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本付録に含めた表のうち、表 2.7.4.7-1 を除くいずれの表も各試験（210 試験、201 試験、及び 203 試験）の CSR の 16.2 項（5.3.5.2-1/HBI-8000-210/CSR/16.2 項、5.3.3.2-1/HBI-8000-201/CSR/16.2 項、5.3.5.4-1/HBI-8000-203/CSR/16.2 項）に含まれる Listing から集計した。

表 2.7.4.7-1 注目すべき有害事象の定義（210 試験及び 203 試験）

AESI group	Term level	Term
血小板減少症	SMQ	造血障害による血小板減少症（SMQ）（狭域）
	PT	血小板減少症+血小板数減少 [a]
好中球減少症	PT	無顆粒球症
	PT	自己免疫性好中球減少症
	PT	周期性好中球減少症
	PT	発熱性好中球減少症
	PT	顆粒球数減少
	PT	顆粒球減少症
	PT	特発性好中球減少症
	PT	白血球減少症
	PT	骨髄球数減少
	PT	骨髄球百分率減少
	PT	好中球減少症
	PT	好中球数減少
	PT	好中球百分率減少
	PT	白血球検査異常
	PT	白血球数減少
	PT	好中球減少症+好中球数減少 [a]（210 試験）
		好中球減少症+好中球数減少+顆粒球減少症 [a]（203 試験）
	PT	白血球減少症+白血球数減少 [a]
感染症	SOC	感染症および寄生虫症
ウイルス再活性化	PT	後天性免疫不全症候群
	PT	急性Ｂ型肝炎
	PT	急性Ｃ型肝炎
	PT	急性ＨＩＶ感染
	PT	アデノウイルス性肝炎
	PT	エイズ胆管症
	PT	エイズ関連症候群
	PT	エイズ関連合併症
	PT	エイズ網膜症
	PT	無症候性ＨＩＶ感染
	PT	無症候性ウイルス性肝炎
	PT	ＢＫウイルス感染
	PT	血中ＨＣＶ－ＲＮＡ量測定限界以下
	PT	血中ＨＩＶ－ＲＮＡ量測定限界以下
	PT	血中ＨＩＶ－ＲＮＡ減少
	PT	血中ＨＩＶ－ＲＮＡ増加
	PT	慢性Ｂ型肝炎
	PT	慢性Ｃ型肝炎
	PT	先天性Ｂ型肝炎感染症
	PT	サイトメガロウイルス性脈絡網膜炎
	PT	サイトメガロウイルス性大腸炎
	PT	サイトメガロウイルス性十二指腸炎
	PT	サイトメガロウイルス性小腸炎
	PT	サイトメガロウイルス性腸炎
	PT	サイトメガロウイルス性胃炎
	PT	サイトメガロウイルス性胃腸炎
	PT	サイトメガロウイルス性消化管感染
	PT	サイトメガロウイルス性胃腸潰瘍

AESI group	Term level	Term
	PT	サイトメガロウイルス肝炎
	PT	サイトメガロウイルス感染
	PT	サイトメガロウイルス性単核症
	PT	サイトメガロウイルス性皮膚粘膜潰瘍
	PT	サイトメガロウイルス性脊髄髄膜神経根炎
	PT	サイトメガロウイルス性心筋炎
	PT	サイトメガロウイルス性食道炎
	PT	サイトメガロウイルス性膵炎
	PT	サイトメガロウイルス性心膜炎
	PT	サイトメガロウイルス症候群
	PT	サイトメガロウイルス検査陽性
	PT	サイトメガロウイルス性尿路感染
	PT	サイトメガロウイルス血症
	PT	播種性サイトメガロウイルス感染
	PT	播種性水痘帯状疱疹ワクチンウイルス感染
	PT	サイトメガロウイルス性脳炎
	PT	水痘後脳炎
	PT	末期エイズ
	PT	エイズ腸炎
	PT	エプスタイン・バーウイルス血症
	PT	エプスタイン・バーウイルス抗体
	PT	エプスタイン・バーウイルス抗体陽性
	PT	エプスタイン・バーウイルス抗原陽性
	PT	エプスタイン・バーウイルス感染
	PT	エプスタイン・バーウイルス検査陽性
	PT	ＨＢＶ－ＤＮＡポリメラーゼ増加
	PT	肝カンジダ症
	PT	肝ガス壊疽
	PT	Ａ型肝炎
	PT	Ａ型肝炎抗体
	PT	Ａ型肝炎抗体異常
	PT	Ａ型肝炎抗体正常
	PT	Ａ型肝炎抗体陽性
	PT	Ａ型肝炎抗原
	PT	Ａ型肝炎抗原陽性
	PT	Ａ型肝炎ウイルス検査陽性
	PT	Ｂ型肝炎
	PT	Ｂ型肝炎抗体
	PT	Ｂ型肝炎抗体異常
	PT	Ｂ型肝炎抗体正常
	PT	Ｂ型肝炎抗体陽性
	PT	Ｂ型肝炎抗原
	PT	Ｂ型肝炎抗原陽性
	PT	Ｂ型肝炎コア抗体
	PT	Ｂ型肝炎コア抗体陽性
	PT	Ｂ型肝炎コア抗原
	PT	Ｂ型肝炎コア抗原陽性
	PT	Ｂ型肝炎ＤＮＡ測定陽性
	PT	Ｂ型肝炎ＤＮＡ減少
	PT	Ｂ型肝炎ＤＮＡ増加
	PT	Ｂ型肝炎ｅ抗体
	PT	Ｂ型肝炎ｅ抗体陽性
	PT	Ｂ型肝炎ｅ抗原
	PT	Ｂ型肝炎ｅ抗原陽性
	PT	Ｂ型肝炎表面抗体
	PT	Ｂ型肝炎表面抗体陽性
	PT	Ｂ型肝炎表面抗原
	PT	Ｂ型肝炎表面抗原陽性

AESI group	Term level	Term
	PT	Ｂ型肝炎ウイルス検査陽性
	PT	Ｃ型肝炎
	PT	Ｃ型肝炎抗体
	PT	Ｃ型肝炎抗体陽性
	PT	Ｃ型肝炎コア抗体
	PT	Ｃ型肝炎コア抗体陽性
	PT	Ｃ型肝炎ＲＮＡ
	PT	Ｃ型肝炎ＲＮＡ減少
	PT	Ｃ型肝炎ＲＮＡ変動
	PT	Ｃ型肝炎ＲＮＡ増加
	PT	Ｃ型肝炎ＲＮＡ陽性
	PT	Ｃ型肝炎ウイルス検査陽性
	PT	Ｄ型肝炎
	PT	Ｄ型肝炎抗体
	PT	Ｄ型肝炎抗体陽性
	PT	Ｄ型肝炎抗原
	PT	Ｄ型肝炎抗原陽性
	PT	Ｄ型肝炎ＲＮＡ
	PT	Ｄ型肝炎ＲＮＡ陽性
	PT	Ｄ型肝炎ウイルス検査陽性
	PT	Ｅ型肝炎
	PT	Ｅ型肝炎抗体
	PT	Ｅ型肝炎抗体異常
	PT	Ｅ型肝炎抗体陽性
	PT	Ｅ型肝炎抗原
	PT	Ｅ型肝炎抗原陽性
	PT	Ｅ型肝炎ウイルス検査陽性
	PT	Ｆ型肝炎
	PT	Ｇ型肝炎
	PT	Ｈ型肝炎
	PT	伝染性単核症肝炎
	PT	ムンプス性肝炎
	PT	非Ａ非Ｂ型肝炎
	PT	非Ａ非Ｂ非Ｃ型肝炎
	PT	輸血後肝炎
	PT	トキソプラズマ性肝炎
	PT	ウイルス性肝炎
	PT	肝炎ウイルス検査陽性
	PT	肝炎ウイルス関連腎症
	PT	肝脾カンジダ症
	PT	単純ヘルペス脳炎
	PT	単純ヘルペス肝炎
	PT	帯状疱疹
	PT	皮膚播種性帯状疱疹
	PT	播種性帯状疱疹
	PT	神経合併症を伴う帯状疱疹感染
	PT	耳帯状疱疹
	PT	ＨＩＶ抗体
	PT	ＨＩＶ抗体陽性
	PT	ＨＩＶ抗原
	PT	ＨＩＶ抗原陽性
	PT	ＨＩＶ関連腎症
	PT	ＨＩＶ心筋症
	PT	ＨＩＶ腸症
	PT	ＨＩＶ感染
	PT	ＨＩＶ感染ＣＤＣ分類Ａ
	PT	ＨＩＶ感染ＣＤＣ分類Ｂ
	PT	ＨＩＶ感染ＣＤＣ分類Ｃ

AESI group	Term level	Term
	PT	ＣＤＣ分類第１群ＨＩＶ感染
	PT	ＣＤＣ分類第２群ＨＩＶ感染
	PT	ＣＤＣ分類第３群ＨＩＶ感染
	PT	ＣＤＣ分類第４群ＨＩＶ感染
	PT	ＣＤＣ分類第４群サブグループＡのＨＩＶ感染
	PT	ＣＤＣ分類第４群サブグループＢのＨＩＶ感染
	PT	ＣＤＣ分類第４群サブグループＣ１のＨＩＶ感染
	PT	ＣＤＣ分類第４群サブグループＣ２のＨＩＶ感染
	PT	ＣＤＣ分類第４群サブグループＤのＨＩＶ感染
	PT	ＣＤＣ分類第４群サブグループＥのＨＩＶ感染
	PT	ＨＩＶ感染ＷＨＯ分類臨床ステージ１
	PT	ＨＩＶ感染ＷＨＯ分類臨床ステージ２
	PT	ＨＩＶ感染ＷＨＯ分類臨床ステージ３
	PT	ＨＩＶ感染ＷＨＯ分類臨床ステージ４
	PT	ＨＩＶ末梢性ニューロパチー
	PT	ＨＩＶ検査陽性
	PT	ＨＩＶ消耗症候群
	PT	ヒトヘルペスウイルス６血清学的検査陽性
	PT	ヒトヘルペスウイルス８検査陽性
	PT	ヒトヘルペスウイルス８感染
	PT	ヒトポリオーマウイルス感染
	PT	伝染性単核症
	PT	ＣＳＦ中ＪＣウイルス検査陽性
	PT	ＪＣウイルス感染
	PT	エイズ関連カポジ肉腫
	PT	リンパ増殖性障害
	PT	リンパ増殖性障害、寛解期
	PT	ヘルペス性髄膜炎
	PT	複数病原体ＰＣＲ検査
	PT	眼部単純ヘルペス
	PT	眼帯状疱疹
	PT	口腔内毛様白斑症
	PT	周産期ＨＩＶ感染
	PT	持続性全身性リンパ節腫脹
	PT	サイトメガロウイルス性肺炎
	PT	ヘルペスウイルス肺炎
	PT	ポリオーマウイルス検査陽性
	PT	ポリオーマウイルス関連腎症
	PT	進行性多巣性白質脳症
	PT	レトロウイルス感染
	PT	レトロウイルスリバウンド症候群
	PT	持続的ウイルス反応
	PT	水痘
	PT	水痘ウイルス検査陽性
	PT	肝炎ウイルスキャリアー
	PT	ウイルス検査陽性
トルサード　ド　ポアント/QT 延長	SMQ	トルサード　ド　ポアント／QT 延長（SMQ）（狭域）
過敏症	SMQ	アナフィラキシー反応（SMQ）（狭域）
	SMQ	重症皮膚副作用（SMQ）（狭域）
	PT	薬物過敏症
	PT	過敏症
間質性肺疾患	SMQ	間質性肺疾患（SMQ）（狭域）
心臓障害	SOC	心臓障害
ウイルス再活性化を除く肝障害	SMQ	肝臓の先天性、家族性、新生児および遺伝性障害（SMQ）（狭域）
	SMQ	薬剤に関連する肝障害－包括的検索（SMQ）（狭域）
	SMQ	明確にアルコール関連と報告された肝障害（SMQ）（狭域）
	SMQ	妊娠関連の肝障害（SMQ）（狭域）

AESI group	Term level	Term
	PT	肝包虫症
	PT	梅毒性肝炎
	PT	肝膿瘍
	PT	門脈膿血症
	PT	肝住血吸虫症
	PT	ワイル病
	PT	肝嚢胞感染
	PT	ジアノッティ・クロスティ症候群
	PT	肝感染
	PT	肝胆道系感染
	PT	Ｂ型肝炎再活性化
	PT	肝アメーバ症
	PT	細菌性肝感染
	PT	蠕虫性肝感染
	PT	真菌性肝感染
	PT	投薬中断後肝炎
	PT	周産期ＨＢＶ感染
	PT	肝脾膿瘍
貧血	PT	貧血
	PT	ヘモグロビン減少
	PT	貧血+ヘモグロビン減少 [a]
リンパ球減少症	PT	リンパ球減少症
	PT	リンパ球数減少
	PT	リンパ球減少症+リンパ球数減少 [a]

PT = Preferred Term; SOC = System Organ Class; SMQ = Standard MedDRA Query
a: Grouped terms for haematological AEs.
MedDRA version 21.1

表 2.7.4.7-2　曝露状況の概要（210 試験）（安全性解析対象集団）

Variable (unit)	Statistic	40 mg (N=23)
Duration of exposure (days)	n	23
	Mean	65.9
	SD	95.3
	Median	35.0
	Minimum	7
	Maximum	388
Number of times study drug is administered	n	23
	Mean	15.6
	SD	23.4
	Median	8.0
	Minimum	2
	Maximum	96
Number of cycles	n	23
	Mean	2.355
	SD	3.402
	Median	1.250
	Minimum	0.25
	Maximum	13.86
Cumulative exposure (mg)	n	23
	Mean	480.4
	SD	592.4
	Median	310.0
	Minimum	80
	Maximum	2260

Source: Listing 16.2.5.1
Duration of exposure (days) = (Date of last study drug – Date of first study drug + 3), if date of last study drug minus date of first study drug is multiple of 7. Else, Duration of exposure (days) = (Date of last study drug – Date of first study drug + 4).
Number of times study drug is administered = the number of study drug administration where dose is greater than 0 mg.
Number of cycles = (Date of last study drug – Date of first study drug + 3) / 28, if date of last study drug minus date of first study drug is multiple of 7. Else, number of cycles = (Date of last study drug – Date of first study drug + 4) / 28.
Last study drug date is the date of last study drug administered as collected in case report form.

Variable (unit)	Statistic	40 mg (N=23)
Dose intensity (mg/cycle)	n	23
	Mean	254.591
	SD	61.446
	Median	260.000
	Minimum	138.51
	Maximum	333.33
Relative dose intensity	n	23
	Mean	0.796
	SD	0.192
	Median	0.810
	Minimum	0.43
	Maximum	1.04
Number of subjects who had dose reduction	n (%)	10 (43.5%)
40mg to 30mg (only 1 dose reduction)	n (%)	7 (30.4%)
40mg to 30mg to 20mg (2 dose reductions excluding 1 dose reduction)	n (%)	3 (13.0%)
Number of subjects who had at least one dose interruptions	n (%)	13 (56.5%)
Cycles with dose interruptions		
Number of subjects where dose interruption occurred only at 1 cycle	n (%)	6 (26.1%)
Number of subjects where dose interruption occurred at a maximum 2 cycles	n (%)	3 (13.0%)
Number of subjects where dose interruption occurred at a maximum 3 cycles	n (%)	2 (8.7%)
Number of subjects where dose interruption occurred at a maximum 4 cycles	n (%)	0 (0.0%)
Number of subjects where dose interruption occurred more than 5 cycles	n (%)	2 (8.7%)

Source: Listing 16.2.5.1

% = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Dose intensity (mg/cycle) = Cumulative Exposure (mg) / Number of cycles.
Relative dose intensity = dose intensity (mg/cycle) / plan dose intensity. Where plan dose intensity is 320 mg/cycle.
Dose interruption is defined as the subject who did not have dose administered at a scheduled timepoint, and this is captured up to the last dose administered as collected in case report form.
Dose intensity and relative dose intensity are calculated based on the last dose administered as collected in case report form.

Variable (unit)	Statistic	40 mg (N=23)
Time to first dose interruption (days)	n	13
	Mean	19.2
	SD	8.3
	Median	18.0
	Minimum	7
	Maximum	40
Time to first dose reduction (days)	n	10
	Mean	42.0
	SD	16.2
	Median	38.0
	Minimum	25
	Maximum	78
Time of administration from last meal (minutes)	n *	354
	Mean	40.9
	SD	28.5
	Median	30.0
	Minimum	5
	Maximum	250
Number of subjects who had at least one overdose	n (%)	0 (0.0%)

Source: Listing 16.2.5.1

% = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

***** denoted the total number of regular meals consumed prior to study drug administration by subjects in the analysis set.

Time to first dose interruption (days) = date of the last dose administered prior to dose interruption + 3 – date of first dose + 1.

Time to first dose reduction (days) = date of the 1st dose administered that is less than 40 mg – date of first dose + 1.

Time of administration from last meal (minutes) = Datetime of study drug – Datetime of most recent ingestion of food before study drug. Meal time is calculated for any regular meal consumed prior to study drug administration.

Overdose is defined as subjects who took more than 320 mg in a 28 days cycle. Particularly for this overdose calculation, 28 days cycle is calculated from C1D1.

表 2.7.4.7-3　曝露状況の概要（201 試験）（安全性解析対象集団）

Variable (unit)	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Duration of exposure (day)	n	7	7	14
	Mean	58.4	103.0	80.7
	SD	42.04	89.90	71.28
	Median	62.0	56.0	59.0
	Minimum	4	24	4
	Maximum	119	239	239
Number of times study drug administered	n	7	7	14
	Mean	15.0	23.3	19.1
	SD	11.09	18.63	15.35
	Median	14.0	16.0	15.0
	Minimum	1	6	1
	Maximum	34	52	52

SOURCE: Listing 16.2.5.1
Duration of exposure = (Date of last study drug - Date of first study drug + 3), if date of last study drug minus date of first study drug is multiple of 7. Else, duration of exposure = (Date of last study drug - Date of first study drug + 4).
Number of times study drug administered = the number of study drug administration where dose is greater than 0mg.
Number of cycles = (Date of last study drug - Date of first study drug + 3) / 28, if date of last study drug minus date of first study drug is multiple of 7. Else, number of cycles = (Date of last study drug - Date of first study drug + 4) / 28.
% = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Percentages of planned dose received = [(Number of times study drug administered)/(Number of times planned dose administered)] * 100.
Number of times planned dose administered : Number of Cycles *8
Dose intensity (mg/body/week) = Cumulative Exposure / (Number of cycles *4)

Variable (unit)	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Number of cycles	n	7	7	14
	Mean	2.087	3.679	2.883
	SD	1.5014	3.2108	2.5457
	Median	2.214	2.000	2.107
	Minimum	0.14	0.86	0.14
	Maximum	4.25	8.54	8.54
Cumulative exposure (mg)	n	7	7	14
	Mean	434.3	762.9	598.6
	SD	302.54	565.79	468.04
	Median	420.0	610.0	455.0
	Minimum	30	220	30
	Maximum	910	1630	1630
Number of patients who had dose reduction	n (%)	1 (14.3%)	5 (71.4%)	6 (42.9%)

SOURCE: Listing 16.2.5.1
Duration of exposure = (Date of last study drug - Date of first study drug + 3), if date of last study drug minus date of first study drug is multiple of 7. Else, duration of exposure = (Date of last study drug - Date of first study drug + 4).
Number of times study drug administered = the number of study drug administration where dose is greater than 0mg.
Number of cycles = (Date of last study drug - Date of first study drug + 3) / 28, if date of last study drug minus date of first study drug is multiple of 7. Else, number of cycles = (Date of last study drug - Date of first study drug + 4) / 28.
% = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Percentages of planned dose received = [(Number of times study drug administered)/(Number of times planned dose administered)] * 100.
Number of times planned dose administered : Number of Cycles *8
Dose intensity (mg/body/week) = Cumulative Exposure / (Number of cycles *4)

Variable (unit)	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Percentages of planned dose received	n	7	7	14
	Mean	90.74	84.95	87.84
	SD	9.733	11.204	10.520
	Median	90.32	81.25	87.50
	Minimum	76.6	74.8	74.8
	Maximum	100.0	100.0	100.0
Dose intensity (mg/body/week)	n	7	7	14
	Mean	53.52	59.52	56.52
	SD	5.300	15.457	11.530
	Median	53.53	53.75	53.64
	Minimum	45.9	43.6	43.6
	Maximum	60.0	80.0	80.0

SOURCE: Listing 16.2.5.1
Duration of exposure = (Date of last study drug - Date of first study drug + 3), if date of last study drug minus date of first study drug is multiple of 7. Else, duration of exposure = (Date of last study drug - Date of first study drug + 4).
Number of times study drug administered = the number of study drug administration where dose is greater than 0mg.
Number of cycles = (Date of last study drug - Date of first study drug + 3) / 28, if date of last study drug minus date of first study drug is multiple of 7. Else, number of cycles = (Date of last study drug - Date of first study drug + 4) / 28.
% = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Percentages of planned dose received = [(Number of times study drug administered)/(Number of times planned dose administered)] * 100.
Number of times planned dose administered : Number of Cycles *8
Dose intensity (mg/body/week) = Cumulative Exposure / (Number of cycles *4)

表 2.7.4.7-4　曝露状況の概要（203 試験）（安全性解析対象集団）

Variable (unit)	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Duration of exposure (days)	n	39	16	55
	Mean	125.2	111.7	121.3
	SD	132.3	133.0	131.4
	Median	80.0	54.0	80.0
	Minimum	10	22	10
	Maximum	580	486	580
Number of times study drug is administered	n	39	16	55
	Mean	31.4	29.2	30.7
	SD	36.3	37.8	36.4
	Median	16.0	14.0	16.0
	Minimum	3	6	3
	Maximum	164	139	164
Number of cycles	n	39	16	55
	Mean	4.473	3.989	4.332
	SD	4.724	4.749	4.692
	Median	2.857	1.929	2.857
	Minimum	0.36	0.79	0.36
	Maximum	20.71	17.36	20.71
Cumulative exposure (mg)	n	39	16	55
	Mean	1087.9	1112.5	1095.1
	SD	1256.6	1490.0	1314.5
	Median	640.0	540.0	600.0
	Minimum	110	220	110
	Maximum	6560	5560	6560

Source: Listing 16.2.5.1
Duration of exposure (days) = (Date of last study drug – Date of first study drug + 3), if date of last study drug minus date of first study drug is multiple of 7. Else, Duration of exposure (days) = (Date of last study drug – Date of first study drug + 4).
Number of times study drug is administered = the number of study drug administration where dose is greater than 0 mg.
Number of cycles = (Date of last study drug – Date of first study drug + 3) / 28, if date of last study drug minus date of first study drug is multiple of 7. Else, number of cycles = (Date of last study drug – Date of first study drug + 4) / 28.
Last study drug date is the date of last study drug administered as collected in case report form.

Variable (unit)	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Dose intensity (mg/cycle)	n	39	16	55
	Mean	247.7	271.4	254.6
	SD	65.4	58.3	63.8
	Median	237.0	291.6	273.2
	Minimum	133	166	133
	Maximum	336	332	336
Relative dose intensity	n	39	16	55
	Mean	0.774	0.848	0.796
	SD	0.204	0.182	0.199
	Median	0.741	0.911	0.854
	Minimum	0.42	0.52	0.42
	Maximum	1.05	1.04	1.05
Number of subjects who had dose reduction	n (%)	21 (53.8)	5 (31.3)	26 (47.3)
40mg to 30mg (only 1 dose reduction)	n (%)	15 (38.5)	5 (31.3)	20 (36.4)
40mg to 30mg to 20mg (2 dose reductions excluding 1 dose reduction)	n (%)	6 (15.4)	0 (0.0)	6 (10.9)
Number of subjects who had at least one dose interruptions	n (%)	27 (69.2)	10 (62.5)	37 (67.3)
Cycles with dose interruptions				
Number of subjects where dose interruption occurred only at 1 cycle	n (%)	7 (17.9)	6 (37.5)	13 (23.6)
Number of subjects where dose interruption occurred at a maximum 2 cycles	n (%)	9 (23.1)	2 (12.5)	11 (20.0)
Number of subjects where dose interruption occurred at a maximum 3 cycles	n (%)	7 (17.9)	1 (6.3)	8 (14.5)
Number of subjects where dose interruption occurred at a maximum 4 cycles	n (%)	1 (2.6)	0 (0.0)	1 (1.8)
Number of subjects where dose interruption occurred more than 5 cycles	n (%)	3 (7.7)	1 (6.3)	4 (7.3)

Source: Listing 16.2.5.1
% = percentages of subjects are calculated relative to the number of subjects in the respective country within the analysis set.
Dose intensity (mg/cycle) = Cumulative Exposure (mg) / Number of cycles.
Relative dose intensity = dose intensity (mg/cycle) / plan dose intensity. Where plan dose intensity is 320 mg/cycle.
Dose interruption is defined as the subject who did not have dose administered at a scheduled timepoint, and this is captured up to the last dose administered as collected in case report form.
Dose intensity and relative dose intensity are calculated based on the last dose administered as collected in case report form.

Variable (unit)	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Time to first dose interruption (days)	n	27	10	37
	Mean	39.1	43.9	40.4
	SD	70.3	65.6	68.2
	Median	15.0	21.5	15.0
	Minimum	4	7	4
	Maximum	366	224	366
Time to first dose reduction (days)	n	21	5	26
	Mean	50.7	34.6	47.6
	SD	35.5	20.9	33.5
	Median	36.0	31.0	32.5
	Minimum	11	15	11
	Maximum	127	70	127
Time of administration from last meal (minutes)	n*	1216	467	1683
	Mean	32.8	33.2	32.9
	SD	9.8	14.9	11.4
	Median	30.0	30.0	30.0
	Minimum	5	20	5
	Maximum	180	150	180
Number of subjects who had at least one overdose	n (%)	1 (2.6)	4 (25.0)	5 (9.1)

Source: Listing 16.2.5.1
% = percentages of subjects are calculated relative to the number of subjects in the respective country within the analysis set.
* denoted the total number of regular meals consumed prior to study drug administration by subjects in the analysis set.
Time to first dose interruption (days) = date of the last dose administered prior to dose interruption + 3 – date of first dose + 1.
Time to first dose reduction (days) = date of the 1st dose administered that is less than 40 mg – date of first dose + 1.
Time of administration from last meal (minutes) = Datetime of study drug – Datetime of most recent ingestion of food before study drug. Meal time is calculated for any regular meal consumed prior to study drug administration.
Overdose is defined as subjects who took more than 320 mg in a 28 days cycle. Particularly for this overdose calculation, 28 days cycle is calculated from C1D1.

表 2.7.4.7-5　被験者の内訳（210 試験）（全同意取得例）

Description	40 mg (N=29) n (%)
Consented	29
Screening failure	6
Treated with at least one dose of HBI-8000 (Safety Analysis Set)	23 (100.0%)
Full Analysis Set (FAS)	23 (100.0%)
Per Protocol Set	23 (100.0%)
Subjects who are on study drug treatment	0 (0.0%)
Subjects who had study drug treatment discontinuation	23 (100.0%)
Primary reason for study drug treatment discontinuation	
Unacceptable toxicity (adverse event)	8 (34.8%)
Progression disease	12 (52.2%)
Decision by the Investigator to permanently discontinue study drug administration	0 (0.0%)
Inter-current illness that would, in the judgment of the Investigator, affect clinical assessments, subject safety, or follow-up significantly	0 (0.0%)
Significant protocol deviations that jeopardize the usefulness of the data	0 (0.0%)
Repeated subject noncompliance	0 (0.0%)
Withdrew consent	2 (8.7%)
Other	1 (4.3%)

Source: Listing 16.2.1 and 16.2.5.1

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the Safety Analysis set;
Percentages for study drug treatment discontinuation reasons are calculated based on the number of subjects in the Safety Analysis set who discontinued.
Progression disease in primary reason for study drug treatment discontinuation is defined as progression of the disease under study, which also included clinical progression disease, except for isolated progression in skin lesion.

Description	40 mg (N=29) n (%)
Subjects in FAS who completed 1 cycle of treatment (including subjects discontinued before C2D1 with >=75% protocol specified dose of 320mg)	16 (69.6%)
Subjects in FAS who did not complete 1 cycle of treatment (where study medication taken within cycle 1 is <75% protocol specified dose of 320mg)	7 (30.4%)
Subjects completed the study participation	13 (56.5%)
Primary reason for completing the study participation	
Lost to follow-up	0 (0.0%)
Death	12 (92.3%)
Withdrew consent	1 (7.7%)
Study reached pre-defined end	0 (0.0%)
Other	0 (0.0%)

Source: Listing 16.2.1 and 16.2.5.1

n = number of subjects; % = percentages of subjects calculated relative to the total number of subjects in the Safety Analysis set.
Percentages for subjects who did or did not complete 1 cycle of treatment are calculated based on the number of subjects in the Full Analysis Set.
Percentages for primary reason for completing the study participation are calculated based on the number of subjects who completed study participation in the Safety Analysis set.

表 2.7.4.7-6　被験者の内訳（201 試験）（全同意取得例）

Description	30 mg (N=15) n (%)	40 mg (N=7) n (%)	Total (N=22) n (%)
Enrolled	15	7	22
Screening Failure	8	0	8
Treated with at least one dose of HBI-8000 (Safety Analysis Set)	7 (46.7%)	7 (100.0%)	14 (63.6%)
Treated with 2 or more dose of HBI-8000 and have valid efficacy assessment at screening and post-dose (Efficacy Analysis Set)	6 (40.0%)	7 (100.0%)	13 (59.1%)
Discontinued	7 (46.7%)	7 (100.0%)	14 (63.6%)
Primary reason for discontinuation			
Adverse event	2 (28.6%)	3 (42.9%)	5 (35.7%)
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tumor progression	3 (42.9%)	1 (14.3%)	4 (28.6%)
Unacceptable toxicity including: QTc prolongation >= Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
Become HBV positive during the study	0 (0.0%)	0 (0.0%)	0 (0.0%)
Significant protocol deviation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Patient non-compliance	0 (0.0%)	0 (0.0%)	0 (0.0%)
Patient request to withdraw informed consent	0 (0.0%)	1 (14.3%)	1 (7.1%)
Decision by the investigator to permanently discontinue HBI-8000	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
Start of another anti-cancer treatment protocol	0 (0.0%)	0 (0.0%)	0 (0.0%)
In the event of sponsor or regulatory authorities obtain safety information which does not allow continuation the study	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.1
n = number of patients; % = percentage of patients calculated relative to the total number of enrolled patients in each cohort.
Percentage for discontinuation reasons is calculated based on the number of patients who had discontinuation in each cohort of the analysis set.

Description	30 mg (N=15) n (%)	40 mg (N=7) n (%)	Total (N=22) n (%)
Intercurrent, non-clear illness that would, in the judgment of the investigator, affect clinical assessments, patient safety, or follow-up to a significant degree	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sponsor decides to discontinue development of HBI-8000 or the study	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lost to follow-up	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	2 (28.6%)	1 (14.3%)	3 (21.4%)

SOURCE: Listing 16.2.1
n = number of patients; % = percentage of patients calculated relative to the total number of enrolled patients in each cohort.
Percentage for discontinuation reasons is calculated based on the number of patients who had discontinuation in each cohort of the analysis set.

表 2.7.4.7-7　被験者の内訳（203 試験）（全同意取得例）

Description	Japan (N=52) n (%)	Korea (N=22) n (%)	Total (N=74) n (%)
Consented	52	22	74
Screening failure	13	6	19
Treated with at least one dose of HBI-8000 (Safety Analysis Set)	39 (100.0)	16 (100.0)	55 (100.0)
Full Analysis Set (FAS)	37 (94.9)	12 (75.0)	49 (89.1)
Per Protocol Set	34 (87.2)	12 (75.0)	46 (83.6)
Subjects who are on study drug treatment	7 (17.9)	1 (6.3)	8 (14.5)
Subjects who had study drug treatment discontinuation	32 (82.1)	15 (93.8)	47 (85.5)
Primary reason for study drug treatment discontinuation			
Unacceptable toxicity (adverse event)	15 (46.9)	2 (13.3)	17 (36.2)
Progression disease	15 (46.9)	9 (60.0)	24 (51.1)
Decision by the Investigator to permanently discontinue study drug administration	0 (0.0)	0 (0.0)	0 (0.0)
Inter-current illness that would, in the judgment of the Investigator, affect clinical assessments, subject safety, or follow-up significantly	0 (0.0)	0 (0.0)	0 (0.0)
Significant protocol deviations that jeopardize the usefulness of the data	0 (0.0)	0 (0.0)	0 (0.0)
Repeated subject noncompliance	0 (0.0)	1 (6.7)	1 (2.1)
Withdrew consent	2 (6.3)	3 (20.0)	5 (10.6)
Other	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.1 and 16.2.5.1
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in the respective country within Safety Analysis set;
Percentages for study drug treatment discontinuation reasons are calculated based on the number of subjects in the respective country within Safety Analysis set who discontinued.
Progression disease in primary reason for study drug treatment discontinuation is defined as progression of the disease under study, which also included clinical progression disease, except for isolated progression in skin lesion.

Description	Japan (N=52) n (%)	Korea (N=22) n (%)	Total (N=74) n (%)
Subjects in FAS who completed 1 cycle of treatment (including subjects discontinued before C2D1 with >=75% protocol specified dose of 320mg)	31 (83.8)	12 (100.0)	43 (87.8)
Subjects in FAS who did not complete 1 cycle of treatment (where study medication taken within cycle 1 is <75% protocol specified dose of 320mg)	6 (16.2)	0 (0.0)	6 (12.2)
Subjects completed the study participation	14 (35.9)	13 (81.3)	27 (49.1)
Primary reason for completing the study participation			
Lost to follow-up	0 (0.0)	1 (7.7)	1 (3.7)
Death	14 (100.0)	4 (30.8)	18 (66.7)
Withdrew consent	0 (0.0)	8 (61.5)	8 (29.6)
Study reached pre-defined end	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.1 and 16.2.5.1
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in the respective country within Safety Analysis set.
Percentages for subjects who did or did not complete 1 cycle of treatment are calculated based on the number of subjects in the respective country within Full Analysis Set.
Percentages for primary reason for completing the study participation are calculated based on the number of subjects who completed study participation in the respective country within Safety Analysis set.

表 2.7.4.7-8　人口統計学的特性及びその他のベースライン特性（210 試験）（安全性解析対象集団）

Characteristic (unit)	Category	Statistic	40 mg (N=23)
Age (years)		n	23
		Mean	73.4
		SD	7.1
		Median	72.0
		Minimum	60
		Maximum	89
	<65	n (%)	1 (4.3%)
	>=65 to <75	n (%)	13 (56.5%)
	>=75	n (%)	9 (39.1%)
Sex	Male	n (%)	15 (65.2%)
	Female	n (%)	8 (34.8%)
Race	Asian	n (%)	23 (100.0%)
	Other	n (%)	0 (0.0%)
	Not Reported	n (%)	0 (0.0%)
Ethnicity	Japanese	n (%)	23 (100.0%)
	Other	n (%)	0 (0.0%)
	Not Reported	n (%)	0 (0.0%)
ECOG Performance Status	0	n (%)	12 (52.2%)
	1	n (%)	10 (43.5%)
	2	n (%)	1 (4.3%)
	3	n (%)	0 (0.0%)
	4	n (%)	0 (0.0%)

Source: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.1, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.
Absolute lymphocyte count is not total absolute lymphocyte count, it is merely the normal absolute lymphocyte count.

Characteristic (unit)	Category	Statistic	40 mg (N=23)
Height (cm)		n	23
		Mean	158.47
		SD	8.68
		Median	158.00
		Minimum	143.0
		Maximum	176.0
Weight (kg)		n	23
		Mean	54.04
		SD	10.35
		Median	52.70
		Minimum	34.4
		Maximum	70.7
BMI (kg/m^2)		n	23
		Mean	21.440
		SD	3.348
		Median	21.290
		Minimum	15.88
		Maximum	29.60
Serum calcium (mmol/L)	<=ULN	n (%)	22 (95.7%)
	>ULN	n (%)	1 (4.3%)
LDH (U/L)	<=ULN	n (%)	8 (34.8%)
	>ULN	n (%)	15 (65.2%)

Source: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.1, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.
Absolute lymphocyte count is not total absolute lymphocyte count, it is merely the normal absolute lymphocyte count.

Characteristic (unit)	Category	Statistic	40 mg (N=23)
LDH (U/L)	<=300 (U/L)	n (%)	13 (56.5%)
	>300 (U/L)	n (%)	10 (43.5%)
Abnormal lymphocyte percent (Proportion of 1)		n	23
		Mean	0.1061
		SD	0.2088
		Median	0.0000
		Minimum	0.000
		Maximum	0.740
Absolute abnormal lymphocyte count (10^9/L)		n	23
		Mean	1.3385
		SD	3.1741
		Median	0.0000
		Minimum	0.000
		Maximum	13.401
Absolute lymphocyte count (10^9/L)		n	23
		Mean	0.9973
		SD	0.8866
		Median	0.8586
		Minimum	0.000
		Maximum	4.100
Corrected Calcium (mg/dL)	<=10.0 (mg/dL)	n (%)	19 (82.6%)
	>10.0 (mg/dL)	n (%)	4 (17.4%)

Source: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.1, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.
Absolute lymphocyte count is not total absolute lymphocyte count, it is merely the normal absolute lymphocyte count.

Characteristic (unit)	Category	Statistic	40 mg (N=23)
Corrected Calcium (mg/dL)		n	23
		Mean	9.579
		SD	0.670
		Median	9.460
		Minimum	8.76
		Maximum	11.54
HBsAg	Positive	n (%)	0 (0.0%)
	Negative	n (%)	23 (100.0%)
	Not Done	n (%)	0 (0.0%)
Anti-HBs	Positive	n (%)	7 (30.4%)
	Negative	n (%)	16 (69.6%)
	Not Done	n (%)	0 (0.0%)
Anti-HBc	Positive	n (%)	9 (39.1%)
	Negative	n (%)	14 (60.9%)
	Not Done	n (%)	0 (0.0%)
HBV-DNA	Positive	n (%)	0 (0.0%)
	Negative	n (%)	14 (60.9%)
	Not Done	n (%)	9 (39.1%)
HCV Antibody	Positive	n (%)	0 (0.0%)
	Negative	n (%)	23 (100.0%)
	Not Done	n (%)	0 (0.0%)

Source: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.1, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.
Absolute lymphocyte count is not total absolute lymphocyte count, it is merely the normal absolute lymphocyte count.

Characteristic (unit)	Category	Statistic	40 mg (N=23)
HTLV-I Antibody	Positive	n (%)	23 (100.0%)
	Negative	n (%)	0 (0.0%)
	Not Done	n (%)	0 (0.0%)
Hepatitis Assessment Result	Active	n (%)	0 (0.0%)
	Non Active	n (%)	23 (100.0%)
Maximum length of long dimension of target lesion (mm) based on Investigator Response Assessment		n	19
		Mean	34.3
		SD	20.4
		Median	26.0
		Minimum	18
		Maximum	93
Sum of 2-dimension products of target lesions (mm^2) based on Investigator Response Assessment		n	19
		Mean	2328.8
		SD	3940.3
		Median	1150.0
		Minimum	234
		Maximum	17591

Source: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.1, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.
Absolute lymphocyte count is not total absolute lymphocyte count, it is merely the normal absolute lymphocyte count.

Characteristic (unit)	Category	Statistic	40 mg (N=23)
Bone Marrow Infiltration	Positive	n (%)	6 (26.1%)
	Undetermined	n (%)	2 (8.7%)
	Negative	n (%)	15 (65.2%)
	Not Done	n (%)	0 (0.0%)
Hepatic enlargement and splenomegaly	Not Done	n (%)	0 (0.0%)
Hepatic enlargement result	Present	n (%)	2 (8.7%)
	Absent	n (%)	21 (91.3%)
Splenomegaly result	Present	n (%)	4 (17.4%)
	Absent	n (%)	19 (82.6%)
Hepatic enlargement result and splenomegaly result	Present	n (%)	1 (4.3%)

Source: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.1, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.
Absolute lymphocyte count is not total absolute lymphocyte count, it is merely the normal absolute lymphocyte count.

表 2.7.4.7-9　疾患特性（210 試験）（安全性解析対象集団）

Description	Subtype/Category	40 mg (N=23) n (%)
Diagnosis at screening	Adult T-cell Lymphoma:	23 (100.0%)
	Acute	13 (56.5%)
	Lymphoma	8 (34.8%)
	Unfavorable Chronic	2 (8.7%)
Duration since initial diagnosis (years)	n	23
	Mean	3.019
	SD	4.838
	Median	1.500
	Minimum	0.31
	Maximum	21.95
Duration since initial diagnosis by category	> 5 years	3 (13.0%)
	<= 5 years	20 (87.0%)
Duration from most recent progression (days)	n	23
	Mean	47.6
	SD	80.4
	Median	26.0
	Minimum	3
	Maximum	371
Duration from most recent progression by category	> 1 month	8 (34.8%)
	<= 1 month	15 (65.2%)

Source: Listing 16.2.4.3

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Duration since initial diagnosis (years)= (informed consent date - date of 1st diagnosis + 1)/365.25.
Duration from most recent progression (days) = (first study drug date - date of most recent progression + 1).
Duration from most recent progression (months) = (first study drug date - date of most recent progression + 1)/ 30.4375.

