	1 (4.5)	0
大動脈弁閉鎖不全症	0	1 (6.7)
心不全	0	1 (6.7)
多臓器機能不全症候群	0	1 (6.7)
末梢性ニューロパチー	0	1 (6.7)
間質性肺疾患	0	1 (6.7)
肺臓炎	0	1 (6.7)

Source: 5.3.5.3-2-D2301 試験-Table 14.3.1-1.18j
RUX 群の発現率の降順
MedDRA version 23.0

Table 7-27 慢性 GVHD の臨床的に注目すべき有害事象の要約（D2301 試験，SAF，日本人，データカットオフまで）

	RUX N=22		BAT N=15	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
感染症				
感染症（結核を除く）	19 (86.4)	11 (50.0)	12 (80.0)	5 (33.3)
肺炎	8 (36.4)	7 (31.8)	5 (33.3)	4 (26.7)
日和見感染	1 (4.5)	0	1 (6.7)	1 (6.7)
サイトメガロウイルス感染／感染症	2 (9.1)	1 (4.5)	2 (13.3)	1 (6.7)
尿路感染	2 (9.1)	2 (9.1)	5 (33.3)	1 (6.7)
敗血症／敗血症性ショック	1 (4.5)	1 (4.5)	1 (6.7)	1 (6.7)
帯状疱疹	1 (4.5)	1 (4.5)	0	0
その他の感染	15 (68.2)	4 (18.2)	10 (66.7)	2 (13.3)
血球減少				
血小板減少症	8 (36.4)	7 (31.8)	3 (20.0)	3 (20.0)
赤血球減少症	10 (45.5)	6 (27.3)	1 (6.7)	1 (6.7)
白血球減少症	6 (27.3)	6 (27.3)	6 (40.0)	4 (26.7)
出血性事象				
出血性事象	3 (13.6)	1 (4.5)	6 (40.0)	1 (6.7)

	RUX N=22		BAT N=15	
Safety topic	All grades n (%)	Grade ≥ 3 n (%)	All grades n (%)	Grade ≥ 3 n (%)
挫傷	1 (4.5)	0	1 (6.7)	0
その他の出血性事象	2 (9.1)	1 (4.5)	5 (33.3)	1 (6.7)
その他				
トランスアミナーゼ上昇	4 (18.2)	2 (9.1)	0	0
脂質異常	5 (22.7)	2 (9.1)	3 (20.0)	2 (13.3)
高血圧	3 (13.6)	1 (4.5)	1 (6.7)	1 (6.7)
血栓塞栓症	1 (4.5)	0	0	0
骨折	1 (4.5)	0	1 (6.7)	0
体重増加	1 (4.5)	0	0	0

Source: 5.3.5.3-2-D2301 試験-Table 14.3.1-1.24j
MedDRA version 23.0

2.7.5 参考文献

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1 2.7.1 「生物薬剤学試験及び関連する分析法」で使用した参考文献

該当なし

2 2.7.2 「臨床薬理試験」で使用した参考文献

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