表 2.7.4.7-10　人口統計学的特性及びその他のベースライン特性（201 試験）（安全性解析対象集団）

Characteristic (unit)	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Age (years)		n	7	7	14
		Mean	70.9	65.1	68.0
		SD	9.44	6.54	8.35
		Median	72.0	63.0	69.0
		Minimum	53	57	53
		Maximum	81	76	81
Sex	Male	n (%)	4 (57.1%)	3 (42.9%)	7 (50.0%)
	Female	n (%)	3 (42.9%)	4 (57.1%)	7 (50.0%)
Race	Asian	n (%)	7 (100.0%)	7 (100.0%)	14 (100.0%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not reported	n	0	0	0
Ethnicity	Japanese	n (%)	7 (100.0%)	7 (100.0%)	14 (100.0%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Unknown	n	0	0	0

SOURCE: Listing 16.2.4.1 and Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set with data.
BMI = body mass index
ECOG = Eastern Cooperative Oncology Group

Characteristic (unit)	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
ECOG Performance Status	0	n (%)	4 (57.1%)	5 (71.4%)	9 (64.3%)
	1	n (%)	3 (42.9%)	2 (28.6%)	5 (35.7%)
	2	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Height (cm)		n	7	7	14
		Mean	160.30	156.04	158.17
		SD	11.657	7.703	9.746
		Median	161.10	158.80	159.90
		Minimum	138.3	146.6	138.3
		Maximum	171.1	167.4	171.1
Weight (kg)		n	7	7	14
		Mean	58.97	63.31	61.14
		SD	11.700	12.257	11.730
		Median	62.00	66.50	62.90
		Minimum	41.6	44.1	41.6
		Maximum	75.9	77.8	77.8

SOURCE: Listing 16.2.4.1 and Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set with data.
BMI = body mass index
ECOG = Eastern Cooperative Oncology Group

Characteristic (unit)	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
BMI (kg/m^2)		n	7	7	14
		Mean	22.83	25.84	24.33
		SD	3.108	3.579	3.578
		Median	22.20	25.68	24.21
		Minimum	17.7	19.7	17.7
		Maximum	27.3	29.8	29.8
Smoking history	Never	n (%)	4 (57.1%)	4 (57.1%)	8 (57.1%)
	Former	n (%)	3 (42.9%)	2 (28.6%)	5 (35.7%)
	Current	n (%)	0 (0.0%)	1 (14.3%)	1 (7.1%)
Duration of tobacco use:					
Former smokers (years)		n	3	2	5
		Mean	26.7	37.5	31.0
		SD	7.64	9.19	9.25
		Median	25.0	37.5	31.0
		Minimum	20	31	20
		Maximum	35	44	44

SOURCE: Listing 16.2.4.1 and Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set with data.
BMI = body mass index
ECOG = Eastern Cooperative Oncology Group

Characteristic (unit)	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Current smokers (years)		n	0	1	1
		Mean	-	16.0	16.0
		SD	-	-	-
		Median	-	16.0	16.0
		Minimum	-	16	16
		Maximum	-	16	16
Alcohol history	Never	n (%)	1 (14.3%)	3 (42.9%)	4 (28.6%)
	Former	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Current	n (%)	6 (85.7%)	4 (57.1%)	10 (71.4%)
History of drug abuse	Yes	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	No	n (%)	7 (100.0%)	7 (100.0%)	14 (100.0%)

SOURCE: Listing 16.2.4.1 and Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set with data.
BMI = body mass index
ECOG = Eastern Cooperative Oncology Group

表 2.7.4.7-11　疾患特性（201 試験）（安全性解析対象集団）

Description	Category	Type	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Initial diagnosis	Mature B-cell neoplasm	Follicular lymphoma	0 (0.0%)	2 (28.6%)	2 (14.3%)
		Extranodal marginal zone B-cell lymphoma of mucosa-associated	1 (14.3%)	0 (0.0%)	1 (7.1%)
		Diffuse large b-cell lymphoma NOS	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Mature T-cell and NK-cell neoplasm	N	3	4	7
		Adult T-cell leukemia/lymphoma	1 (33.3%)	4 (100.0%)	5 (71.4%)
		Peripheral T-cell lymphoma	2 (66.7%)	0 (0.0%)	2 (28.6%)
	Other		1 (14.3%)	0 (0.0%)	1 (7.1%)
HTLV-1 Result	Positive		1 (14.3%)	4 (57.1%)	5 (35.7%)
	Negative		2 (28.6%)	0 (0.0%)	2 (14.3%)
	Not done		0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.4.4
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Percentage of mature T-cell and NK-cell neoplasm results is calculated based on the number of patients with mature T-cell and NK-cell neoplasm in each cohort of the analysis set with data.
Subject [redacted] had initial diagnosis of ADULT T-CELL LEUKEMIA/LYMPHOMA, however there was no data available for relapse.

Description	Category	Type	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Most recent relapse	Mature B-cell neoplasm	Follicular lymphoma	0 (0.0%)	2 (28.6%)	2 (14.3%)
		Extranodal marginal zone B-cell lymphoma of mucosa-associated	1 (14.3%)	0 (0.0%)	1 (7.1%)
		Diffuse large B-cell lymphoma nos	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Mature T-cell and NK-cell neoplasm	N	3	3	6
		Adult T-cell leukemia/lymphoma	1 (33.3%)	3 (100.0%)	4 (66.7%)
		Peripheral T-cell lymphoma	2 (66.7%)	0 (0.0%)	2 (33.3%)
	Other		1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.4
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Percentage of mature T-cell and NK-cell neoplasm results is calculated based on the number of patients with mature T-cell and NK-cell neoplasm in each cohort of the analysis set with data.
Subject [redacted] had initial diagnosis of ADULT T-CELL LEUKEMIA/LYMPHOMA, however there was no data available for relapse.

Description	Category	Type	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Stage	Ann Arbor	I	1 (14.3%)	0 (0.0%)	1 (7.1%)
		II	1 (14.3%)	3 (42.9%)	4 (28.6%)
		IIa	1 (14.3%)	0 (0.0%)	1 (7.1%)
		III	0 (0.0%)	1 (14.3%)	1 (7.1%)
		IV	4 (57.1%)	1 (14.3%)	5 (35.7%)
		Not applicable	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Other	I	0 (0.0%)	0 (0.0%)	0 (0.0%)
		II	0 (0.0%)	0 (0.0%)	0 (0.0%)
		IIa	0 (0.0%)	0 (0.0%)	0 (0.0%)
		III	0 (0.0%)	0 (0.0%)	0 (0.0%)
		IV	0 (0.0%)	0 (0.0%)	0 (0.0%)
		Not applicable	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.4.4
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Percentage of mature T-cell and NK-cell neoplasm results is calculated based on the number of patients with mature T-cell and NK-cell neoplasm in each cohort of the analysis set with data.
Subject [redacted] had initial diagnosis of ADULT T-CELL LEUKEMIA/LYMPHOMA however there was no data available for relapse.

表 2.7.4.7-12　人口統計学的特性及びその他のベースライン特性（203 試験）（安全性解析対象集団）

Characteristic (unit)	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Age (years)		n	39	16	55
		Mean	68.9	64.7	67.7
		SD	12.1	10.7	11.7
		Median	73.0	67.0	71.0
		Minimum	38	44	38
		Maximum	87	79	87
	<65	n (%)	8 (20.5%)	7 (43.8%)	15 (27.3%)
	>=65 to <75	n (%)	17 (43.6%)	6 (37.5%)	23 (41.8%)
	>=75	n (%)	14 (35.9%)	3 (18.8%)	17 (30.9%)
Sex	Male	n (%)	28 (71.8%)	7 (43.8%)	35 (63.6%)
	Female	n (%)	11 (28.2%)	9 (56.3%)	20 (36.4%)
Race	Asian	n (%)	39 (100.0%)	16 (100.0%)	55 (100.0%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not Reported	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ethnicity	Japanese	n (%)	39 (100.0%)	0 (0.0%)	39 (70.9%)
	Korean	n (%)	0 (0.0%)	16 (100.0%)	16 (29.1%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not Reported	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ECOG Performance Status	0	n (%)	26 (66.7%)	2 (12.5%)	28 (50.9%)
	1	n (%)	12 (30.8%)	13 (81.3%)	25 (45.5%)
	2	n (%)	1 (2.6%)	1 (6.3%)	2 (3.6%)
	3	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.

Characteristic (unit)	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Height (cm)		n	39	16	55
		Mean	163.18	159.88	162.22
		SD	8.96	9.55	9.18
		Median	162.00	160.10	162.00
		Minimum	148.0	142.5	142.5
		Maximum	189.6	177.7	189.6
Weight (kg)		n	39	16	55
		Mean	58.52	56.93	58.05
		SD	11.59	9.79	11.03
		Median	57.10	58.50	57.40
		Minimum	36.4	41.3	36.4
		Maximum	88.2	69.3	88.2
BMI (kg/m^2)		n	39	16	55
		Mean	21.842	22.248	21.960
		SD	3.062	3.176	3.071
		Median	22.281	22.309	22.281
		Minimum	14.47	15.54	14.47
		Maximum	29.00	27.09	29.00
LDH (U/L)	<=ULN	n (%)	19 (48.7%)	7 (43.8%)	26 (47.3%)
	>ULN	n (%)	20 (51.3%)	9 (56.3%)	29 (52.7%)
LDH (U/L)	<=300 (U/L)	n (%)	31 (79.5%)	8 (50.0%)	39 (70.9%)
	>300 (U/L)	n (%)	8 (20.5%)	8 (50.0%)	16 (29.1%)

SOURCE: Listing 16 2.4 1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.

Characteristic (unit)	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
HBsAg	Positive	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Negative	n (%)	39 (100.0%)	16 (100.0%)	55 (100.0%)
	Not Done	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anti-HBs	Positive	n (%)	6 (15.4%)	7 (43.8%)	13 (23.6%)
	Negative	n (%)	32 (82.1%)	9 (56.3%)	41 (74.5%)
	Not Done	n (%)	1 (2.6%)	0 (0.0%)	1 (1.8%)
Anti-HBc	Positive	n (%)	6 (15.4%)	7 (43.8%)	13 (23.6%)
	Negative	n (%)	32 (82.1%)	9 (56.3%)	41 (74.5%)
	Not Done	n (%)	1 (2.6%)	0 (0.0%)	1 (1.8%)
HBV-DNA	Positive	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Negative	n (%)	24 (61.5%)	11 (68.8%)	35 (63.6%)
	Not Done	n (%)	15 (38.5%)	5 (31.3%)	20 (36.4%)
HCV Antibody	Positive	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Negative	n (%)	39 (100.0%)	16 (100.0%)	55 (100.0%)
	Not Done	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hepatitis Assessment Result	Active	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Non Active	n (%)	39 (100.0%)	14 (87.5%)	53 (96.4%)

SOURCE: Listing 16 2.4 1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.

Characteristic (unit)	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Maximum length of long dimension of target lesion (mm) based on Investigator Response Assessment		n	39	16	55
		Mean	32.0	30.9	31.7
		SD	13.5	15.2	13.9
		Median	28.0	23.5	28.0
		Minimum	17	16	16
		Maximum	70	70	70
Sum of 2-dimension products of target lesions (mm^2) based on Investigator Response Assessment		n	39	16	55
		Mean	1380.1	1660.6	1461.7
		SD	1051.8	1497.9	1190.9
		Median	1092.0	1107.0	1092.0
		Minimum	162	234	162
		Maximum	4487	5516	5516
Bone Marrow Infiltration	Positive	n (%)	12 (30.8%)	2 (12.5%)	14 (25.5%)
	Undetermined	n (%)	5 (12.8%)	0 (0.0%)	5 (9.1%)
	Negative	n (%)	22 (56.4%)	7 (43.8%)	29 (52.7%)
	Not Done	n (%)	0 (0.0%)	7 (43.8%)	7 (12.7%)

SOURCE: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.

Characteristic (unit)	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Hepatic enlargement and splenomegaly	Not Done	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hepatic enlargement result	Present	n (%)	0 (0.0%)	3 (18.8%)	3 (5.5%)
	Absent	n (%)	39 (100.0%)	13 (81.3%)	52 (94.5%)
Splenomegaly result	Present	n (%)	4 (10.3%)	1 (6.3%)	5 (9.1%)
	Absent	n (%)	35 (89.7%)	15 (93.8%)	50 (90.9%)
Hepatic enlargement result and splenomegaly result	Present	n (%)	0 (0.0%)	1 (6.3%)	1 (1.8%)

SOURCE: Listing 16.2.4.1, 16.2.5.3, 16.2.5.8, 16.2.5.9, 16.2.7.2, 16.2.7.5 and 16.2.11.1
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
For maximum length of long dimension of target lesion, subjects who had multiple target lesions only have the biggest length of long dimension target lesion included in this analysis.

表 2.7.4.7-13　疾患特性（203 試験）（安全性解析対象集団）

Description	Subtype/Category	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Diagnosis at screening and confirmed by Central Pathology Review	Peripheral T-cell Lymphoma (PTCL):	38 (97.4%)	14 (87.5%)	52 (94.5%)
	Peripheral T-Cell Lymphoma Not Otherwise Specified (PTCL-NOS)	27 (69.2%)	10 (62.5%)	37 (67.3%)
	Angioimmunoblastic T-Cell Lymphoma (AITL)	8 (20.5%)	2 (12.5%)	10 (18.2%)
	Anaplastic Large-Cell Lymphoma (ALCL), ALK+	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Anaplastic Large-Cell Lymphoma (ALCL), ALK-	2 (5.1%)	1 (6.3%)	3 (5.5%)
	Enteropathy-Type T-Cell Lymphoma (EATL)	1 (2.6%)	1 (6.3%)	2 (3.6%)
	Hepatosplenic T-Cell Lymphoma (HSTCL)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Subcutaneous Panniculitis-Like T-Cell Lymphoma (SPTCL)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Non-PTCL	1 (2.6%)	1 (6.3%)	2 (3.6%)
Diagnosis at screening assessed by Investigator	Peripheral T-cell Lymphoma (PTCL):	39 (100.0%)	16 (100.0%)	55 (100.0%)
	Peripheral T-Cell Lymphoma Not Otherwise Specified (PTCL-NOS)	22 (56.4%)	6 (37.5%)	28 (50.9%)
	Angioimmunoblastic T-Cell Lymphoma (AITL)	14 (35.9%)	7 (43.8%)	21 (38.2%)
	Anaplastic Large-Cell Lymphoma (ALCL), ALK+	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Anaplastic Large-Cell Lymphoma (ALCL), ALK-	2 (5.1%)	2 (12.5%)	4 (7.3%)
	Enteropathy-Type T-Cell Lymphoma (EATL)	1 (2.6%)	1 (6.3%)	2 (3.6%)
	Hepatosplenic T-Cell Lymphoma (HSTCL)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Subcutaneous Panniculitis-Like T-Cell Lymphoma (SPTCL)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Other PTCL	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.4.3

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
Duration since initial diagnosis (years)= (informed consent date - date of 1st diagnosis + 1)/365.25.
Duration from most recent progression (days) = (first study drug date - date of most recent progression + 1).
Duration from most recent progression (months) = (first study drug date - date of most recent progression + 1)/ 30.4375.
Central pathology reviewer could not confirm subject [redacted] disease subtype, due to the reason that subject's tumor slides were not submitted for central pathology review.

Description	Subtype/Category	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Duration since initial diagnosis (years)	n	39	16	55
	Mean	3.133	2.576	2.971
	SD	3.190	3.262	3.191
	Median	1.202	1.392	1.339
	Minimum	0.06	0.35	0.06
	Maximum	10.95	12.88	12.88
Duration since initial diagnosis by category	> 5 years	10 (25.6%)	3 (18.8%)	13 (23.6%)
	<= 5 years	29 (74.4%)	13 (81.3%)	42 (76.4%)
Duration from most recent progression (days)	n	39	16	55
	Mean	53.0	50.3	52.2
	SD	99.7	54.8	88.5
	Median	27.0	26.0	27.0
	Minimum	9	7	7
	Maximum	605	205	605
Duration from most recent progression by category	> 1 months	17 (43.6%)	7 (43.8%)	24 (43.6%)
	<= 1 months	22 (56.4%)	9 (56.3%)	31 (56.4%)

SOURCE: Listing 16.2.4.3

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
Duration since initial diagnosis (years)= (informed consent date - date of 1st diagnosis + 1)/365.25.
Duration from most recent progression (days) = (first study drug date - date of most recent progression + 1).
Duration from most recent progression (months) = (first study drug date - date of most recent progression + 1)/ 30.4375.
Central pathology reviewer could not confirm subject[redacted] disease subtype, due to the reason that subject's tumor slides were not submitted for central pathology review.

表 2.7.4.7-14　がんに対する前治療（210 試験）（安全性解析対象集団）

Description	Category	Statistic	40 mg (N=23)
Number of subjects with at least one treatment agent type		n	23
Type of previous cancer therapy	Chemotherapy alone	n (%)	17 (73.9%)
	Chemotherapy plus Mogamulizumab Therapy	n (%)	11 (47.8%)
	Mogamulizumab Monotherapy	n (%)	12 (52.2%)
	Radiotherapy	n (%)	2 (8.7%)
	Hematopoietic stem cell transplantation	n (%)	0 (0.0%)
	Other prior therapy	n (%)	3 (13.0%)
Number of subjects with:	Mogamulizumab tolerance	n (%)	13 (56.5%)
	Mogamulizumab in-tolerance	n (%)	10 (43.5%)
Total number of previous cancer therapy regimens	1 regimen	n (%)	5 (21.7%)
	2 regimens	n (%)	6 (26.1%)
	3 regimens	n (%)	4 (17.4%)
	4 regimens	n (%)	4 (17.4%)
	5 or more regimens	n (%)	4 (17.4%)
	2 or more regimens	n (%)	18 (78.3%)
		Median	3.0
Refractory, recurrent, relapsed and undetermined ATL based on last previous treatment	Refractory	n (%)	5 (21.7%)
	Recurrent	n (%)	13 (56.5%)
	Relapsed	n (%)	5 (21.7%)
	Undetermined	n (%)	0 (0.0%)

Source: Listing 16.2.4.4

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects may have more than one type of cancer therapy. Data for mogamulizumab monotherapy and combination therapy are provided by Medical Reviewer.
Number of regimens are provided by Medical Reviewer. Previous cancer therapy regimens included other prior therapy, radiotherapy and chemotherapy.
Subjects with refractory, recurrent, relapsed and undetermined ATL are confirmed by Medical Expert.

Description	Category	Statistic	40 mg (N=23)
Days from end of the last immediate previous treatment	< 3 months	n (%)	12 (52.2%)
	>=3 months	n (%)	11 (47.8%)
Number of days from end of the last immediate previous treatment (days)		n	23
		Mean	131.0
		SD	138.6
		Median	89.0
		Minimum	30
		Maximum	496
Chemotherapy	Total number of regimens		
	1 regimen	n (%)	6 (26.1%)
	2 regimens	n (%)	6 (26.1%)
	3 regimens	n (%)	3 (13.0%)
	4 regimens	n (%)	5 (21.7%)
	5 or more regimens	n (%)	3 (13.0%)
	2 or more regimens	n (%)	17 (73.9%)
		Median	2.0

Source: Listing 16.2.4.4

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Days from end of the last immediate previous treatment (months) = (date of first study drug – end date of last immediate previous treatment + 1)/30.4375
Number of days from end of the last immediate previous treatment (days) = date of first study drug – end date of last immediate previous treatment + 1
Data for total number of regimens is provided by Medical Reviewer.
Total number of regimens for chemotherapy and the last immediate previous chemotherapy best response included mogamulizumab therapy.
Chemotherapy included molecular targeted therapy and others.

Description	Category	Statistic	40 mg (N=23)
The last immediate previous chemotherapy best response	Complete response (CR)	n (%)	4 (17.4%)
	Unconfirmed complete response (CRu)	n (%)	1 (4.3%)
	Partial response (PR)	n (%)	8 (34.8%)
	Stable disease (SD)	n (%)	3 (13.0%)
	Relapsed disease or progressive disease (PD)	n (%)	5 (21.7%)
	Not assessable	n	2
	Unknown	n	0
Type of transplantation	Autologous transplantation	n (%)	0 (0.0%)
	Allogeneic transplantation	n (%)	0 (0.0%)
The last immediate previous radiotherapy best response	Complete response (CR)	n (%)	1 (4.3%)
	Unconfirmed complete response (CRu)	n (%)	0 (0.0%)
	Partial response (PR)	n (%)	0 (0.0%)
	Stable disease (SD)	n (%)	0 (0.0%)
	Relapsed disease or progressive disease (PD)	n (%)	0 (0.0%)
	Not assessable	n	0
	Unknown	n	1
The last immediate previous mogamulizumab therapy best response	Complete response (CR)	n (%)	3 (13.0%)
	Unconfirmed complete response (CRu)	n (%)	0 (0.0%)
	Partial response (PR)	n (%)	6 (26.1%)
	Stable disease (SD)	n (%)	2 (8.7%)
	Relapsed disease or progressive disease (PD)	n (%)	1 (4.3%)
	Not assessable	n	2
	Unknown	n	0

Source: Listing 16.2.4.4

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Best response for last immediate previous mogamulizumab therapy included monotherapy and combination therapy. In the event when combination therapy was used, best response from the mogamulizumab treatment is presented.

Last immediate previous mogamulizumab therapy applies to subjects who had mogamulizumab therapy (either monotherapy or combination therapy) as last immediate therapy before the administration of tucidinostat.

Total number of regimens for chemotherapy and the last immediate previous chemotherapy best response included mogamulizumab therapy.

Description	Category	Statistic	40 mg (N=23)
Number of days from end of the last immediate previous Mogamulizumab therapy (days)		n	14
		Mean	210.1
		SD	159.1
		Median	134.0
		Minimum	30
		Maximum	534

Source: Listing 16.2.4.4

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Last immediate previous mogamulizumab therapy applies to subjects who had mogamulizumab therapy (either monotherapy or combination therapy) as last immediate therapy before the administration of tucidinostat.

表 2.7.4.7-15　がんに対する前治療（201 試験）（安全性解析対象集団）

Description	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Number of patients with at least one treatment agent type		n	7	7	14
Previous Treatment agent type	Chemotherapy	n (%)	7 (100.0%)	7 (100.0%)	14 (100.0%)
	Radiation therapy	n (%)	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Biologic	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Myeloablative therapy	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Immuno therapy	n (%)	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Immuno-conjugated therapy	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	UV light therapy	n (%)	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Steroid therapy	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Previous Chemotherapy best response	Complete response	n (%)	4 (57.1%)	3 (42.9%)	7 (50.0%)
	Unconfirmed complete response	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Partial response	n (%)	0 (0.0%)	3 (42.9%)	3 (21.4%)
	Stable disease	n (%)	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Progressive disease	n (%)	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Not evaluable	n	0	0	0
	Unknown	n	1	0	1

SOURCE: Listing 16.2.4.5
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Patients may have more than one type of treatment agent.
Percentage of best responses, radiation source and type of UV light therapy is calculated based on the number of patients with chemotherapy, radiation therapy and UV light therapy in each cohort of the analysis set, respectively.
If patients had more than one chemotherapy regimen, best response to any prior therapy is presented. The number of cycle denotes the highest number of cycles given among all prior chemotherapy regimens.

Description	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Number of cycles	Chemotherapy	n	7	7	14
		Mean	6.4	5.9	6.1
		SD	1.62	2.48	2.03
		Median	6.0	6.0	6.0
		Minimum	5	2	2
		Maximum	10	8	10
Radiation source	X-ray	n (%)	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Gamma-ray	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Electron ray	n (%)	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type of UV light therapy	PUVA	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	UVA	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	UVB	n (%)	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Other	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.4.5
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Patients may have more than one type of treatment agent.
Percentage of best responses, radiation source and type of UV light therapy is calculated based on the number of patients with chemotherapy, radiation therapy and UV light therapy in each cohort of the analysis set, respectively.
If patients had more than one chemotherapy regimen, best response to any prior therapy is presented. The number of cycle denotes the highest number of cycles given among all prior chemotherapy regimens.

Description	Category	Statistic	30 mg (N=7)	40 mg (N=7)	Total (N=14)
Total number of regimen		n	7	7	14
		Mean	3.0	3.1	3.1
		SD	2.89	2.27	2.50
		Median	2.0	3.0	2.5
		Minimum	1	1	1
		Maximum	9	8	9

SOURCE: Listing 16.2.4.5
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Patients may have more than one type of treatment agent.
Percentage of best responses, radiation source and type of UV light therapy is calculated based on the number of patients with chemotherapy, radiation therapy and UV light therapy in each cohort of the analysis set, respectively.
If patients had more than one chemotherapy regimen, best response to any prior therapy is presented. The number of cycle denotes the highest number of cycles given among all prior chemotherapy regimens.

表 2.7.4.7-16　がんに対する前治療（203 試験）（安全性解析対象集団）

Description	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Number of subjects with at least one treatment agent type		n	39	16	55
Type of previous cancer therapy	Chemotherapy	n (%)	39 (100.0%)	16 (100.0%)	55 (100.0%)
	Other anticancer therapy	n (%)	14 (35.9%)	2 (12.5%)	16 (29.1%)
	Brentuximab vedotin	n (%)	1 (2.6%)	1 (6.3%)	2 (3.6%)
	Darinaparsin	n (%)	7 (17.9%)	1 (6.3%)	8 (14.5%)
	E7777[a]	n (%)	2 (5.1%)	0 (0.0%)	2 (3.6%)
	Forodesine	n (%)	6 (15.4%)	0 (0.0%)	6 (10.9%)
	Mogamulizumab	n (%)	1 (2.6%)	0 (0.0%)	1 (1.8%)
	Rituximab	n (%)	2 (5.1%)	0 (0.0%)	2 (3.6%)
	Romidepsin	n (%)	4 (10.3%)	0 (0.0%)	4 (7.3%)
	Radiotherapy	n (%)	4 (10.3%)	2 (12.5%)	6 (10.9%)
	Hematopoietic stem cell transplantation	n (%)	2 (5.1%)	4 (25.0%)	6 (10.9%)
	Other prior therapy	n (%)	1 (2.6%)	1 (6.3%)	2 (3.6%)
Total number of previous cancer therapy regimens	1 regimen	n (%)	15 (38.5%)	2 (12.5%)	17 (30.9%)
	2 regimens	n (%)	10 (25.6%)	8 (50.0%)	18 (32.7%)
	3 regimens	n (%)	7 (17.9%)	1 (6.3%)	8 (14.5%)
	4 regimens	n (%)	2 (5.1%)	2 (12.5%)	4 (7.3%)
	5 or more regimens	n (%)	5 (12.8%)	3 (18.8%)	8 (14.5%)
	2 or more regimens	n (%)	24 (61.5%)	14 (87.5%)	38 (69.1%)
		Median	2.0	2.0	2.0
Refractory, relapsed and undetermined PTCL based on last previous treatment	Refractory	n (%)	15 (38.5%)	8 (50.0%)	23 (41.8%)
	Relapsed	n (%)	24 (61.5%)	8 (50.0%)	32 (58.2%)
	Undetermined	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.4.4

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set.
a: development code for denileukin diftitox
Subjects may have more than one type of therapy.
Subjects with refractory, relapsed and undetermined PTCL are confirmed by Medical Expert.
Previous cancer therapy regimens included other prior therapy, radiotherapy and chemotherapy.

Description	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Days from end of the last immediate previous treatment	< 3 months	n (%)	20 (51.3%)	7 (43.8%)	27 (49.1%)
	>=3 months	n (%)	19 (48.7%)	9 (56.3%)	28 (50.9%)
Number of days from end of the last immediate previous treatment (days)		n	39	16	55
		Mean	344.6	253.2	318.0
		SD	724.1	516.5	667.0
		Median	88.0	110.5	97.0
		Minimum	29	30	29
		Maximum	3861	2154	3861
Chemotherapy	Total number of regimens				
	1 regimen	n (%)	17 (43.6%)	3 (18.8%)	20 (36.4%)
	2 regimens	n (%)	10 (25.6%)	7 (43.8%)	17 (30.9%)
	3 regimens	n (%)	6 (15.4%)	2 (12.5%)	8 (14.5%)
	4 regimens	n (%)	3 (7.7%)	2 (12.5%)	5 (9.1%)
	5 or more regimens	n (%)	3 (7.7%)	2 (12.5%)	5 (9.1%)
	2 or more regimens	n (%)	22 (56.4%)	13 (81.3%)	35 (63.6%)
		Median	2.0	2.0	2.0
The last immediate previous chemotherapy best response	Complete response (CR)	n (%)	13 (33.3%)	4 (25.0%)	17 (30.9%)
	Unconfirmed complete response (CRu)	n (%)	1 (2.6%)	0 (0.0%)	1 (1.8%)
	Partial response (PR)	n (%)	10 (25.6%)	3 (18.8%)	13 (23.6%)
	Stable disease (SD)	n (%)	11 (28.2%)	1 (6.3%)	12 (21.8%)
	Relapsed disease or progressive disease (PD)	n (%)	4 (10.3%)	6 (37.5%)	10 (18.2%)
	Not assessable	n	0	1	1
	Unknown	n	0	1	1

SOURCE: Listing 16.2.4.4

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set.
Number of days from end of the last immediate previous treatment (days) = date of first study drug – end date of last immediate previous treatment + 1
Days from end of the last immediate previous treatment (months) = (date of first study drug – end date of last immediate previous treatment + 1)/30.4375

Description	Category	Statistic	Japan (N=39)	Korea (N=16)	Total (N=55)
Type of transplantation	Autologous transplantation	n (%)	2 (5.1%)	4 (25.0%)	6 (10.9%)
	Allogeneic transplantation	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
The last immediate previous radiotherapy best response	Complete response (CR)	n (%)	2 (5.1%)	0 (0.0%)	2 (3.6%)
	Unconfirmed complete response (CRu)	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Partial response (PR)	n (%)	0 (0.0%)	1 (6.3%)	1 (1.8%)
	Stable disease (SD)	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Relapsed disease or progressive disease (PD)	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not assessable	n	0	0	0
	Unknown	n	2	1	3

SOURCE: Listing 16.2.4.4

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set.

表 2.7.4.7-17　併用薬（210 試験）（安全性解析対象集団）

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
Number of subjects with at least one concomitant medication	23 (100.0%)
ADRENERGICS, INHALANTS	1 (4.3%)
FLUTICASONE;VILANTEROL	1 (4.3%)
AGENTS AGAINST AMOEBIASIS AND OTHER PROTOZOAL DISEASES	2 (8.7%)
SAMTIREL	2 (8.7%)
AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL FISSURES FOR TOPICAL USE	1 (4.3%)
POSTERISAN FORTE /01567801/	1 (4.3%)
ALL OTHER THERAPEUTIC PRODUCTS	1 (4.3%)
CALCIUM POLYSTYRENE SULFONATE	1 (4.3%)
ANESTHETICS, LOCAL	3 (13.0%)
LIDOCAINE	1 (4.3%)
MEPIVACAINE HYDROCHLORIDE	1 (4.3%)
STROCAIN /00130301/	1 (4.3%)
XYLOCAINE /00033401/	1 (4.3%)
ANGIOTENSIN II ANTAGONISTS, PLAIN	1 (4.3%)
AZILVA	1 (4.3%)
ANTACIDS	2 (8.7%)
MAGMITT	2 (8.7%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
ANTI-ACNE PREPARATIONS FOR TOPICAL USE	2 (8.7%)
ACUATIM	1 (4.3%)
SAHNE	1 (4.3%)
ANTI-PARATHYROID AGENTS	2 (8.7%)
ELCITONIN	2 (8.7%)
ANTIDIARRHEAL MICROORGANISMS	3 (13.0%)
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	1 (4.3%)
BIO-THREE	1 (4.3%)
BIOFERMIN R	1 (4.3%)
ANTIEMETICS AND ANTINAUSEANTS	3 (13.0%)
CEPHADOL	1 (4.3%)
DIFENIDOL	1 (4.3%)
TRAVELMIN /00517301/	1 (4.3%)
ANTIFUNGALS FOR TOPICAL USE	2 (8.7%)
KETOCONAZOLE	1 (4.3%)
NITRAZEN	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS	2 (8.7%)
AIPHAGAN	1 (4.3%)
CARTEOLOL HYDROCHLORIDE	1 (4.3%)
COSOPT	1 (4.3%)
TAFLUPROST	1 (4.3%)
ANTIGOUT PREPARATIONS	10 (43.5%)
FEBURIC	8 (34.8%)
ALLOPURINOL	1 (4.3%)
FEBUXOSTAT	1 (4.3%)
ANTIHISTAMINES FOR SYSTEMIC USE	9 (39.1%)
OLOPATADINE HYDROCHLORIDE	5 (21.7%)
XYZAL	3 (13.0%)
ALLELOCK	1 (4.3%)
FEXOFENADINE	1 (4.3%)
FEXOFENADINE HYDROCHLORIDE	1 (4.3%)
LEVOCETIRIZINE HYDROCHLORIDE	1 (4.3%)
POLARAMINE	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
ANTIINFECTIVES	1 (4.3%)
CRAVIT	1 (4.3%)
TARIVID /00731801/	1 (4.3%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	9 (39.1%)
LOXOPROFEN	3 (13.0%)
LOXOPROFEN SODIUM HYDRATE	2 (8.7%)
CELECOXIB	1 (4.3%)
DICLOFENAC SODIUM	1 (4.3%)
LOXONIN	1 (4.3%)
LOXOPROFEN NA	1 (4.3%)
SALAZOSULFAPYRIDINE	1 (4.3%)
ANTIMYCOTICS FOR SYSTEMIC USE	8 (34.8%)
ITRACONAZOLE	3 (13.0%)
FLUCONAZOLE	2 (8.7%)
ITRIZOLE	2 (8.7%)
FUNGIZONE	1 (4.3%)
ANTISEPTICS AND DISINFECTANTS	1 (4.3%)
ISODINE /00080001/	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
ANTITHROMBOTIC AGENTS	7 (30.4%)
BAYASPIRIN	2 (8.7%)
CLOPIDOGREL SULFATE	2 (8.7%)
ELIQUIS	1 (4.3%)
LIMAPROST ALFADEX	1 (4.3%)
SARPOGRELATE HYDROCHLORIDE	1 (4.3%)
ANXIOLYTICS	2 (8.7%)
ALPRAZOLAM	1 (4.3%)
DIAZEPAM	1 (4.3%)
BELLADONNA AND DERIVATIVES, PLAIN	1 (4.3%)
SCOPOLAMINE BUTYLBROMIDE	1 (4.3%)
BETA BLOCKING AGENTS	2 (8.7%)
ATENOLOL	1 (4.3%)
CARVEDILOL	1 (4.3%)
METOPROLOL TARTRATE	1 (4.3%)
BILE THERAPY	2 (8.7%)
URSO /00465701/	1 (4.3%)
URSODEOXYCHOLIC ACID	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	5 (21.7%)
EQUA	2 (8.7%)
ACTOS	1 (4.3%)
GLUBES	1 (4.3%)
METFORMIN HYDROCHLORIDE	1 (4.3%)
SITAGLIPTIN PHOSPHATE MONOHYDRATE	1 (4.3%)
TENELIA	1 (4.3%)
TENELIGLIPTIN HYDROBROMIDE	1 (4.3%)
CALCIUM	1 (4.3%)
ASPARA-CA	1 (4.3%)
CHEMOTHERAPEUTICS FOR TOPICAL USE	1 (4.3%)
REFLAP	1 (4.3%)
CORTICOSTEROIDS FOR SYSTEMIC USE, COMBINATIONS	1 (4.3%)
CELESTAMINE /01221101/	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	9 (39.1%)
PREDNISOLONE	5 (21.7%)
PREDONINE /00016201/	3 (13.0%)
DEXAMETHASONE SODIUM PHOSPHATE	1 (4.3%)
SAXIZON	1 (4.3%)
CORTICOSTEROIDS, COMBINATIONS WITH ANTIBIOTICS	2 (8.7%)
DERMOSOL G	1 (4.3%)
RINDERON-VG	1 (4.3%)
CORTICOSTEROIDS, OTHER COMBINATIONS	1 (4.3%)
EURAX H	1 (4.3%)
CORTICOSTEROIDS, PLAIN	6 (26.1%)
METHADERM	2 (8.7%)
ANAMIDOL	1 (4.3%)
ANTEBATE	1 (4.3%)
BETAMETHASONE BUTYRATE PROPIONATE	1 (4.3%)
CLOBETASOL PROPIONATE	1 (4.3%)
DERMOVATE	1 (4.3%)
RINDERON-V	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECTORANTS	1 (4.3%)
CODEINE PHOSPHATE	1 (4.3%)
DECONGESTANTS AND ANTIALLERGICS	1 (4.3%)
LIVOSTIN	1 (4.3%)
DIRECT ACTING ANTIVIRALS	6 (26.1%)
ACICLOVIR	4 (17.4%)
ENTECAVIR	1 (4.3%)
VICCLOX /00587301/	1 (4.3%)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	1 (4.3%)
BENET	1 (4.3%)
DRUGS FOR CONSTIPATION	12 (52.2%)
MAGNESIUM OXIDE	9 (39.1%)
SENNOSIDE /00571901/	4 (17.4%)
AMITIZA	2 (8.7%)
MAGMITT	2 (8.7%)
LINZESS	1 (4.3%)
PICOSULFATE	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	20 (87.0%)
LANSOPRAZOLE	4 (17.4%)
OMEPRAZOLE	3 (13.0%)
RABEPRAZOLE SODIUM	3 (13.0%)
REBAMIPIDE	3 (13.0%)
TAKECAB	3 (13.0%)
ESOMEPRAZOLE	2 (8.7%)
RABEPRAZOLE	2 (8.7%)
ESOMEPRAZOLE MAGNESIUM	1 (4.3%)
IRSOGLADINE MALEATE	1 (4.3%)
LEVOGLUTAMIDE W/SODIUM GUALENATE HYDRATE	1 (4.3%)
PARIET	1 (4.3%)
DRUGS FOR TREATMENT OF TUBERCULOSIS	3 (13.0%)
ISONIAZID	2 (8.7%)
ISCOTIN /00030201/	1 (4.3%)
DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY	2 (8.7%)
TAMSULOSIN HYDROCHLORIDE	1 (4.3%)
URIEF	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
EMOLLIENTS AND PROTECTIVES	13 (56.5%)
HIRUDOID	6 (26.1%)
HEPARINOID	5 (21.7%)
BESOFTEN	3 (13.0%)
PROPETO	3 (13.0%)
UREA	1 (4.3%)
VASELINE /00473501/	1 (4.3%)
EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRESSANTS	2 (8.7%)
L-CARBOCYSTEINE	1 (4.3%)
MUCODYNE	1 (4.3%)
RESPLEN	1 (4.3%)
HIGH-CEILING DIURETICS	6 (26.1%)
LUPRAC	3 (13.0%)
DIART	2 (8.7%)
AZOSEMIDE	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
HYPNOTICS AND SEDATIVES	13 (56.5%)
BROTIZOLAM	5 (21.7%)
ZOLPIDEM TARTRATE	4 (17.4%)
ZOPICLONE	2 (8.7%)
ESTAZOLAM	1 (4.3%)
FLUNITRAZEPAM	1 (4.3%)
LUNESTA	1 (4.3%)
NITRAZEPAM	1 (4.3%)
RILMAZAFONE HYDROCHLORIDE	1 (4.3%)
ROZEREM	1 (4.3%)
ZOLPIDEM	1 (4.3%)
I.V. SOLUTION ADDITIVES	1 (4.3%)
ISOTONIC SODIUM CHLORIDE SOLUTION	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		40 mg (N=23) n (%)
I.V. SOLUTIONS		6 (26.1%)
BFLUID		4 (17.4%)
KCL		1 (4.3%)
SODIUM CHLORIDE		1 (4.3%)
SOLDEM		1 (4.3%)
SOLDEM 1		1 (4.3%)
YD SOLITA T NO.1		1 (4.3%)
YD SOLITA T NO.3G		1 (4.3%)
IMMUNOSTIMULANTS		6 (26.1%)
FILGRASTIM		4 (17.4%)
FILGRASTIM BS	/06441101/	2 (8.7%)
NEUTROGIN		1 (4.3%)
NEUTROPINE		1 (4.3%)
INSULINS AND ANALOGUES		2 (8.7%)
HUMALOG		1 (4.3%)
HUMULIN R		1 (4.3%)
INSULIN GLARGINE RECOMBINANT		1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
LIPID MODIFYING AGENTS, COMBINATIONS	1 (4.3%)
CADUET	1 (4.3%)
LIPID MODIFYING AGENTS, PLAIN	6 (26.1%)
ATORVASTATIN	1 (4.3%)
EPADEL-S	1 (4.3%)
FENOFIBRATE	1 (4.3%)
LIPIDIL	1 (4.3%)
LIVARO	1 (4.3%)
PRAVASTATIN SODIUM	1 (4.3%)
ROSUVASTATIN CALCIUM	1 (4.3%)
LOW-CEILING DIURETICS, THIAZIDES	1 (4.3%)
HYDROCHLOROTHIAZIDE	1 (4.3%)
OPIOIDS	1 (4.3%)
TRAMAL	1 (4.3%)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	3 (13.0%)
MIYA-BM	3 (13.0%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
OTHER ANALGESICS AND ANTIPYRETICS	8 (34.8%)
CALONAL	4 (17.4%)
ACETAMINOPHEN	3 (13.0%)
ACELIO	1 (4.3%)
LYRICA	1 (4.3%)
LYRICA OD	1 (4.3%)
OTHER BETA-LACTAM ANTIBACTERIALS	7 (30.4%)
CEFCAPENE PIVOXIL HYDROCHLORIDE	2 (8.7%)
CEFDITOREN PIVOXIL	1 (4.3%)
CEFON /00883901/	1 (4.3%)
CEFTRIAXONE	1 (4.3%)
FAROPENEM SODIUM	1 (4.3%)
MAXIPIME	1 (4.3%)
MEROPENEM	1 (4.3%)
OTHER CARDIAC PREPARATIONS	3 (13.0%)
UBIDECARENONE	2 (8.7%)
ADETPHOS	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
OTHER DERMATOLOGICAL PREPARATIONS	1 (4.3%)
AZUNOL /00620101/	1 (4.3%)
OTHER NUTRIENTS	1 (4.3%)
SQUALENE	1 (4.3%)
OTHER OPHTHALMOLOGICALS	1 (4.3%)
DIQUAS	1 (4.3%)
TEARBALANCE	1 (4.3%)
OTHER PLAIN VITAMIN PREPARATIONS	2 (8.7%)
PANTOSIN	1 (4.3%)
PYRIDOXAL PHOSPHATE	1 (4.3%)
POTASSIUM	1 (4.3%)
K-SUPPLY	1 (4.3%)
POTASSIUM-SPARING AGENTS	2 (8.7%)
SPIRONOLACTONE	2 (8.7%)
PROPULSIVES	1 (4.3%)
DOMPERIDONE	1 (4.3%)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIRECT CARDIAC EFFECTS	1 (4.3%)
DILTIAZEM HYDROCHLORIDE	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	5 (21.7%)
AMLODIPINE	2 (8.7%)
AMLODIPINE BESILATE	2 (8.7%)
BENIDIPINE HYDROCHLORIDE	1 (4.3%)
STOMATOLOGICAL PREPARATIONS	6 (26.1%)
AZUNOL GARGLE LIQUID	2 (8.7%)
DEXALTIN	2 (8.7%)
AMPHOTERICIN B	1 (4.3%)
POPIYODON	1 (4.3%)
TRIAMCINOLONE ACETONIDE	1 (4.3%)
SULFONAMIDES AND TRIMETHOPRIM	14 (60.9%)
BAKTAR	7 (30.4%)
BACTRAMIN	3 (13.0%)
BACTAR	2 (8.7%)
SULFAMETHOXAZOLE W/TRIMETHOPRIM	2 (8.7%)
DAIPHEN	1 (4.3%)
THROAT PREPARATIONS	1 (4.3%)
SP TROCHES	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
THYROID PREPARATIONS	2 (8.7%)
LEVOTHYROXINE SODIUM	1 (4.3%)
THYRADIN	1 (4.3%)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	6 (26.1%)
KETOPROFEN	2 (8.7%)
INDOMETACIN	1 (4.3%)
LOXOPROFEN SODIUM HYDRATE	1 (4.3%)
MOHRUS	1 (4.3%)
SALONPAS /07673501/	1 (4.3%)
VOLTAREN /00372301/	1 (4.3%)
VASODILATORS USED IN CARDIAC DISEASES	2 (8.7%)
FRANDOL	1 (4.3%)
ISOSORBIDE DINITRATE	1 (4.3%)
NICORANDIL	1 (4.3%)
VIRAL VACCINES	1 (4.3%)
INFLUENZA HA VACCINE	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	40 mg (N=23) n (%)
VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO	4 (17.4%)
EDIROL	2 (8.7%)
ALFACALCIDOL	1 (4.3%)
CALFINA	1 (4.3%)
VITAMIN B12 AND FOLIC ACID	2 (8.7%)
MECOBALAMIN	1 (4.3%)
METHYCOBAL	1 (4.3%)
X-RAY CONTRAST MEDIA, IODINATED	6 (26.1%)
OMNIPAQUE	3 (13.0%)
IOVERIN	2 (8.7%)
IOPAMIDOL	1 (4.3%)
IOPROMIDE	1 (4.3%)
OYPALOMIN	1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		40 mg (N=23) n (%)
ATC Class Level 3 not Available		6 (26.1%)
DIAMOX	/00016901/	1 (4.3%)
KAKKONTO	/07985901/	1 (4.3%)
KEISHIKAJUTSUBUTO		1 (4.3%)
NUTRIENTS NOS		1 (4.3%)
OPHTHALMOLOGICALS		1 (4.3%)
SOLACET F		1 (4.3%)

Source: Listing 16.2.4.5

WHO-DDE Version 01SEP2017 was used to code medications.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

表 2.7.4.7-18　併用薬（201 試験）（安全性解析対象集団）

ATC class level 3 WHO-DDE drug name		30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one concomitant medication		7 (100.0%)	7 (100.0%)	14 (100.0%)
STOMATOLOGICAL PREPARATIONS		1 (14.3%)	1 (14.3%)	2 (14.3%)
XYLOCAINE	/00033401/	1 (14.3%)	0 (0.0%)	1 (7.1%)
GLYCERIN	/00200601/	1 (14.3%)	0 (0.0%)	1 (7.1%)
SODIUM GUALENATE HYDRATE		1 (14.3%)	1 (14.3%)	2 (14.3%)
TETRACYCLINE PRESTERON		1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTACIDS		1 (14.3%)	2 (28.6%)	3 (21.4%)
MACMET	/00091001/	0 (0.0%)	1 (14.3%)	1 (7.1%)
MAGMITT		1 (14.3%)	1 (14.3%)	2 (14.3%)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFL		3 (42.9%)	6 (85.7%)	9 (64.3%)
AZUNOL	/00317302/	1 (14.3%)	0 (0.0%)	1 (7.1%)
ISALON		0 (0.0%)	1 (14.3%)	1 (7.1%)
HACHIAZULE	/00523101/	1 (14.3%)	0 (0.0%)	1 (7.1%)
OMEPRAZOLE		1 (14.3%)	0 (0.0%)	1 (7.1%)
FAMOTIDINE		0 (0.0%)	2 (28.6%)	2 (14.3%)
TEPRENONE		1 (14.3%)	0 (0.0%)	1 (7.1%)
SELBEX		1 (14.3%)	0 (0.0%)	1 (7.1%)
REBAMIPIDE		1 (14.3%)	0 (0.0%)	1 (7.1%)
LANSOPRAZOLE		1 (14.3%)	1 (14.3%)	2 (14.3%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
LANSOPRAZOLE TOWA	0 (0.0%)	1 (14.3%)	1 (7.1%)
ESOMEPRAZOLE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ESOMEPRAZOLE MAGNESIUM	0 (0.0%)	1 (14.3%)	1 (7.1%)
PROPULSIVES	1 (14.3%)	1 (14.3%)	2 (14.3%)
METOCLOPRAMIDE	0 (0.0%)	1 (14.3%)	1 (7.1%)
MOSAPRIDE CITRATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTIEMETICS AND ANTINAUSEANTS	1 (14.3%)	1 (14.3%)	2 (14.3%)
PROCHLORPERAZINE MALEATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
GRANISETRON HYDROCHLORIDE	0 (0.0%)	1 (14.3%)	1 (7.1%)
BILE THERAPY	0 (0.0%)	1 (14.3%)	1 (7.1%)
URSODEOXYCHOLIC ACID	0 (0.0%)	1 (14.3%)	1 (7.1%)
LIVER THERAPY, LIPOTROPICS	0 (0.0%)	1 (14.3%)	1 (7.1%)
GLYCYRRHIZIC ACID	0 (0.0%)	1 (14.3%)	1 (7.1%)
DRUGS FOR CONSTIPATION	2 (28.6%)	4 (57.1%)	6 (42.9%)
POLYCARBOPHIL CALCIUM	0 (0.0%)	1 (14.3%)	1 (7.1%)
SENNOSIDE /00571901/	0 (0.0%)	1 (14.3%)	1 (7.1%)
PURSENNIDE /00571901/	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
SENNOSIDE A+B CALCIUM	0 (0.0%)	2 (28.6%)	2 (14.3%)
MAGNESIUM OXIDE	1 (14.3%)	1 (14.3%)	2 (14.3%)
MAGLAX	0 (0.0%)	1 (14.3%)	1 (7.1%)
DAIKENCHUTO	0 (0.0%)	1 (14.3%)	1 (7.1%)
ANTIDIARRHEAL MICROORGANISMS	0 (0.0%)	3 (42.9%)	3 (21.4%)
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	0 (0.0%)	1 (14.3%)	1 (7.1%)
BIO-THREE	0 (0.0%)	2 (28.6%)	2 (14.3%)
OTHER ANTIDIARRHEALS	0 (0.0%)	1 (14.3%)	1 (7.1%)
ALBUMIN TANNATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
INSULINS AND ANALOGUES	0 (0.0%)	2 (28.6%)	2 (14.3%)
INSULIN HUMAN	0 (0.0%)	1 (14.3%)	1 (7.1%)
HUMULIN R	0 (0.0%)	1 (14.3%)	1 (7.1%)
TRESIBA	0 (0.0%)	1 (14.3%)	1 (7.1%)
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	1 (14.3%)	2 (28.6%)	3 (21.4%)
METGLUCO	0 (0.0%)	1 (14.3%)	1 (7.1%)
GLIMEPIRIDE	0 (0.0%)	1 (14.3%)	1 (7.1%)
EQUA	0 (0.0%)	1 (14.3%)	1 (7.1%)
SITAGLIPTIN PHOSPHATE MONOHYDRATE	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
GLACTIV	0 (0.0%)	1 (14.3%)	1 (7.1%)
VITAMIN B1, PLAIN AND IN COMBINATION WITH VITAMIN	1 (14.3%)	0 (0.0%)	1 (7.1%)
ALINAMIN F /00257801/	1 (14.3%)	0 (0.0%)	1 (7.1%)
OTHER PLAIN VITAMIN PREPARATIONS	1 (14.3%)	1 (14.3%)	2 (14.3%)
PANTETHINE	1 (14.3%)	1 (14.3%)	2 (14.3%)
OTHER VITAMIN PRODUCTS, COMBINATIONS	1 (14.3%)	0 (0.0%)	1 (7.1%)
VITAMEDIN /00274301/	1 (14.3%)	0 (0.0%)	1 (7.1%)
CALCIUM	0 (0.0%)	2 (28.6%)	2 (14.3%)
CALCIUM LACTATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
CALCIUM L-ASPARTATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
POTASSIUM	1 (14.3%)	0 (0.0%)	1 (7.1%)
POTASSIUM CHLORIDE	1 (14.3%)	0 (0.0%)	1 (7.1%)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	1 (14.3%)	2 (28.6%)	3 (21.4%)
CLOSTRIDIUM BUTYRICUM	1 (14.3%)	1 (14.3%)	2 (14.3%)
GLYCINE	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
ANTITHROMBOTIC AGENTS	2 (28.6%)	1 (14.3%)	3 (21.4%)
BAYASPIRIN	0 (0.0%)	1 (14.3%)	1 (7.1%)
HEPARIN SODIUM	1 (14.3%)	0 (0.0%)	1 (7.1%)
HEPAFLUSH	1 (14.3%)	0 (0.0%)	1 (7.1%)
VITAMIN B12 AND FOLIC ACID	1 (14.3%)	0 (0.0%)	1 (7.1%)
MECOBALAMIN	1 (14.3%)	0 (0.0%)	1 (7.1%)
I.V. SOLUTIONS	0 (0.0%)	1 (14.3%)	1 (7.1%)
HARTMAN G-3	0 (0.0%)	1 (14.3%)	1 (7.1%)
REPLAS	0 (0.0%)	1 (14.3%)	1 (7.1%)
LACTATE RINGER	0 (0.0%)	1 (14.3%)	1 (7.1%)
HIGH-CEILING DIURETICS	1 (14.3%)	0 (0.0%)	1 (7.1%)
FUROSEMIDE	1 (14.3%)	0 (0.0%)	1 (7.1%)
POTASSIUM-SPARING AGENTS	2 (28.6%)	0 (0.0%)	2 (14.3%)
SPIRONOLACTONE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ALDACTONE A	1 (14.3%)	0 (0.0%)	1 (7.1%)
AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL FISSU	1 (14.3%)	0 (0.0%)	1 (7.1%)
HYDROCORTISONE ACETATE	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
ESCHERICHIA COLI	1 (14.3%)	0 (0.0%)	1 (7.1%)
NERIPROCT	1 (14.3%)	0 (0.0%)	1 (7.1%)
BORRAZA G	1 (14.3%)	0 (0.0%)	1 (7.1%)
POSTERISAN FORTE /01567801/	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTIVARICOSE THERAPY	0 (0.0%)	1 (14.3%)	1 (7.1%)
HEPARINOID	0 (0.0%)	1 (14.3%)	1 (7.1%)
BETA BLOCKING AGENTS	2 (28.6%)	0 (0.0%)	2 (14.3%)
TENORMIN	2 (28.6%)	0 (0.0%)	2 (14.3%)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VAS	2 (28.6%)	2 (28.6%)	4 (28.6%)
AMLODIPINE BESILATE	1 (14.3%)	2 (28.6%)	3 (21.4%)
NORVASC	2 (28.6%)	0 (0.0%)	2 (14.3%)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIRECT CAR	0 (0.0%)	1 (14.3%)	1 (7.1%)
DILTIAZEM HYDROCHLORIDE R	0 (0.0%)	1 (14.3%)	1 (7.1%)
ACE INHIBITORS, PLAIN	1 (14.3%)	0 (0.0%)	1 (7.1%)
LONGES	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANGIOTENSIN II ANTAGONISTS, PLAIN	1 (14.3%)	1 (14.3%)	2 (14.3%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
CANDESARTAN CILEXETIL	0 (0.0%)	1 (14.3%)	1 (7.1%)
BLOPRESS	1 (14.3%)	0 (0.0%)	1 (7.1%)
LIPID MODIFYING AGENTS, PLAIN	0 (0.0%)	2 (28.6%)	2 (14.3%)
BEZAFIBRATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
CRESTOR	0 (0.0%)	1 (14.3%)	1 (7.1%)
EMOLLIENTS AND PROTECTIVES	2 (28.6%)	1 (14.3%)	3 (21.4%)
UREPEARL	1 (14.3%)	0 (0.0%)	1 (7.1%)
HEPARINOID	1 (14.3%)	1 (14.3%)	2 (14.3%)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS,	1 (14.3%)	1 (14.3%)	2 (14.3%)
DIPHENHYDRAMINE	0 (0.0%)	1 (14.3%)	1 (7.1%)
RESTAMIN /00000401/	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTIBIOTICS FOR TOPICAL USE	0 (0.0%)	1 (14.3%)	1 (7.1%)
GENTAMICIN SULFATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
CHEMOTHERAPEUTICS FOR TOPICAL USE	1 (14.3%)	0 (0.0%)	1 (7.1%)
METRONIDAZOLE	1 (14.3%)	0 (0.0%)	1 (7.1%)
SULFADIAZINE SILVER	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
CORTICOSTEROIDS, PLAIN	3 (42.9%)	1 (14.3%)	4 (28.6%)
BETAMETHASONE	1 (14.3%)	0 (0.0%)	1 (7.1%)
BETAMETHASONE BUTYRATE PROPIONATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTEBATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
DIFLUPREDNATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY	1 (14.3%)	0 (0.0%)	1 (7.1%)
TAMSULOSIN HCL	1 (14.3%)	0 (0.0%)	1 (7.1%)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	1 (14.3%)	1 (14.3%)	2 (14.3%)
PREDNISOLONE	0 (0.0%)	1 (14.3%)	1 (7.1%)
KENALOG IN ORABASE	1 (14.3%)	0 (0.0%)	1 (7.1%)
THYROID PREPARATIONS	1 (14.3%)	0 (0.0%)	1 (7.1%)
LEVOTHYROXINE SODIUM	1 (14.3%)	0 (0.0%)	1 (7.1%)
OTHER BETA-LACTAM ANTIBACTERIALS	0 (0.0%)	3 (42.9%)	3 (21.4%)
CEFPODOXIME PROXETIL	0 (0.0%)	1 (14.3%)	1 (7.1%)
CEFDINIR	0 (0.0%)	1 (14.3%)	1 (7.1%)
MEROPENEM	0 (0.0%)	1 (14.3%)	1 (7.1%)
CEFCAPENE PIVOXIL HYDROCHLORIDE	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
SULFONAMIDES AND TRIMETHOPRIM	0 (0.0%)	1 (14.3%)	1 (7.1%)
SULFAMETHOXAZOLE	0 (0.0%)	1 (14.3%)	1 (7.1%)
BACTRAMIN	0 (0.0%)	1 (14.3%)	1 (7.1%)
TRIMETHOPRIM	0 (0.0%)	1 (14.3%)	1 (7.1%)
ANTIMYCOTICS FOR SYSTEMIC USE	0 (0.0%)	3 (42.9%)	3 (21.4%)
AMPHOTERICIN B	0 (0.0%)	1 (14.3%)	1 (7.1%)
MYCOSYST	0 (0.0%)	1 (14.3%)	1 (7.1%)
MICAFUNGIN SODIUM	0 (0.0%)	1 (14.3%)	1 (7.1%)
DIRECT ACTING ANTIVIRALS	1 (14.3%)	2 (28.6%)	3 (21.4%)
ACICLOVIR	1 (14.3%)	2 (28.6%)	3 (21.4%)
IMMUNOSTIMULANTS	0 (0.0%)	2 (28.6%)	2 (14.3%)
FILGRASTIM	0 (0.0%)	1 (14.3%)	1 (7.1%)
GRAN	0 (0.0%)	1 (14.3%)	1 (7.1%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-S	0 (0.0%)	4 (57.1%)	4 (28.6%)
FLURBIPROFEN AXETIL	0 (0.0%)	1 (14.3%)	1 (7.1%)
LOBU	0 (0.0%)	1 (14.3%)	1 (7.1%)
LOXOPROFEN SODIUM HYDRATE	0 (0.0%)	2 (28.6%)	2 (14.3%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	1 (14.3%)	0 (0.0%)	1 (7.1%)
MOHRUS	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTIGOUT PREPARATIONS	4 (57.1%)	1 (14.3%)	5 (35.7%)
ALLOPURINOL	1 (14.3%)	0 (0.0%)	1 (7.1%)
SALOBEL	0 (0.0%)	1 (14.3%)	1 (7.1%)
FEBUXOSTAT	1 (14.3%)	0 (0.0%)	1 (7.1%)
FEBURIC	2 (28.6%)	0 (0.0%)	2 (14.3%)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	0 (0.0%)	1 (14.3%)	1 (7.1%)
ALENDRONATE SODIUM HYDRATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
ANESTHETICS, LOCAL	0 (0.0%)	1 (14.3%)	1 (7.1%)
LIDOCAINE HYDROCHLORIDE MONOHYDRATE	0 (0.0%)	1 (14.3%)	1 (7.1%)
OTHER ANALGESICS AND ANTIPYRETICS	3 (42.9%)	2 (28.6%)	5 (35.7%)
ACETAMINOPHEN	3 (42.9%)	0 (0.0%)	3 (21.4%)
CALONAL	0 (0.0%)	2 (28.6%)	2 (14.3%)
CAFFEINE W/PARACETAMOL/PROMETHAZINE/SALICYLAM	0 (0.0%)	1 (14.3%)	1 (7.1%)
ANXIOLYTICS	0 (0.0%)	1 (14.3%)	1 (7.1%)
ETIZOLAM	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
HYPNOTICS AND SEDATIVES	2 (28.6%)	2 (28.6%)	4 (28.6%)
NITRAZEPAM	1 (14.3%)	0 (0.0%)	1 (7.1%)
SILECE	0 (0.0%)	1 (14.3%)	1 (7.1%)
ESTAZOLAM	0 (0.0%)	1 (14.3%)	1 (7.1%)
ZOPICLONE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ZOLPIDEM TARTRATE	1 (14.3%)	1 (14.3%)	2 (14.3%)
MYSLEE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTI-DEMENTIA DRUGS	0 (0.0%)	1 (14.3%)	1 (7.1%)
ARICEPT	0 (0.0%)	1 (14.3%)	1 (7.1%)
AGENTS AGAINST AMOEBIASIS AND OTHER PROTOZOAL DISE	0 (0.0%)	3 (42.9%)	3 (21.4%)
ATOVAQUONE	0 (0.0%)	2 (28.6%)	2 (14.3%)
SAMTIREL	0 (0.0%)	1 (14.3%)	1 (7.1%)
AGENTS AGAINST LEISHMANIASIS AND TRYPANOSOMIASIS	2 (28.6%)	0 (0.0%)	2 (14.3%)
BENAMBAX	1 (14.3%)	0 (0.0%)	1 (7.1%)
PENTAMIDINE ISETIONATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
THROAT PREPARATIONS	1 (14.3%)	0 (0.0%)	1 (7.1%)
SP TROCHES	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHAL	1 (14.3%)	0 (0.0%)	1 (7.1%)
INTAL	1 (14.3%)	0 (0.0%)	1 (7.1%)
ADRENERGICS FOR SYSTEMIC USE	1 (14.3%)	0 (0.0%)	1 (7.1%)
SULTANOL	1 (14.3%)	0 (0.0%)	1 (7.1%)
EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRE	0 (0.0%)	2 (28.6%)	2 (14.3%)
CARBOCISTEINE	0 (0.0%)	1 (14.3%)	1 (7.1%)
AMBROXOL HYDROCHLORIDE	0 (0.0%)	1 (14.3%)	1 (7.1%)
MUCOSAL /00546002/	0 (0.0%)	1 (14.3%)	1 (7.1%)
COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECT	0 (0.0%)	2 (28.6%)	2 (14.3%)
DEXTROMETHORPHAN HYDROBROMIDE	0 (0.0%)	2 (28.6%)	2 (14.3%)
MEDICON /00048102/	0 (0.0%)	1 (14.3%)	1 (7.1%)
ASTOMIN /00426502/	0 (0.0%)	1 (14.3%)	1 (7.1%)
ANTIHISTAMINES FOR SYSTEMIC USE	1 (14.3%)	1 (14.3%)	2 (14.3%)
FEXOFENADINE	1 (14.3%)	0 (0.0%)	1 (7.1%)
OLOPATADINE HYDROCHLORIDE	0 (0.0%)	1 (14.3%)	1 (7.1%)
BEPOTASTINE BESILATE	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
ANTIINFECTIVES	1 (14.3%)	0 (0.0%)	1 (7.1%)
MOXIFLOXACIN HYDROCHLORIDE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTIINFLAMMATORY AGENTS	1 (14.3%)	1 (14.3%)	2 (14.3%)
FLUOROMETHOLONE	0 (0.0%)	1 (14.3%)	1 (7.1%)
ODOMEL	1 (14.3%)	0 (0.0%)	1 (7.1%)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS	1 (14.3%)	0 (0.0%)	1 (7.1%)
TIMOLOL MALEATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
DECONGESTANTS AND ANTIALLERGICS	0 (0.0%)	1 (14.3%)	1 (7.1%)
TRANILAST	0 (0.0%)	1 (14.3%)	1 (7.1%)
OTHER OPHTHALMOLOGICALS	2 (28.6%)	0 (0.0%)	2 (14.3%)
PIRENOXINE	1 (14.3%)	0 (0.0%)	1 (7.1%)
SODIUM HYALURONATE	1 (14.3%)	0 (0.0%)	1 (7.1%)
ALL OTHER THERAPEUTIC PRODUCTS	0 (0.0%)	1 (14.3%)	1 (7.1%)
DL-METHIONINE	0 (0.0%)	1 (14.3%)	1 (7.1%)
MAGNETIC RESONANCE IMAGING CONTRAST MEDIA	1 (14.3%)	0 (0.0%)	1 (7.1%)
MAGNESCOPE	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

ATC class level 3 WHO-DDE drug name	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
ATC Class Level 3 not Available	0 (0.0%)	1 (14.3%)	1 (7.1%)
HERBAL PREPARATION	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.4.6
WHO-DDE Version 01Sep2016 was used to code medications.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
ATC class = Anatomical Therapeutic Chemical class
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of treatment.

表 2.7.4.7-19　併用薬（203 試験）（安全性解析対象集団）

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with at least one concomitant medication	39 (100.0)	16 (100.0)	55 (100.0)
ADRENERGICS FOR SYSTEMIC USE	1 (2.6)	1 (6.3)	2 (3.6)
HOKUNALIN /00654901/	1 (2.6)	0	1 (1.8)
METHYLEPHEDRINE HCL	0	1 (6.3)	1 (1.8)
ADRENERGICS, INHALANTS	6 (15.4)	0	6 (10.9)
SULTANOL	2 (5.1)	0	2 (3.6)
ADOAIR	1 (2.6)	0	1 (1.8)
PROCATEROL HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
SALBUTAMOL SULFATE	1 (2.6)	0	1 (1.8)
VENETLIN	1 (2.6)	0	1 (1.8)
AGENTS AGAINST AMOEBIASIS AND OTHER PROTOZOAL DISEASES	2 (5.1)	0	2 (3.6)
ATOVAQUONE	2 (5.1)	0	2 (3.6)
AGENTS AGAINST LEISHMANIASIS AND TRYPANOSOMIASIS	5 (12.8)	1 (6.3)	6 (10.9)
BENAMBAX	3 (7.7)	0	3 (5.5)
PENTAMIDINE ISETIONATE	2 (5.1)	0	2 (3.6)
PENTAMIDINE	0	1 (6.3)	1 (1.8)
AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL FISSURES FOR TOPICAL USE	1 (2.6)	0	1 (1.8)
POSTERISAN FORTE /01567801/	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ALL OTHER THERAPEUTIC PRODUCTS	1 (2.6)	1 (6.3)	2 (3.6)
ARGAMATE	1 (2.6)	0	1 (1.8)
FERBON	0	1 (6.3)	1 (1.8)
AMINOGLYCOSIDE ANTIBACTERIALS	1 (2.6)	1 (6.3)	2 (3.6)
GENTACIN	1 (2.6)	0	1 (1.8)
TOBRAMYCIN	0	1 (6.3)	1 (1.8)
ANESTHETICS, GENERAL	0	1 (6.3)	1 (1.8)
PROPOFOL	0	1 (6.3)	1 (1.8)
REMIFENTANIL	0	1 (6.3)	1 (1.8)
ANESTHETICS, LOCAL	7 (17.9)	2 (12.5)	9 (16.4)
XYLOCAINE /00033402/	3 (7.7)	0	3 (5.5)
LIDOCAINE	1 (2.6)	1 (6.3)	2 (3.6)
LIDOCAINE HYDROCHLORIDE MONOHYDRATE	2 (5.1)	0	2 (3.6)
XYLOCAINE WITH EPINEPHRINE	2 (5.1)	0	2 (3.6)
LIDOCAINE HCL	0	1 (6.3)	1 (1.8)
XYLOCAINE VISCOUS	1 (2.6)	0	1 (1.8)
ANGIOTENSIN II ANTAGONISTS, COMBINATIONS	1 (2.6)	0	1 (1.8)
CO DIO COMBINATION	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ANGIOTENSIN II ANTAGONISTS, PLAIN	8 (20.5)	1 (6.3)	9 (16.4)
OLMESARTAN MEDOXOMIL	2 (5.1)	0	2 (3.6)
TELMISARTAN	2 (5.1)	0	2 (3.6)
VALSARTAN	2 (5.1)	0	2 (3.6)
ATACAND	0	1 (6.3)	1 (1.8)
MICARDIS	1 (2.6)	0	1 (1.8)
OLMESARTAN OD	1 (2.6)	0	1 (1.8)
ANTACIDS	2 (5.1)	1 (6.3)	3 (5.5)
SODIUM BICARBONATE	2 (5.1)	0	2 (3.6)
ALMAGATE	0	1 (6.3)	1 (1.8)
ANTI-ACNE PREPARATIONS FOR TOPICAL USE	1 (2.6)	0	1 (1.8)
ACUATIM	1 (2.6)	0	1 (1.8)
ANTIARRHYTHMICS, CLASS I AND III	0	1 (6.3)	1 (1.8)
PROPAFENONE	0	1 (6.3)	1 (1.8)
ANTIBIOTICS FOR TOPICAL USE	3 (7.7)	1 (6.3)	4 (7.3)
GENTACIN	2 (5.1)	0	2 (3.6)
BEAROBAN	0	1 (6.3)	1 (1.8)
GENTAMICIN SULFATE	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ANTIDEPRESSANTS	2 (5.1)	0	2 (3.6)
CYMBALTA	1 (2.6)	0	1 (1.8)
TRAZODONE HCL	1 (2.6)	0	1 (1.8)
ANTIDIARRHEAL MICROORGANISMS	5 (12.8)	1 (6.3)	6 (10.9)
BIO-THREE	2 (5.1)	0	2 (3.6)
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	0	1 (6.3)	1 (1.8)
BIOFERMIN /07746301/	1 (2.6)	0	1 (1.8)
BIOFERMIN /14521401/	1 (2.6)	0	1 (1.8)
LACTOBACILLUS ACIDOPHILUS	0	1 (6.3)	1 (1.8)
LACTOMIN	1 (2.6)	0	1 (1.8)
ANTIEMETICS AND ANTINAUSEANTS	0	2 (12.5)	2 (3.6)
EMEND /01627301/	0	1 (6.3)	1 (1.8)
RAMOSETRON HYDROCHLORIDE	0	1 (6.3)	1 (1.8)
ANTIFUNGALS FOR TOPICAL USE	1 (2.6)	0	1 (1.8)
LULICONAZOLE	1 (2.6)	0	1 (1.8)
TERBINAFINE HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS	1 (2.6)	1 (6.3)	2 (3.6)
CARTEOLOL HYDROCHLORIDE	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
COSOPT	0	1 (6.3)	1 (1.8)
ANTIGOUT PREPARATIONS	9 (23.1)	0	9 (16.4)
FEBURIC	5 (12.8)	0	5 (9.1)
FEBUXOSTAT	3 (7.7)	0	3 (5.5)
ALLOPURINOL	1 (2.6)	0	1 (1.8)
ANTIHISTAMINES FOR SYSTEMIC USE	11 (28.2)	9 (56.3)	20 (36.4)
OLOPATADINE HYDROCHLORIDE	5 (12.8)	0	5 (9.1)
FEXOFENADINE	1 (2.6)	2 (12.5)	3 (5.5)
BEPOTASTINE BESILATE	1 (2.6)	1 (6.3)	2 (3.6)
CHLORPHENIRAMINE MALEATE	0	2 (12.5)	2 (3.6)
FEXOFENADINE HYDROCHLORIDE	2 (5.1)	0	2 (3.6)
PENIRAMIN	0	2 (12.5)	2 (3.6)
ADIPAM /00058402/	0	1 (6.3)	1 (1.8)
BEPOTAN	0	1 (6.3)	1 (1.8)
CHLORPHENIRAMINE /00072501/	0	1 (6.3)	1 (1.8)
DEXCHLORPHENIRAMINE MALEATE	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
EBASTEL	0	1 (6.3)	1 (1.8)
EMEDASTINE DIFUMARATE	0	1 (6.3)	1 (1.8)
EPINASTINE HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
LEVOCETIRIZINE HCL	0	1 (6.3)	1 (1.8)
LORATADINE	0	1 (6.3)	1 (1.8)
MEQUITAZINE	0	1 (6.3)	1 (1.8)
NEORESTAR	1 (2.6)	0	1 (1.8)
OLOPATADINE	0	1 (6.3)	1 (1.8)
PLAKON	0	1 (6.3)	1 (1.8)
POLARAMINE	1 (2.6)	0	1 (1.8)
TALION /01587402/	0	1 (6.3)	1 (1.8)
XYZAL	1 (2.6)	0	1 (1.8)
ANTIINFECTIVES	5 (12.8)	1 (6.3)	6 (10.9)
OFLOXACIN	2 (5.1)	0	2 (3.6)
COLISTIN SODIUM METHANESULFONATE	1 (2.6)	0	1 (1.8)
CRAVIT	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16 2.4 5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
LEVOFLOXACIN	1 (2.6)	0	1 (1.8)
LEVOFLOXACIN HYDRATE	1 (2.6)	0	1 (1.8)
TARIVID OTIC	0	1 (6.3)	1 (1.8)
VEGAMOX	1 (2.6)	0	1 (1.8)
ANTIINFLAMMATORY AGENTS	4 (10.3)	0	4 (7.3)
FLUOROMETHOLONE	2 (5.1)	0	2 (3.6)
DICLOD	1 (2.6)	0	1 (1.8)
FLUMETHOLON	1 (2.6)	0	1 (1.8)
NEVANAC	1 (2.6)	0	1 (1.8)
PRANOPROFEN	1 (2.6)	0	1 (1.8)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	15 (38.5)	8 (50.0)	23 (41.8)
LOXOPROFEN SODIUM HYDRATE	4 (10.3)	0	4 (7.3)
CELECOXIB	2 (5.1)	1 (6.3)	3 (5.5)
CAROL-F	0	2 (12.5)	2 (3.6)
LOBU	2 (5.1)	0	2 (3.6)
LOXOPROFEN	1 (2.6)	1 (6.3)	2 (3.6)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

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ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
NAPROXEN	2 (5.1)	0	2 (3.6)
AIRTAL	0	1 (6.3)	1 (1.8)
ARGININE W/IBUPROFEN	0	1 (6.3)	1 (1.8)
DICLOFENAC SODIUM	1 (2.6)	0	1 (1.8)
HYDROXYCHLOROQUINE	0	1 (6.3)	1 (1.8)
KETOPROFEN	1 (2.6)	0	1 (1.8)
KETOROLAC TROMETHAMINE	0	1 (6.3)	1 (1.8)
LOXONIN	1 (2.6)	0	1 (1.8)
LOXOPROFEN NA	1 (2.6)	0	1 (1.8)
LOXOPROFEN SODIUM	1 (2.6)	0	1 (1.8)
MELOXICAM	0	1 (6.3)	1 (1.8)
MOBIC	0	1 (6.3)	1 (1.8)
NAXEN S	0	1 (6.3)	1 (1.8)
SERACTIL	0	1 (6.3)	1 (1.8)
SOLANTAL	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
VOLTAREN /00372301/	1 (2.6)	0	1 (1.8)
ZALTOPROFEN	0	1 (6.3)	1 (1.8)
ANTIMIGRAINE PREPARATIONS	1 (2.6)	0	1 (1.8)
AMERGE	1 (2.6)	0	1 (1.8)
IMIGRAN /01044801/	1 (2.6)	0	1 (1.8)
MIGSIS	1 (2.6)	0	1 (1.8)
ANTIMYCOTICS FOR SYSTEMIC USE	3 (7.7)	0	3 (5.5)
ITRIZOLE	2 (5.1)	0	2 (3.6)
ITRACONAZOLE	1 (2.6)	0	1 (1.8)
ANTIPROPULSIVES	2 (5.1)	2 (12.5)	4 (7.3)
LOPERAMIDE HYDROCHLORIDE	2 (5.1)	0	2 (3.6)
LOPMIN	0	2 (12.5)	2 (3.6)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	4 (10.3)	0	4 (7.3)
RESTAMIN KOWA	2 (5.1)	0	2 (3.6)
DIPHENHYDRAMINE	1 (2.6)	0	1 (1.8)
LIDOCAINE	1 (2.6)	0	1 (1.8)
ANTIPSYCHOTICS	0	1 (6.3)	1 (1.8)
OLANZAPINE	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ANTISEPTICS AND DISINFECTANTS		2 (5.1)	0	2 (3.6)
CADEX	/00082201/	1 (2.6)	0	1 (1.8)
ISODINE	/00080001/	1 (2.6)	0	1 (1.8)
ANTITHROMBOTIC AGENTS		9 (23.1)	3 (18.8)	12 (21.8)
ASPIRIN	/00002701/	2 (5.1)	0	2 (3.6)
HEPARIN SODIUM		1 (2.6)	1 (6.3)	2 (3.6)
RIVAROXABAN		1 (2.6)	1 (6.3)	2 (3.6)
APIXABAN		1 (2.6)	0	1 (1.8)
BAYASPIRIN		1 (2.6)	0	1 (1.8)
GIGKYOTACIN		0	1 (6.3)	1 (1.8)
HEPAFLUSH		1 (2.6)	0	1 (1.8)
HEPARIN NA LOCK		1 (2.6)	0	1 (1.8)
LIXIANA		1 (2.6)	0	1 (1.8)
PRAZAXA		1 (2.6)	0	1 (1.8)
STREPTODORNASE W/STREPTOKINASE		0	1 (6.3)	1 (1.8)
WARFARIN POTASSIUM		1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

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Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ANTIVARICOSE THERAPY	1 (2.6)	0	1 (1.8)
HEPARINOID	1 (2.6)	0	1 (1.8)
ANXIOLYTICS	4 (10.3)	2 (12.5)	6 (10.9)
CERCINE	2 (5.1)	0	2 (3.6)
CLOBAZAM	0	1 (6.3)	1 (1.8)
CLOTIAZEPAM	1 (2.6)	0	1 (1.8)
ETIZOLAM	1 (2.6)	0	1 (1.8)
LORAZEPAM	0	1 (6.3)	1 (1.8)
TOFISOPAM	0	1 (6.3)	1 (1.8)
ASCORBIC ACID (VITAMIN C), INCL. COMBINATIONS	1 (2.6)	0	1 (1.8)
CINAL	1 (2.6)	0	1 (1.8)
BACTERIAL AND VIRAL VACCINES, COMBINED	0	1 (6.3)	1 (1.8)
PENTAXIM	0	1 (6.3)	1 (1.8)
BACTERIAL VACCINES	0	1 (6.3)	1 (1.8)
PREVENAR	0	1 (6.3)	1 (1.8)
BELLADONNA AND DERIVATIVES, PLAIN	2 (5.1)	1 (6.3)	3 (5.5)
SCOPOLAMINE BUTYLBROMIDE	2 (5.1)	0	2 (3.6)
BUSCOPAN	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

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Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
BETA BLOCKING AGENTS	3 (7.7)	1 (6.3)	4 (7.3)
BISOPROLOL FUMARATE	2 (5.1)	0	2 (3.6)
AROTINOLOL HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
CARVEDILOL	0	1 (6.3)	1 (1.8)
BETA-LACTAM ANTIBACTERIALS, PENICILLINS	3 (7.7)	3 (18.8)	6 (10.9)
AMOXICILLIN HYDRATE	2 (5.1)	0	2 (3.6)
NAFCILLIN	0	1 (6.3)	1 (1.8)
TAZOCIN	0	1 (6.3)	1 (1.8)
TAZOLACTAM	0	1 (6.3)	1 (1.8)
TAZOPERAN	0	1 (6.3)	1 (1.8)
TAZOPIPE	1 (2.6)	0	1 (1.8)
BILE THERAPY	3 (7.7)	3 (18.8)	6 (10.9)
URSODEOXYCHOLIC ACID	3 (7.7)	0	3 (5.5)
UDCA	0	2 (12.5)	2 (3.6)
URSA	0	1 (6.3)	1 (1.8)
BLOOD AND RELATED PRODUCTS	0	1 (6.3)	1 (1.8)
ALBUMIN	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	9 (23.1)	2 (12.5)	11 (20.0)
SITAGLIPTIN PHOSPHATE MONOHYDRATE	5 (12.8)	0	5 (9.1)
GLACTIV	1 (2.6)	0	1 (1.8)
GLIMEPIRIDE	1 (2.6)	0	1 (1.8)
GLIMIN	0	1 (6.3)	1 (1.8)
LINAGLIPTIN	1 (2.6)	0	1 (1.8)
METFORMIN	0	1 (6.3)	1 (1.8)
METFORMIN HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
METGLUCO	1 (2.6)	0	1 (1.8)
PIOGLITAZONE	1 (2.6)	0	1 (1.8)
SITAGLIPTIN	0	1 (6.3)	1 (1.8)
SUINY	1 (2.6)	0	1 (1.8)
TENELIGLIPTIN HYDROBROMIDE	1 (2.6)	0	1 (1.8)
TRAZENTA	1 (2.6)	0	1 (1.8)
CALCIUM	1 (2.6)	1 (6.3)	2 (3.6)
CALCIUM W/MAGNESIUM	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
DICAMAX-D	0	1 (6.3)	1 (1.8)
CAPILLARY STABILIZING AGENTS	0	1 (6.3)	1 (1.8)
VENITOL	0	1 (6.3)	1 (1.8)
CARDIOVASCULAR SYSTEM	1 (2.6)	0	1 (1.8)
MYOVIEW /02203201/	1 (2.6)	0	1 (1.8)
CORTICOSTEROIDS FOR SYSTEMIC USE, COMBINATIONS	2 (5.1)	0	2 (3.6)
BETAMETHASONE W/DEXCHLORPHENIRAMINE MALEATE	2 (5.1)	0	2 (3.6)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	6 (15.4)	6 (37.5)	12 (21.8)
PREDNISOLONE	3 (7.7)	3 (18.8)	6 (10.9)
HYDROCORTISONE SODIUM SUCCINATE	2 (5.1)	1 (6.3)	3 (5.5)
CALCORT	0	1 (6.3)	1 (1.8)
HYDROCORTISONE	0	1 (6.3)	1 (1.8)
HYDROCORTISONE SODIUM	0	1 (6.3)	1 (1.8)
METHYLPREDNISOLONE SODIUM SUCCINATE	1 (2.6)	0	1 (1.8)
PREDNIN	1 (2.6)	0	1 (1.8)
TRIAMCINOLONE	0	1 (6.3)	1 (1.8)
CORTICOSTEROIDS, COMBINATIONS WITH ANTIBIOTICS	2 (5.1)	0	2 (3.6)
DERMOSOL G	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
STRONG RESTAMIN	1 (2.6)	0	1 (1.8)
CORTICOSTEROIDS, PLAIN	13 (33.3)	5 (31.3)	18 (32.7)
ANTEBATE	4 (10.3)	0	4 (7.3)
DERMOVATE	2 (5.1)	1 (6.3)	3 (5.5)
ALMETA	2 (5.1)	0	2 (3.6)
DESOWEN	0	2 (12.5)	2 (3.6)
LACTICARE HC /00028601/	0	2 (12.5)	2 (3.6)
LOCOID	2 (5.1)	0	2 (3.6)
ANFLAVATE	1 (2.6)	0	1 (1.8)
BETAMETHASONE BUTYRATE PROPIONATE	1 (2.6)	0	1 (1.8)
CLOBETASONE BUTYRATE	1 (2.6)	0	1 (1.8)
DESOXYMETHASONE	0	1 (6.3)	1 (1.8)
DIFLUPREDNATE	1 (2.6)	0	1 (1.8)
DRENISON /00182901/	1 (2.6)	0	1 (1.8)
ESPERSON	0	1 (6.3)	1 (1.8)
HYDROCORTISONE	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

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ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
LIDOMEX	1 (2.6)	0	1 (1.8)
METHADERM	1 (2.6)	0	1 (1.8)
METHYLPREDNISOLONE ACEPONATE	0	1 (6.3)	1 (1.8)
MYSER /01249201/	1 (2.6)	0	1 (1.8)
PSOREX	0	1 (6.3)	1 (1.8)
RINDERON DP	1 (2.6)	0	1 (1.8)
RINDERON-V	1 (2.6)	0	1 (1.8)
SOLVEGA	1 (2.6)	0	1 (1.8)
COUGH SUPPRESSANTS AND EXPECTORANTS, COMBINATIONS	0	1 (6.3)	1 (1.8)
COUGH S	0	1 (6.3)	1 (1.8)
COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECTORANTS	2 (5.1)	2 (12.5)	4 (7.3)
ASVERIN /00465502/	1 (2.6)	0	1 (1.8)
CODEINE	0	1 (6.3)	1 (1.8)
COUGH SYRUP /06155801/	0	1 (6.3)	1 (1.8)
MEDICON /00048102/	1 (2.6)	0	1 (1.8)
DECONGESTANTS AND ANTIALLERGICS	1 (2.6)	1 (6.3)	2 (3.6)
ALESION	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
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ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
OLOPATADINE	0	1 (6.3)	1 (1.8)
DECONGESTANTS AND OTHER NASAL PREPARATIONS FOR TOPICAL USE	1 (2.6)	2 (12.5)	3 (5.5)
AVAMYS	0	1 (6.3)	1 (1.8)
AZELASTINE HCL	0	1 (6.3)	1 (1.8)
MOMETASONE FUROATE	0	1 (6.3)	1 (1.8)
NASONEX	1 (2.6)	0	1 (1.8)
DIGESTIVES, INCL. ENZYMES	0	3 (18.8)	3 (5.5)
PHAZYME COMPLEX	0	2 (12.5)	2 (3.6)
BESZYME	0	1 (6.3)	1 (1.8)
DIRECT ACTING ANTIVIRALS	13 (33.3)	1 (6.3)	14 (25.5)
ACICLOVIR	8 (20.5)	0	8 (14.5)
VICCLOX /00587301/	3 (7.7)	0	3 (5.5)
ACLOVA /00587301/	0	1 (6.3)	1 (1.8)
ENTECAVIR MONOHYDRATE	1 (2.6)	0	1 (1.8)
PERAMIVIR	1 (2.6)	0	1 (1.8)
VALGANCICLOVIR HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
VALTREX	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
XOFLUZA		1 (2.6)	0	1 (1.8)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION		2 (5.1)	0	2 (3.6)
ACTONEL		1 (2.6)	0	1 (1.8)
SODIUM RISEDRONATE HYDRATE		1 (2.6)	0	1 (1.8)
DRUGS FOR CONSTIPATION		18 (46.2)	2 (12.5)	20 (36.4)
MAGNESIUM OXIDE		10 (25.6)	0	10 (18.2)
MAGMITT		3 (7.7)	0	3 (5.5)
SENNOSIDE	/00571901/	3 (7.7)	0	3 (5.5)
BISACODYL		1 (2.6)	0	1 (1.8)
DUPHALAC EASY		0	1 (6.3)	1 (1.8)
GLYCERIN	/00200601/	1 (2.6)	0	1 (1.8)
LACTULOSE		0	1 (6.3)	1 (1.8)
LAXOBERON		1 (2.6)	0	1 (1.8)
LUBIPROSTONE		1 (2.6)	0	1 (1.8)
MACROGOL		1 (2.6)	0	1 (1.8)
MAGCOROL P		1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
NIFLEC	1 (2.6)	0	1 (1.8)
PICOSULFATE NA	1 (2.6)	0	1 (1.8)
PURSENNID /00571902/	1 (2.6)	0	1 (1.8)
SENNARIDE	1 (2.6)	0	1 (1.8)
SENNOSIDE A+B CALCIUM	1 (2.6)	0	1 (1.8)
SODIUM PICOSULFATE	1 (2.6)	0	1 (1.8)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	4 (10.3)	2 (12.5)	6 (10.9)
DIMETHICONE	2 (5.1)	0	2 (3.6)
BALGIN ANTIFOAMING	1 (2.6)	0	1 (1.8)
BROMOCTYL	0	1 (6.3)	1 (1.8)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDE	0	1 (6.3)	1 (1.8)
GASCON	1 (2.6)	0	1 (1.8)
GLYCOPYRROLATE /00196201/	0	1 (6.3)	1 (1.8)
MENOCTYL	0	1 (6.3)	1 (1.8)
OCTYLONIUM BROMIDE	0	1 (6.3)	1 (1.8)
SPAROD	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
TIRAM /01183002/	0	1 (6.3)	1 (1.8)
TIROPRAMIDE HYDROCHLORIDE	0	1 (6.3)	1 (1.8)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	26 (66.7)	11 (68.8)	37 (67.3)
LANSOPRAZOLE	7 (17.9)	2 (12.5)	9 (16.4)
REBAMIPIDE	5 (12.8)	1 (6.3)	6 (10.9)
NEXIUM /01479302/	3 (7.7)	2 (12.5)	5 (9.1)
RABEPRAZOLE SODIUM	5 (12.8)	0	5 (9.1)
ESOMEPRAZOLE MAGNESIUM	3 (7.7)	0	3 (5.5)
IRSOGLADINE MALEATE	2 (5.1)	1 (6.3)	3 (5.5)
ALBIS D	0	2 (12.5)	2 (3.6)
FAMOTIDINE	1 (2.6)	1 (6.3)	2 (3.6)
MUCOSTA	0	2 (12.5)	2 (3.6)
RABIET	0	2 (12.5)	2 (3.6)
RANITIDINE	0	2 (12.5)	2 (3.6)
AZUNOL /00317302/	1 (2.6)	0	1 (1.8)
CALCIUM CARBONATE W/SODIUM ALGINATE/SODIUM BI	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

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ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
CURAN		0	1 (6.3)	1 (1.8)
EUPATILIN		0	1 (6.3)	1 (1.8)
GASTER	/00706001/	0	1 (6.3)	1 (1.8)
LANSOPRAZOLE TEVA		1 (2.6)	0	1 (1.8)
LANSOPRAZOLE TOWA		1 (2.6)	0	1 (1.8)
LANSTON		0	1 (6.3)	1 (1.8)
LANSTON LFDT		0	1 (6.3)	1 (1.8)
OMEPRAZOLE		1 (2.6)	0	1 (1.8)
POLAPREZINC		1 (2.6)	0	1 (1.8)
RABEPRAZOLE NA		1 (2.6)	0	1 (1.8)
STOGAR		0	1 (6.3)	1 (1.8)
TAKECAB		1 (2.6)	0	1 (1.8)
TEPRENONE		1 (2.6)	0	1 (1.8)
ULCERLMIN		0	1 (6.3)	1 (1.8)
ULCERMIN	/00434701/	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16 2.4 5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
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Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY		3 (7.7)	1 (6.3)	4 (7.3)
AVOLVE		1 (2.6)	0	1 (1.8)
FLIVAS		1 (2.6)	0	1 (1.8)
SILODOSIN		1 (2.6)	0	1 (1.8)
TAMSULOSIN		0	1 (6.3)	1 (1.8)
URIEF		1 (2.6)	0	1 (1.8)
EMOLLIENTS AND PROTECTIVES		13 (33.3)	0	13 (23.6)
HIRUDOID		6 (15.4)	0	6 (10.9)
HEPARINOID		5 (12.8)	0	5 (9.1)
WHITE PETROLATUM		2 (5.1)	0	2 (3.6)
BESOFTEN		1 (2.6)	0	1 (1.8)
JUVELA	/00110502/	1 (2.6)	0	1 (1.8)
PETROLATUM		1 (2.6)	0	1 (1.8)
SALICYLIC ACID		1 (2.6)	0	1 (1.8)
UREA		1 (2.6)	0	1 (1.8)
VASELINE	/01007601/	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRESSANTS	6 (15.4)	4 (25.0)	10 (18.2)
CARBOCISTEINE	2 (5.1)	0	2 (3.6)
ERDOSTEINE	0	2 (12.5)	2 (3.6)
ACETYLCYSTEINE	0	1 (6.3)	1 (1.8)
AMBROXOL	0	1 (6.3)	1 (1.8)
AMBROXOL HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
BISOLVON	1 (2.6)	0	1 (1.8)
MUCODYNE	1 (2.6)	0	1 (1.8)
MUCOMYST /00082801/	0	1 (6.3)	1 (1.8)
RESPLEN	1 (2.6)	0	1 (1.8)
HIGH-CEILING DIURETICS	1 (2.6)	2 (12.5)	3 (5.5)
FUROSEMIDE	0	2 (12.5)	2 (3.6)
AZOSEMIDE	1 (2.6)	0	1 (1.8)
HYPNOTICS AND SEDATIVES	10 (25.6)	3 (18.8)	13 (23.6)
ZOLPIDEM TARTRATE	3 (7.7)	1 (6.3)	4 (7.3)
BROTIZOLAM	2 (5.1)	0	2 (3.6)
ZOLPIDEM	1 (2.6)	1 (6.3)	2 (3.6)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ARON	0	1 (6.3)	1 (1.8)
BELSOMRA	1 (2.6)	0	1 (1.8)
ESZOPICLONE	1 (2.6)	0	1 (1.8)
LUNESTA	1 (2.6)	0	1 (1.8)
MELATONIN	0	1 (6.3)	1 (1.8)
MYSLEE	1 (2.6)	0	1 (1.8)
RAMELTEON	1 (2.6)	0	1 (1.8)
ROZEREM	1 (2.6)	0	1 (1.8)
SUVOREXANT	1 (2.6)	0	1 (1.8)
I.V. SOLUTION ADDITIVES	3 (7.7)	5 (31.3)	8 (14.5)
MAGNESIUM SULFATE	0	3 (18.8)	3 (5.5)
NORMAL SALINE	2 (5.1)	0	2 (3.6)
CALCIUM CHLORIDE	0	1 (6.3)	1 (1.8)
CALCIUM GLUCONATE	0	1 (6.3)	1 (1.8)
KCL	0	1 (6.3)	1 (1.8)
PHOSTEN	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16 2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

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ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
SODIUM BICARBONATE	0	1 (6.3)	1 (1.8)
SODIUM CHLORIDE	1 (2.6)	0	1 (1.8)
TAMIPOOL	0	1 (6.3)	1 (1.8)
I.V. SOLUTIONS	5 (12.8)	4 (25.0)	9 (16.4)
BFLUID	3 (7.7)	0	3 (5.5)
ELEJECT	1 (2.6)	0	1 (1.8)
FULCALIQ	1 (2.6)	0	1 (1.8)
KCL	0	1 (6.3)	1 (1.8)
LACTEC G	1 (2.6)	0	1 (1.8)
LIPIDS NOS	0	1 (6.3)	1 (1.8)
NORMAL SALINE	1 (2.6)	0	1 (1.8)
OLIMEL N9E	0	1 (6.3)	1 (1.8)
OMAPONE PERI	0	1 (6.3)	1 (1.8)
POTACOL R	1 (2.6)	0	1 (1.8)
POTASSIUM CHLORIDE	1 (2.6)	0	1 (1.8)
SODIUM CHLORIDE	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
SOLDEM 1		1 (2.6)	0	1 (1.8)
IMMUNOGLOBULINS		1 (2.6)	0	1 (1.8)
VENOGLOBULIN IH		1 (2.6)	0	1 (1.8)
IMMUNOSTIMULANTS		15 (38.5)	4 (25.0)	19 (34.5)
FILGRASTIM		6 (15.4)	1 (6.3)	7 (12.7)
FILGRASTIM BS	/06441101/	3 (7.7)	0	3 (5.5)
FILGRASTIM RECOMBINANT		2 (5.1)	0	2 (3.6)
GRASIN		0	2 (12.5)	2 (3.6)
LENOGRASTIM		2 (5.1)	0	2 (3.6)
NEUTROGIN		2 (5.1)	0	2 (3.6)
G LASTA		1 (2.6)	0	1 (1.8)
G-CSF		0	1 (6.3)	1 (1.8)
GRAN		1 (2.6)	0	1 (1.8)
INSULINS AND ANALOGUES		3 (7.7)	3 (18.8)	6 (10.9)
INSULIN HUMAN		2 (5.1)	0	2 (3.6)
NOVORAPID		0	2 (12.5)	2 (3.6)
INSULIN		0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
INSULIN ASPART	1 (2.6)	0	1 (1.8)
INSULIN GLARGINE	0	1 (6.3)	1 (1.8)
LANTUS	0	1 (6.3)	1 (1.8)
TOUJEO	0	1 (6.3)	1 (1.8)
INTESTINAL ADSORBENTS	0	3 (18.8)	3 (5.5)
SMECTA /07327601/	0	2 (12.5)	2 (3.6)
DIOSMECTITE	0	1 (6.3)	1 (1.8)
INTESTINAL ANTIINFECTIVES	0	1 (6.3)	1 (1.8)
NORMIX	0	1 (6.3)	1 (1.8)
IRON PREPARATIONS	2 (5.1)	0	2 (3.6)
FERROUS SODIUM CITRATE	2 (5.1)	0	2 (3.6)
IRRIGATING SOLUTIONS	1 (2.6)	0	1 (1.8)
NORMAL SALINE	1 (2.6)	0	1 (1.8)
LIPID MODIFYING AGENTS, PLAIN	9 (23.1)	1 (6.3)	10 (18.2)
ATORVASTATIN	2 (5.1)	0	2 (3.6)
ATORVASTATIN CALCIUM	1 (2.6)	0	1 (1.8)
BEZAFIBRATE	1 (2.6)	0	1 (1.8)
CRESTOR	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

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Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ETHYL ICOSAPENTATE	1 (2.6)	0	1 (1.8)
LIVALO	1 (2.6)	0	1 (1.8)
PRAVASTATIN	1 (2.6)	0	1 (1.8)
PRAVASTATIN SODIUM	1 (2.6)	0	1 (1.8)
SIMVASTATIN	0	1 (6.3)	1 (1.8)
ZETIA	1 (2.6)	0	1 (1.8)
LIVER THERAPY, LIPOTROPICS	1 (2.6)	1 (6.3)	2 (3.6)
HEPA-MERZ /01390204/	0	1 (6.3)	1 (1.8)
HISHIPHAGEN COMBINATION	1 (2.6)	0	1 (1.8)
LOW-CEILING DIURETICS, THIAZIDES	1 (2.6)	0	1 (1.8)
TRICHLORMETHIAZIDE	1 (2.6)	0	1 (1.8)
MUSCLE RELAXANTS, CENTRALLY ACTING AGENTS	1 (2.6)	1 (6.3)	2 (3.6)
BACLOFEN	0	1 (6.3)	1 (1.8)
EPERISONE HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
EXOPERINE	0	1 (6.3)	1 (1.8)
MUSCLE RELAXANTS, PERIPHERALLY ACTING AGENTS	0	1 (6.3)	1 (1.8)
ROCUMERON	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
MYDRIATICS AND CYCLOPLEGICS	1 (2.6)	0	1 (1.8)
MYDRIN-P	1 (2.6)	0	1 (1.8)
NASAL DECONGESTANTS FOR SYSTEMIC USE	1 (2.6)	2 (12.5)	3 (5.5)
ACTIFED /00005601/	0	1 (6.3)	1 (1.8)
ALLEGRA D	0	1 (6.3)	1 (1.8)
CONTAC 600 PLUS	1 (2.6)	0	1 (1.8)
PSEUDOEPHEDRINE	0	1 (6.3)	1 (1.8)
OPIOIDS	8 (20.5)	8 (50.0)	16 (29.1)
TRAMAL	3 (7.7)	0	3 (5.5)
TRAMCET	3 (7.7)	0	3 (5.5)
TARGIN	0	2 (12.5)	2 (3.6)
ULTRACET SEMI	0	2 (12.5)	2 (3.6)
DUROGESIC	0	1 (6.3)	1 (1.8)
FENTORA	0	1 (6.3)	1 (1.8)
IRCODON	0	1 (6.3)	1 (1.8)
MORPHINE	0	1 (6.3)	1 (1.8)
NUCYNTA ER	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16 2.4 5

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ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
OXYCODONE	0	1 (6.3)	1 (1.8)
OXYCODONE HYDROCHLORIDE	1 (2.6)	0	1 (1.8)
PABRON S ALPHA	1 (2.6)	0	1 (1.8)
TACOPEN	0	1 (6.3)	1 (1.8)
TRIDOL	0	1 (6.3)	1 (1.8)
ULTRACET	0	1 (6.3)	1 (1.8)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	7 (17.9)	1 (6.3)	8 (14.5)
MIYA-BM	6 (15.4)	0	6 (10.9)
POLAPREZINC	1 (2.6)	1 (6.3)	2 (3.6)
OTHER ANALGESICS AND ANTIPYRETICS	22 (56.4)	4 (25.0)	26 (47.3)
ACETAMINOPHEN	8 (20.5)	4 (25.0)	12 (21.8)
CALONAL	8 (20.5)	0	8 (14.5)
LYRICA OD	3 (7.7)	0	3 (5.5)
CYMBALTA	1 (2.6)	1 (6.3)	2 (3.6)
BUFFERIN A /01754001/	1 (2.6)	0	1 (1.8)
DENOGAN	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
GABAPENTIN	0	1 (6.3)	1 (1.8)
PL	1 (2.6)	0	1 (1.8)
PREGABALIN	1 (2.6)	0	1 (1.8)
PROPACETAMOL HYDROCHLORIDE	0	1 (6.3)	1 (1.8)
OTHER ANTIANEMIC PREPARATIONS	0	3 (18.8)	3 (5.5)
NESP	0	3 (18.8)	3 (5.5)
OTHER ANTIBACTERIALS	0	3 (18.8)	3 (5.5)
METRONIDAZOLE	0	2 (12.5)	2 (3.6)
FLASINYL	0	1 (6.3)	1 (1.8)
TEICONIN	0	1 (6.3)	1 (1.8)
OTHER BETA-LACTAM ANTIBACTERIALS	6 (15.4)	5 (31.3)	11 (20.0)
CEFDINIR	2 (5.1)	1 (6.3)	3 (5.5)
CEFCAPENE PIVOXIL HYDROCHLORIDE	2 (5.1)	0	2 (3.6)
CEFPODOXIME	0	2 (12.5)	2 (3.6)
CEFACLOR	0	1 (6.3)	1 (1.8)
CEFDITOREN PIVOXIL	0	1 (6.3)	1 (1.8)
CEFEPIME DIHYDROCHLORIDE	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

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ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
CEFEPIME HCL	0	1 (6.3)	1 (1.8)
CEFTRIAXONE	0	1 (6.3)	1 (1.8)
CEPHRADINE MONOHYDRATE	0	1 (6.3)	1 (1.8)
FAROPENEM SODIUM	1 (2.6)	0	1 (1.8)
MAXIPIME	1 (2.6)	0	1 (1.8)
MEIACT MS	1 (2.6)	0	1 (1.8)
MEROPEN /01250501/	0	1 (6.3)	1 (1.8)
MEROPENEM	1 (2.6)	0	1 (1.8)
OTHER CARDIAC PREPARATIONS	1 (2.6)	0	1 (1.8)
ADENOSINE	1 (2.6)	0	1 (1.8)
OTHER COLD PREPARATIONS	1 (2.6)	0	1 (1.8)
OTHER COLD PREPARATIONS	1 (2.6)	0	1 (1.8)
OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS	0	1 (6.3)	1 (1.8)
ATROVENT UDV	0	1 (6.3)	1 (1.8)
OTHER HEMATOLOGICAL AGENTS	2 (5.1)	0	2 (3.6)
PRONASE	1 (2.6)	0	1 (1.8)
PRONASE MS	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
OTHER MINERAL SUPPLEMENTS	3 (7.7)	4 (25.0)	7 (12.7)
MAGNESIUM OXIDE	0	2 (12.5)	2 (3.6)
SODIUM CHLORIDE	2 (5.1)	0	2 (3.6)
JOULIE SOL	0	1 (6.3)	1 (1.8)
MAGMITT	1 (2.6)	0	1 (1.8)
MAGNESIUM LACTATE W/PYRIDOXINE HYDROCHLORIDE	0	1 (6.3)	1 (1.8)
MAGO /07349401/	0	1 (6.3)	1 (1.8)
ZINC SULFATE HEPTAHYDRATE	0	1 (6.3)	1 (1.8)
OTHER NUTRIENTS	0	4 (25.0)	4 (7.3)
ENCOVER	0	3 (18.8)	3 (5.5)
WINUF PERI	0	1 (6.3)	1 (1.8)
OTHER OPHTHALMOLOGICALS	5 (12.8)	1 (6.3)	6 (10.9)
KARY UNI /00528801/	2 (5.1)	0	2 (3.6)
SODIUM HYALURONATE	2 (5.1)	0	2 (3.6)
CYANOCOBALAMIN	1 (2.6)	0	1 (1.8)
DIQUAS	1 (2.6)	0	1 (1.8)
LANOLIN ANHYDROUS	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
OTHER OTOLOGICALS	1 (2.6)	0	1 (1.8)
GLYCERIN /00200601/	1 (2.6)	0	1 (1.8)
SODIUM BICARBONATE	1 (2.6)	0	1 (1.8)
OTHER SYSTEMIC DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	0	1 (6.3)	1 (1.8)
LUKIO	0	1 (6.3)	1 (1.8)
OTHER VITAMIN PRODUCTS, COMBINATIONS	2 (5.1)	0	2 (3.6)
HERBAL NOS W/VITAMINS NOS	1 (2.6)	0	1 (1.8)
VITAMINS, OTHER COMBINATIONS	1 (2.6)	0	1 (1.8)
PARASYMPATHOMIMETICS	0	2 (12.5)	2 (3.6)
BETHANECHOL	0	1 (6.3)	1 (1.8)
PYRIDOSTIGMINE BROMIDE	0	1 (6.3)	1 (1.8)
PERIPHERAL VASODILATORS	2 (5.1)	0	2 (3.6)
PLETAAL	1 (2.6)	0	1 (1.8)
PRORENAL	1 (2.6)	0	1 (1.8)
POTASSIUM	4 (10.3)	1 (6.3)	5 (9.1)
POTASSIUM ASPARTATE	2 (5.1)	0	2 (3.6)
K-CONTIN	0	1 (6.3)	1 (1.8)
KCL	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16 2.4 5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
POTASSIUM CHLORIDE		1 (2.6)	0	1 (1.8)
SLOW-K		1 (2.6)	0	1 (1.8)
POTASSIUM-SPARING AGENTS		1 (2.6)	0	1 (1.8)
SPIRONOLACTONE		1 (2.6)	0	1 (1.8)
PROGESTOGENS		0	1 (6.3)	1 (1.8)
MEGESTROL		0	1 (6.3)	1 (1.8)
PROPULSIVES		7 (17.9)	4 (25.0)	11 (20.0)
PRAMIEL	/00041901/	2 (5.1)	0	2 (3.6)
PRIMPERAN		2 (5.1)	0	2 (3.6)
TERPERAN		2 (5.1)	0	2 (3.6)
ACOTIAMIDE HYDROCHLORIDE		1 (2.6)	0	1 (1.8)
ITOPRIDE		0	1 (6.3)	1 (1.8)
ITOPRIDE HCL		0	1 (6.3)	1 (1.8)
MACPERAN		0	1 (6.3)	1 (1.8)
MECOOL		0	1 (6.3)	1 (1.8)
METOCLOPRAMIDE		1 (2.6)	0	1 (1.8)
METOCLOPRAMIDE HCL		0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
QUINOLONE ANTIBACTERIALS	1 (2.6)	4 (25.0)	5 (9.1)
CRAVIT	0	2 (12.5)	2 (3.6)
LEVOPLUS /01278901/	0	1 (6.3)	1 (1.8)
MOXIFLOXACIN	0	1 (6.3)	1 (1.8)
TOSUFLOXACIN TOSILATE MONOHYDRATE	1 (2.6)	0	1 (1.8)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIRECT CARDIAC EFFECTS	0	1 (6.3)	1 (1.8)
DILTIAZEM	0	1 (6.3)	1 (1.8)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	9 (23.1)	1 (6.3)	10 (18.2)
AMLODIPINE	4 (10.3)	0	4 (7.3)
AMLODIPINE BESILATE	3 (7.7)	0	3 (5.5)
AMLODIN	1 (2.6)	0	1 (1.8)
AMODIPIN	0	1 (6.3)	1 (1.8)
NIFEDIPINE	1 (2.6)	0	1 (1.8)
STOMATOLOGICAL PREPARATIONS	9 (23.1)	1 (6.3)	10 (18.2)
AZUNOL GARGLE LIQUID	4 (10.3)	0	4 (7.3)
SODIUM GUALENATE HYDRATE	2 (5.1)	0	2 (3.6)
BENZYDAMINE HCL	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ISOTONIC SODIUM CHLORIDE SOLUTION	1 (2.6)	0	1 (1.8)
LIDOCAINE HCL	0	1 (6.3)	1 (1.8)
NYSTATIN	0	1 (6.3)	1 (1.8)
POVIDONE-IODINE	1 (2.6)	0	1 (1.8)
SODIUM CHLORIDE	1 (2.6)	0	1 (1.8)
SULFONAMIDES AND TRIMETHOPRIM	19 (48.7)	2 (12.5)	21 (38.2)
DAIPHEN	11 (28.2)	0	11 (20.0)
BACTRAMIN	4 (10.3)	0	4 (7.3)
BAKTAR	4 (10.3)	0	4 (7.3)
SEPTRIN	0	1 (6.3)	1 (1.8)
SULFAMETHOXAZOLE W/TRIMETHOPRIM	0	1 (6.3)	1 (1.8)
THROAT PREPARATIONS	3 (7.7)	0	3 (5.5)
AZ COMBINATION	1 (2.6)	0	1 (1.8)
NEOSTELIN GREEN	1 (2.6)	0	1 (1.8)
SODIUM BICARBONATE W/SODIUM GUALENATE HYDRATE	1 (2.6)	0	1 (1.8)
THYROID PREPARATIONS	2 (5.1)	1 (6.3)	3 (5.5)
LEVOTHYROXINE	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16 2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
LEVOTHYROXINE SODIUM	1 (2.6)	0	1 (1.8)
THYRADIN	1 (2.6)	0	1 (1.8)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	8 (20.5)	2 (12.5)	10 (18.2)
KETOPROFEN	4 (10.3)	0	4 (7.3)
BENZYDAMINE HYDROCHLORIDE	0	1 (6.3)	1 (1.8)
FELBINAC PAP	1 (2.6)	0	1 (1.8)
LOXONIN	1 (2.6)	0	1 (1.8)
LOXOPROFEN SODIUM HYDRATE	1 (2.6)	0	1 (1.8)
MOHRUS	1 (2.6)	0	1 (1.8)
PIROXICAM	0	1 (6.3)	1 (1.8)
SUMILU STICK	1 (2.6)	0	1 (1.8)
ZEPOLAS	1 (2.6)	0	1 (1.8)
UROLOGICALS	2 (5.1)	0	2 (3.6)
SOLIFENACIN SUCCINATE	1 (2.6)	0	1 (1.8)
TOVIAZ	1 (2.6)	0	1 (1.8)
VASODILATORS USED IN CARDIAC DISEASES	2 (5.1)	0	2 (3.6)
ISOSORBIDE MONONITRATE	1 (2.6)	0	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
NITOROL	1 (2.6)	0	1 (1.8)
NITROGLYCERIN	1 (2.6)	0	1 (1.8)
VIRAL VACCINES	1 (2.6)	1 (6.3)	2 (3.6)
INFLUENZA HA VACCINE	1 (2.6)	0	1 (1.8)
INFLUENZA VACCINE INACT SAG 4V	0	1 (6.3)	1 (1.8)
VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO	2 (5.1)	0	2 (3.6)
EDIROL	2 (5.1)	0	2 (3.6)
VITAMIN B-COMPLEX, INCL. COMBINATIONS	1 (2.6)	1 (6.3)	2 (3.6)
ASCORBIC ACID W/VITAMIN B NOS	0	1 (6.3)	1 (1.8)
EBIOS	1 (2.6)	0	1 (1.8)
VITAMIN B12 AND FOLIC ACID	7 (17.9)	1 (6.3)	8 (14.5)
MECOBALAMIN	5 (12.8)	0	5 (9.1)
METHYCOBAL	2 (5.1)	0	2 (3.6)
FOLIC ACID	0	1 (6.3)	1 (1.8)
VITAMIN K AND OTHER HEMOSTATICS	0	1 (6.3)	1 (1.8)
ROMIPLATE	0	1 (6.3)	1 (1.8)
VITAMIN K1	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16 2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
X-RAY CONTRAST MEDIA, IODINATED	21 (53.8)	0	21 (38.2)
OMNIPAQUE	8 (20.5)	0	8 (14.5)
IOPAMIDOL	6 (15.4)	0	6 (10.9)
IOPAMIRON	5 (12.8)	0	5 (9.1)
IOHEXOL	4 (10.3)	0	4 (7.3)
IOMEPROL	2 (5.1)	0	2 (3.6)
IOMERON	2 (5.1)	0	2 (3.6)
IOPAQUE	2 (5.1)	0	2 (3.6)
OPTIRAY	1 (2.6)	0	1 (1.8)
ATC Class Level 3 not Available	9 (23.1)	10 (62.5)	19 (34.5)
MEGESTROL	0	5 (31.3)	5 (9.1)
HERBAL PREPARATION	1 (2.6)	2 (12.5)	3 (5.5)
MEGACE F	0	3 (18.8)	3 (5.5)
DIAMOX /00016901/	2 (5.1)	0	2 (3.6)
SHAKUYAKUKANZOTO	2 (5.1)	0	2 (3.6)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (5.1)	0	2 (3.6)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.
n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;
ATC class = Anatomical Therapeutic Chemical class.
Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

ATC class level 3 WHO-DDE drug name		Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
ADJUST-A		1 (2.6)	0	1 (1.8)
ALOSENN	/00476901/	1 (2.6)	0	1 (1.8)
DAIKENCHUTO		1 (2.6)	0	1 (1.8)
HOCHUEKKITO	/07973001/	1 (2.6)	0	1 (1.8)
JUVELA	/00526901/	1 (2.6)	0	1 (1.8)
LEGALON		0	1 (6.3)	1 (1.8)
MEGACE		0	1 (6.3)	1 (1.8)
MEGESTROL ACETATE		0	1 (6.3)	1 (1.8)
SILYMARIN	/01131701/	0	1 (6.3)	1 (1.8)

SOURCE: Listing 16.2.4.5

WHO-DDE Version 01SEP2018 was used to code medications.

n = number of subjects; % = percentages are calculated based on the number of subjects in the respective country within the analysis set;

ATC class = Anatomical Therapeutic Chemical class.

Concomitant medications = medications started prior to, on or after the first dose of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the treatment. End of treatment is defined as end of treatment visit which is approximately 30 (± 3) days after the last dosing of study drug or before the initiation of new cancer treatment, whichever is earlier.

表 2.7.4.7-20　有害事象の概要（210 試験）（安全性解析対象集団）

Description	40 mg (N=23)
	n (%)
Number of subjects with	
At least one TEAE	23 (100.0%)
At least one TEAE related to the study drug	23 (100.0%)
At least one serious TEAE	7 (30.4%)
At least one serious TEAE related to the study drug	6 (26.1%)
At least one TEAE leading to dose reduction or interruption	16 (69.6%)
At least one TEAE leading to study drug discontinuation	9 (39.1%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	18 (78.3%)
At least one TEAE with grade 3 or higher and related to the study drug	18 (78.3%)

Source: Listing 16.2.6.1

Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-21　有害事象の概要（201 試験）（安全性解析対象集団）

Description	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with			
At least one TEAE	6 (85.7%)	7 (100.0%)	13 (92.9%)
At least one TEAE related to the study drug	6 (85.7%)	7 (100.0%)	13 (92.9%)
At least one serious TEAE	1 (14.3%)	1 (14.3%)	2 (14.3%)
At least one serious TEAE related to the study drug	0 (0.0%)	1 (14.3%)	1 (7.1%)
A TEAE leading to dose reduction or delay	4 (57.1%)	4 (57.1%)	8 (57.1%)
A TEAE leading to study drug discontinuation	2 (28.6%)	4 (57.1%)	6 (42.9%)
A TEAE leading to death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Severity			
Grade 1: Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)
Grade 2: Moderate	1 (14.3%)	1 (14.3%)	2 (14.3%)
Grade 3: Severe	5 (71.4%)	4 (57.1%)	9 (64.3%)
Grade 4: Life-Threatening	0 (0.0%)	2 (28.6%)	2 (14.3%)
Grade 5: Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Grade 3 or higher	5 (71.4%)	6 (85.7%)	11 (78.6%)

SOURCE: Listing 16.2.6.3
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Description	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Causal relationship			
Unrelated	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unlikely	0 (0.0%)	0 (0.0%)	0 (0.0%)
Possible	0 (0.0%)	1 (14.3%)	1 (7.1%)
Probable	4 (57.1%)	3 (42.9%)	7 (50.0%)
Definite	2 (28.6%)	3 (42.9%)	5 (35.7%)

SOURCE: Listing 16.2.6.3
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

表 2.7.4.7-22　有害事象の概要（203 試験）（安全性解析対象集団）

Description	Japan (N=39)	Korea (N=16)	Total (N=55)
	n (%)	n (%)	n (%)
Number of subjects with			
At least one TEAE	39 (100.0)	16 (100.0)	55 (100.0)
At least one TEAE related to the study drug	39 (100.0)	12 (75.0)	51 (92.7)
At least one serious TEAE	11 (28.2)	3 (18.8)	14 (25.5)
At least one serious TEAE related to the study drug	8 (20.5)	2 (12.5)	10 (18.2)
At least one TEAE leading to dose reduction or interruption	31 (79.5)	9 (56.3)	40 (72.7)
At least one TEAE leading to study drug discontinuation	15 (38.5)	3 (18.8)	18 (32.7)
At least one TEAE leading to death	0 (0.0)	1 (6.3)	1 (1.8)
At least one TEAE with grade 3 or higher	34 (87.2)	12 (75.0)	46 (83.6)
At least one TEAE with grade 3 or higher and related to the study drug	33 (84.6)	9 (56.3)	42 (76.4)

Source: Listing 16.2.6.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-23　有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	40 mg (N=23) n (%)
Number of subjects with at least one TEAE	23(100.0%)
血液およびリンパ系障害	19(82.6%)
血小板減少症*	18(78.3%)
好中球減少症*	12(52.2%)
白血球減少症*	10(43.5%)
貧血*	9(39.1%)
リンパ球減少症*	2(8.7%)
好酸球増加症	1(4.3%)
発熱性好中球減少症	1(4.3%)
心臓障害	2(8.7%)
第一度房室ブロック	1(4.3%)
動悸	1(4.3%)
眼障害	1(4.3%)
ドライアイ	1(4.3%)
胃腸障害	9(39.1%)
下痢	6(26.1%)
腹痛	3(13.0%)
悪心	3(13.0%)
口内炎	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
一般・全身障害および投与部位の状態	13(56.5%)
倦怠感	7(30.4%)
疲労	3(13.0%)
発熱	3(13.0%)
悪寒	1(4.3%)
非心臓性胸痛	1(4.3%)
末梢性浮腫	1(4.3%)
感染症および寄生虫症	7(30.4%)
細菌感染	1(4.3%)
サイトメガロウイルス感染	1(4.3%)
医療機器関連感染	1(4.3%)
麦粒腫	1(4.3%)
口腔カンジダ症	1(4.3%)
ニューモシスチス・イロベチイ肺炎	1(4.3%)
皮膚感染	1(4.3%)
扁桃炎	1(4.3%)
上気道感染	1(4.3%)
尿路感染	1(4.3%)
傷害、中毒および処置合併症	1(4.3%)
挫傷	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
臨床検査	10(43.5%)
体重減少	4(17.4%)
アスパラギン酸アミノトランスフェラーゼ増加	2(8.7%)
γ－グルタミルトランスフェラーゼ増加	2(8.7%)
アラニンアミノトランスフェラーゼ増加	1(4.3%)
血中アルカリホスファターゼ増加	1(4.3%)
血中乳酸脱水素酵素増加	1(4.3%)
脳性ナトリウム利尿ペプチド増加	1(4.3%)
好酸球数増加	1(4.3%)
リパーゼ増加	1(4.3%)
代謝および栄養障害	13(56.5%)
食欲減退	8(34.8%)
低アルブミン血症	3(13.0%)
低ナトリウム血症	2(8.7%)
高カルシウム血症	1(4.3%)
低カリウム血症	1(4.3%)
低リン酸血症	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
筋骨格系および結合組織障害	7(30.4%)
背部痛	4(17.4%)
関節痛	1(4.3%)
脊椎すべり症	1(4.3%)
尺骨突き上げ症候群	1(4.3%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1(4.3%)
腫瘍疼痛	1(4.3%)
神経系障害	9(39.1%)
味覚異常	4(17.4%)
頭痛	2(8.7%)
味覚消失	1(4.3%)
認知障害	1(4.3%)
浮動性めまい	1(4.3%)
傾眠	1(4.3%)
腎および尿路障害	1(4.3%)
尿瘻	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
呼吸器、胸郭および縦隔障害	4(17.4%)
急性呼吸不全	1(4.3%)
鼻出血	1(4.3%)
間質性肺疾患	1(4.3%)
口腔咽頭痛	1(4.3%)
皮膚および皮下組織障害	8(34.8%)
接触皮膚炎	1(4.3%)
湿疹	1(4.3%)
紅斑	1(4.3%)
多形紅斑	1(4.3%)
光線過敏性反応	1(4.3%)
そう痒症	1(4.3%)
発疹	1(4.3%)
皮膚剥脱	1(4.3%)
皮膚潰瘍	1(4.3%)
血管障害	1(4.3%)
高血圧	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

表 2.7.4.7-24　有害事象の発現割合（201 試験）（安全性解析対象集団）

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one TEAE	6 (85.7%)	7 (100.0%)	13 (92.9%)
血液およびリンパ系障害	5 (71.4%)	5 (71.4%)	10 (71.4%)
貧血	5 (71.4%)	0 (0.0%)	5 (35.7%)
白血球減少症	1 (14.3%)	0 (0.0%)	1 (7.1%)
好中球減少症	1 (14.3%)	2 (28.6%)	3 (21.4%)
血小板減少症	2 (28.6%)	4 (57.1%)	6 (42.9%)
先天性、家族性および遺伝性障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
表皮融解	1 (14.3%)	0 (0.0%)	1 (7.1%)
耳および迷路障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
回転性めまい	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
胃腸障害	3 (42.9%)	4 (57.1%)	7 (50.0%)
腹痛	1 (14.3%)	1 (14.3%)	2 (14.3%)
便秘	0 (0.0%)	1 (14.3%)	1 (7.1%)
下痢	3 (42.9%)	1 (14.3%)	4 (28.6%)
口内乾燥	0 (0.0%)	1 (14.3%)	1 (7.1%)
腸炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
悪心	1 (14.3%)	2 (28.6%)	3 (21.4%)
口内炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
嘔吐	1 (14.3%)	0 (0.0%)	1 (7.1%)
一般・全身障害および投与部位の状態	4 (57.1%)	3 (42.9%)	7 (50.0%)
疲労	3 (42.9%)	1 (14.3%)	4 (28.6%)
治癒不良	0 (0.0%)	1 (14.3%)	1 (7.1%)
末梢性浮腫	1 (14.3%)	0 (0.0%)	1 (7.1%)
発熱	1 (14.3%)	2 (28.6%)	3 (21.4%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
感染症および寄生虫症	2 (28.6%)	3 (42.9%)	5 (35.7%)
結膜炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
膀胱炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
鼻咽頭炎	0 (0.0%)	2 (28.6%)	2 (14.3%)
食道カンジダ症	0 (0.0%)	1 (14.3%)	1 (7.1%)
咽頭炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
副鼻腔炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
傷害、中毒および処置合併症	0 (0.0%)	1 (14.3%)	1 (7.1%)
挫傷	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
臨床検査	4 (57.1%)	7 (100.0%)	11 (78.6%)
アラニンアミノトランスフェラーゼ増加	0 (0.0%)	1 (14.3%)	1 (7.1%)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0%)	1 (14.3%)	1 (7.1%)
血中クレアチンホスホキナーゼ増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
Ｃ－反応性蛋白増加	1 (14.3%)	1 (14.3%)	2 (14.3%)
低比重リポ蛋白増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
リンパ球数減少	1 (14.3%)	0 (0.0%)	1 (7.1%)
好中球数減少	2 (28.6%)	0 (0.0%)	2 (14.3%)
血小板数減少	3 (42.9%)	3 (42.9%)	6 (42.9%)
体重減少	1 (14.3%)	2 (28.6%)	3 (21.4%)
体重増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
白血球数減少	3 (42.9%)	1 (14.3%)	4 (28.6%)
トランスアミナーゼ上昇	0 (0.0%)	1 (14.3%)	1 (7.1%)
胸部コンピュータ断層撮影異常	0 (0.0%)	1 (14.3%)	1 (7.1%)
トロポニンＩ増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
血中アルカリホスファターゼ増加	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
代謝および栄養障害	4 (57.1%)	6 (85.7%)	10 (71.4%)
糖尿病	0 (0.0%)	1 (14.3%)	1 (7.1%)
高血糖	0 (0.0%)	1 (14.3%)	1 (7.1%)
高マグネシウム血症	1 (14.3%)	0 (0.0%)	1 (7.1%)
高トリグリセリド血症	1 (14.3%)	1 (14.3%)	2 (14.3%)
高尿酸血症	2 (28.6%)	0 (0.0%)	2 (14.3%)
低カルシウム血症	0 (0.0%)	3 (42.9%)	3 (21.4%)
低カリウム血症	2 (28.6%)	1 (14.3%)	3 (21.4%)
低マグネシウム血症	0 (0.0%)	1 (14.3%)	1 (7.1%)
血液量減少症	0 (0.0%)	1 (14.3%)	1 (7.1%)
食欲減退	1 (14.3%)	2 (28.6%)	3 (21.4%)
筋骨格系および結合組織障害	1 (14.3%)	2 (28.6%)	3 (21.4%)
背部痛	0 (0.0%)	2 (28.6%)	2 (14.3%)
筋肉痛	1 (14.3%)	0 (0.0%)	1 (7.1%)
筋骨格系胸痛	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
神経系障害	3 (42.9%)	1 (14.3%)	4 (28.6%)
味覚異常	2 (28.6%)	1 (14.3%)	3 (21.4%)
頭痛	1 (14.3%)	1 (14.3%)	2 (14.3%)
パーキンソニズム	1 (14.3%)	0 (0.0%)	1 (7.1%)
精神障害	1 (14.3%)	1 (14.3%)	2 (14.3%)
不眠症	1 (14.3%)	1 (14.3%)	2 (14.3%)
腎および尿路障害	2 (28.6%)	1 (14.3%)	3 (21.4%)
血尿	1 (14.3%)	0 (0.0%)	1 (7.1%)
頻尿	1 (14.3%)	0 (0.0%)	1 (7.1%)
蛋白尿	1 (14.3%)	0 (0.0%)	1 (7.1%)
尿管結石症	0 (0.0%)	1 (14.3%)	1 (7.1%)
呼吸器、胸郭および縦隔障害	2 (28.6%)	0 (0.0%)	2 (14.3%)
胸水	1 (14.3%)	0 (0.0%)	1 (7.1%)
口腔咽頭不快感	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
皮膚および皮下組織障害	2 (28.6%)	1 (14.3%)	3 (21.4%)
多形紅斑	0 (0.0%)	1 (14.3%)	1 (7.1%)
結節性紅斑	0 (0.0%)	1 (14.3%)	1 (7.1%)
全身性皮疹	1 (14.3%)	0 (0.0%)	1 (7.1%)
斑状丘疹状皮疹	0 (0.0%)	1 (14.3%)	1 (7.1%)
不全角化	1 (14.3%)	0 (0.0%)	1 (7.1%)
血管周囲細胞浸潤性皮膚炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
血管障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
低血圧	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

表 2.7.4.7-25　有害事象の発現割合（203 試験）（安全性解析対象集団）

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with at least one TEAE	39(100.0)	16(100.0)	55(100.0)
血液およびリンパ系障害	38(97.4)	14(87.5)	52(94.5)
血小板減少症*	35(89.7)	11(68.8)	46(83.6)
好中球減少症*	28(71.8)	3(18.8)	31(56.4)
白血球減少症*	24(61.5)	0	24(43.6)
貧血*	14(35.9)	4(25.0)	18(32.7)
リンパ球減少症*	16(41.0)	0	16(29.1)
発熱性好中球減少症	2(5.1)	1(6.3)	3(5.5)
再生不良性貧血	1(2.6)	0	1(1.8)
好酸球増加症	0	1(6.3)	1(1.8)
心臓障害	6(15.4)	1(6.3)	7(12.7)
動悸	3(7.7)	0	3(5.5)
心房細動	1(2.6)	1(6.3)	2(3.6)
不安定狭心症	1(2.6)	0	1(1.8)
不整脈	1(2.6)	0	1(1.8)
心嚢液貯留	1(2.6)	0	1(1.8)
耳および迷路障害	1(2.6)	1(6.3)	2(3.6)
回転性めまい	1(2.6)	0	1(1.8)
耳痛	0	1(6.3)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
眼障害	4(10.3)	1(6.3)	5(9.1)
ドライアイ	1(2.6)	0	1(1.8)
白内障	0	1(6.3)	1(1.8)
結膜出血	1(2.6)	0	1(1.8)
角膜炎	1(2.6)	0	1(1.8)
霧視	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
胃腸障害	25(64.1)	7(43.8)	32(58.2)
下痢	14(35.9)	3(18.8)	17(30.9)
悪心	9(23.1)	3(18.8)	12(21.8)
嘔吐	2(5.1)	1(6.3)	3(5.5)
腹痛	1(2.6)	2(12.5)	3(5.5)
上腹部痛	2(5.1)	0	2(3.6)
口内炎	0	2(12.5)	2(3.6)
齲歯	2(5.1)	0	2(3.6)
便秘	1(2.6)	0	1(1.8)
口腔粘膜血腫	1(2.6)	0	1(1.8)
心窩部不快感	1(2.6)	0	1(1.8)
歯痛	1(2.6)	0	1(1.8)
消化不良	1(2.6)	0	1(1.8)
痔出血	1(2.6)	0	1(1.8)
肛門出血	1(2.6)	0	1(1.8)
胃潰瘍	0	1(6.3)	1(1.8)
胃炎	0	1(6.3)	1(1.8)
腹部不快感	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
一般・全身障害および投与部位の状態	19(48.7)	8(50.0)	27(49.1)
発熱	5(12.8)	6(37.5)	11(20.0)
倦怠感	8(20.5)	0	8(14.5)
疲労	4(10.3)	2(12.5)	6(10.9)
末梢性浮腫	2(5.1)	2(12.5)	4(7.3)
インフルエンザ様疾患	0	2(12.5)	2(3.6)
無力症	0	2(12.5)	2(3.6)
カテーテル留置部位腫脹	1(2.6)	0	1(1.8)
口渇	1(2.6)	0	1(1.8)
歩行障害	1(2.6)	0	1(1.8)
溢出	1(2.6)	0	1(1.8)
胸痛	1(2.6)	0	1(1.8)
胸部不快感	1(2.6)	0	1(1.8)
免疫系障害	1(2.6)	0	1(1.8)
薬物過敏症	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
感染症および寄生虫症	15(38.5)	4(25.0)	19(34.5)
上気道感染	2(5.1)	2(12.5)	4(7.3)
咽頭炎	3(7.7)	0	3(5.5)
インフルエンザ	2(5.1)	0	2(3.6)
上咽頭炎	2(5.1)	0	2(3.6)
気管支炎	2(5.1)	0	2(3.6)
結膜炎	2(5.1)	0	2(3.6)
サイトメガロウイルス感染	1(2.6)	0	1(1.8)
ニューモシスチス・イロベチイ肺炎	1(2.6)	0	1(1.8)
ブドウ球菌皮膚感染	0	1(6.3)	1(1.8)
帯状疱疹	1(2.6)	0	1(1.8)
感染性小腸結腸炎	0	1(6.3)	1(1.8)
肺炎	0	1(6.3)	1(1.8)
胃腸炎	0	1(6.3)	1(1.8)
膀胱炎	1(2.6)	0	1(1.8)
膿痂疹	1(2.6)	0	1(1.8)
鼻炎	1(2.6)	0	1(1.8)
傷害、中毒および処置合併症	1(2.6)	2(12.5)	3(5.5)
処置による疼痛	0	1(6.3)	1(1.8)
爪損傷	1(2.6)	0	1(1.8)
胃瘻管部合併症	0	1(6.3)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
臨床検査	24(61.5)	1(6.3)	25(45.5)
γ－グルタミルトランスフェラーゼ増加	8(20.5)	0	8(14.5)
血中アルカリホスファターゼ増加	8(20.5)	0	8(14.5)
アスパラギン酸アミノトランスフェラーゼ増加	7(17.9)	0	7(12.7)
体重減少	6(15.4)	0	6(10.9)
アラニンアミノトランスフェラーゼ増加	5(12.8)	0	5(9.1)
心電図ＱＴ延長	5(12.8)	0	5(9.1)
Ｃ－反応性蛋白増加	2(5.1)	1(6.3)	3(5.5)
好酸球数増加	2(5.1)	0	2(3.6)
脳性ナトリウム利尿ペプチド増加	2(5.1)	0	2(3.6)
血中クレアチニン増加	2(5.1)	0	2(3.6)
リパーゼ増加	1(2.6)	0	1(1.8)
体重増加	1(2.6)	0	1(1.8)
尿中血陽性	1(2.6)	0	1(1.8)
心胸郭比増加	1(2.6)	0	1(1.8)
心電図Ｔ波逆転	1(2.6)	0	1(1.8)
血中クレアチンホスホキナーゼ増加	1(2.6)	0	1(1.8)
血中クレアチンホスホキナーゼＭＢ増加	1(2.6)	0	1(1.8)
血中コレステロール増加	1(2.6)	0	1(1.8)
血中免疫グロブリンＡ減少	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
代謝および栄養障害	16(41.0)	9(56.3)	25(45.5)
食欲減退	8(20.5)	5(31.3)	13(23.6)
低アルブミン血症	4(10.3)	1(6.3)	5(9.1)
低カリウム血症	3(7.7)	2(12.5)	5(9.1)
低カルシウム血症	2(5.1)	1(6.3)	3(5.5)
低ナトリウム血症	2(5.1)	0	2(3.6)
低蛋白血症	1(2.6)	0	1(1.8)
糖尿病	1(2.6)	0	1(1.8)
高カリウム血症	1(2.6)	0	1(1.8)
高トリグリセリド血症	1(2.6)	0	1(1.8)
高マグネシウム血症	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
筋骨格系および結合組織障害	15(38.5)	4(25.0)	19(34.5)
筋痙縮	5(12.8)	0	5(9.1)
背部痛	4(10.3)	1(6.3)	5(9.1)
筋肉疲労	1(2.6)	1(6.3)	2(3.6)
筋肉痛	2(5.1)	0	2(3.6)
出血性関節症	1(2.6)	0	1(1.8)
四肢痛	1(2.6)	0	1(1.8)
筋力低下	0	1(6.3)	1(1.8)
筋骨格硬直	1(2.6)	0	1(1.8)
肩回旋筋腱板症候群	0	1(6.3)	1(1.8)
腱炎	1(2.6)	0	1(1.8)
関節炎	1(2.6)	0	1(1.8)
関節痛	1(2.6)	0	1(1.8)
関節腫脹	1(2.6)	0	1(1.8)
頚部痛	1(2.6)	0	1(1.8)
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(7.7)	1(6.3)	4(7.3)
腫瘍疼痛	1(2.6)	1(6.3)	2(3.6)
末梢性Ｔ細胞性リンパ腫、組織型不明	1(2.6)	0	1(1.8)
皮膚乳頭腫	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
神経系障害	7(17.9)	2(12.5)	9(16.4)
頭痛	4(10.3)	2(12.5)	6(10.9)
味覚異常	2(5.1)	0	2(3.6)
失神寸前の状態	1(2.6)	0	1(1.8)
感覚鈍麻	1(2.6)	0	1(1.8)
末梢性感覚ニューロパチー	1(2.6)	0	1(1.8)
浮動性めまい	1(2.6)	0	1(1.8)
精神障害	4(10.3)	1(6.3)	5(9.1)
不眠症	3(7.7)	1(6.3)	4(7.3)
譫妄	2(5.1)	0	2(3.6)
腎および尿路障害	2(5.1)	0	2(3.6)
急性腎障害	1(2.6)	0	1(1.8)
蛋白尿	1(2.6)	0	1(1.8)
血尿	1(2.6)	0	1(1.8)
生殖系および乳房障害	0	1(6.3)	1(1.8)
陰嚢浮腫	0	1(6.3)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
呼吸器、胸郭および縦隔障害	14(35.9)	7(43.8)	21(38.2)
咳嗽	2(5.1)	4(25.0)	6(10.9)
呼吸困難	2(5.1)	2(12.5)	4(7.3)
肺臓炎	3(7.7)	1(6.3)	4(7.3)
口腔咽頭痛	2(5.1)	1(6.3)	3(5.5)
胸水	2(5.1)	0	2(3.6)
鼻出血	2(5.1)	0	2(3.6)
しゃっくり	0	1(6.3)	1(1.8)
アレルギー性鼻炎	0	1(6.3)	1(1.8)
上気道の炎症	1(2.6)	0	1(1.8)
労作性呼吸困難	0	1(6.3)	1(1.8)
咽頭知覚不全	1(2.6)	0	1(1.8)
湿性咳嗽	0	1(6.3)	1(1.8)
発声障害	0	1(6.3)	1(1.8)
間質性肺疾患	1(2.6)	0	1(1.8)
鼻漏	0	1(6.3)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
皮膚および皮下組織障害	18(46.2)	5(31.3)	23(41.8)
発疹	3(7.7)	2(12.5)	5(9.1)
蕁麻疹	3(7.7)	2(12.5)	5(9.1)
全身性そう痒症	1(2.6)	1(6.3)	2(3.6)
斑状丘疹状皮疹	2(5.1)	0	2(3.6)
紅斑	2(5.1)	0	2(3.6)
紫斑	2(5.1)	0	2(3.6)
ざ瘡様皮膚炎	1(2.6)	0	1(1.8)
そう痒性皮疹	1(2.6)	0	1(1.8)
全身性剥脱性皮膚炎	1(2.6)	0	1(1.8)
全身紅斑	1(2.6)	0	1(1.8)
多形紅斑	1(2.6)	0	1(1.8)
点状出血	1(2.6)	0	1(1.8)
皮脂欠乏性湿疹	1(2.6)	0	1(1.8)
皮膚乾燥	1(2.6)	0	1(1.8)
皮膚疼痛	1(2.6)	0	1(1.8)
色素沈着障害	1(2.6)	0	1(1.8)
褥瘡性潰瘍	1(2.6)	0	1(1.8)
血管障害	2(5.1)	1(6.3)	3(5.5)
低血圧	1(2.6)	0	1(1.8)
末梢動脈閉塞性疾患	1(2.6)	0	1(1.8)
深部静脈血栓症	0	1(6.3)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-26　治験薬と関連性のある有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	40 mg (N=23) n (%)
Number of subjects with at least one related TEAE	23(100.0%)
血液およびリンパ系障害	19(82.6%)
血小板減少症*	18(78.3%)
好中球減少症*	12(52.2%)
白血球減少症*	10(43.5%)
貧血*	9(39.1%)
リンパ球減少症*	2(8.7%)
好酸球増加症	1(4.3%)
発熱性好中球減少症	1(4.3%)
心臓障害	2(8.7%)
第一度房室ブロック	1(4.3%)
動悸	1(4.3%)
胃腸障害	7(30.4%)
下痢	5(21.7%)
悪心	3(13.0%)
腹痛	1(4.3%)
口内炎	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
一般・全身障害および投与部位の状態	10(43.5%)
倦怠感	7(30.4%)
疲労	2(8.7%)
発熱	2(8.7%)
悪寒	1(4.3%)
末梢性浮腫	1(4.3%)
感染症および寄生虫症	5(21.7%)
サイトメガロウイルス感染	1(4.3%)
医療機器関連感染	1(4.3%)
口腔カンジダ症	1(4.3%)
ニューモシスチス・イロベチイ肺炎	1(4.3%)
皮膚感染	1(4.3%)
尿路感染	1(4.3%)
臨床検査	8(34.8%)
体重減少	4(17.4%)
アスパラギン酸アミノトランスフェラーゼ増加	2(8.7%)
γ－グルタミルトランスフェラーゼ増加	2(8.7%)
アラニンアミノトランスフェラーゼ増加	1(4.3%)
血中アルカリホスファターゼ増加	1(4.3%)
好酸球数増加	1(4.3%)
リパーゼ増加	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
代謝および栄養障害	12(52.2%)
食欲減退	8(34.8%)
低アルブミン血症	3(13.0%)
低ナトリウム血症	2(8.7%)
低カリウム血症	1(4.3%)
低リン酸血症	1(4.3%)
筋骨格系および結合組織障害	1(4.3%)
関節痛	1(4.3%)
神経系障害	7(30.4%)
味覚異常	4(17.4%)
味覚消失	1(4.3%)
頭痛	1(4.3%)
傾眠	1(4.3%)
腎および尿路障害	1(4.3%)
尿瘻	1(4.3%)
呼吸器、胸郭および縦隔障害	2(8.7%)
鼻出血	1(4.3%)
間質性肺疾患	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	40 mg (N=23) n (%)
皮膚および皮下組織障害	5(21.7%)
紅斑	1(4.3%)
多形紅斑	1(4.3%)
光線過敏性反応	1(4.3%)
そう痒症	1(4.3%)
発疹	1(4.3%)
皮膚潰瘍	1(4.3%)
血管障害	1(4.3%)
高血圧	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-27　治験薬と関連性のある有害事象（201 試験）（安全性解析対象集団）

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one related TEAE	6 (85.7%)	7 (100.0%)	13 (92.9%)
血液およびリンパ系障害	5 (71.4%)	5 (71.4%)	10 (71.4%)
貧血	5 (71.4%)	0 (0.0%)	5 (35.7%)
白血球減少症	1 (14.3%)	0 (0.0%)	1 (7.1%)
好中球減少症	1 (14.3%)	2 (28.6%)	3 (21.4%)
血小板減少症	2 (28.6%)	4 (57.1%)	6 (42.9%)
先天性、家族性および遺伝性障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
表皮融解	1 (14.3%)	0 (0.0%)	1 (7.1%)
胃腸障害	3 (42.9%)	4 (57.1%)	7 (50.0%)
腹痛	1 (14.3%)	1 (14.3%)	2 (14.3%)
便秘	0 (0.0%)	1 (14.3%)	1 (7.1%)
下痢	2 (28.6%)	1 (14.3%)	3 (21.4%)
口内乾燥	0 (0.0%)	1 (14.3%)	1 (7.1%)
悪心	1 (14.3%)	2 (28.6%)	3 (21.4%)
口内炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
嘔吐	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
一般・全身障害および投与部位の状態	3 (42.9%)	2 (28.6%)	5 (35.7%)
疲労	3 (42.9%)	1 (14.3%)	4 (28.6%)
発熱	1 (14.3%)	2 (28.6%)	3 (21.4%)
感染症および寄生虫症	2 (28.6%)	3 (42.9%)	5 (35.7%)
結膜炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
膀胱炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
鼻咽頭炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
食道カンジダ症	0 (0.0%)	1 (14.3%)	1 (7.1%)
咽頭炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
副鼻腔炎	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
臨床検査	4 (57.1%)	7 (100.0%)	11 (78.6%)
アラニンアミノトランスフェラーゼ増加	0 (0.0%)	1 (14.3%)	1 (7.1%)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0%)	1 (14.3%)	1 (7.1%)
血中クレアチンホスホキナーゼ増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
Ｃ－反応性蛋白増加	1 (14.3%)	1 (14.3%)	2 (14.3%)
低比重リポ蛋白増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
リンパ球数減少	1 (14.3%)	0 (0.0%)	1 (7.1%)
好中球数減少	2 (28.6%)	0 (0.0%)	2 (14.3%)
血小板数減少	3 (42.9%)	3 (42.9%)	6 (42.9%)
体重減少	1 (14.3%)	2 (28.6%)	3 (21.4%)
白血球数減少	3 (42.9%)	1 (14.3%)	4 (28.6%)
トランスアミナーゼ上昇	0 (0.0%)	1 (14.3%)	1 (7.1%)
胸部コンピュータ断層撮影異常	0 (0.0%)	1 (14.3%)	1 (7.1%)
血中アルカリホスファターゼ増加	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
代謝および栄養障害	4 (57.1%)	4 (57.1%)	8 (57.1%)
糖尿病	0 (0.0%)	1 (14.3%)	1 (7.1%)
高トリグリセリド血症	1 (14.3%)	1 (14.3%)	2 (14.3%)
高尿酸血症	2 (28.6%)	0 (0.0%)	2 (14.3%)
低カルシウム血症	0 (0.0%)	2 (28.6%)	2 (14.3%)
低カリウム血症	2 (28.6%)	0 (0.0%)	2 (14.3%)
食欲減退	1 (14.3%)	2 (28.6%)	3 (21.4%)
筋骨格系および結合組織障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
筋肉痛	1 (14.3%)	0 (0.0%)	1 (7.1%)
筋骨格系胸痛	1 (14.3%)	0 (0.0%)	1 (7.1%)
神経系障害	3 (42.9%)	1 (14.3%)	4 (28.6%)
味覚異常	2 (28.6%)	1 (14.3%)	3 (21.4%)
頭痛	1 (14.3%)	1 (14.3%)	2 (14.3%)
精神障害	0 (0.0%)	1 (14.3%)	1 (7.1%)
不眠症	0 (0.0%)	1 (14.3%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
腎および尿路障害	2 (28.6%)	0 (0.0%)	2 (14.3%)
血尿	1 (14.3%)	0 (0.0%)	1 (7.1%)
頻尿	1 (14.3%)	0 (0.0%)	1 (7.1%)
蛋白尿	1 (14.3%)	0 (0.0%)	1 (7.1%)
呼吸器、胸郭および縦隔障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
口腔咽頭不快感	1 (14.3%)	0 (0.0%)	1 (7.1%)
皮膚および皮下組織障害	2 (28.6%)	1 (14.3%)	3 (21.4%)
多形紅斑	0 (0.0%)	1 (14.3%)	1 (7.1%)
結節性紅斑	0 (0.0%)	1 (14.3%)	1 (7.1%)
全身性皮疹	1 (14.3%)	0 (0.0%)	1 (7.1%)
斑状丘疹状皮疹	0 (0.0%)	1 (14.3%)	1 (7.1%)
不全角化	1 (14.3%)	0 (0.0%)	1 (7.1%)
血管周囲細胞浸潤性皮膚炎	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

表 2.7.4.7-28　治験薬と関連性のある有害事象（203 試験）（安全性解析対象集団）

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with at least one related TEAE	39(100.0)	12(75.0)	51(92.7)
血液およびリンパ系障害	38(97.4)	9(56.3)	47(85.5)
血小板減少症*	35(89.7)	7(43.8)	42(76.4)
好中球減少症*	28(71.8)	3(18.8)	31(56.4)
白血球減少症*	21(53.8)	0	21(38.2)
リンパ球減少症*	16(41.0)	0	16(29.1)
貧血*	11(28.2)	1(6.3)	12(21.8)
発熱性好中球減少症	2(5.1)	1(6.3)	3(5.5)
再生不良性貧血	1(2.6)	0	1(1.8)
心臓障害	4(10.3)	0	4(7.3)
動悸	2(5.1)	0	2(3.6)
不整脈	1(2.6)	0	1(1.8)
心嚢液貯留	1(2.6)	0	1(1.8)
心房細動	1(2.6)	0	1(1.8)
耳および迷路障害	1(2.6)	0	1(1.8)
回転性めまい	1(2.6)	0	1(1.8)
眼障害	1(2.6)	0	1(1.8)
結膜出血	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
胃腸障害	20(51.3)	5(31.3)	25(45.5)
悪心	9(23.1)	2(12.5)	11(20.0)
下痢	9(23.1)	1(6.3)	10(18.2)
便秘	1(2.6)	0	1(1.8)
嘔吐	1(2.6)	0	1(1.8)
心窩部不快感	1(2.6)	0	1(1.8)
消化不良	1(2.6)	0	1(1.8)
胃炎	0	1(6.3)	1(1.8)
腹痛	0	1(6.3)	1(1.8)
腹部不快感	1(2.6)	0	1(1.8)
齲歯	1(2.6)	0	1(1.8)
一般・全身障害および投与部位の状態	16(41.0)	1(6.3)	17(30.9)
倦怠感	8(20.5)	0	8(14.5)
疲労	4(10.3)	0	4(7.3)
末梢性浮腫	2(5.1)	0	2(3.6)
発熱	2(5.1)	0	2(3.6)
歩行障害	1(2.6)	0	1(1.8)
無力症	0	1(6.3)	1(1.8)
胸部不快感	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
感染症および寄生虫症	7(17.9)	1(6.3)	8(14.5)
気管支炎	2(5.1)	0	2(3.6)
サイトメガロウイルス感染	1(2.6)	0	1(1.8)
ニューモシスチス・イロベチイ肺炎	1(2.6)	0	1(1.8)
上咽頭炎	1(2.6)	0	1(1.8)
肺炎	0	1(6.3)	1(1.8)
膀胱炎	1(2.6)	0	1(1.8)
膿痂疹	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
臨床検査	19(48.7)	1(6.3)	20(36.4)
γ－グルタミルトランスフェラーゼ増加	7(17.9)	0	7(12.7)
血中アルカリホスファターゼ増加	6(15.4)	0	6(10.9)
心電図ＱＴ延長	5(12.8)	0	5(9.1)
アスパラギン酸アミノトランスフェラーゼ増加	4(10.3)	0	4(7.3)
アラニンアミノトランスフェラーゼ増加	4(10.3)	0	4(7.3)
体重減少	2(5.1)	0	2(3.6)
好酸球数増加	2(5.1)	0	2(3.6)
血中クレアチニン増加	2(5.1)	0	2(3.6)
Ｃ－反応性蛋白増加	1(2.6)	1(6.3)	2(3.6)
リパーゼ増加	1(2.6)	0	1(1.8)
心胸郭比増加	1(2.6)	0	1(1.8)
心電図Ｔ波逆転	1(2.6)	0	1(1.8)
脳性ナトリウム利尿ペプチド増加	1(2.6)	0	1(1.8)
血中クレアチンホスホキナーゼ増加	1(2.6)	0	1(1.8)
血中クレアチンホスホキナーゼＭＢ増加	1(2.6)	0	1(1.8)
血中免疫グロブリンＡ減少	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
代謝および栄養障害	12(30.8)	4(25.0)	16(29.1)
食欲減退	8(20.5)	4(25.0)	12(21.8)
低アルブミン血症	2(5.1)	0	2(3.6)
低カリウム血症	2(5.1)	0	2(3.6)
低カルシウム血症	2(5.1)	0	2(3.6)
低ナトリウム血症	2(5.1)	0	2(3.6)
糖尿病	1(2.6)	0	1(1.8)
筋骨格系および結合組織障害	7(17.9)	0	7(12.7)
筋痙縮	3(7.7)	0	3(5.5)
四肢痛	1(2.6)	0	1(1.8)
筋肉疲労	1(2.6)	0	1(1.8)
筋骨格硬直	1(2.6)	0	1(1.8)
背部痛	1(2.6)	0	1(1.8)
関節炎	1(2.6)	0	1(1.8)
関節腫脹	1(2.6)	0	1(1.8)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1(2.6)	0	1(1.8)
末梢性Ｔ細胞性リンパ腫、組織型不明	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
神経系障害	4(10.3)	0	4(7.3)
味覚異常	2(5.1)	0	2(3.6)
頭痛	2(5.1)	0	2(3.6)
浮動性めまい	1(2.6)	0	1(1.8)
腎および尿路障害	1(2.6)	0	1(1.8)
蛋白尿	1(2.6)	0	1(1.8)
呼吸器、胸郭および縦隔障害	8(20.5)	1(6.3)	9(16.4)
肺臓炎	3(7.7)	1(6.3)	4(7.3)
呼吸困難	2(5.1)	0	2(3.6)
咳嗽	1(2.6)	0	1(1.8)
胸水	1(2.6)	0	1(1.8)
間質性肺疾患	1(2.6)	0	1(1.8)
鼻出血	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
皮膚および皮下組織障害	10(25.6)	2(12.5)	12(21.8)
発疹	2(5.1)	1(6.3)	3(5.5)
蕁麻疹	3(7.7)	0	3(5.5)
全身性そう痒症	1(2.6)	1(6.3)	2(3.6)
紫斑	2(5.1)	0	2(3.6)
ざ瘡様皮膚炎	1(2.6)	0	1(1.8)
全身性剥脱性皮膚炎	1(2.6)	0	1(1.8)
多形紅斑	1(2.6)	0	1(1.8)
斑状丘疹状皮疹	1(2.6)	0	1(1.8)
点状出血	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-29　重症度別の有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any Grade	23(100.0%)	13(56.5%)	23(100.0%)
	Grade 1	3(13.0%)	2(8.7%)	1(4.3%)
	Grade 2	2(8.7%)	10(43.5%)	4(17.4%)
	Grade 3	9(39.1%)	0(0.0%)	9(39.1%)
	Grade 4	9(39.1%)	1(4.3%)	9(39.1%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	18(78.3%)	1(4.3%)	18(78.3%)
血液およびリンパ系障害	Any Grade	19(82.6%)	0(0.0%)	19(82.6%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 3	8(34.8%)	0(0.0%)	8(34.8%)
	Grade 4	8(34.8%)	0(0.0%)	8(34.8%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	16(69.6%)	0(0.0%)	16(69.6%)
血小板減少症*	Any Grade	18(78.3%)	0(0.0%)	18(78.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	5(21.7%)	0(0.0%)	5(21.7%)
	Grade 3	6(26.1%)	0(0.0%)	6(26.1%)
	Grade 4	6(26.1%)	0(0.0%)	6(26.1%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	12(52.2%)	0(0.0%)	12(52.2%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
好中球减少症*	Any Grade	12(52.2%)	0(0.0%)	12(52.2%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 3	7(30.4%)	0(0.0%)	7(30.4%)
	Grade 4	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	10(43.5%)	0(0.0%)	10(43.5%)
白血球减少症*	Any Grade	10(43.5%)	0(0.0%)	10(43.5%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 3	7(30.4%)	0(0.0%)	7(30.4%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	7(30.4%)	0(0.0%)	7(30.4%)
貧血*	Any Grade	9(39.1%)	0(0.0%)	9(39.1%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 3	5(21.7%)	0(0.0%)	5(21.7%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	5(21.7%)	0(0.0%)	5(21.7%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
リンパ球減少症*	Any Grade	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
好酸球増加症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
発熱性好中球減少症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
心臓障害	Any Grade	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 1	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
第一度房室ブロック	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
動悸	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
眼障害	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
ドライアイ	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
胃腸障害	Any Grade	7(30.4%)	2(8.7%)	9(39.1%)
	Grade 1	6(26.1%)	1(4.3%)	7(30.4%)
	Grade 2	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
下痢	Any Grade	5(21.7%)	1(4.3%)	6(26.1%)
	Grade 1	4(17.4%)	1(4.3%)	5(21.7%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
腹痛	Any Grade	1(4.3%)	2(8.7%)	3(13.0%)
	Grade 1	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
悪心	Any Grade	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 1	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
口内炎	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
一般・全身障害および投与部位の状態	Any Grade	10(43.5%)	3(13.0%)	13(56.5%)
	Grade 1	7(30.4%)	2(8.7%)	9(39.1%)
	Grade 2	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 3	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	2(8.7%)	0(0.0%)	2(8.7%)
倦怠感	Any Grade	7(30.4%)	0(0.0%)	7(30.4%)
	Grade 1	5(21.7%)	0(0.0%)	5(21.7%)
	Grade 2	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
疲労	Any Grade	2(8.7%)	1(4.3%)	3(13.0%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	2(8.7%)	0(0.0%)	2(8.7%)
発熱	Any Grade	2(8.7%)	1(4.3%)	3(13.0%)
	Grade 1	2(8.7%)	1(4.3%)	3(13.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
悪寒	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
非心臓性胸痛	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
末梢性浮腫	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
感染症および寄生虫症	Any Grade	5(21.7%)	4(17.4%)	7(30.4%)
	Grade 1	1(4.3%)	1(4.3%)	1(4.3%)
	Grade 2	1(4.3%)	3(13.0%)	3(13.0%)
	Grade 3	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	3(13.0%)	0(0.0%)	3(13.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
細菌感染	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
サイトメガロウイルス感染	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
医療機器関連感染	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
麦粒腫	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
口腔カンジダ症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
皮膚感染	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
扁桃炎	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
上気道感染	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
尿路感染	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
傷害、中毒および処置合併症	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
挫傷	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
臨床検査	Any Grade	8(34.8%)	2(8.7%)	10(43.5%)
	Grade 1	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 2	3(13.0%)	2(8.7%)	5(21.7%)
	Grade 3	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 4	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	3(13.0%)	0(0.0%)	3(13.0%)
体重減少	Any Grade	4(17.4%)	0(0.0%)	4(17.4%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
アスパラギン酸アミノトランスフェラーゼ増加	Any Grade	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 1	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
γーグルタミルトランスフェラーゼ増加	Any Grade	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
アラニンアミノトランスフェラーゼ増加	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
血中アルカリホスファターゼ増加	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
血中乳酸脱水素酵素増加	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
脳性ナトリウム利尿ペプチド増加	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
好酸球数増加	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
リパーゼ増加	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
代謝および栄養障害	Any Grade	12(52.2%)	1(4.3%)	13(56.5%)
	Grade 1	4(17.4%)	1(4.3%)	5(21.7%)
	Grade 2	6(26.1%)	0(0.0%)	6(26.1%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	2(8.7%)	0(0.0%)	2(8.7%)
食欲減退	Any Grade	8(34.8%)	0(0.0%)	8(34.8%)
	Grade 1	4(17.4%)	0(0.0%)	4(17.4%)
	Grade 2	4(17.4%)	0(0.0%)	4(17.4%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
低アルブミン血症	Any Grade	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
低ナトリウム血症	Any Grade	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
高カルシウム血症	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
低カリウム血症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
低リン酸血症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
筋骨格系および結合組織障害	Any Grade	1(4.3%)	6(26.1%)	7(30.4%)
	Grade 1	0(0.0%)	5(21.7%)	5(21.7%)
	Grade 2	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
背部痛	Any Grade	0(0.0%)	4(17.4%)	4(17.4%)
	Grade 1	0(0.0%)	3(13.0%)	3(13.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
関節痛	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
脊椎すべり症	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each relationship column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
尺骨突き上げ症候群	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
腫瘍疼痛	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
神経系障害	Any Grade	7(30.4%)	3(13.0%)	9(39.1%)
	Grade 1	5(21.7%)	2(8.7%)	6(26.1%)
	Grade 2	2(8.7%)	1(4.3%)	3(13.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
味覚異常	Any Grade	4(17.4%)	0(0.0%)	4(17.4%)
	Grade 1	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 2	2(8.7%)	0(0.0%)	2(8.7%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
頭痛	Any Grade	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 1	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
味覚消失	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
認知障害	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
浮動性めまい	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
傾眠	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
腎および尿路障害	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
尿瘻	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	Any Grade	2(8.7%)	2(8.7%)	4(17.4%)
	Grade 1	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	1(4.3%)	1(4.3%)	2(8.7%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	1(4.3%)	2(8.7%)
急性呼吸不全	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	1(4.3%)	1(4.3%)
鼻出血	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
間質性肺疾患	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
口腔咽頭痛	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
皮膚および皮下組織障害	Any Grade	5(21.7%)	3(13.0%)	8(34.8%)
	Grade 1	3(13.0%)	1(4.3%)	4(17.4%)
	Grade 2	2(8.7%)	2(8.7%)	4(17.4%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
接触皮膚炎	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
湿疹	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
紅斑	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
多形紅斑	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
光線過敏性反応	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
そう痒症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
発疹	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
皮膚剥脱	Any Grade	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 1	0(0.0%)	1(4.3%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
皮膚潰瘍	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	0(0.0%)	0(0.0%)	0(0.0%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
血管障害	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
高血圧	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI-CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each relationship column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

表 2.7.4.7-30　重症度別の有害事象（201 試験）（安全性解析対象集団）

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one TEAE	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 3	5 (71.4%)	4 (57.1%)	9 (64.3%)
	Grade 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
血液およびリンパ系障害	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 3	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
貧血	Grade 1	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
白血球減少症	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
好中球減少症	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
血小板減少症	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 3	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
先天性、家族性および遺伝性障害	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
表皮融解	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
耳および迷路障害	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
回転性めまい	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
胃腸障害	Grade 1	1 (14.3%)	3 (42.9%)	4 (28.6%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
腹痛	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
便秘	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
下痢	Grade 1	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
口内乾燥	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
腸炎	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
悪心	Grade 1	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
口内炎	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
嘔吐	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
一般・全身障害および投与部位の状態	Grade 1	2 (28.6%)	2 (28.6%)	4 (28.6%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
疲労	Grade 1	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
治癒不良	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
末梢性浮腫	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
発熱	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
感染症および寄生虫症	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	1 (14.3%)	2 (28.6%)	3 (21.4%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
結膜炎	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
膀胱炎	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
鼻咽頭炎	Grade 1	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
食道カンジダ症	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
咽頭炎	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
副鼻腔炎	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
傷害、中毒および処置合併症	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
挫傷	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
臨床検査	Grade 1	1 (14.3%)	2 (28.6%)	3 (21.4%)
	Grade 2	0 (0.0%)	3 (42.9%)	3 (21.4%)
	Grade 3	3 (42.9%)	2 (28.6%)	5 (35.7%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
アラニンアミノトランスフェラーゼ増加	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
アスパラギン酸アミノトランスフェラーゼ増加	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
血中クレアチンホスホキナーゼ増加	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ｃ－反応性蛋白増加	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
低比重リポ蛋白増加	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
リンパ球数減少	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
好中球数減少	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
血小板数減少	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	3 (42.9%)	3 (42.9%)	6 (42.9%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
体重减少	Grade 1	1 (14.3%)	2 (28.6%)	3 (21.4%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
体重增加	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
白血球数减少	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
トランスアミナーゼ上昇	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
胸部コンピュータ断層撮影異常	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
トロポニンＩ増加	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
血中アルカリホスファターゼ増加	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
代謝および栄養障害	Grade 1	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 2	2 (28.6%)	3 (42.9%)	5 (35.7%)
	Grade 3	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
糖尿病	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
高血糖	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
高マグネシウム血症	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
高トリグリセリド血症	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
高尿酸血症	Grade 1	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
低カルシウム血症	Grade 1	0 (0.0%)	3 (42.9%)	3 (21.4%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
低カリウム血症	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
低マグネシウム血症	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
血液量減少症	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
食欲減退	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
筋骨格系および結合組織障害	Grade 1	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
背部痛	Grade 1	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
筋肉痛	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
筋骨格系胸痛	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
神経系障害	Grade 1	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
味覚異常	Grade 1	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
頭痛	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
パーキンソニズム	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
精神障害	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
不眠症	Grade 1	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
腎および尿路障害	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
血尿	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
頻尿	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
蛋白尿	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
尿管結石症	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
呼吸器、胸郭および縦隔障害	Grade 1	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
胸水	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
口腔咽頭不快感	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
皮膚および皮下組織障害	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
多形紅斑	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
結節性紅斑	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
全身性皮疹	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
斑状丘疹状皮疹	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
不全角化	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

System organ class Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
血管周囲細胞浸潤性皮膚炎	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
血管障害	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
低血圧	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Patients with more than one TEAE will be counted once in the worst severity category.

表 2.7.4.7-31　重症度別の有害事象（203 試験）（安全性解析対象集団）

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any Grade	39(100.0)	31(79.5)	39(100.0)
	Grade 1	2(5.1)	5(12.8)	1(2.6)
	Grade 2	4(10.3)	15(38.5)	4(10.3)
	Grade 3	22(56.4)	10(25.6)	22(56.4)
	Grade 4	11(28.2)	1(2.6)	12(30.8)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	33(84.6)	11(28.2)	34(87.2)
血液およびリンパ系障害	Any Grade	38(97.4)	7(17.9)	38(97.4)
	Grade 1	1(2.6)	2(5.1)	1(2.6)
	Grade 2	6(15.4)	1(2.6)	6(15.4)
	Grade 3	20(51.3)	3(7.7)	19(48.7)
	Grade 4	11(28.2)	1(2.6)	12(30.8)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	31(79.5)	4(10.3)	31(79.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血小板減少症*	Any Grade	35(89.7)	1(2.6)	35(89.7)
	Grade 1	7(17.9)	0(0.0)	6(15.4)
	Grade 2	7(17.9)	0(0.0)	7(17.9)
	Grade 3	14(35.9)	0(0.0)	14(35.9)
	Grade 4	7(17.9)	1(2.6)	8(20.5)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	21(53.8)	1(2.6)	22(56.4)
好中球減少症*	Any Grade	28(71.8)	0(0.0)	28(71.8)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	10(25.6)	0(0.0)	10(25.6)
	Grade 3	13(33.3)	0(0.0)	13(33.3)
	Grade 4	4(10.3)	0(0.0)	4(10.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	17(43.6)	0(0.0)	17(43.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
白血球減少症*	Any Grade	21(53.8)	3(7.7)	24(61.5)
	Grade 1	1(2.6)	1(2.6)	2(5.1)
	Grade 2	10(25.6)	1(2.6)	11(28.2)
	Grade 3	9(23.1)	1(2.6)	10(25.6)
	Grade 4	1(2.6)	0(0.0)	1(2.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	10(25.6)	1(2.6)	11(28.2)
リンパ球減少症*	Any Grade	16(41.0)	0(0.0)	16(41.0)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	3(7.7)	0(0.0)	3(7.7)
	Grade 3	10(25.6)	0(0.0)	10(25.6)
	Grade 4	2(5.1)	0(0.0)	2(5.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	12(30.8)	0(0.0)	12(30.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
貧血*	Any Grade	11(28.2)	3(7.7)	14(35.9)
	Grade 1	1(2.6)	1(2.6)	2(5.1)
	Grade 2	5(12.8)	0(0.0)	5(12.8)
	Grade 3	4(10.3)	2(5.1)	6(15.4)
	Grade 4	1(2.6)	0(0.0)	1(2.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	5(12.8)	2(5.1)	7(17.9)
発熱性好中球減少症	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
再生不良性貧血	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	1(2.6)	0(0.0)	1(2.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
心臓障害	Any Grade	4(10.3)	2(5.1)	6(15.4)
	Grade 1	2(5.1)	1(2.6)	3(7.7)
	Grade 2	2(5.1)	0(0.0)	2(5.1)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
動悸	Any Grade	2(5.1)	1(2.6)	3(7.7)
	Grade 1	2(5.1)	1(2.6)	3(7.7)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
不安定狭心症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
不整脈	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心房細動	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
心嚢液貯留	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
耳および迷路障害	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
回転性めまい	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
眼障害	Any Grade	1(2.6)	3(7.7)	4(10.3)
	Grade 1	1(2.6)	2(5.1)	3(7.7)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
結膜出血	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
ドライアイ	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
角膜炎	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
霧視	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
胃腸障害	Any Grade	20(51.3)	13(33.3)	25(64.1)
	Grade 1	10(25.6)	11(28.2)	14(35.9)
	Grade 2	10(25.6)	1(2.6)	10(25.6)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)
下痢	Any Grade	9(23.1)	6(15.4)	14(35.9)
	Grade 1	5(12.8)	5(12.8)	9(23.1)
	Grade 2	4(10.3)	1(2.6)	5(12.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
悪心	Any Grade	9(23.1)	0(0.0)	9(23.1)
	Grade 1	4(10.3)	0(0.0)	4(10.3)
	Grade 2	5(12.8)	0(0.0)	5(12.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
上腹部痛	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	2(5.1)	2(5.1)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
齲歯	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)
嘔吐	Any Grade	1(2.6)	2(5.1)	2(5.1)
	Grade 1	1(2.6)	2(5.1)	2(5.1)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
腹部不快感	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
腹痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
肛門出血	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
便秘	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
消化不良	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心窩部不快感	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
痔出血	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
口腔粘膜血腫	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
歯痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
一般・全身障害および投与部位の状態	Any Grade	16(41.0)	6(15.4)	19(48.7)
	Grade 1	9(23.1)	5(12.8)	11(28.2)
	Grade 2	6(15.4)	1(2.6)	7(17.9)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
倦怠感	Any Grade	8(20.5)	0(0.0)	8(20.5)
	Grade 1	5(12.8)	0(0.0)	5(12.8)
	Grade 2	3(7.7)	0(0.0)	3(7.7)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
発熱	Any Grade	2(5.1)	3(7.7)	5(12.8)
	Grade 1	1(2.6)	3(7.7)	4(10.3)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
疲労	Any Grade	4(10.3)	0(0.0)	4(10.3)
	Grade 1	3(7.7)	0(0.0)	3(7.7)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
末梢性浮腫	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
カテーテル留置部位腫脹	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胸部不快感	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
胸痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
溢出	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
歩行障害	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
口渇	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
免疫系障害	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
薬物過敏症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	7(17.9)	11(28.2)	15(38.5)
	Grade 1	2(5.1)	2(5.1)	2(5.1)
	Grade 2	4(10.3)	8(20.5)	12(30.8)
	Grade 3	1(2.6)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	1(2.6)	1(2.6)
咽頭炎	Any Grade	0(0.0)	3(7.7)	3(7.7)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(5.1)	2(5.1)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
気管支炎	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(5.1)	0(0.0)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
結膜炎	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
インフルエンザ	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(5.1)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
上咽頭炎	Any Grade	1(2.6)	2(5.1)	2(5.1)
	Grade 1	1(2.6)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
上気道感染	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(5.1)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
膀胱炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=39) n (%)
サイトメガロウイルス感染	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
帯状疱疹	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
膿痂疹	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
鼻炎	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
傷害、中毒および処置合併症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
爪損傷	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
臨床検査	Any Grade	19(48.7)	11(28.2)	24(61.5)
	Grade 1	7(17.9)	6(15.4)	9(23.1)
	Grade 2	8(20.5)	4(10.3)	10(25.6)
	Grade 3	4(10.3)	1(2.6)	5(12.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	4(10.3)	1(2.6)	5(12.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血中アルカリホスファターゼ増加	Any Grade	6(15.4)	2(5.1)	8(20.5)
	Grade 1	3(7.7)	1(2.6)	4(10.3)
	Grade 2	2(5.1)	1(2.6)	3(7.7)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
γーグルタミルトランスフェラーゼ増加	Any Grade	7(17.9)	1(2.6)	8(20.5)
	Grade 1	1(2.6)	1(2.6)	2(5.1)
	Grade 2	3(7.7)	0(0.0)	3(7.7)
	Grade 3	3(7.7)	0(0.0)	3(7.7)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(7.7)	0(0.0)	3(7.7)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
アスパラギン酸アミノトランスフェラーゼ増加	Any Grade	4(10.3)	4(10.3)	7(17.9)
	Grade 1	2(5.1)	4(10.3)	5(12.8)
	Grade 2	2(5.1)	0(0.0)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
体重減少	Any Grade	2(5.1)	4(10.3)	6(15.4)
	Grade 1	1(2.6)	2(5.1)	3(7.7)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
アラニンアミノトランスフェラーゼ増加	Any Grade	4(10.3)	3(7.7)	5(12.8)
	Grade 1	2(5.1)	3(7.7)	3(7.7)
	Grade 2	2(5.1)	0(0.0)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心電図ＱＴ延長	Any Grade	5(12.8)	0(0.0)	5(12.8)
	Grade 1	4(10.3)	0(0.0)	4(10.3)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血中クレアチニン増加	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
脳性ナトリウム利尿ペプチド増加	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	1(2.6)	1(2.6)	2(5.1)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
C－反応性蛋白増加	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
好酸球数増加	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血中コレステロール増加	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血中クレアチンホスホキナーゼＭＢ増加	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血中クレアチンホスホキナーゼ増加	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血中免疫グロブリンA減少	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
尿中血陽性	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心胸郭比増加	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
心電図Ｔ波逆転	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
リパーゼ増加	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
体重増加	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
代謝および栄養障害	Any Grade	12(30.8)	6(15.4)	16(41.0)
	Grade 1	2(5.1)	1(2.6)	2(5.1)
	Grade 2	7(17.9)	5(12.8)	11(28.2)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	1(2.6)	0(0.0)	1(2.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(7.7)	0(0.0)	3(7.7)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
食欲減退	Any Grade	8(20.5)	0(0.0)	8(20.5)
	Grade 1	2(5.1)	0(0.0)	2(5.1)
	Grade 2	4(10.3)	0(0.0)	4(10.3)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
低アルブミン血症	Any Grade	2(5.1)	2(5.1)	4(10.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(5.1)	2(5.1)	4(10.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
低カリウム血症	Any Grade	2(5.1)	1(2.6)	3(7.7)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	1(2.6)	0(0.0)	1(2.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
低カルシウム血症	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(5.1)	0(0.0)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
低ナトリウム血症	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
糖尿病	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
高カリウム血症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
高マグネシウム血症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
高トリグリセリド血症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
低蛋白血症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
筋骨格系および結合組織障害	Any Grade	7(17.9)	11(28.2)	15(38.5)
	Grade 1	6(15.4)	6(15.4)	9(23.1)
	Grade 2	1(2.6)	5(12.8)	6(15.4)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
筋痙縮	Any Grade	3(7.7)	2(5.1)	5(12.8)
	Grade 1	3(7.7)	0(0.0)	3(7.7)
	Grade 2	0(0.0)	2(5.1)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
背部痛	Any Grade	1(2.6)	3(7.7)	4(10.3)
	Grade 1	0(0.0)	2(5.1)	2(5.1)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
筋肉痛	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	2(5.1)	2(5.1)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
関節痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
関節炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
出血性関節症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
関節腫脹	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
筋肉疲労	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
筋骨格硬直	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
頚部痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
四肢痛	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
腱炎	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any Grade	1(2.6)	2(5.1)	3(7.7)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
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N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
末梢性Ｔ細胞性リンパ腫、組織型不明	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
皮膚乳頭腫	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
腫瘍疼痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
神経系障害	Any Grade	4(10.3)	5(12.8)	7(17.9)
	Grade 1	3(7.7)	2(5.1)	4(10.3)
	Grade 2	1(2.6)	3(7.7)	3(7.7)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
頭痛	Any Grade	2(5.1)	2(5.1)	4(10.3)
	Grade 1	2(5.1)	1(2.6)	3(7.7)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
味覚異常	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
浮動性めまい	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
感覚鈍麻	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
末梢性感覚ニューロパチー	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
失神寸前の状態	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
精神障害	Any Grade	0(0.0)	4(10.3)	4(10.3)
	Grade 1	0(0.0)	3(7.7)	3(7.7)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
不眠症	Any Grade	0(0.0)	3(7.7)	3(7.7)
	Grade 1	0(0.0)	2(5.1)	2(5.1)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
譫妄	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
腎および尿路障害	Any Grade	1(2.6)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	0(0.0)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
急性腎障害	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血尿	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
蛋白尿	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
呼吸器、胸郭および縦隔障害	Any Grade	8(20.5)	7(17.9)	14(35.9)
	Grade 1	3(7.7)	2(5.1)	4(10.3)
	Grade 2	3(7.7)	3(7.7)	6(15.4)
	Grade 3	2(5.1)	2(5.1)	4(10.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	2(5.1)	4(10.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
肺臓炎	Any Grade	3(7.7)	0(0.0)	3(7.7)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
咳嗽	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
呼吸困難	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
鼻出血	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
口腔咽頭痛	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胸水	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
咽頭知覚不全	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
間質性肺疾患	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
上気道の炎症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)
皮膚および皮下組織障害	Any Grade	10(25.6)	10(25.6)	18(46.2)
	Grade 1	5(12.8)	6(15.4)	9(23.1)
	Grade 2	5(12.8)	4(10.3)	9(23.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
発疹	Any Grade	2(5.1)	1(2.6)	3(7.7)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
蕁麻疹	Any Grade	3(7.7)	0(0.0)	3(7.7)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	3(7.7)	0(0.0)	3(7.7)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
紅斑	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(5.1)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
紫斑	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	2(5.1)	0(0.0)	2(5.1)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
斑状丘疹状皮疹	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
褥瘡性潰瘍	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
ざ瘡様皮膚炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
全身性剥脱性皮膚炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
皮膚乾燥	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
皮脂欠乏性湿疹	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
多形紅斑	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
全身紅斑	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
皮膚疼痛	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
点状出血	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
色素沈着障害	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
全身性そう痒症	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
そう痒性皮疹	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血管障害	Any Grade	0(0.0)	2(5.1)	2(5.1)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
低血圧	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
末梢動脈閉塞性疾患	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any Grade	12(75.0)	14(87.5)	16(100.0)
	Grade 1	1(6.3)	2(12.5)	0(0.0)
	Grade 2	2(12.5)	7(43.8)	4(25.0)
	Grade 3	7(43.8)	3(18.8)	8(50.0)
	Grade 4	1(6.3)	2(12.5)	3(18.8)
	Grade 5	1(6.3)	0(0.0)	1(6.3)
	>=Grade 3	9(56.3)	5(31.3)	12(75.0)
血液およびリンパ系障害	Any Grade	9(56.3)	6(37.5)	14(87.5)
	Grade 1	1(6.3)	0(0.0)	1(6.3)
	Grade 2	2(12.5)	2(12.5)	3(18.8)
	Grade 3	5(31.3)	3(18.8)	8(50.0)
	Grade 4	1(6.3)	1(6.3)	2(12.5)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	6(37.5)	4(25.0)	10(62.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
血小板減少症*	Any Grade	7(43.8)	4(25.0)	11(68.8)
	Grade 1	2(12.5)	0(0.0)	2(12.5)
	Grade 2	2(12.5)	1(6.3)	3(18.8)
	Grade 3	3(18.8)	2(12.5)	5(31.3)
	Grade 4	0(0.0)	1(6.3)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(18.8)	3(18.8)	6(37.5)
貧血*	Any Grade	1(6.3)	3(18.8)	4(25.0)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(12.5)	2(12.5)
	Grade 3	1(6.3)	1(6.3)	2(12.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	1(6.3)	2(12.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
好中球減少症*	Any Grade	3(18.8)	0(0.0)	3(18.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(12.5)	0(0.0)	2(12.5)
	Grade 4	1(6.3)	0(0.0)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(18.8)	0(0.0)	3(18.8)
好酸球増加症	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
発熱性好中球減少症	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
心臓障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
心房細動	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
耳および迷路障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
耳痛	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
眼障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
白内障	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胃腸障害	Any Grade	5(31.3)	6(37.5)	7(43.8)
	Grade 1	0(0.0)	3(18.8)	1(6.3)
	Grade 2	4(25.0)	3(18.8)	5(31.3)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
下痢	Any Grade	1(6.3)	2(12.5)	3(18.8)
	Grade 1	0(0.0)	2(12.5)	2(12.5)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
悪心	Any Grade	2(12.5)	1(6.3)	3(18.8)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	2(12.5)	0(0.0)	2(12.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
腹痛	Any Grade	1(6.3)	1(6.3)	2(12.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(6.3)	1(6.3)	2(12.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
口内炎	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
胃潰瘍	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胃炎	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(6.3)	0(0.0)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
嘔吐	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
一般・全身障害および投与部位の状態	Any Grade	1(6.3)	7(43.8)	8(50.0)
	Grade 1	1(6.3)	3(18.8)	4(25.0)
	Grade 2	0(0.0)	4(25.0)	4(25.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
発熱	Any Grade	0(0.0)	6(37.5)	6(37.5)
	Grade 1	0(0.0)	6(37.5)	6(37.5)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
無力症	Any Grade	1(6.3)	1(6.3)	2(12.5)
	Grade 1	1(6.3)	0(0.0)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
疲労	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
インフルエンザ様疾患	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
末梢性浮腫	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(12.5)	2(12.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
感染症および寄生虫症	Any Grade	1(6.3)	4(25.0)	4(25.0)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	2(12.5)	1(6.3)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(6.3)	0(0.0)	1(6.3)
	>=Grade 3	1(6.3)	1(6.3)	2(12.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
上気道感染	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(12.5)	2(12.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
感染性小腸結腸炎	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(6.3)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
胃腸炎	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
肺炎	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(6.3)	0(0.0)	1(6.3)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
ブドウ球菌皮膚感染	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(6.3)	1(6.3)
傷害、中毒および処置合併症	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	2(12.5)	2(12.5)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
胃瘻管部合併症	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
処置による疼痛	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
臨床検査	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
C－反応性蛋白増加	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
代謝および栄養障害	Any Grade	4(25.0)	5(31.3)	9(56.3)
	Grade 1	2(12.5)	1(6.3)	3(18.8)
	Grade 2	2(12.5)	2(12.5)	4(25.0)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	1(6.3)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	2(12.5)	2(12.5)
食欲減退	Any Grade	4(25.0)	1(6.3)	5(31.3)
	Grade 1	2(12.5)	1(6.3)	3(18.8)
	Grade 2	2(12.5)	0(0.0)	2(12.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
低カリウム血症	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	1(6.3)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(6.3)	1(6.3)
低アルブミン血症	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
低カルシウム血症	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(6.3)	1(6.3)
筋骨格系および結合組織障害	Any Grade	0(0.0)	4(25.0)	4(25.0)
	Grade 1	0(0.0)	2(12.5)	2(12.5)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(6.3)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
背部痛	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
筋肉疲労	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(6.3)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(6.3)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
筋力低下	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
肩回旋筋腱板症候群	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
腫瘍疼痛	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
神経系障害	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
頭痛	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
精神障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
不眠症	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
生殖系および乳房障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
陰嚢浮腫	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	Any Grade	1(6.3)	7(43.8)	7(43.8)
	Grade 1	0(0.0)	4(25.0)	3(18.8)
	Grade 2	0(0.0)	3(18.8)	3(18.8)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
咳嗽	Any Grade	0(0.0)	4(25.0)	4(25.0)
	Grade 1	0(0.0)	4(25.0)	4(25.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
呼吸困難	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
発声障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
労作性呼吸困難	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
しゃっくり	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
口腔咽頭痛	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
肺臓炎	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
湿性咳嗽	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
アレルギー性鼻炎	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
鼻漏	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
皮膚および皮下組織障害	Any Grade	2(12.5)	3(18.8)	5(31.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	1(6.3)	2(12.5)	3(18.8)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
発疹	Any Grade	1(6.3)	1(6.3)	2(12.5)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
蕁麻疹	Any Grade	0(0.0)	2(12.5)	2(12.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(12.5)	2(12.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
全身性そう痒症	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(6.3)	0(0.0)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血管障害	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
深部静脈血栓症	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(6.3)	1(6.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any Grade	51(92.7)	45(81.8)	55(100.0)
	Grade 1	3(5.5)	7(12.7)	1(1.8)
	Grade 2	6(10.9)	22(40.0)	8(14.5)
	Grade 3	29(52.7)	13(23.6)	30(54.5)
	Grade 4	12(21.8)	3(5.5)	15(27.3)
	Grade 5	1(1.8)	0(0.0)	1(1.8)
	>=Grade 3	42(76.4)	16(29.1)	46(83.6)
血液およびリンパ系障害	Any Grade	47(85.5)	13(23.6)	52(94.5)
	Grade 1	2(3.6)	2(3.6)	2(3.6)
	Grade 2	8(14.5)	3(5.5)	9(16.4)
	Grade 3	25(45.5)	6(10.9)	27(49.1)
	Grade 4	12(21.8)	2(3.6)	14(25.5)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	37(67.3)	8(14.5)	41(74.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
血小板减少症*	Any Grade	42(76.4)	5(9.1)	46(83.6)
	Grade 1	9(16.4)	0(0.0)	8(14.5)
	Grade 2	9(16.4)	1(1.8)	10(18.2)
	Grade 3	17(30.9)	2(3.6)	19(34.5)
	Grade 4	7(12.7)	2(3.6)	9(16.4)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	24(43.6)	4(7.3)	28(50.9)
好中球减少症*	Any Grade	31(56.4)	0(0.0)	31(56.4)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	10(18.2)	0(0.0)	10(18.2)
	Grade 3	15(27.3)	0(0.0)	15(27.3)
	Grade 4	5(9.1)	0(0.0)	5(9.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	20(36.4)	0(0.0)	20(36.4)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
白血球減少症*	Any Grade	21(38.2)	3(5.5)	24(43.6)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	10(18.2)	1(1.8)	11(20.0)
	Grade 3	9(16.4)	1(1.8)	10(18.2)
	Grade 4	1(1.8)	0(0.0)	1(1.8)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	10(18.2)	1(1.8)	11(20.0)
貧血*	Any Grade	12(21.8)	6(10.9)	18(32.7)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	5(9.1)	2(3.6)	7(12.7)
	Grade 3	5(9.1)	3(5.5)	8(14.5)
	Grade 4	1(1.8)	0(0.0)	1(1.8)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	6(10.9)	3(5.5)	9(16.4)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
リンパ球減少症*	Any Grade	16(29.1)	0(0.0)	16(29.1)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	3(5.5)	0(0.0)	3(5.5)
	Grade 3	10(18.2)	0(0.0)	10(18.2)
	Grade 4	2(3.6)	0(0.0)	2(3.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	12(21.8)	0(0.0)	12(21.8)
発熱性好中球減少症	Any Grade	3(5.5)	0(0.0)	3(5.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	3(5.5)	0(0.0)	3(5.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	0(0.0)	3(5.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
再生不良性貧血	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	1(1.8)	0(0.0)	1(1.8)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
好酸球増加症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
心臓障害	Any Grade	4(7.3)	3(5.5)	7(12.7)
	Grade 1	2(3.6)	1(1.8)	3(5.5)
	Grade 2	2(3.6)	1(1.8)	3(5.5)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)
動悸	Any Grade	2(3.6)	1(1.8)	3(5.5)
	Grade 1	2(3.6)	1(1.8)	3(5.5)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
心房細動	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
不安定狭心症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
不整脈	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心嚢液貯留	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
耳および迷路障害	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
耳痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
回転性めまい	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
眼障害	Any Grade	1(1.8)	4(7.3)	5(9.1)
	Grade 1	1(1.8)	3(5.5)	4(7.3)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
白内障	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
結膜出血	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
ドライアイ	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
角膜炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
霧視	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胃腸障害	Any Grade	25(45.5)	19(34.5)	32(58.2)
	Grade 1	10(18.2)	14(25.5)	15(27.3)
	Grade 2	14(25.5)	4(7.3)	15(27.3)
	Grade 3	1(1.8)	1(1.8)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	1(1.8)	2(3.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
下痢	Any Grade	10(18.2)	8(14.5)	17(30.9)
	Grade 1	5(9.1)	7(12.7)	11(20.0)
	Grade 2	4(7.3)	1(1.8)	5(9.1)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
悪心	Any Grade	11(20.0)	1(1.8)	12(21.8)
	Grade 1	4(7.3)	1(1.8)	5(9.1)
	Grade 2	7(12.7)	0(0.0)	7(12.7)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
腹痛	Any Grade	1(1.8)	2(3.6)	3(5.5)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
嘔吐	Any Grade	1(1.8)	3(5.5)	3(5.5)
	Grade 1	1(1.8)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
上腹部痛	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
齲歯	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
口内炎	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
腹部不快感	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
肛門出血	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
便秘	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
消化不良	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心窩部不快感	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
胃潰瘍	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胃炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
痔出血	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
口腔粘膜血腫	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
歯痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
一般・全身障害および投与部位の状態	Any Grade	17(30.9)	13(23.6)	27(49.1)
	Grade 1	10(18.2)	8(14.5)	15(27.3)
	Grade 2	6(10.9)	5(9.1)	11(20.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
発熱	Any Grade	2(3.6)	9(16.4)	11(20.0)
	Grade 1	1(1.8)	9(16.4)	10(18.2)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
倦怠感	Any Grade	8(14.5)	0(0.0)	8(14.5)
	Grade 1	5(9.1)	0(0.0)	5(9.1)
	Grade 2	3(5.5)	0(0.0)	3(5.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
疲労	Any Grade	4(7.3)	2(3.6)	6(10.9)
	Grade 1	3(5.5)	1(1.8)	4(7.3)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
末梢性浮腫	Any Grade	2(3.6)	2(3.6)	4(7.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	2(3.6)	3(5.5)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
無力症	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
インフルエンザ様疾患	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
カテーテル留置部位腫脹	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胸部不快感	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
胸痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
溢出	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
歩行障害	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
口渇	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
免疫系障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
薬物過敏症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	8(14.5)	15(27.3)	19(34.5)
	Grade 1	2(3.6)	3(5.5)	3(5.5)
	Grade 2	4(7.3)	10(18.2)	13(23.6)
	Grade 3	1(1.8)	2(3.6)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(1.8)	0(0.0)	1(1.8)
	>=Grade 3	2(3.6)	2(3.6)	3(5.5)
上気道感染	Any Grade	0(0.0)	4(7.3)	4(7.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	4(7.3)	4(7.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
咽頭炎	Any Grade	0(0.0)	3(5.5)	3(5.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)
気管支炎	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(3.6)	0(0.0)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
結膜炎	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
インフルエンザ	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
上咽頭炎	Any Grade	1(1.8)	2(3.6)	2(3.6)
	Grade 1	1(1.8)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
膀胱炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
サイトメガロウイルス感染	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
感染性小腸結腸炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
胃腸炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
帯状疱疹	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
膿痂疹	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
肺炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(1.8)	0(0.0)	1(1.8)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
鼻炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
ブドウ球菌皮膚感染	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)
傷害、中毒および処置合併症	Any Grade	0(0.0)	3(5.5)	3(5.5)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
胃瘻管部合併症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
爪損傷	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
処置による疼痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
臨床検査	Any Grade	20(36.4)	11(20.0)	25(45.5)
	Grade 1	7(12.7)	6(10.9)	9(16.4)
	Grade 2	8(14.5)	4(7.3)	10(18.2)
	Grade 3	5(9.1)	1(1.8)	6(10.9)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	5(9.1)	1(1.8)	6(10.9)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
血中アルカリホスファターゼ増加	Any Grade	6(10.9)	2(3.6)	8(14.5)
	Grade 1	3(5.5)	1(1.8)	4(7.3)
	Grade 2	2(3.6)	1(1.8)	3(5.5)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
γーグルタミルトランスフェラーゼ増加	Any Grade	7(12.7)	1(1.8)	8(14.5)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	3(5.5)	0(0.0)	3(5.5)
	Grade 3	3(5.5)	0(0.0)	3(5.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	0(0.0)	3(5.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
アスパラギン酸アミノトランスフェラーゼ増加	Any Grade	4(7.3)	4(7.3)	7(12.7)
	Grade 1	2(3.6)	4(7.3)	5(9.1)
	Grade 2	2(3.6)	0(0.0)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
体重減少	Any Grade	2(3.6)	4(7.3)	6(10.9)
	Grade 1	1(1.8)	2(3.6)	3(5.5)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
アラニンアミノトランスフェラーゼ増加	Any Grade	4(7.3)	3(5.5)	5(9.1)
	Grade 1	2(3.6)	3(5.5)	3(5.5)
	Grade 2	2(3.6)	0(0.0)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心電図ＱＴ延長	Any Grade	5(9.1)	0(0.0)	5(9.1)
	Grade 1	4(7.3)	0(0.0)	4(7.3)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
C－反応性蛋白増加	Any Grade	2(3.6)	1(1.8)	3(5.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
血中クレアチニン増加	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
脳性ナトリウム利尿ペプチド増加	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
好酸球数増加	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
血中コレステロール増加	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血中クレアチンホスホキナーゼＭＢ増加	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
血中クレアチンホスホキナーゼ増加	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血中免疫グロブリンA減少	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
尿中血陽性	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心胸郭比増加	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
心電図Ｔ波逆転	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
リパーゼ増加	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
体重増加	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
代謝および栄養障害	Any Grade	16(29.1)	11(20.0)	25(45.5)
	Grade 1	4(7.3)	2(3.6)	5(9.1)
	Grade 2	9(16.4)	7(12.7)	15(27.3)
	Grade 3	2(3.6)	1(1.8)	3(5.5)
	Grade 4	1(1.8)	1(1.8)	2(3.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	2(3.6)	5(9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
食欲減退	Any Grade	12(21.8)	1(1.8)	13(23.6)
	Grade 1	4(7.3)	1(1.8)	5(9.1)
	Grade 2	6(10.9)	0(0.0)	6(10.9)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
低アルブミン血症	Any Grade	2(3.6)	3(5.5)	5(9.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(3.6)	3(5.5)	5(9.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
低カリウム血症	Any Grade	2(3.6)	3(5.5)	5(9.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	2(3.6)	3(5.5)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	1(1.8)	1(1.8)	2(3.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	1(1.8)	2(3.6)
低カルシウム血症	Any Grade	2(3.6)	1(1.8)	3(5.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(3.6)	0(0.0)	2(3.6)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
低ナトリウム血症	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
糖尿病	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
高カリウム血症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
高マグネシウム血症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
高トリグリセリド血症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
低蛋白血症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
筋骨格系および結合組織障害	Any Grade	7(12.7)	15(27.3)	19(34.5)
	Grade 1	6(10.9)	8(14.5)	11(20.0)
	Grade 2	1(1.8)	6(10.9)	7(12.7)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)
背部痛	Any Grade	1(1.8)	4(7.3)	5(9.1)
	Grade 1	0(0.0)	3(5.5)	3(5.5)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
筋痙縮	Any Grade	3(5.5)	2(3.6)	5(9.1)
	Grade 1	3(5.5)	0(0.0)	3(5.5)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
筋肉疲労	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
筋肉痛	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
関節痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
関節炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
出血性関節症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
関節腫脹	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
筋力低下	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
筋骨格硬直	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
頚部痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
四肢痛	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
肩回旋筋腱板症候群	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
腱炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any Grade	1(1.8)	3(5.5)	4(7.3)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
腫瘍疼痛	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
末梢性Ｔ細胞性リンパ腫、組織型不明	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
皮膚乳頭腫	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
神経系障害	Any Grade	4(7.3)	7(12.7)	9(16.4)
	Grade 1	3(5.5)	3(5.5)	5(9.1)
	Grade 2	1(1.8)	4(7.3)	4(7.3)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
頭痛	Any Grade	2(3.6)	4(7.3)	6(10.9)
	Grade 1	2(3.6)	2(3.6)	4(7.3)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
味覚異常	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
浮動性めまい	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
感覚鈍麻	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
末梢性感覚ニューロパチー	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
失神寸前の状態	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
精神障害	Any Grade	0(0.0)	5(9.1)	5(9.1)
	Grade 1	0(0.0)	3(5.5)	3(5.5)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
不眠症	Any Grade	0(0.0)	4(7.3)	4(7.3)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
譫妄	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
腎および尿路障害	Any Grade	1(1.8)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	0(0.0)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
急性腎障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血尿	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
蛋白尿	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
生殖系および乳房障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
陰嚢浮腫	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
呼吸器、胸郭および縦隔障害	Any Grade	9(16.4)	14(25.5)	21(38.2)
	Grade 1	3(5.5)	6(10.9)	7(12.7)
	Grade 2	3(5.5)	6(10.9)	9(16.4)
	Grade 3	3(5.5)	2(3.6)	5(9.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	2(3.6)	5(9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
咳嗽	Any Grade	1(1.8)	5(9.1)	6(10.9)
	Grade 1	1(1.8)	4(7.3)	5(9.1)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
呼吸困難	Any Grade	2(3.6)	2(3.6)	4(7.3)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
肺臓炎	Any Grade	4(7.3)	0(0.0)	4(7.3)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
口腔咽頭痛	Any Grade	0(0.0)	3(5.5)	3(5.5)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
鼻出血	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
胸水	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
咽頭知覚不全	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
発声障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
労作性呼吸困難	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
しゃっくり	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
間質性肺疾患	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
湿性咳嗽	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
アレルギー性鼻炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
鼻漏	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
上気道の炎症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)
皮膚および皮下組織障害	Any Grade	12(21.8)	13(23.6)	23(41.8)
	Grade 1	5(9.1)	7(12.7)	10(18.2)
	Grade 2	6(10.9)	6(10.9)	12(21.8)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
発疹	Any Grade	3(5.5)	2(3.6)	5(9.1)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
蕁麻疹	Any Grade	3(5.5)	2(3.6)	5(9.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	3(5.5)	2(3.6)	5(9.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
紅斑	Any Grade	0(0.0)	2(3.6)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	2(3.6)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
全身性そう痒症	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(3.6)	0(0.0)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
紫斑	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	2(3.6)	0(0.0)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
斑状丘疹状皮疹	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
褥瘡性潰瘍	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
ざ瘡様皮膚炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
全身性剥脱性皮膚炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
皮膚乾燥	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
皮脂欠乏性湿疹	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
多形紅斑	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
全身紅斑	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
皮膚疼痛	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
点状出血	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
色素沈着障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
そう痒性皮疹	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血管障害	Any Grade	0(0.0)	3(5.5)	3(5.5)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
深部静脈血栓症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
低血圧	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
末梢動脈閉塞性疾患	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-32　発現時期別の有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any period	23	23 (100.0%)	0 (0.0%)	23 (100.0%)
	<4 Weeks	23	23 (100.0%)	0 (0.0%)	23 (100.0%)
	4 - <8 Weeks	17	13 (76.5%)	0 (0.0%)	13 (76.5%)
	8 - <12 Weeks	12	7 (58.3%)	1 (8.3%)	8 (66.7%)
	12 - <16 Weeks	6	6 (100.0%)	0 (0.0%)	6 (100.0%)
	>=16 Weeks	3	3 (100.0%)	0 (0.0%)	3 (100.0%)
血液およびリンパ系障害	Any period	23	19 (82.6%)	0 (0.0%)	19 (82.6%)
	<4 Weeks	23	19 (82.6%)	0 (0.0%)	19 (82.6%)
	4 - <8 Weeks	17	13 (76.5%)	0 (0.0%)	13 (76.5%)
	8 - <12 Weeks	12	6 (50.0%)	0 (0.0%)	6 (50.0%)
	12 - <16 Weeks	6	5 (83.3%)	0 (0.0%)	5 (83.3%)
	>=16 Weeks	3	3 (100.0%)	0 (0.0%)	3 (100.0%)
血小板減少症*	Any period	23	18 (78.3%)	0 (0.0%)	18 (78.3%)
	<4 Weeks	23	18 (78.3%)	0 (0.0%)	18 (78.3%)
	4 - <8 Weeks	17	7 (41.2%)	0 (0.0%)	7 (41.2%)
	8 - <12 Weeks	12	3 (25.0%)	0 (0.0%)	3 (25.0%)
	12 - <16 Weeks	6	2 (33.3%)	0 (0.0%)	2 (33.3%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
好中球减少症*	Any period	23	12 (52.2%)	0 (0.0%)	12 (52.2%)
	<4 Weeks	23	10 (43.5%)	0 (0.0%)	10 (43.5%)
	4 - <8 Weeks	17	9 (52.9%)	0 (0.0%)	9 (52.9%)
	8 - <12 Weeks	12	4 (33.3%)	0 (0.0%)	4 (33.3%)
	12 - <16 Weeks	6	3 (50.0%)	0 (0.0%)	3 (50.0%)
	>=16 Weeks	3	2 (66.7%)	0 (0.0%)	2 (66.7%)
白血球减少症*	Any period	23	10 (43.5%)	0 (0.0%)	10 (43.5%)
	<4 Weeks	23	8 (34.8%)	0 (0.0%)	8 (34.8%)
	4 - <8 Weeks	17	9 (52.9%)	0 (0.0%)	9 (52.9%)
	8 - <12 Weeks	12	5 (41.7%)	0 (0.0%)	5 (41.7%)
	12 - <16 Weeks	6	2 (33.3%)	0 (0.0%)	2 (33.3%)
	>=16 Weeks	3	2 (66.7%)	0 (0.0%)	2 (66.7%)
貧血*	Any period	23	9 (39.1%)	0 (0.0%)	9 (39.1%)
	<4 Weeks	23	4 (17.4%)	0 (0.0%)	4 (17.4%)
	4 - <8 Weeks	17	6 (35.3%)	0 (0.0%)	6 (35.3%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	1 (16.7%)	0 (0.0%)	1 (16.7%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
リンパ球減少症*	Any period	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	2 (11.8%)	0 (0.0%)	2 (11.8%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	1 (16.7%)	0 (0.0%)	1 (16.7%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)
好酸球増加症	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
発熱性好中球減少症	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
心臓障害	Any period	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	<4 Weeks	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
第一度房室ブロック	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
動悸	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
眼障害	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	1 (8.3%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
ドライアイ	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	1 (8.3%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
胃腸障害	Any period	23	7 (30.4%)	2 (8.7%)	9 (39.1%)
	<4 Weeks	23	6 (26.1%)	1 (4.3%)	7 (30.4%)
	4 - <8 Weeks	17	2 (11.8%)	1 (5.9%)	3 (17.6%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
下痢	Any period	23	5 (21.7%)	1 (4.3%)	6 (26.1%)
	<4 Weeks	23	3 (13.0%)	1 (4.3%)	4 (17.4%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)
腹痛	Any period	23	1 (4.3%)	2 (8.7%)	3 (13.0%)
	<4 Weeks	23	1 (4.3%)	1 (4.3%)	2 (8.7%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
悪心	Any period	23	3 (13.0%)	0 (0.0%)	3 (13.0%)
	<4 Weeks	23	3 (13.0%)	0 (0.0%)	3 (13.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
口内炎	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
一般・全身障害および投与部位の状態	Any period	23	10 (43.5%)	3 (13.0%)	13 (56.5%)
	<4 Weeks	23	7 (30.4%)	3 (13.0%)	10 (43.5%)
	4 - <8 Weeks	17	4 (23.5%)	0 (0.0%)	4 (23.5%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)
倦怠感	Any period	23	7 (30.4%)	0 (0.0%)	7 (30.4%)
	<4 Weeks	23	6 (26.1%)	0 (0.0%)	6 (26.1%)
	4 - <8 Weeks	17	2 (11.8%)	0 (0.0%)	2 (11.8%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
疲労	Any period	23	2 (8.7%)	1 (4.3%)	3 (13.0%)
	<4 Weeks	23	1 (4.3%)	1 (4.3%)	2 (8.7%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)
発熱	Any period	23	2 (8.7%)	1 (4.3%)	3 (13.0%)
	<4 Weeks	23	1 (4.3%)	1 (4.3%)	2 (8.7%)
	4 - <8 Weeks	17	2 (11.8%)	0 (0.0%)	2 (11.8%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
悪寒	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
非心臓性胸痛	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
末梢性浮腫	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
感染症および寄生虫症	Any period	23	5 (21.7%)	2 (8.7%)	7 (30.4%)
	<4 Weeks	23	1 (4.3%)	2 (8.7%)	3 (13.0%)
	4 - <8 Weeks	17	3 (17.6%)	1 (5.9%)	4 (23.5%)
	8 - <12 Weeks	12	2 (16.7%)	0 (0.0%)	2 (16.7%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
細菌感染	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
サイトメガロウイルス感染	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
医療機器関連感染	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
麦粒腫	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	1 (33.3%)	1 (33.3%)
口腔カンジダ症	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
ニューモシスチス・イロベチイ肺炎	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
皮膚感染	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
扁桃炎	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
上気道感染	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
尿路感染	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	1 (33.3%)	0 (0.0%)	1 (33.3%)
傷害、中毒および処置合併症	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
挫傷	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
臨床検査	Any period	23	8 (34.8%)	2 (8.7%)	10 (43.5%)
	<4 Weeks	23	6 (26.1%)	1 (4.3%)	7 (30.4%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	1 (16.7%)	0 (0.0%)	1 (16.7%)
	>=16 Weeks	3	0 (0.0%)	1 (33.3%)	1 (33.3%)
体重減少	Any period	23	4 (17.4%)	0 (0.0%)	4 (17.4%)
	<4 Weeks	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	1 (16.7%)	0 (0.0%)	1 (16.7%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
アスパラギン酸アミノトランスフェラーゼ増加	Any period	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	<4 Weeks	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
γーグルタミルトランスフェラーゼ増加	Any period	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	<4 Weeks	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
アラニンアミノトランスフェラーゼ増加	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
血中アルカリホスファターゼ増加	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
血中乳酸脱水素酵素増加	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
脳性ナトリウム利尿ペプチド増加	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	1 (33.3%)	1 (33.3%)
好酸球数増加	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
リパーゼ増加	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
代謝および栄養障害	Any period	23	12 (52.2%)	1 (4.3%)	13 (56.5%)
	<4 Weeks	23	12 (52.2%)	1 (4.3%)	13 (56.5%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
食欲減退	Any period	23	8 (34.8%)	0 (0.0%)	8 (34.8%)
	<4 Weeks	23	8 (34.8%)	0 (0.0%)	8 (34.8%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
低アルブミン血症	Any period	23	3 (13.0%)	0 (0.0%)	3 (13.0%)
	<4 Weeks	23	3 (13.0%)	0 (0.0%)	3 (13.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
低ナトリウム血症	Any period	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	<4 Weeks	23	2 (8.7%)	0 (0.0%)	2 (8.7%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
高カルシウム血症	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
低カリウム血症	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
低リン酸血症	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
筋骨格系および結合組織障害	Any period	23	1 (4.3%)	6 (26.1%)	7 (30.4%)
	<4 Weeks	23	0 (0.0%)	4 (17.4%)	4 (17.4%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	1 (8.3%)	1 (8.3%)	2 (16.7%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
背部痛	Any period	23	0 (0.0%)	4 (17.4%)	4 (17.4%)
	<4 Weeks	23	0 (0.0%)	3 (13.0%)	3 (13.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	1 (8.3%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
関節痛	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
脊椎すべり症	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
尺骨突き上げ症候群	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
腫瘍疼痛	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
神経系障害	Any period	23	7 (30.4%)	2 (8.7%)	9 (39.1%)
	<4 Weeks	23	6 (26.1%)	1 (4.3%)	7 (30.4%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	1 (16.7%)	0 (0.0%)	1 (16.7%)
	>=16 Weeks	3	0 (0.0%)	1 (33.3%)	1 (33.3%)
味覚異常	Any period	23	4 (17.4%)	0 (0.0%)	4 (17.4%)
	<4 Weeks	23	3 (13.0%)	0 (0.0%)	3 (13.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	1 (16.7%)	0 (0.0%)	1 (16.7%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
頭痛	Any period	23	1 (4.3%)	1 (4.3%)	2 (8.7%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	1 (33.3%)	1 (33.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
味覚消失	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
認知障害	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
浮動性めまい	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
傾眠	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
腎および尿路障害	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
尿瘻	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	Any period	23	2 (8.7%)	2 (8.7%)	4 (17.4%)
	<4 Weeks	23	1 (4.3%)	1 (4.3%)	2 (8.7%)
	4 - <8 Weeks	17	1 (5.9%)	1 (5.9%)	2 (11.8%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
急性呼吸不全	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
鼻出血	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
間質性肺疾患	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
口腔咽頭痛	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	1 (5.9%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
皮膚および皮下組織障害	Any period	23	5 (21.7%)	3 (13.0%)	8 (34.8%)
	<4 Weeks	23	2 (8.7%)	2 (8.7%)	4 (17.4%)
	4 - <8 Weeks	17	3 (17.6%)	0 (0.0%)	3 (17.6%)
	8 - <12 Weeks	12	1 (8.3%)	1 (8.3%)	2 (16.7%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
接触皮膚炎	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
湿疹	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	1 (8.3%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
紅斑	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
多形紅斑	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
光線過敏性反応	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
そう痒症	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
発疹	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
皮膚剥脱	Any period	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	1 (4.3%)	1 (4.3%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
皮膚潰瘍	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	0 (0.0%)	0 (0.0%)	0 (0.0%)
	8 - <12 Weeks	12	1 (8.3%)	0 (0.0%)	1 (8.3%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total
			n (%)	n (%)	n (%)
血管障害	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
高血圧	Any period	23	1 (4.3%)	0 (0.0%)	1 (4.3%)
	<4 Weeks	23	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4 - <8 Weeks	17	1 (5.9%)	0 (0.0%)	1 (5.9%)
	8 - <12 Weeks	12	0 (0.0%)	0 (0.0%)	0 (0.0%)
	12 - <16 Weeks	6	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=16 Weeks	3	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. n = number of subjects; % = percentages are based on number of subjects at risk at the particular interval; Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period. Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

表 2.7.4.7-33　発現時期別の有害事象（203 試験）（安全性解析対象集団）

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any period	39	39 (100.0)	0 (0.0)	39 (100.0)
	<4 Weeks	39	36 (92.3)	1 (2.6)	37 (94.9)
	4 - <8 Weeks	37	29 (78.4)	5 (13.5)	34 (91.9)
	8 - <12 Weeks	29	22 (75.9)	4 (13.8)	26 (89.7)
	12 - <16 Weeks	23	14 (60.9)	2 (8.7)	16 (69.6)
	>=16 Weeks	18	14 (77.8)	1 (5.6)	15 (83.3)
血液およびリンパ系障害	Any period	39	38 (97.4)	0 (0.0)	38 (97.4)
	<4 Weeks	39	36 (92.3)	1 (2.6)	37 (94.9)
	4 - <8 Weeks	37	22 (59.5)	2 (5.4)	24 (64.9)
	8 - <12 Weeks	29	18 (62.1)	1 (3.4)	19 (65.5)
	12 - <16 Weeks	23	11 (47.8)	0 (0.0)	11 (47.8)
	>=16 Weeks	18	13 (72.2)	0 (0.0)	13 (72.2)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level.　Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
血小板减少症*	Any period	39	35 (89.7)	0 (0.0)	35 (89.7)
	<4 Weeks	39	29 (74.4)	0 (0.0)	29 (74.4)
	4 - <8 Weeks	37	10 (27.0)	0 (0.0)	10 (27.0)
	8 - <12 Weeks	29	4 (13.8)	0 (0.0)	4 (13.8)
	12 - <16 Weeks	23	8 (34.8)	0 (0.0)	8 (34.8)
	>=16 Weeks	18	10 (55.6)	0 (0.0)	10 (55.6)
好中球减少症*	Any period	39	28 (71.8)	0 (0.0)	28 (71.8)
	<4 Weeks	39	20 (51.3)	0 (0.0)	20 (51.3)
	4 - <8 Weeks	37	13 (35.1)	0 (0.0)	13 (35.1)
	8 - <12 Weeks	29	11 (37.9)	0 (0.0)	11 (37.9)
	12 - <16 Weeks	23	2 (8.7)	0 (0.0)	2 (8.7)
	>=16 Weeks	18	9 (50.0)	0 (0.0)	9 (50.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
白血球減少症*	Any period	39	21 (53.8)	3 (7.7)	24 (61.5)
	<4 Weeks	39	15 (38.5)	2 (5.1)	17 (43.6)
	4 - <8 Weeks	37	9 (24.3)	1 (2.7)	10 (27.0)
	8 - <12 Weeks	29	7 (24.1)	1 (3.4)	8 (27.6)
	12 - <16 Weeks	23	5 (21.7)	0 (0.0)	5 (21.7)
	>=16 Weeks	18	4 (22.2)	1 (5.6)	5 (27.8)
リンパ球減少症*	Any period	39	16 (41.0)	0 (0.0)	16 (41.0)
	<4 Weeks	39	7 (17.9)	0 (0.0)	7 (17.9)
	4 - <8 Weeks	37	6 (16.2)	0 (0.0)	6 (16.2)
	8 - <12 Weeks	29	5 (17.2)	0 (0.0)	5 (17.2)
	12 - <16 Weeks	23	3 (13.0)	0 (0.0)	3 (13.0)
	>=16 Weeks	18	5 (27.8)	0 (0.0)	5 (27.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
貧血*	Any period	39	11 (28.2)	3 (7.7)	14 (35.9)
	<4 Weeks	39	7 (17.9)	1 (2.6)	8 (20.5)
	4 - <8 Weeks	37	4 (10.8)	2 (5.4)	6 (16.2)
	8 - <12 Weeks	29	3 (10.3)	0 (0.0)	3 (10.3)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
発熱性好中球減少症	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
再生不良性貧血	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	Any period	39	4 (10.3)	2 (5.1)	6 (15.4)
	<4 Weeks	39	2 (5.1)	1 (2.6)	3 (7.7)
	4 - <8 Weeks	37	2 (5.4)	1 (2.7)	3 (8.1)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
動悸	Any period	39	2 (5.1)	1 (2.6)	3 (7.7)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	2 (5.4)	0 (0.0)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
不安定狭心症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
不整脈	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
心房細動	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
心嚢液貯留	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
回転性めまい	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	Any period	39	1 (2.6)	3 (7.7)	4 (10.3)
	<4 Weeks	39	1 (2.6)	2 (5.1)	3 (7.7)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
結膜出血	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
ドライアイ	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
角膜炎	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
霧視	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
胃腸障害	Any period	39	20 (51.3)	5 (12.8)	25 (64.1)
	<4 Weeks	39	15 (38.5)	4 (10.3)	19 (48.7)
	4 - <8 Weeks	37	3 (8.1)	4 (10.8)	7 (18.9)
	8 - <12 Weeks	29	1 (3.4)	1 (3.4)	2 (6.9)
	12 - <16 Weeks	23	0 (0.0)	1 (4.3)	1 (4.3)
	>=16 Weeks	18	3 (16.7)	3 (16.7)	6 (33.3)
下痢	Any period	39	9 (23.1)	5 (12.8)	14 (35.9)
	<4 Weeks	39	7 (17.9)	3 (7.7)	10 (25.6)
	4 - <8 Weeks	37	3 (8.1)	1 (2.7)	4 (10.8)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	1 (4.3)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
悪心	Any period	39	9 (23.1)	0 (0.0)	9 (23.1)
	<4 Weeks	39	6 (15.4)	0 (0.0)	6 (15.4)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	2 (11.1)	0 (0.0)	2 (11.1)
上腹部痛	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
齲歯	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	1 (5.6)	2 (11.1)
嘔吐	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
腹部不快感	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
肛門出血	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
便秘	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
消化不良	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
痔出血	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
口腔粘膜血腫	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
歯痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
一般・全身障害および投与部位の状態	Any period	39	16 (41.0)	3 (7.7)	19 (48.7)
	<4 Weeks	39	12 (30.8)	1 (2.6)	13 (33.3)
	4 - <8 Weeks	37	3 (8.1)	2 (5.4)	5 (13.5)
	8 - <12 Weeks	29	2 (6.9)	1 (3.4)	3 (10.3)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	2 (11.1)	1 (5.6)	3 (16.7)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
倦怠感	Any period	39	8 (20.5)	0 (0.0)	8 (20.5)
	<4 Weeks	39	7 (17.9)	0 (0.0)	7 (17.9)
	4 - <8 Weeks	37	2 (5.4)	0 (0.0)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
発熱	Any period	39	2 (5.1)	3 (7.7)	5 (12.8)
	<4 Weeks	39	1 (2.6)	2 (5.1)	3 (7.7)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	1 (3.4)	1 (3.4)	2 (6.9)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
疲労	Any period	39	4 (10.3)	0 (0.0)	4 (10.3)
	<4 Weeks	39	3 (7.7)	0 (0.0)	3 (7.7)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)
末梢性浮腫	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
カテーテル留置部位腫脹	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
胸痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
溢出	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
歩行障害	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
口渇	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
免疫系障害	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
感染症および寄生虫症	Any period	39	7 (17.9)	8 (20.5)	15 (38.5)
	<4 Weeks	39	1 (2.6)	3 (7.7)	4 (10.3)
	4 - <8 Weeks	37	3 (8.1)	1 (2.7)	4 (10.8)
	8 - <12 Weeks	29	0 (0.0)	2 (6.9)	2 (6.9)
	12 - <16 Weeks	23	2 (8.7)	0 (0.0)	2 (8.7)
	>=16 Weeks	18	1 (5.6)	5 (27.8)	6 (33.3)
咽頭炎	Any period	39	0 (0.0)	3 (7.7)	3 (7.7)
	<4 Weeks	39	0 (0.0)	2 (5.1)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
気管支炎	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	2 (5.4)	0 (0.0)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
インフルエンザ	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
上咽頭炎	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	2 (11.1)	2 (11.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
上気道感染	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
膀胱炎	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
サイトメガロウイルス感染	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
膿痂疹	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
ニューモシスチス・イロベチイ肺炎	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
鼻炎	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
爪損傷	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
臨床検査	Any period	39	19 (48.7)	5 (12.8)	24 (61.5)
	<4 Weeks	39	10 (25.6)	2 (5.1)	12 (30.8)
	4 - <8 Weeks	37	6 (16.2)	4 (10.8)	10 (27.0)
	8 - <12 Weeks	29	3 (10.3)	4 (13.8)	7 (24.1)
	12 - <16 Weeks	23	5 (21.7)	2 (8.7)	7 (30.4)
	>=16 Weeks	18	6 (33.3)	1 (5.6)	7 (38.9)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
血中アルカリホスファターゼ増加	Any period	39	6 (15.4)	2 (5.1)	8 (20.5)
	<4 Weeks	39	2 (5.1)	1 (2.6)	3 (7.7)
	4 - <8 Weeks	37	3 (8.1)	0 (0.0)	3 (8.1)
	8 - <12 Weeks	29	1 (3.4)	1 (3.4)	2 (6.9)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
γーグルタミルトランスフェラーゼ増加	Any period	39	7 (17.9)	1 (2.6)	8 (20.5)
	<4 Weeks	39	5 (12.8)	0 (0.0)	5 (12.8)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
アスパラギン酸アミノトランスフェラーゼ増加	Any period	39	4 (10.3)	3 (7.7)	7 (17.9)
	<4 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	4 - <8 Weeks	37	3 (8.1)	1 (2.7)	4 (10.8)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	2 (8.7)	0 (0.0)	2 (8.7)
	>=16 Weeks	18	1 (5.6)	1 (5.6)	2 (11.1)
体重減少	Any period	39	2 (5.1)	4 (10.3)	6 (15.4)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	1 (3.4)	1 (3.4)	2 (6.9)
	12 - <16 Weeks	23	0 (0.0)	1 (4.3)	1 (4.3)
	>=16 Weeks	18	1 (5.6)	1 (5.6)	2 (11.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
アラニンアミノトランスフェラーゼ増加	Any period	39	4 (10.3)	1 (2.6)	5 (12.8)
	<4 Weeks	39	3 (7.7)	0 (0.0)	3 (7.7)
	4 - <8 Weeks	37	2 (5.4)	0 (0.0)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
心電図ＱＴ延長	Any period	39	5 (12.8)	0 (0.0)	5 (12.8)
	<4 Weeks	39	2 (5.1)	0 (0.0)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	2 (11.1)	0 (0.0)	2 (11.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in ‘Any Period’ level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
血中クレアチニン増加	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	2 (8.7)	0 (0.0)	2 (8.7)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)
脳性ナトリウム利尿ペプチド増加	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
Ｃ－反応性蛋白増加	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
血中コレステロール増加	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼＭＢ増加	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
血中クレアチンホスホキナーゼ増加	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
血中免疫グロブリンA減少	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
尿中血陽性	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	1 (4.3)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
心胸郭比増加	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
心電図Ｔ波逆転	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ増加	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
体重増加	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	Any period	39	12 (30.8)	4 (10.3)	16 (41.0)
	<4 Weeks	39	9 (23.1)	3 (7.7)	12 (30.8)
	4 - <8 Weeks	37	1 (2.7)	1 (2.7)	2 (5.4)
	8 - <12 Weeks	29	3 (10.3)	1 (3.4)	4 (13.8)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
食欲減退	Any period	39	8 (20.5)	0 (0.0)	8 (20.5)
	<4 Weeks	39	7 (17.9)	0 (0.0)	7 (17.9)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
低アルブミン血症	Any period	39	2 (5.1)	2 (5.1)	4 (10.3)
	<4 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
低カリウム血症	Any period	39	2 (5.1)	1 (2.6)	3 (7.7)
	<4 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
低ナトリウム血症	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	2 (5.1)	0 (0.0)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
高カリウム血症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
高マグネシウム血症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
高トリグリセリド血症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
低蛋白血症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
筋骨格系および結合組織障害	Any period	39	7 (17.9)	8 (20.5)	15 (38.5)
	<4 Weeks	39	3 (7.7)	3 (7.7)	6 (15.4)
	4 - <8 Weeks	37	4 (10.8)	1 (2.7)	5 (13.5)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	2 (8.7)	2 (8.7)
	>=16 Weeks	18	2 (11.1)	3 (16.7)	5 (27.8)
筋痙縮	Any period	39	3 (7.7)	2 (5.1)	5 (12.8)
	<4 Weeks	39	2 (5.1)	0 (0.0)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	1 (5.6)	2 (11.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
背部痛	Any period	39	1 (2.6)	3 (7.7)	4 (10.3)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	2 (11.1)	2 (11.1)
筋肉痛	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	1 (4.3)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
関節痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
関節炎	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
出血性関節症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	1 (4.3)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
筋肉疲労	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
頚部痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
腱炎	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any period	39	1 (2.6)	2 (5.1)	3 (7.7)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	2 (5.4)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in ‘Any Period’ level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
末梢性Ｔ細胞性リンパ腫、組織型不明	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
腫瘍疼痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	Any period	39	4 (10.3)	3 (7.7)	7 (17.9)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	3 (8.1)	1 (2.7)	4 (10.8)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	2 (11.1)	2 (11.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
頭痛	Any period	39	2 (5.1)	2 (5.1)	4 (10.3)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	1 (2.7)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
味覚異常	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	2 (5.4)	0 (0.0)	2 (5.4)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
浮動性めまい	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
末梢性感覚ニューロパチー	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
失神寸前の状態	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
精神障害	Any period	39	0 (0.0)	4 (10.3)	4 (10.3)
	<4 Weeks	39	0 (0.0)	2 (5.1)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	Any period	39	0 (0.0)	3 (7.7)	3 (7.7)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
譫妄	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
急性腎障害	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
血尿	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
蛋白尿	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	Any period	39	8 (20.5)	6 (15.4)	14 (35.9)
	<4 Weeks	39	2 (5.1)	3 (7.7)	5 (12.8)
	4 - <8 Weeks	37	1 (2.7)	1 (2.7)	2 (5.4)
	8 - <12 Weeks	29	3 (10.3)	1 (3.4)	4 (13.8)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	2 (11.1)	1 (5.6)	3 (16.7)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
肺臓炎	Any period	39	3 (7.7)	0 (0.0)	3 (7.7)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	1 (4.3)	0 (0.0)	1 (4.3)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)
咳嗽	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
呼吸困難	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
口腔咽頭痛	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)
胸水	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
咽頭知覚不全	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
間質性肺疾患	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
上気道の炎症	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	Any period	39	10 (25.6)	8 (20.5)	18 (46.2)
	<4 Weeks	39	5 (12.8)	2 (5.1)	7 (17.9)
	4 - <8 Weeks	37	2 (5.4)	6 (16.2)	8 (21.6)
	8 - <12 Weeks	29	4 (13.8)	2 (6.9)	6 (20.7)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
発疹	Any period	39	2 (5.1)	1 (2.6)	3 (7.7)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	Any period	39	3 (7.7)	0 (0.0)	3 (7.7)
	<4 Weeks	39	2 (5.1)	0 (0.0)	2 (5.1)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
紅斑	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
紫斑	Any period	39	2 (5.1)	0 (0.0)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	1 (2.7)	0 (0.0)	1 (2.7)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
斑状丘疹状皮疹	Any period	39	1 (2.6)	1 (2.6)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	1 (3.4)	2 (6.9)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
褥瘡性潰瘍	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
ざ瘡様皮膚炎	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
全身性剥脱性皮膚炎	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	1 (5.6)	0 (0.0)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
皮膚乾燥	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
皮脂欠乏性湿疹	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
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TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
多形紅斑	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
全身紅斑	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
皮膚疼痛	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
色素沈着障害	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
全身性そう痒症	Any period	39	1 (2.6)	0 (0.0)	1 (2.6)
	<4 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
そう痒性皮疹	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	Any period	39	0 (0.0)	2 (5.1)	2 (5.1)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Japan

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=39)
			n (%)	n (%)	n (%)
低血圧	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	1 (2.7)	1 (2.7)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	0 (0.0)	0 (0.0)
末梢動脈閉塞性疾患	Any period	39	0 (0.0)	1 (2.6)	1 (2.6)
	<4 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	37	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	23	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	18	0 (0.0)	1 (5.6)	1 (5.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any period	16	12 (75.0)	4 (25.0)	16 (100.0)
	<4 Weeks	16	9 (56.3)	6 (37.5)	15 (93.8)
	4 - <8 Weeks	15	8 (53.3)	4 (26.7)	12 (80.0)
	8 - <12 Weeks	10	3 (30.0)	1 (10.0)	4 (40.0)
	12 - <16 Weeks	6	1 (16.7)	0 (0.0)	1 (16.7)
	>=16 Weeks	4	3 (75.0)	1 (25.0)	4 (100.0)
血液およびリンパ系障害	Any period	16	9 (56.3)	5 (31.3)	14 (87.5)
	<4 Weeks	16	8 (50.0)	3 (18.8)	11 (68.8)
	4 - <8 Weeks	15	5 (33.3)	3 (20.0)	8 (53.3)
	8 - <12 Weeks	10	3 (30.0)	0 (0.0)	3 (30.0)
	12 - <16 Weeks	6	1 (16.7)	0 (0.0)	1 (16.7)
	>=16 Weeks	4	2 (50.0)	0 (0.0)	2 (50.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
血小板減少症*	Any period	16	7 (43.8)	4 (25.0)	11 (68.8)
	<4 Weeks	16	7 (43.8)	2 (12.5)	9 (56.3)
	4 - <8 Weeks	15	2 (13.3)	3 (20.0)	5 (33.3)
	8 - <12 Weeks	10	2 (20.0)	0 (0.0)	2 (20.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	0 (0.0)	1 (25.0)
貧血*	Any period	16	1 (6.3)	3 (18.8)	4 (25.0)
	<4 Weeks	16	1 (6.3)	1 (6.3)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	2 (13.3)	2 (13.3)
	8 - <12 Weeks	10	1 (10.0)	0 (0.0)	1 (10.0)
	12 - <16 Weeks	6	1 (16.7)	0 (0.0)	1 (16.7)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
好中球減少症*	Any period	16	3 (18.8)	0 (0.0)	3 (18.8)
	<4 Weeks	16	2 (12.5)	0 (0.0)	2 (12.5)
	4 - <8 Weeks	15	3 (20.0)	0 (0.0)	3 (20.0)
	8 - <12 Weeks	10	1 (10.0)	0 (0.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	0 (0.0)	1 (25.0)
好酸球増加症	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
発熱性好中球減少症	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	1 (6.3)	0 (0.0)	1 (6.3)
	4 - <8 Weeks	15	1 (6.7)	0 (0.0)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
心房細動	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
耳痛	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
白内障	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	Any period	16	5 (31.3)	2 (12.5)	7 (43.8)
	<4 Weeks	16	5 (31.3)	1 (6.3)	6 (37.5)
	4 - <8 Weeks	15	1 (6.7)	4 (26.7)	5 (33.3)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	1 (25.0)	2 (50.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
下痢	Any period	16	1 (6.3)	2 (12.5)	3 (18.8)
	<4 Weeks	16	1 (6.3)	0 (0.0)	1 (6.3)
	4 - <8 Weeks	15	1 (6.7)	2 (13.3)	3 (20.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	0 (0.0)	1 (25.0)
悪心	Any period	16	2 (12.5)	1 (6.3)	3 (18.8)
	<4 Weeks	16	2 (12.5)	1 (6.3)	3 (18.8)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
腹痛	Any period	16	1 (6.3)	1 (6.3)	2 (12.5)
	<4 Weeks	16	1 (6.3)	0 (0.0)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
胃潰瘍	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)
胃炎	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	1 (6.3)	0 (0.0)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
嘔吐	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	Any period	16	1 (6.3)	7 (43.8)	8 (50.0)
	<4 Weeks	16	1 (6.3)	4 (25.0)	5 (31.3)
	4 - <8 Weeks	15	0 (0.0)	5 (33.3)	5 (33.3)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
発熱	Any period	16	0 (0.0)	6 (37.5)	6 (37.5)
	<4 Weeks	16	0 (0.0)	2 (12.5)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	4 (26.7)	4 (26.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
無力症	Any period	16	1 (6.3)	1 (6.3)	2 (12.5)
	<4 Weeks	16	1 (6.3)	0 (0.0)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
疲労	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	2 (12.5)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	2 (12.5)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
末梢性浮腫	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	2 (13.3)	2 (13.3)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	Any period	16	1 (6.3)	3 (18.8)	4 (25.0)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	1 (6.7)	0 (0.0)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	2 (50.0)	2 (50.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
上気道感染	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)
感染性小腸結腸炎	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
胃腸炎	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)
肺炎	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	1 (6.7)	0 (0.0)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
ブドウ球菌皮膚感染	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
胃瘻管部合併症	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
臨床検査	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	1 (6.7)	0 (0.0)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
C－反応性蛋白増加	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	1 (6.7)	0 (0.0)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
代謝および栄養障害	Any period	16	4 (25.0)	5 (31.3)	9 (56.3)
	<4 Weeks	16	2 (12.5)	1 (6.3)	3 (18.8)
	4 - <8 Weeks	15	2 (13.3)	2 (13.3)	4 (26.7)
	8 - <12 Weeks	10	1 (10.0)	1 (10.0)	2 (20.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	1 (25.0)	2 (50.0)
食欲減退	Any period	16	4 (25.0)	1 (6.3)	5 (31.3)
	<4 Weeks	16	2 (12.5)	0 (0.0)	2 (12.5)
	4 - <8 Weeks	15	2 (13.3)	0 (0.0)	2 (13.3)
	8 - <12 Weeks	10	1 (10.0)	0 (0.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	1 (25.0)	2 (50.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
低カリウム血症	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
低アルブミン血症	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
低カルシウム血症	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	Any period	16	0 (0.0)	4 (25.0)	4 (25.0)
	<4 Weeks	16	0 (0.0)	3 (18.8)	3 (18.8)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
背部痛	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
筋力低下	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related n (%)	Not Related n (%)	Total (N=16) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍疼痛	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
神経系障害	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	2 (12.5)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	2 (12.5)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
精神障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
生殖系および乳房障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢浮腫	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	Any period	16	1 (6.3)	6 (37.5)	7 (43.8)
	<4 Weeks	16	0 (0.0)	5 (31.3)	5 (31.3)
	4 - <8 Weeks	15	0 (0.0)	3 (20.0)	3 (20.0)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	1 (25.0)	2 (50.0)
咳嗽	Any period	16	0 (0.0)	4 (25.0)	4 (25.0)
	<4 Weeks	16	0 (0.0)	2 (12.5)	2 (12.5)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
呼吸困難	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)
発声障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
労作性呼吸困難	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)
しゃっくり	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
口腔咽頭痛	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	1 (25.0)	0 (0.0)	1 (25.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
湿性咳嗽	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	1 (25.0)	1 (25.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
鼻漏	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	Any period	16	2 (12.5)	3 (18.8)	5 (31.3)
	<4 Weeks	16	1 (6.3)	1 (6.3)	2 (12.5)
	4 - <8 Weeks	15	1 (6.7)	1 (6.7)	2 (13.3)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
発疹	Any period	16	1 (6.3)	1 (6.3)	2 (12.5)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	1 (6.7)	0 (0.0)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	1 (10.0)	1 (10.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	Any period	16	0 (0.0)	2 (12.5)	2 (12.5)
	<4 Weeks	16	0 (0.0)	1 (6.3)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
全身性そう痒症	Any period	16	1 (6.3)	0 (0.0)	1 (6.3)
	<4 Weeks	16	1 (6.3)	0 (0.0)	1 (6.3)
	4 - <8 Weeks	15	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Korea

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=16)
			n (%)	n (%)	n (%)
深部静脈血栓症	Any period	16	0 (0.0)	1 (6.3)	1 (6.3)
	<4 Weeks	16	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	15	0 (0.0)	1 (6.7)	1 (6.7)
	8 - <12 Weeks	10	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	6	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	4	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	Any period	55	51 (92.7)	4 (7.3)	55 (100.0)
	<4 Weeks	55	45 (81.8)	7 (12.7)	52 (94.5)
	4 - <8 Weeks	52	37 (71.2)	9 (17.3)	46 (88.5)
	8 - <12 Weeks	39	25 (64.1)	5 (12.8)	30 (76.9)
	12 - <16 Weeks	29	15 (51.7)	2 (6.9)	17 (58.6)
	>=16 Weeks	22	17 (77.3)	2 (9.1)	19 (86.4)
血液およびリンパ系障害	Any period	55	47 (85.5)	5 (9.1)	52 (94.5)
	<4 Weeks	55	44 (80.0)	4 (7.3)	48 (87.3)
	4 - <8 Weeks	52	27 (51.9)	5 (9.6)	32 (61.5)
	8 - <12 Weeks	39	21 (53.8)	1 (2.6)	22 (56.4)
	12 - <16 Weeks	29	12 (41.4)	0 (0.0)	12 (41.4)
	>=16 Weeks	22	15 (68.2)	0 (0.0)	15 (68.2)
血小板減少症*	Any period	55	42 (76.4)	4 (7.3)	46 (83.6)
	<4 Weeks	55	36 (65.5)	2 (3.6)	38 (69.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
血小板减少症*	4 - <8 Weeks	52	12 (23.1)	3 (5.8)	15 (28.8)
	8 - <12 Weeks	39	6 (15.4)	0 (0.0)	6 (15.4)
	12 - <16 Weeks	29	8 (27.6)	0 (0.0)	8 (27.6)
	>=16 Weeks	22	11 (50.0)	0 (0.0)	11 (50.0)
好中球减少症*	Any period	55	31 (56.4)	0 (0.0)	31 (56.4)
	<4 Weeks	55	22 (40.0)	0 (0.0)	22 (40.0)
	4 - <8 Weeks	52	16 (30.8)	0 (0.0)	16 (30.8)
	8 - <12 Weeks	39	12 (30.8)	0 (0.0)	12 (30.8)
	12 - <16 Weeks	29	2 (6.9)	0 (0.0)	2 (6.9)
	>=16 Weeks	22	10 (45.5)	0 (0.0)	10 (45.5)
白血球减少症*	Any period	55	21 (38.2)	3 (5.5)	24 (43.6)
	<4 Weeks	55	15 (27.3)	2 (3.6)	17 (30.9)
	4 - <8 Weeks	52	9 (17.3)	1 (1.9)	10 (19.2)
	8 - <12 Weeks	39	7 (17.9)	1 (2.6)	8 (20.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
白血球減少症*	12 - <16 Weeks	29	5 (17.2)	0 (0.0)	5 (17.2)
	>=16 Weeks	22	4 (18.2)	1 (4.5)	5 (22.7)
貧血*	Any period	55	12 (21.8)	6 (10.9)	18 (32.7)
	<4 Weeks	55	8 (14.5)	2 (3.6)	10 (18.2)
	4 - <8 Weeks	52	4 (7.7)	4 (7.7)	8 (15.4)
	8 - <12 Weeks	39	4 (10.3)	0 (0.0)	4 (10.3)
	12 - <16 Weeks	29	2 (6.9)	0 (0.0)	2 (6.9)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球減少症*	Any period	55	16 (29.1)	0 (0.0)	16 (29.1)
	<4 Weeks	55	7 (12.7)	0 (0.0)	7 (12.7)
	4 - <8 Weeks	52	6 (11.5)	0 (0.0)	6 (11.5)
	8 - <12 Weeks	39	5 (12.8)	0 (0.0)	5 (12.8)
	12 - <16 Weeks	29	3 (10.3)	0 (0.0)	3 (10.3)
	>=16 Weeks	22	5 (22.7)	0 (0.0)	5 (22.7)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
発熱性好中球減少症	Any period	55	3 (5.5)	0 (0.0)	3 (5.5)
	<4 Weeks	55	2 (3.6)	0 (0.0)	2 (3.6)
	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
再生不良性貧血	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
好酸球増加症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
好酸球増加症	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	Any period	55	4 (7.3)	3 (5.5)	7 (12.7)
	<4 Weeks	55	2 (3.6)	2 (3.6)	4 (7.3)
	4 - <8 Weeks	52	2 (3.8)	1 (1.9)	3 (5.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
動悸	Any period	55	2 (3.6)	1 (1.8)	3 (5.5)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
動悸	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
心房細動	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
不安定狭心症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
不整脈	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
心嚢液貯留	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
耳および迷路障害	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
回転性めまい	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	Any period	55	1 (1.8)	4 (7.3)	5 (9.1)
	<4 Weeks	55	1 (1.8)	3 (5.5)	4 (7.3)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
白内障	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
結膜出血	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
ドライアイ	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
角膜炎	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
角膜炎	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
霧視	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	Any period	55	25 (45.5)	7 (12.7)	32 (58.2)
	<4 Weeks	55	20 (36.4)	5 (9.1)	25 (45.5)
	4 - <8 Weeks	52	4 (7.7)	8 (15.4)	12 (23.1)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
胃腸障害	12 - <16 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	>=16 Weeks	22	4 (18.2)	4 (18.2)	8 (36.4)
下痢	Any period	55	10 (18.2)	7 (12.7)	17 (30.9)
	<4 Weeks	55	8 (14.5)	3 (5.5)	11 (20.0)
	4 - <8 Weeks	52	4 (7.7)	3 (5.8)	7 (13.5)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
悪心	Any period	55	11 (20.0)	1 (1.8)	12 (21.8)
	<4 Weeks	55	8 (14.5)	1 (1.8)	9 (16.4)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	2 (9.1)	0 (0.0)	2 (9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
腹痛	Any period	55	1 (1.8)	2 (3.6)	3 (5.5)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	2 (3.8)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	Any period	55	1 (1.8)	2 (3.6)	3 (5.5)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
上腹部痛	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
上腹部痛	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	1 (4.5)	2 (9.1)
口内炎	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
口内炎	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
肛門出血	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
便秘	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
心窩部不快感	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
胃炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
胃炎	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
口腔粘膜血腫	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
歯痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
一般・全身障害および投与部位の状態	Any period	55	17 (30.9)	10 (18.2)	27 (49.1)
	<4 Weeks	55	13 (23.6)	5 (9.1)	18 (32.7)
	4 - <8 Weeks	52	3 (5.8)	7 (13.5)	10 (19.2)
	8 - <12 Weeks	39	2 (5.1)	1 (2.6)	3 (7.7)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	2 (9.1)	1 (4.5)	3 (13.6)
発熱	Any period	55	2 (3.6)	9 (16.4)	11 (20.0)
	<4 Weeks	55	1 (1.8)	4 (7.3)	5 (9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
発熱	4 - <8 Weeks	52	1 (1.9)	4 (7.7)	5 (9.6)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	Any period	55	8 (14.5)	0 (0.0)	8 (14.5)
	<4 Weeks	55	7 (12.7)	0 (0.0)	7 (12.7)
	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
疲労	Any period	55	4 (7.3)	2 (3.6)	6 (10.9)
	<4 Weeks	55	3 (5.5)	2 (3.6)	5 (9.1)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
疲労	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
末梢性浮腫	Any period	55	2 (3.6)	2 (3.6)	4 (7.3)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	2 (3.8)	3 (5.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
無力症	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
インフルエンザ様疾患	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	2 (3.6)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
カテーテル留置部位腫脹	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
胸部不快感	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
溢出	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
溢出	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
歩行障害	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
口渇	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
免疫系障害	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	Any period	55	8 (14.5)	11 (20.0)	19 (34.5)
	<4 Weeks	55	1 (1.8)	4 (7.3)	5 (9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
感染症および寄生虫症	4 - <8 Weeks	52	4 (7.7)	1 (1.9)	5 (9.6)
	8 - <12 Weeks	39	0 (0.0)	3 (7.7)	3 (7.7)
	12 - <16 Weeks	29	2 (6.9)	0 (0.0)	2 (6.9)
	>=16 Weeks	22	1 (4.5)	7 (31.8)	8 (36.4)
上気道感染	Any period	55	0 (0.0)	4 (7.3)	4 (7.3)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	2 (9.1)	2 (9.1)
咽頭炎	Any period	55	0 (0.0)	3 (5.5)	3 (5.5)
	<4 Weeks	55	0 (0.0)	2 (3.6)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
咽頭炎	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
気管支炎	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related n (%)	Not Related n (%)	Total (N=55) n (%)
インフルエンザ	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
上咽頭炎	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	2 (9.1)	2 (9.1)
膀胱炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
膀胱炎	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
サイトメガロウイルス感染	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
感染性小腸結腸炎	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
帯状疱疹	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
膿痂疹	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
ニューモシスチス・イロベチイ肺炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
肺炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
肺炎	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
ブドウ球菌皮膚感染	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	Any period	55	0 (0.0)	3 (5.5)	3 (5.5)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	2 (9.1)	2 (9.1)
胃瘻管部合併症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
爪損傷	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
処置による疼痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
臨床検査	Any period	55	20 (36.4)	5 (9.1)	25 (45.5)
	<4 Weeks	55	10 (18.2)	2 (3.6)	12 (21.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
臨床検査	4 - <8 Weeks	52	7 (13.5)	4 (7.7)	11 (21.2)
	8 - <12 Weeks	39	3 (7.7)	4 (10.3)	7 (17.9)
	12 - <16 Weeks	29	5 (17.2)	2 (6.9)	7 (24.1)
	>=16 Weeks	22	6 (27.3)	1 (4.5)	7 (31.8)
血中アルカリホスファターゼ増加	Any period	55	6 (10.9)	2 (3.6)	8 (14.5)
	<4 Weeks	55	2 (3.6)	1 (1.8)	3 (5.5)
	4 - <8 Weeks	52	3 (5.8)	0 (0.0)	3 (5.8)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
γーグルタミルトランスフェラーゼ増加	Any period	55	7 (12.7)	1 (1.8)	8 (14.5)
	<4 Weeks	55	5 (9.1)	0 (0.0)	5 (9.1)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
γーグルタミルトランスフェラーゼ増加	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
アスパラギン酸アミノトランスフェラーゼ増加	Any period	55	4 (7.3)	3 (5.5)	7 (12.7)
	<4 Weeks	55	1 (1.8)	1 (1.8)	2 (3.6)
	4 - <8 Weeks	52	3 (5.8)	1 (1.9)	4 (7.7)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	2 (6.9)	0 (0.0)	2 (6.9)
	>=16 Weeks	22	1 (4.5)	1 (4.5)	2 (9.1)
体重減少	Any period	55	2 (3.6)	4 (7.3)	6 (10.9)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	12 - <16 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	>=16 Weeks	22	1 (4.5)	1 (4.5)	2 (9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
アラニンアミノトランスフェラーゼ増加	Any period	55	4 (7.3)	1 (1.8)	5 (9.1)
	<4 Weeks	55	3 (5.5)	0 (0.0)	3 (5.5)
	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
心電図ＱＴ延長	Any period	55	5 (9.1)	0 (0.0)	5 (9.1)
	<4 Weeks	55	2 (3.6)	0 (0.0)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	2 (9.1)	0 (0.0)	2 (9.1)
Ｃ－反応性蛋白増加	Any period	55	2 (3.6)	1 (1.8)	3 (5.5)
	<4 Weeks	55	1 (1.8)	1 (1.8)	2 (3.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in ‘Any Period’ level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
Ｃ－反応性蛋白増加	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	2 (6.9)	0 (0.0)	2 (6.9)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
脳性ナトリウム利尿ペプチド増加	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
脳性ナトリウム利尿ペプチド増加	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
血中クレアチンホスホキナーゼＭＢ増加	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
血中クレアチンホスホキナーゼ増加	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
血中免疫グロブリンＡ減少	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in ‘Any Period’ level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
血中免疫グロブリンA減少	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
尿中血陽性	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
心胸郭比増加	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
心胸郭比増加	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
心電図Ｔ波逆転	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ増加	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
体重増加	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	Any period	55	16 (29.1)	9 (16.4)	25 (45.5)
	<4 Weeks	55	11 (20.0)	4 (7.3)	15 (27.3)
	4 - <8 Weeks	52	3 (5.8)	3 (5.8)	6 (11.5)
	8 - <12 Weeks	39	4 (10.3)	2 (5.1)	6 (15.4)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	2 (9.1)	3 (13.6)
食欲減退	Any period	55	12 (21.8)	1 (1.8)	13 (23.6)
	<4 Weeks	55	9 (16.4)	0 (0.0)	9 (16.4)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
食欲減退	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	2 (5.1)	0 (0.0)	2 (5.1)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	1 (4.5)	2 (9.1)
低アルブミン血症	Any period	55	2 (3.6)	3 (5.5)	5 (9.1)
	<4 Weeks	55	1 (1.8)	1 (1.8)	2 (3.6)
	4 - <8 Weeks	52	1 (1.9)	1 (1.9)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	Any period	55	2 (3.6)	3 (5.5)	5 (9.1)
	<4 Weeks	55	1 (1.8)	1 (1.8)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related n (%)	Not Related n (%)	Total (N=55) n (%)
低カリウム血症	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	Any period	55	2 (3.6)	1 (1.8)	3 (5.5)
	<4 Weeks	55	1 (1.8)	1 (1.8)	2 (3.6)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	2 (3.6)	0 (0.0)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
糖尿病	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
高カリウム血症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
高マグネシウム血症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
高マグネシウム血症	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
低蛋白血症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
低蛋白血症	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	Any period	55	7 (12.7)	12 (21.8)	19 (34.5)
	<4 Weeks	55	3 (5.5)	6 (10.9)	9 (16.4)
	4 - <8 Weeks	52	4 (7.7)	2 (3.8)	6 (11.5)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	2 (6.9)	2 (6.9)
	>=16 Weeks	22	2 (9.1)	3 (13.6)	5 (22.7)
背部痛	Any period	55	1 (1.8)	4 (7.3)	5 (9.1)
	<4 Weeks	55	0 (0.0)	2 (3.6)	2 (3.6)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	2 (9.1)	2 (9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
筋痙縮	Any period	55	3 (5.5)	2 (3.6)	5 (9.1)
	<4 Weeks	55	2 (3.6)	0 (0.0)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	1 (4.5)	2 (9.1)
筋肉疲労	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	1 (1.9)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
筋肉痛	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
関節痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
関節炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
関節炎	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
出血性関節症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	1 (3.4)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
筋力低下	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
頚部痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
頚部痛	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
肩回旋筋腱板症候群	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
腱炎	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any period	55	1 (1.8)	3 (5.5)	4 (7.3)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	2 (3.8)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
腫瘍疼痛	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
末梢性Ｔ細胞性リンパ腫、組織型不明	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
皮膚乳頭腫	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	Any period	55	4 (7.3)	5 (9.1)	9 (16.4)
	<4 Weeks	55	1 (1.8)	2 (3.6)	3 (5.5)
	4 - <8 Weeks	52	3 (5.8)	1 (1.9)	4 (7.7)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	2 (9.1)	2 (9.1)
頭痛	Any period	55	2 (3.6)	4 (7.3)	6 (10.9)
	<4 Weeks	55	1 (1.8)	2 (3.6)	3 (5.5)
	4 - <8 Weeks	52	1 (1.9)	1 (1.9)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
頭痛	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
味覚異常	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	2 (3.8)	0 (0.0)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
感覚鈍麻	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
末梢性感覚ニューロパチー	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
失神寸前の状態	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
失神寸前の状態	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	Any period	55	0 (0.0)	5 (9.1)	5 (9.1)
	<4 Weeks	55	0 (0.0)	3 (5.5)	3 (5.5)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	Any period	55	0 (0.0)	4 (7.3)	4 (7.3)
	<4 Weeks	55	0 (0.0)	2 (3.6)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
不眠症	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
譫妄	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
急性腎障害	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
血尿	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
蛋白尿	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
蛋白尿	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢浮腫	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
陰嚢浮腫	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	Any period	55	9 (16.4)	12 (21.8)	21 (38.2)
	<4 Weeks	55	2 (3.6)	8 (14.5)	10 (18.2)
	4 - <8 Weeks	52	1 (1.9)	4 (7.7)	5 (9.6)
	8 - <12 Weeks	39	3 (7.7)	2 (5.1)	5 (12.8)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	3 (13.6)	2 (9.1)	5 (22.7)
咳嗽	Any period	55	1 (1.8)	5 (9.1)	6 (10.9)
	<4 Weeks	55	0 (0.0)	2 (3.6)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	2 (3.8)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	1 (4.5)	2 (9.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
呼吸困難	Any period	55	2 (3.6)	2 (3.6)	4 (7.3)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
肺臓炎	Any period	55	4 (7.3)	0 (0.0)	4 (7.3)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	1 (3.4)	0 (0.0)	1 (3.4)
	>=16 Weeks	22	2 (9.1)	0 (0.0)	2 (9.1)
口腔咽頭痛	Any period	55	0 (0.0)	3 (5.5)	3 (5.5)
	<4 Weeks	55	0 (0.0)	2 (3.6)	2 (3.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
口腔咽頭痛	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
鼻出血	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
胸水	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	1 (1.8)	1 (1.8)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
胸水	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
咽頭知覚不全	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
発声障害	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
労作性呼吸困難	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
しゃっくり	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
間質性肺疾患	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
間質性肺疾患	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related n (%)	Not Related n (%)	Total (N=55) n (%)
アレルギー性鼻炎	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
鼻漏	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
皮膚および皮下組織障害	Any period	55	12 (21.8)	11 (20.0)	23 (41.8)
	<4 Weeks	55	6 (10.9)	3 (5.5)	9 (16.4)
	4 - <8 Weeks	52	3 (5.8)	7 (13.5)	10 (19.2)
	8 - <12 Weeks	39	4 (10.3)	3 (7.7)	7 (17.9)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
発疹	Any period	55	3 (5.5)	2 (3.6)	5 (9.1)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	1 (1.9)	1 (1.9)	2 (3.8)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	Any period	55	3 (5.5)	2 (3.6)	5 (9.1)
	<4 Weeks	55	2 (3.6)	1 (1.8)	3 (5.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
蕁麻疹	4 - <8 Weeks	52	1 (1.9)	1 (1.9)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	Any period	55	0 (0.0)	2 (3.6)	2 (3.6)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
全身性そう痒症	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	2 (3.6)	0 (0.0)	2 (3.6)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
全身性そう痒症	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
紫斑	Any period	55	2 (3.6)	0 (0.0)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	1 (1.9)	0 (0.0)	1 (1.9)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	Any period	55	1 (1.8)	1 (1.8)	2 (3.6)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	1 (2.6)	2 (5.1)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
褥瘡性潰瘍	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
ざ瘡様皮膚炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
全身性剥脱性皮膚炎	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
全身性剥脱性皮膚炎	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	1 (2.6)	0 (0.0)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	1 (4.5)	0 (0.0)	1 (4.5)
皮膚乾燥	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
皮脂欠乏性湿疹	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
皮脂欠乏性湿疹	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
多形紅斑	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
全身紅斑	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
皮膚疼痛	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	1 (1.8)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	Any period	55	1 (1.8)	0 (0.0)	1 (1.8)
	<4 Weeks	55	1 (1.8)	0 (0.0)	1 (1.8)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
色素沈着障害	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	1 (2.6)	1 (2.6)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
そう痒性皮疹	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	Any period	55	0 (0.0)	3 (5.5)	3 (5.5)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	2 (3.8)	2 (3.8)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
血管障害	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)
深部静脈血栓症	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	1 (1.9)	1 (1.9)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;

Number of subjects at risk is defined as subjects on treatment at a particular study week.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

Study week = (start date of adverse event – date of first study drug + 1)/7.

Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.

Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.

TEAE of overdose is not included in this analysis.

Country: Overall

System organ class Preferred term	Study Week	Subject at Risk	Related	Not Related	Total (N=55)
			n (%)	n (%)	n (%)
末梢動脈閉塞性疾患	Any period	55	0 (0.0)	1 (1.8)	1 (1.8)
	<4 Weeks	55	0 (0.0)	0 (0.0)	0 (0.0)
	4 - <8 Weeks	52	0 (0.0)	0 (0.0)	0 (0.0)
	8 - <12 Weeks	39	0 (0.0)	0 (0.0)	0 (0.0)
	12 - <16 Weeks	29	0 (0.0)	0 (0.0)	0 (0.0)
	>=16 Weeks	22	0 (0.0)	1 (4.5)	1 (4.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.; n = number of subjects; % = percentages are based on number of subjects in a country at risk at the particular interval;
Number of subjects at risk is defined as subjects on treatment at a particular study week.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Study week = (start date of adverse event – date of first study drug + 1)/7.
Subjects whose TEAEs occurred more than once in the same PT and in the same period are counted once in that particular PT and period.
Subjects who had more than one AEs occurring at different period within the same PT are counted once in 'Any Period' level. Subjects with more than one TEAE in a particular period are counted once in the worst relationship.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-34　死亡に至った有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	40 mg (N=23) n (%)
No observation.	

Source: Listing 16.2.6.4
MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-35　死亡に至った有害事象（201 試験）（安全性解析対象集団）

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Not Applicable			

SOURCE: Listing 16.2.6.6
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

表 2.7.4.7-36　死亡に至った有害事象（203 試験）（安全性解析対象集団）

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with TEAE leading to death	0	1(6.3)	1(1.8)
感染症および寄生虫症	0	1(6.3)	1(1.8)
肺炎	0	1(6.3)	1(1.8)

Source: Listing 16.2.6.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-37　重篤な有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	40 mg (N=23) n (%)
Number of subjects with at least one serious TEAE	7(30.4%)
血液およびリンパ系障害	2(8.7%)
血小板減少症*	2(8.7%)
好中球減少症*	1(4.3%)
心臓障害	1(4.3%)
動悸	1(4.3%)
感染症および寄生虫症	2(8.7%)
ニューモシスチス・イロベチイ肺炎	1(4.3%)
尿路感染	1(4.3%)
呼吸器、胸郭および縦隔障害	2(8.7%)
急性呼吸不全	1(4.3%)
間質性肺疾患	1(4.3%)

Source: Listing 16.2.6.3

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-38　重篤な有害事象（201 試験）（安全性解析対象集団）

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one serious TEAE	1 (14.3%)	1 (14.3%)	2 (14.3%)
胃腸障害	0 (0.0%)	1 (14.3%)	1 (7.1%)
腹痛	0 (0.0%)	1 (14.3%)	1 (7.1%)
腸炎	0 (0.0%)	1 (14.3%)	1 (7.1%)
神経系障害	1 (14.3%)	0 (0.0%)	1 (7.1%)
パーキンソニズム	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.5
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

表 2.7.4.7-39　重篤な有害事象（203 試験）（安全性解析対象集団）

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with at least one serious TEAE	11(28.2)	3(18.8)	14(25.5)
血液およびリンパ系障害	2(5.1)	1(6.3)	3(5.5)
発熱性好中球減少症	1(2.6)	1(6.3)	2(3.6)
再生不良性貧血	1(2.6)	0	1(1.8)
心臓障害	1(2.6)	0	1(1.8)
不安定狭心症	1(2.6)	0	1(1.8)
一般・全身障害および投与部位の状態	0	2(12.5)	2(3.6)
疲労	0	1(6.3)	1(1.8)
発熱	0	1(6.3)	1(1.8)
感染症および寄生虫症	1(2.6)	1(6.3)	2(3.6)
ニューモシスチス・イロベチイ肺炎	1(2.6)	0	1(1.8)
咽頭炎	1(2.6)	0	1(1.8)
肺炎	0	1(6.3)	1(1.8)
臨床検査	1(2.6)	0	1(1.8)
Ｃ－反応性蛋白増加	1(2.6)	0	1(1.8)
代謝および栄養障害	1(2.6)	0	1(1.8)
低ナトリウム血症	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.3

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1(2.6)	0	1(1.8)
末梢性Ｔ細胞性リンパ腫、組織型不明	1(2.6)	0	1(1.8)
腎および尿路障害	1(2.6)	0	1(1.8)
急性腎障害	1(2.6)	0	1(1.8)
呼吸器、胸郭および縦隔障害	3(7.7)	0	3(5.5)
上気道の炎症	1(2.6)	0	1(1.8)
肺臓炎	1(2.6)	0	1(1.8)
間質性肺疾患	1(2.6)	0	1(1.8)
血管障害	1(2.6)	0	1(1.8)
末梢動脈閉塞性疾患	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.3

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-40　治験薬の投与中止に至った有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	40 mg (N=23) n (%)
Number of subjects with at least one TEAE leading to study drug discontinuation	9(39.1%)
血液およびリンパ系障害	5(21.7%)
血小板減少症*	4(17.4%)
好中球減少症*	3(13.0%)
一般・全身障害および投与部位の状態	1(4.3%)
疲労	1(4.3%)
感染症および寄生虫症	1(4.3%)
ニューモシスチス・イロベチイ肺炎	1(4.3%)
臨床検査	1(4.3%)
血中アルカリホスファターゼ増加	1(4.3%)
γ－グルタミルトランスフェラーゼ増加	1(4.3%)
呼吸器、胸郭および縦隔障害	1(4.3%)
間質性肺疾患	1(4.3%)

Source: Listing 16.2.6.2

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-41　重症度別関連性別治験薬の投与中止に至った有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE leading to study drug discontinuation	Any Grade	9 (39.1%)	0 (0.0%)	9 (39.1%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	6 (26.1%)	0 (0.0%)	6 (26.1%)
	Grade 4	3 (13.0%)	0 (0.0%)	3 (13.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	9 (39.1%)	0 (0.0%)	9 (39.1%)
血液およびリンパ系障害	Any Grade	5 (21.7%)	0 (0.0%)	5 (21.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	3 (13.0%)	0 (0.0%)	3 (13.0%)
	Grade 4	2 (8.7%)	0 (0.0%)	2 (8.7%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	5 (21.7%)	0 (0.0%)	5 (21.7%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
血小板减少症*	Any Grade	4 (17.4%)	0 (0.0%)	4 (17.4%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	2 (8.7%)	0 (0.0%)	2 (8.7%)
	Grade 4	2 (8.7%)	0 (0.0%)	2 (8.7%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	4 (17.4%)	0 (0.0%)	4 (17.4%)
好中球减少症*	Any Grade	3 (13.0%)	0 (0.0%)	3 (13.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 3	2 (8.7%)	0 (0.0%)	2 (8.7%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	2 (8.7%)	0 (0.0%)	2 (8.7%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
疲労	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
ニューモシスチス・イロベチイ肺炎	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
臨床検査	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
血中アルカリホスファターゼ増加	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
γーグルタミルトランスフェラーゼ増加	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)
間質性肺疾患	Any Grade	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	1 (4.3%)	0 (0.0%)	1 (4.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=Grade 3	1 (4.3%)	0 (0.0%)	1 (4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-42　治験薬の投与中止に至った有害事象（201 試験）（安全性解析対象集団）

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with TEAE leading to study drug discontinuation	2 (28.6%)	4 (57.1%)	6 (42.9%)
血液およびリンパ系障害	0 (0.0%)	1 (14.3%)	1 (7.1%)
好中球減少症	0 (0.0%)	1 (14.3%)	1 (7.1%)
胃腸障害	0 (0.0%)	1 (14.3%)	1 (7.1%)
腹痛	0 (0.0%)	1 (14.3%)	1 (7.1%)
臨床検査	1 (14.3%)	1 (14.3%)	2 (14.3%)
血中クレアチンホスホキナーゼ増加	1 (14.3%)	0 (0.0%)	1 (7.1%)
胸部コンピュータ断層撮影異常	0 (0.0%)	1 (14.3%)	1 (7.1%)
皮膚および皮下組織障害	1 (14.3%)	1 (14.3%)	2 (14.3%)
多形紅斑	0 (0.0%)	1 (14.3%)	1 (7.1%)
血管周囲細胞浸潤性皮膚炎	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.4
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

表 2.7.4.7-43　治験薬の投与中止に至った有害事象（203 試験）（安全性解析対象集団）

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with at least one TEAE leading to study drug discontinuation	15(38.5)	3(18.8)	18(32.7)
血液およびリンパ系障害	8(20.5)	1(6.3)	9(16.4)
好中球減少症*	4(10.3)	1(6.3)	5(9.1)
血小板減少症*	4(10.3)	0	4(7.3)
リンパ球減少症*	2(5.1)	0	2(3.6)
白血球減少症*	1(2.6)	0	1(1.8)
感染症および寄生虫症	1(2.6)	1(6.3)	2(3.6)
ニューモシスチス・イロベチイ肺炎	1(2.6)	0	1(1.8)
肺炎	0	1(6.3)	1(1.8)
臨床検査	3(7.7)	0	3(5.5)
γ－グルタミルトランスフェラーゼ増加	2(5.1)	0	2(3.6)
脳性ナトリウム利尿ペプチド増加	1(2.6)	0	1(1.8)
血中アルカリホスファターゼ増加	1(2.6)	0	1(1.8)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1(2.6)	0	1(1.8)
末梢性Ｔ細胞性リンパ腫、組織型不明	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.2

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
呼吸器、胸郭および縦隔障害	2(5.1)	1(6.3)	3(5.5)
肺臓炎	1(2.6)	1(6.3)	2(3.6)
呼吸困難	0	1(6.3)	1(1.8)
間質性肺疾患	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.2

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-44　重症度別関連性別治験薬の投与中止に至った有害事象（203 試験）（安全性解析対象集団）

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE leading to study drug discontinuation	Any Grade	14(35.9)	1(2.6)	15(38.5)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	12(30.8)	0(0.0)	12(30.8)
	Grade 4	2(5.1)	0(0.0)	2(5.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	14(35.9)	0(0.0)	14(35.9)
血液およびリンパ系障害	Any Grade	8(20.5)	0(0.0)	8(20.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	6(15.4)	0(0.0)	6(15.4)
	Grade 4	2(5.1)	0(0.0)	2(5.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	8(20.5)	0(0.0)	8(20.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=39) n (%)
好中球減少症*	Any Grade	4(10.3)	0(0.0)	4(10.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	4(10.3)	0(0.0)	4(10.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	4(10.3)	0(0.0)	4(10.3)
血小板減少症*	Any Grade	4(10.3)	0(0.0)	4(10.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	2(5.1)	0(0.0)	2(5.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	4(10.3)	0(0.0)	4(10.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
リンパ球減少症*	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
白血球減少症*	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
臨床検査	Any Grade	2(5.1)	1(2.6)	3(7.7)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
γーグルタミルトランスフェラーゼ増加	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血中アルカリホスファターゼ増加	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
脳性ナトリウム利尿ペプチド増加	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	1(2.6)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=39) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
末梢性Ｔ細胞性リンパ腫、組織型不明	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
間質性肺疾患	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
肺臓炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=16) n (%)
Number of subjects with at least one TEAE leading to study drug discontinuation	Any Grade	3(18.8)	1(6.3)	3(18.8)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(12.5)	0(0.0)	2(12.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(6.3)	0(0.0)	1(6.3)
	>=Grade 3	3(18.8)	0(0.0)	3(18.8)
血液およびリンパ系障害	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=16) n (%)
好中球減少症*	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
感染症および寄生虫症	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(6.3)	0(0.0)	1(6.3)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
肺炎	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(6.3)	0(0.0)	1(6.3)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
呼吸器、胸郭および縦隔障害	Any Grade	1(6.3)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
呼吸困難	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
肺臓炎	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE leading to study drug discontinuation	Any Grade	17(30.9)	2(3.6)	18(32.7)
	Grade 1	0(0.0)	2(3.6)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	14(25.5)	0(0.0)	14(25.5)
	Grade 4	2(3.6)	0(0.0)	2(3.6)
	Grade 5	1(1.8)	0(0.0)	1(1.8)
	>=Grade 3	17(30.9)	0(0.0)	17(30.9)
血液およびリンパ系障害	Any Grade	9(16.4)	0(0.0)	9(16.4)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	7(12.7)	0(0.0)	7(12.7)
	Grade 4	2(3.6)	0(0.0)	2(3.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	9(16.4)	0(0.0)	9(16.4)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
好中球减少症*	Any Grade	5(9.1)	0(0.0)	5(9.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	5(9.1)	0(0.0)	5(9.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	5(9.1)	0(0.0)	5(9.1)
血小板减少症*	Any Grade	4(7.3)	0(0.0)	4(7.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	2(3.6)	0(0.0)	2(3.6)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	4(7.3)	0(0.0)	4(7.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
リンパ球減少症*	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
白血球減少症*	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(1.8)	0(0.0)	1(1.8)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
肺炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	1(1.8)	0(0.0)	1(1.8)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
臨床検査	Any Grade	2(3.6)	1(1.8)	3(5.5)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
γーグルタミルトランスフェラーゼ増加	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
血中アルカリホスファターゼ増加	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
脳性ナトリウム利尿ペプチド増加	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=55) n (%)
末梢性Ｔ細胞性リンパ腫、組織型不明	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
呼吸器、胸郭および縦隔障害	Any Grade	3(5.5)	1(1.8)	3(5.5)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	3(5.5)	0(0.0)	3(5.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	0(0.0)	3(5.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
肺臓炎	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
呼吸困難	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
間質性肺疾患	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-45　治験薬の休薬又は減量に至った有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	40 mg (N=23) n (%)
Number of subjects with at least one dose reduction or dose interruption due to TEAE	16(69.6%)
血液およびリンパ系障害	15(65.2%)
好中球減少症*	10(43.5%)
血小板減少症*	10(43.5%)
一般・全身障害および投与部位の状態	1(4.3%)
疲労	1(4.3%)
感染症および寄生虫症	1(4.3%)
尿路感染	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-46　重症度別関連性別治験薬の休薬又は減量に至った有害事象（210 試験）（安全性解析対象集団）

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE leading to dose reduction or interruption	Any Grade	16(69.6%)	0(0.0%)	16(69.6%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	10(43.5%)	0(0.0%)	10(43.5%)
	Grade 4	6(26.1%)	0(0.0%)	6(26.1%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	16(69.6%)	0(0.0%)	16(69.6%)
血液およびリンパ系障害	Any Grade	15(65.2%)	0(0.0%)	15(65.2%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	9(39.1%)	0(0.0%)	9(39.1%)
	Grade 4	6(26.1%)	0(0.0%)	6(26.1%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	15(65.2%)	0(0.0%)	15(65.2%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
好中球减少症*	Any Grade	10(43.5%)	0(0.0%)	10(43.5%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	7(30.4%)	0(0.0%)	7(30.4%)
	Grade 4	3(13.0%)	0(0.0%)	3(13.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	10(43.5%)	0(0.0%)	10(43.5%)
血小板减少症*	Any Grade	10(43.5%)	0(0.0%)	10(43.5%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	6(26.1%)	0(0.0%)	6(26.1%)
	Grade 4	4(17.4%)	0(0.0%)	4(17.4%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	10(43.5%)	0(0.0%)	10(43.5%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
疲労	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Severity	Related	Not Related	Total (N=23)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
尿路感染	Any Grade	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 1	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 2	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 3	1(4.3%)	0(0.0%)	1(4.3%)
	Grade 4	0(0.0%)	0(0.0%)	0(0.0%)
	Grade 5	0(0.0%)	0(0.0%)	0(0.0%)
	>=Grade 3	1(4.3%)	0(0.0%)	1(4.3%)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events. Severities are graded using NCI CTCAE Version 4.03.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

Subjects are counted only once for the worst grade under each column.

TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.

TEAE of overdose is not included in this analysis.

For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-47　治験薬の休薬又は減量に至った有害事象（201 試験）（安全性解析対象集団）

System organ class Preferred term	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with TEAE leading to dose reduction or delay	4 (57.1%)	4 (57.1%)	8 (57.1%)
血液およびリンパ系障害	1 (14.3%)	1 (14.3%)	2 (14.3%)
貧血	1 (14.3%)	0 (0.0%)	1 (7.1%)
好中球減少症	0 (0.0%)	1 (14.3%)	1 (7.1%)
血小板減少症	0 (0.0%)	1 (14.3%)	1 (7.1%)
一般・全身障害および投与部位の状態	1 (14.3%)	0 (0.0%)	1 (7.1%)
疲労	1 (14.3%)	0 (0.0%)	1 (7.1%)
感染症および寄生虫症	1 (14.3%)	0 (0.0%)	1 (7.1%)
副鼻腔炎	1 (14.3%)	0 (0.0%)	1 (7.1%)
臨床検査	2 (28.6%)	3 (42.9%)	5 (35.7%)
アラニンアミノトランスフェラーゼ増加	0 (0.0%)	1 (14.3%)	1 (7.1%)
好中球数減少	2 (28.6%)	0 (0.0%)	2 (14.3%)
血小板数減少	2 (28.6%)	2 (28.6%)	4 (28.6%)
代謝および栄養障害	0 (0.0%)	1 (14.3%)	1 (7.1%)
高トリグリセリド血症	0 (0.0%)	1 (14.3%)	1 (7.1%)
皮膚および皮下組織障害	1 (14.3%)	1 (14.3%)	2 (14.3%)
結節性紅斑	0 (0.0%)	1 (14.3%)	1 (7.1%)
全身性皮疹	1 (14.3%)	0 (0.0%)	1 (7.1%)

SOURCE: Listing 16.2.6.3
MedDRA Version 19.1 was used to code adverse events.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

表 2.7.4.7-48　治験薬の休薬又は減量に至った有害事象（203 試験）（安全性解析対象集団）

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of subjects with at least one dose reduction or dose interruption due to TEAE	31(79.5)	9(56.3)	40(72.7)
血液およびリンパ系障害	28(71.8)	6(37.5)	34(61.8)
血小板減少症*	18(46.2)	3(18.8)	21(38.2)
好中球減少症*	16(41.0)	3(18.8)	19(34.5)
発熱性好中球減少症	2(5.1)	1(6.3)	3(5.5)
白血球減少症*	2(5.1)	0	2(3.6)
心臓障害	1(2.6)	0	1(1.8)
不安定狭心症	1(2.6)	0	1(1.8)
耳および迷路障害	1(2.6)	0	1(1.8)
回転性めまい	1(2.6)	0	1(1.8)
胃腸障害	1(2.6)	1(6.3)	2(3.6)
下痢	0	1(6.3)	1(1.8)
悪心	1(2.6)	0	1(1.8)
一般・全身障害および投与部位の状態	2(5.1)	1(6.3)	3(5.5)
発熱	1(2.6)	1(6.3)	2(3.6)
末梢性浮腫	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

System organ class Preferred term	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
感染症および寄生虫症	2(5.1)	0	2(3.6)
上咽頭炎	1(2.6)	0	1(1.8)
気管支炎	1(2.6)	0	1(1.8)
臨床検査	2(5.1)	1(6.3)	3(5.5)
Ｃ－反応性蛋白増加	1(2.6)	1(6.3)	2(3.6)
心電図ＱＴ延長	1(2.6)	0	1(1.8)
心電図Ｔ波逆転	1(2.6)	0	1(1.8)
代謝および栄養障害	4(10.3)	0	4(7.3)
食欲減退	3(7.7)	0	3(5.5)
低ナトリウム血症	2(5.1)	0	2(3.6)
皮膚および皮下組織障害	1(2.6)	1(6.3)	2(3.6)
発疹	0	1(6.3)	1(1.8)
蕁麻疹	1(2.6)	0	1(1.8)
血管障害	1(2.6)	0	1(1.8)
末梢動脈閉塞性疾患	1(2.6)	0	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-49　重症度別関連性別治験薬の休薬又は減量に至った有害事象（203 試験）（安全性解析対象集団）

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
Number of subjects with at least one TEAE leading to dose reduction or interruption	Any Grade	29(74.4)	5(12.8)	31(79.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	2(5.1)	2(5.1)	3(7.7)
	Grade 3	19(48.7)	2(5.1)	20(51.3)
	Grade 4	8(20.5)	1(2.6)	9(23.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	27(69.2)	3(7.7)	28(71.8)
血液およびリンパ系障害	Any Grade	27(69.2)	1(2.6)	28(71.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	18(46.2)	0(0.0)	18(46.2)
	Grade 4	8(20.5)	1(2.6)	9(23.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	26(66.7)	1(2.6)	27(69.2)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
血小板減少症*	Any Grade	17(43.6)	1(2.6)	18(46.2)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	12(30.8)	0(0.0)	12(30.8)
	Grade 4	4(10.3)	1(2.6)	5(12.8)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	16(41.0)	1(2.6)	17(43.6)
好中球減少症*	Any Grade	16(41.0)	0(0.0)	16(41.0)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	12(30.8)	0(0.0)	12(30.8)
	Grade 4	4(10.3)	0(0.0)	4(10.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	16(41.0)	0(0.0)	16(41.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
発熱性好中球減少症	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
白血球減少症*	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
心臓障害	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)
不安定狭心症	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
耳および迷路障害	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
回転性めまい	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
胃腸障害	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
悪心	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)
末梢性浮腫	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(2.6)	0(0.0)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(2.6)	0(0.0)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=39) n (%)
発熱	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
感染症および寄生虫症	Any Grade	1(2.6)	1(2.6)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=39) n (%)
気管支炎	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
上咽頭炎	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
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Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
臨床検査	Any Grade	2(5.1)	1(2.6)	2(5.1)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	1(2.6)	1(2.6)	2(5.1)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
C－反応性蛋白増加	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(2.6)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
心電図ＱＴ延長	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
心電図Ｔ波逆転	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	1(2.6)	0(0.0)	1(2.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
代謝および栄養障害	Any Grade	4(10.3)	0(0.0)	4(10.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	3(7.7)	0(0.0)	3(7.7)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(7.7)	0(0.0)	3(7.7)
食欲減退	Any Grade	3(7.7)	0(0.0)	3(7.7)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
低ナトリウム血症	Any Grade	2(5.1)	0(0.0)	2(5.1)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(5.1)	0(0.0)	2(5.1)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(5.1)	0(0.0)	2(5.1)
皮膚および皮下組織障害	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
蕁麻疹	Any Grade	1(2.6)	0(0.0)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(2.6)	0(0.0)	1(2.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血管障害	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Japan

System organ class Preferred term	Severity	Related	Not Related	Total (N=39)
		n (%)	n (%)	n (%)
末梢動脈閉塞性疾患	Any Grade	0(0.0)	1(2.6)	1(2.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(2.6)	1(2.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(2.6)	1(2.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=16) n (%)
Number of subjects with at least one TEAE leading to dose reduction or interruption	Any Grade	8(50.0)	1(6.3)	9(56.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	7(43.8)	0(0.0)	7(43.8)
	Grade 4	1(6.3)	0(0.0)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	8(50.0)	0(0.0)	8(50.0)
血液およびリンパ系障害	Any Grade	6(37.5)	0(0.0)	6(37.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	5(31.3)	0(0.0)	5(31.3)
	Grade 4	1(6.3)	0(0.0)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	6(37.5)	0(0.0)	6(37.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
好中球减少症*	Any Grade	3(18.8)	0(0.0)	3(18.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(12.5)	0(0.0)	2(12.5)
	Grade 4	1(6.3)	0(0.0)	1(6.3)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(18.8)	0(0.0)	3(18.8)
血小板减少症*	Any Grade	3(18.8)	0(0.0)	3(18.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	3(18.8)	0(0.0)	3(18.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(18.8)	0(0.0)	3(18.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=16) n (%)
発熱性好中球減少症	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
胃腸障害	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
下痢	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
一般・全身障害および投与部位の状態	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
発熱	Any Grade	0(0.0)	1(6.3)	1(6.3)
	Grade 1	0(0.0)	1(6.3)	1(6.3)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
臨床検査	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
Ｃ－反応性蛋白増加	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)
皮膚および皮下組織障害	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Korea

System organ class Preferred term	Severity	Related	Not Related	Total (N=16)
		n (%)	n (%)	n (%)
発疹	Any Grade	1(6.3)	0(0.0)	1(6.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(6.3)	0(0.0)	1(6.3)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(6.3)	0(0.0)	1(6.3)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related n (%)	Not Related n (%)	Total (N=55) n (%)
Number of subjects with at least one TEAE leading to dose reduction or interruption	Any Grade	37(67.3)	6(10.9)	40(72.7)
	Grade 1	0(0.0)	1(1.8)	1(1.8)
	Grade 2	2(3.6)	2(3.6)	3(5.5)
	Grade 3	26(47.3)	2(3.6)	27(49.1)
	Grade 4	9(16.4)	1(1.8)	10(18.2)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	35(63.6)	3(5.5)	36(65.5)
血液およびリンパ系障害	Any Grade	33(60.0)	1(1.8)	34(61.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	23(41.8)	0(0.0)	23(41.8)
	Grade 4	9(16.4)	1(1.8)	10(18.2)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	32(58.2)	1(1.8)	33(60.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
血小板减少症*	Any Grade	20(36.4)	1(1.8)	21(38.2)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	15(27.3)	0(0.0)	15(27.3)
	Grade 4	4(7.3)	1(1.8)	5(9.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	19(34.5)	1(1.8)	20(36.4)
好中球减少症*	Any Grade	19(34.5)	0(0.0)	19(34.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	14(25.5)	0(0.0)	14(25.5)
	Grade 4	5(9.1)	0(0.0)	5(9.1)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	19(34.5)	0(0.0)	19(34.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
発熱性好中球減少症	Any Grade	3(5.5)	0(0.0)	3(5.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	3(5.5)	0(0.0)	3(5.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	0(0.0)	3(5.5)
白血球減少症*	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
心臓障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)
不安定狭心症	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
耳および迷路障害	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
回転性めまい	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
胃腸障害	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
下痢	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
悪心	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
一般・全身障害および投与部位の状態	Any Grade	2(3.6)	1(1.8)	3(5.5)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
発熱	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	1(1.8)	1(1.8)	2(3.6)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
末梢性浮腫	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
感染症および寄生虫症	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
気管支炎	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
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Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
上咽頭炎	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
臨床検査	Any Grade	3(5.5)	1(1.8)	3(5.5)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	1(1.8)	1(1.8)	2(3.6)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
Ｃ－反応性蛋白増加	Any Grade	1(1.8)	1(1.8)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	1(1.8)	1(1.8)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
心電図ＱＴ延長	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
心電図Ｔ波逆転	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	1(1.8)	0(0.0)	1(1.8)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
代謝および栄養障害	Any Grade	4(7.3)	0(0.0)	4(7.3)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	3(5.5)	0(0.0)	3(5.5)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	3(5.5)	0(0.0)	3(5.5)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
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Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
食欲減退	Any Grade	3(5.5)	0(0.0)	3(5.5)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)
低ナトリウム血症	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	2(3.6)	0(0.0)	2(3.6)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	2(3.6)	0(0.0)	2(3.6)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
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Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
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For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
皮膚および皮下組織障害	Any Grade	2(3.6)	0(0.0)	2(3.6)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)
発疹	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	1(1.8)	0(0.0)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	1(1.8)	0(0.0)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
蕁麻疹	Any Grade	1(1.8)	0(0.0)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	1(1.8)	0(0.0)	1(1.8)
	Grade 3	0(0.0)	0(0.0)	0(0.0)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	0(0.0)	0(0.0)
血管障害	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

Country: Overall

System organ class Preferred term	Severity	Related	Not Related	Total (N=55)
		n (%)	n (%)	n (%)
末梢動脈閉塞性疾患	Any Grade	0(0.0)	1(1.8)	1(1.8)
	Grade 1	0(0.0)	0(0.0)	0(0.0)
	Grade 2	0(0.0)	0(0.0)	0(0.0)
	Grade 3	0(0.0)	1(1.8)	1(1.8)
	Grade 4	0(0.0)	0(0.0)	0(0.0)
	Grade 5	0(0.0)	0(0.0)	0(0.0)
	>=Grade 3	0(0.0)	1(1.8)	1(1.8)

Source: Listing 16.2.6.1

MedDRA Version 21.1 was used to code adverse events.
Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects are counted only once for the worst grade under each relationship column.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.

表 2.7.4.7-50　注目すべき有害事象（210 試験）（安全性解析対象集団）

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
Number of subjects with at least one Adverse Event of Special Interest		21(91.3%)
「貧血」	Any Grade	9(39.1%)
	Grade 1	1(4.3%)
	Grade 2	3(13.0%)
	Grade 3	5(21.7%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	5(21.7%)
貧血+ヘモグロビン減少	Any Grade	9(39.1%)
	Grade 1	1(4.3%)
	Grade 2	3(13.0%)
	Grade 3	5(21.7%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	5(21.7%)
貧血	Any Grade	8(34.8%)
	Grade 1	1(4.3%)
	Grade 2	3(13.0%)
	Grade 3	4(17.4%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	4(17.4%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
ヘモグロビン減少	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
「心臓障害」	Any Grade	2(8.7%)
	Grade 1	2(8.7%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
第一度房室ブロック	Any Grade	1(4.3%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
動悸	Any Grade	1(4.3%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「ウイルス再活性化を除く肝障害」	Any Grade	3(13.0%)
	Grade 1	2(8.7%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
アスパラギン酸アミノトランスフェラーゼ増加	Any Grade	2(8.7%)
	Grade 1	2(8.7%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
γーグルタミルトランスフェラーゼ増加	Any Grade	2(8.7%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
アラニンアミノトランスフェラーゼ増加	Any Grade	1(4.3%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「過敏症」	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5
MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
多形紅斑	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「感染症」	Any Grade	7(30.4%)
	Grade 1	1(4.3%)
	Grade 2	3(13.0%)
	Grade 3	3(13.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(13.0%)
細菌感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
サイトメガロウイルス感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
医療機器関連感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
麦粒腫	Any Grade	1(4.3%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
口腔カンジダ症	Any Grade	1(4.3%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
皮膚感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
扁桃炎	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
上気道感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
尿路感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
「間質性肺疾患」	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	1(4.3%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
間質性肺疾患	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	1(4.3%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
「リンパ球減少症」	Any Grade	2(8.7%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
リンパ球数減少	Any Grade	2(8.7%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
リンパ球減少症+リンパ球数減少	Any Grade	2(8.7%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
「好中球減少症」	Any Grade	13(56.5%)
	Grade 1	1(4.3%)
	Grade 2	2(8.7%)
	Grade 3	7(30.4%)
	Grade 4	3(13.0%)
	Grade 5	0(0.0%)
	>=Grade 3	10(43.5%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
好中球减少症+好中球数减少	Any Grade	12(52.2%)
	Grade 1	0(0.0%)
	Grade 2	2(8.7%)
	Grade 3	7(30.4%)
	Grade 4	3(13.0%)
	Grade 5	0(0.0%)
	>=Grade 3	10(43.5%)
好中球数减少	Any Grade	11(47.8%)
	Grade 1	0(0.0%)
	Grade 2	2(8.7%)
	Grade 3	7(30.4%)
	Grade 4	2(8.7%)
	Grade 5	0(0.0%)
	>=Grade 3	9(39.1%)
白血球减少症+白血球数减少	Any Grade	10(43.5%)
	Grade 1	1(4.3%)
	Grade 2	2(8.7%)
	Grade 3	7(30.4%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	7(30.4%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
白血球数減少	Any Grade	9(39.1%)
	Grade 1	0(0.0%)
	Grade 2	2(8.7%)
	Grade 3	7(30.4%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	7(30.4%)
発熱性好中球減少症	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(4.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
白血球減少症	Any Grade	1(4.3%)
	Grade 1	1(4.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
好中球減少症	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	1(4.3%)
	Grade 5	0(0.0%)
	>=Grade 3	1(4.3%)
「血小板減少症」	Any Grade	18(78.3%)
	Grade 1	1(4.3%)
	Grade 2	5(21.7%)
	Grade 3	6(26.1%)
	Grade 4	6(26.1%)
	Grade 5	0(0.0%)
	>=Grade 3	12(52.2%)
血小板減少症+血小板数減少	Any Grade	18(78.3%)
	Grade 1	1(4.3%)
	Grade 2	5(21.7%)
	Grade 3	6(26.1%)
	Grade 4	6(26.1%)
	Grade 5	0(0.0%)
	>=Grade 3	12(52.2%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
血小板数減少	Any Grade	15(65.2%)
	Grade 1	1(4.3%)
	Grade 2	5(21.7%)
	Grade 3	4(17.4%)
	Grade 4	5(21.7%)
	Grade 5	0(0.0%)
	>=Grade 3	9(39.1%)
血小板減少症	Any Grade	3(13.0%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	2(8.7%)
	Grade 4	1(4.3%)
	Grade 5	0(0.0%)
	>=Grade 3	3(13.0%)
「ウイルス再活性化」	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

Grouped Term Preferred term	Severity	40 mg (N=23) n (%)
サイトメガロウイルス感染	Any Grade	1(4.3%)
	Grade 1	0(0.0%)
	Grade 2	1(4.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

Source: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.

表 2.7.4.7-51　注目すべき有害事象：血液学的有害事象（201 試験）（安全性解析対象集団）

Grouped Term Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one Adverse Event of Special Interest		5 (71.4%)	7 (100.0%)	12 (85.7%)
白血球減少症（Grouped）	Any Grade	4 (57.1%)	1 (14.3%)	5 (35.7%)
	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	1 (14.3%)	1 (14.3%)	2 (14.3%)
白血球減少症	Any Grade	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 1	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
白血球数減少	Any Grade	3 (42.9%)	1 (14.3%)	4 (28.6%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	1 (14.3%)	1 (14.3%)	2 (14.3%)

SOURCE: Listing 16.2.6.3

MedDRA Version 19.1 was used to code adverse events.

n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.

Grouped Term Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
好中球減少症（Grouped）	Any Grade	3 (42.9%)	2 (28.6%)	5 (35.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	3 (42.9%)	0 (0.0%)	3 (21.4%)
	Grade 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	3 (42.9%)	2 (28.6%)	5 (35.7%)
好中球減少症	Any Grade	1 (14.3%)	2 (28.6%)	3 (21.4%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	1 (14.3%)	2 (28.6%)	3 (21.4%)
好中球数減少	Any Grade	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	2 (28.6%)	0 (0.0%)	2 (14.3%)

SOURCE: Listing 16.2.6.3s

MedDRA Version 19.1 was used to code adverse events.

n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.

Grouped Term Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
血小板减少症（Grouped）	Any Grade	5 (71.4%)	7 (100.0%)	12 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	5 (71.4%)	4 (57.1%)	9 (64.3%)
	Grade 3	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	0 (0.0%)	2 (28.6%)	2 (14.3%)
血小板数减少	Any Grade	3 (42.9%)	3 (42.9%)	6 (42.9%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	3 (42.9%)	3 (42.9%)	6 (42.9%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
血小板减少症	Any Grade	2 (28.6%)	4 (57.1%)	6 (42.9%)
	Grade 1	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 2	2 (28.6%)	1 (14.3%)	3 (21.4%)
	Grade 3	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	0 (0.0%)	2 (28.6%)	2 (14.3%)

SOURCE: Listing 16.2.6.3

MedDRA Version 19.1 was used to code adverse events.

n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.

Grouped Term Preferred term	Severity	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
貧血（Grouped）	Any Grade	5 (71.4%)	0 (0.0%)	5 (35.7%)
	Grade 1	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
貧血	Any Grade	5 (71.4%)	0 (0.0%)	5 (35.7%)
	Grade 1	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 2	2 (28.6%)	0 (0.0%)	2 (14.3%)
	Grade 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	1 (14.3%)	0 (0.0%)	1 (7.1%)
ヘモグロビン減少	Any Grade	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade >= 3	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.6.3

MedDRA Version 19.1 was used to code adverse events.

n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.

表 2.7.4.7-52　注目すべき有害事象（203 試験）（安全性解析対象集団）

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
Number of subjects with at least one Adverse Event of Special Interest		53(96.4%)
「貧血」	Any Grade	18(32.7%)
	Grade 1	2(3.6%)
	Grade 2	7(12.7%)
	Grade 3	8(14.5%)
	Grade 4	1(1.8%)
	Grade 5	0(0.0%)
	>=Grade 3	9(16.4%)
貧血	Any Grade	18(32.7%)
	Grade 1	2(3.6%)
	Grade 2	7(12.7%)
	Grade 3	8(14.5%)
	Grade 4	1(1.8%)
	Grade 5	0(0.0%)
	>=Grade 3	9(16.4%)
貧血+ヘモグロビン減少	Any Grade	18(32.7%)
	Grade 1	2(3.6%)
	Grade 2	7(12.7%)
	Grade 3	8(14.5%)
	Grade 4	1(1.8%)
	Grade 5	0(0.0%)
	>=Grade 3	9(16.4%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
「心臓障害」	Any Grade	7(12.7%)
	Grade 1	3(5.5%)
	Grade 2	3(5.5%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
動悸	Any Grade	3(5.5%)
	Grade 1	3(5.5%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
心房細動	Any Grade	2(3.6%)
	Grade 1	1(1.8%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
不安定狭心症	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
不整脈	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
心嚢液貯留	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
「ウイルス再活性化を除く肝障害」	Any Grade	10(18.2%)
	Grade 1	3(5.5%)
	Grade 2	4(7.3%)
	Grade 3	3(5.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(5.5%)
γ－グルタミルトランスフェラーゼ増加	Any Grade	8(14.5%)
	Grade 1	2(3.6%)
	Grade 2	3(5.5%)
	Grade 3	3(5.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(5.5%)
アスパラギン酸アミノトランスフェラーゼ増加	Any Grade	7(12.7%)
	Grade 1	5(9.1%)
	Grade 2	2(3.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
アラニンアミノトランスフェラーゼ増加	Any Grade	5(9.1%)
	Grade 1	3(5.5%)
	Grade 2	2(3.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「過敏症」	Any Grade	3(5.5%)
	Grade 1	2(3.6%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
全身性剥脱性皮膚炎	Any Grade	1(1.8%)
	Grade 1	1(1.8%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
薬物過敏症	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
多形紅斑	Any Grade	1(1.8%)
	Grade 1	1(1.8%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「感染症」	Any Grade	19(34.5%)
	Grade 1	3(5.5%)
	Grade 2	13(23.6%)
	Grade 3	2(3.6%)
	Grade 4	0(0.0%)
	Grade 5	1(1.8%)
	>=Grade 3	3(5.5%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
上気道感染	Any Grade	4(7.3%)
	Grade 1	0(0.0%)
	Grade 2	4(7.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
咽頭炎	Any Grade	3(5.5%)
	Grade 1	0(0.0%)
	Grade 2	2(3.6%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
気管支炎	Any Grade	2(3.6%)
	Grade 1	0(0.0%)
	Grade 2	2(3.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16 2.6 5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
結膜炎	Any Grade	2(3.6%)
	Grade 1	1(1.8%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
インフルエンザ	Any Grade	2(3.6%)
	Grade 1	0(0.0%)
	Grade 2	2(3.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
上咽頭炎	Any Grade	2(3.6%)
	Grade 1	1(1.8%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
膀胱炎	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
サイトメガロウイルス感染	Any Grade	1(1.8%)
	Grade 1	1(1.8%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
感染性小腸結腸炎	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
胃腸炎	Any Grade	1(1.8%)
	Grade 1	1(1.8%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
帯状疱疹	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
膿痂疹	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
肺炎	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	1(1.8%)
	>=Grade 3	1(1.8%)
鼻炎	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
ブドウ球菌皮膚感染	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
「間質性肺疾患」	Any Grade	5(9.1%)
	Grade 1	1(1.8%)
	Grade 2	1(1.8%)
	Grade 3	3(5.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(5.5%)
肺臓炎	Any Grade	4(7.3%)
	Grade 1	1(1.8%)
	Grade 2	1(1.8%)
	Grade 3	2(3.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(3.6%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
間質性肺疾患	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
「リンパ球減少症」	Any Grade	16(29.1%)
	Grade 1	1(1.8%)
	Grade 2	3(5.5%)
	Grade 3	10(18.2%)
	Grade 4	2(3.6%)
	Grade 5	0(0.0%)
	>=Grade 3	12(21.8%)
リンパ球減少症+リンパ球数減少	Any Grade	16(29.1%)
	Grade 1	1(1.8%)
	Grade 2	3(5.5%)
	Grade 3	10(18.2%)
	Grade 4	2(3.6%)
	Grade 5	0(0.0%)
	>=Grade 3	12(21.8%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
リンパ球数減少	Any Grade	11(20.0%)
	Grade 1	1(1.8%)
	Grade 2	2(3.6%)
	Grade 3	6(10.9%)
	Grade 4	2(3.6%)
	Grade 5	0(0.0%)
	>=Grade 3	8(14.5%)
リンパ球減少症	Any Grade	5(9.1%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	4(7.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	4(7.3%)
「好中球減少症」	Any Grade	35(63.6%)
	Grade 1	0(0.0%)
	Grade 2	11(20.0%)
	Grade 3	19(34.5%)
	Grade 4	5(9.1%)
	Grade 5	0(0.0%)
	>=Grade 3	24(43.6%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
好中球减少症+好中球数减少+顆粒球减少症	Any Grade	31(56.4%)
	Grade 1	1(1.8%)
	Grade 2	10(18.2%)
	Grade 3	15(27.3%)
	Grade 4	5(9.1%)
	Grade 5	0(0.0%)
	>=Grade 3	20(36.4%)
白血球減少症+白血球数減少	Any Grade	24(43.6%)
	Grade 1	2(3.6%)
	Grade 2	11(20.0%)
	Grade 3	10(18.2%)
	Grade 4	1(1.8%)
	Grade 5	0(0.0%)
	>=Grade 3	11(20.0%)
好中球数減少	Any Grade	20(36.4%)
	Grade 1	1(1.8%)
	Grade 2	4(7.3%)
	Grade 3	12(21.8%)
	Grade 4	3(5.5%)
	Grade 5	0(0.0%)
	>=Grade 3	15(27.3%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
白血球数减少	Any Grade	18(32.7%)
	Grade 1	2(3.6%)
	Grade 2	7(12.7%)
	Grade 3	8(14.5%)
	Grade 4	1(1.8%)
	Grade 5	0(0.0%)
	>=Grade 3	9(16.4%)
好中球减少症	Any Grade	11(20.0%)
	Grade 1	0(0.0%)
	Grade 2	6(10.9%)
	Grade 3	3(5.5%)
	Grade 4	2(3.6%)
	Grade 5	0(0.0%)
	>=Grade 3	5(9.1%)
白血球减少症	Any Grade	6(10.9%)
	Grade 1	0(0.0%)
	Grade 2	4(7.3%)
	Grade 3	2(3.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(3.6%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
発熱性好中球減少症	Any Grade	3(5.5%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	3(5.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(5.5%)
顆粒球減少症	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(1.8%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(1.8%)
「血小板減少症」	Any Grade	46(83.6%)
	Grade 1	8(14.5%)
	Grade 2	10(18.2%)
	Grade 3	19(34.5%)
	Grade 4	9(16.4%)
	Grade 5	0(0.0%)
	>=Grade 3	28(50.9%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
血小板减少症+血小板数减少	Any Grade	46(83.6%)
	Grade 1	8(14.5%)
	Grade 2	10(18.2%)
	Grade 3	19(34.5%)
	Grade 4	9(16.4%)
	Grade 5	0(0.0%)
	>=Grade 3	28(50.9%)
血小板数减少	Any Grade	31(56.4%)
	Grade 1	7(12.7%)
	Grade 2	7(12.7%)
	Grade 3	11(20.0%)
	Grade 4	6(10.9%)
	Grade 5	0(0.0%)
	>=Grade 3	17(30.9%)
血小板减少症	Any Grade	15(27.3%)
	Grade 1	1(1.8%)
	Grade 2	3(5.5%)
	Grade 3	8(14.5%)
	Grade 4	3(5.5%)
	Grade 5	0(0.0%)
	>=Grade 3	11(20.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
「トルサード　ド　ポアント／QT 延長」	Any Grade	5(9.1%)
	Grade 1	4(7.3%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
心電図ＱＴ延長	Any Grade	5(9.1%)
	Grade 1	4(7.3%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「ウイルス再活性化」	Any Grade	2(3.6%)
	Grade 1	1(1.8%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Grouped Term Preferred term	Severity	40 mg (N=55) n (%)
サイトメガロウイルス感染	Any Grade	1(1.8%)
	Grade 1	1(1.8%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
帯状疱疹	Any Grade	1(1.8%)
	Grade 1	0(0.0%)
	Grade 2	1(1.8%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5

MedDRA Version 21.1 was used to code adverse events.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

表 2.7.4.7-53　人種別（日本人、韓国人）注目すべき有害事象（203 試験）（安全性解析対象集団）

Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
Number of subjects with at least one Adverse Event of Special Interest		39(100.0%)
「貧血」	Any Grade	14(35.9%)
	Grade 1	2(5.1%)
	Grade 2	5(12.8%)
	Grade 3	6(15.4%)
	Grade 4	1(2.6%)
	Grade 5	0(0.0%)
	>=Grade 3	7(17.9%)
貧血	Any Grade	14(35.9%)
	Grade 1	2(5.1%)
	Grade 2	5(12.8%)
	Grade 3	6(15.4%)
	Grade 4	1(2.6%)
	Grade 5	0(0.0%)
	>=Grade 3	7(17.9%)
貧血+ヘモグロビン減少	Any Grade	14(35.9%)
	Grade 1	2(5.1%)
	Grade 2	5(12.8%)
	Grade 3	6(15.4%)
	Grade 4	1(2.6%)
	Grade 5	0(0.0%)
	>=Grade 3	7(17.9%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1
MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
「心臓障害」	Any Grade	6(15.4%)
	Grade 1	3(7.7%)
	Grade 2	2(5.1%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)
動悸	Any Grade	3(7.7%)
	Grade 1	3(7.7%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
不安定狭心症	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
不整脈	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
心房細動	Any Grade	1(2.6%)
	Grade 1	1(2.6%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
心嚢液貯留	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
「ウイルス再活性化を除く肝障害」	Any Grade	10(25.6%)
	Grade 1	3(7.7%)
	Grade 2	4(10.3%)
	Grade 3	3(7.7%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(7.7%)
γーグルタミルトランスフェラーゼ増加	Any Grade	8(20.5%)
	Grade 1	2(5.1%)
	Grade 2	3(7.7%)
	Grade 3	3(7.7%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	3(7.7%)
アスパラギン酸アミノトランスフェラーゼ増加	Any Grade	7(17.9%)
	Grade 1	5(12.8%)
	Grade 2	2(5.1%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
アラニンアミノトランスフェラーゼ増加	Any Grade	5(12.8%)
	Grade 1	3(7.7%)
	Grade 2	2(5.1%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「過敏症」	Any Grade	3(7.7%)
	Grade 1	2(5.1%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
全身性剥脱性皮膚炎	Any Grade	1(2.6%)
	Grade 1	1(2.6%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
薬物過敏症	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
多形紅斑	Any Grade	1(2.6%)
	Grade 1	1(2.6%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「感染症」	Any Grade	15(38.5%)
	Grade 1	2(5.1%)
	Grade 2	12(30.8%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
咽頭炎	Any Grade	3(7.7%)
	Grade 1	0(0.0%)
	Grade 2	2(5.1%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)
気管支炎	Any Grade	2(5.1%)
	Grade 1	0(0.0%)
	Grade 2	2(5.1%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
結膜炎	Any Grade	2(5.1%)
	Grade 1	1(2.6%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
インフルエンザ	Any Grade	2(5.1%)
	Grade 1	0(0.0%)
	Grade 2	2(5.1%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
上咽頭炎	Any Grade	2(5.1%)
	Grade 1	1(2.6%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
上気道感染	Any Grade	2(5.1%)
	Grade 1	0(0.0%)
	Grade 2	2(5.1%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
膀胱炎	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
サイトメガロウイルス感染	Any Grade	1(2.6%)
	Grade 1	1(2.6%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
帯状疱疹	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
膿痂疹	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
ニューモシスチス・イロベチイ肺炎	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)
鼻炎	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
「間質性肺疾患」	Any Grade	4(10.3%)
	Grade 1	1(2.6%)
	Grade 2	1(2.6%)
	Grade 3	2(5.1%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(5.1%)
肺臓炎	Any Grade	3(7.7%)
	Grade 1	1(2.6%)
	Grade 2	1(2.6%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)
間質性肺疾患	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
「リンパ球減少症」	Any Grade	16(41.0%)
	Grade 1	1(2.6%)
	Grade 2	3(7.7%)
	Grade 3	10(25.6%)
	Grade 4	2(5.1%)
	Grade 5	0(0.0%)
	>=Grade 3	12(30.8%)
リンパ球減少症+リンパ球数減少	Any Grade	16(41.0%)
	Grade 1	1(2.6%)
	Grade 2	3(7.7%)
	Grade 3	10(25.6%)
	Grade 4	2(5.1%)
	Grade 5	0(0.0%)
	>=Grade 3	12(30.8%)
リンパ球数減少	Any Grade	11(28.2%)
	Grade 1	1(2.6%)
	Grade 2	2(5.1%)
	Grade 3	6(15.4%)
	Grade 4	2(5.1%)
	Grade 5	0(0.0%)
	>=Grade 3	8(20.5%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
リンパ球減少症	Any Grade	5(12.8%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	4(10.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	4(10.3%)
「好中球減少症」	Any Grade	32(82.1%)
	Grade 1	0(0.0%)
	Grade 2	11(28.2%)
	Grade 3	17(43.6%)
	Grade 4	4(10.3%)
	Grade 5	0(0.0%)
	>=Grade 3	21(53.8%)
好中球減少症+好中球数減少+顆粒球減少症	Any Grade	28(71.8%)
	Grade 1	1(2.6%)
	Grade 2	10(25.6%)
	Grade 3	13(33.3%)
	Grade 4	4(10.3%)
	Grade 5	0(0.0%)
	>=Grade 3	17(43.6%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
白血球減少症+白血球数減少	Any Grade	24(61.5%)
	Grade 1	2(5.1%)
	Grade 2	11(28.2%)
	Grade 3	10(25.6%)
	Grade 4	1(2.6%)
	Grade 5	0(0.0%)
	>=Grade 3	11(28.2%)
好中球数減少	Any Grade	18(46.2%)
	Grade 1	1(2.6%)
	Grade 2	4(10.3%)
	Grade 3	10(25.6%)
	Grade 4	3(7.7%)
	Grade 5	0(0.0%)
	>=Grade 3	13(33.3%)
白血球数減少	Any Grade	18(46.2%)
	Grade 1	2(5.1%)
	Grade 2	7(17.9%)
	Grade 3	8(20.5%)
	Grade 4	1(2.6%)
	Grade 5	0(0.0%)
	>=Grade 3	9(23.1%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
07MAY2020 03:21

Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
好中球減少症	Any Grade	9(23.1%)
	Grade 1	0(0.0%)
	Grade 2	6(15.4%)
	Grade 3	2(5.1%)
	Grade 4	1(2.6%)
	Grade 5	0(0.0%)
	>=Grade 3	3(7.7%)
白血球減少症	Any Grade	6(15.4%)
	Grade 1	0(0.0%)
	Grade 2	4(10.3%)
	Grade 3	2(5.1%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(5.1%)
発熱性好中球減少症	Any Grade	2(5.1%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	2(5.1%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(5.1%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
07MAY2020 03:21

Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
顆粒球減少症	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(2.6%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(2.6%)
「血小板減少症」	Any Grade	35(89.7%)
	Grade 1	6(15.4%)
	Grade 2	7(17.9%)
	Grade 3	14(35.9%)
	Grade 4	8(20.5%)
	Grade 5	0(0.0%)
	>=Grade 3	22(56.4%)
血小板減少症+血小板数減少	Any Grade	35(89.7%)
	Grade 1	6(15.4%)
	Grade 2	7(17.9%)
	Grade 3	14(35.9%)
	Grade 4	8(20.5%)
	Grade 5	0(0.0%)
	>=Grade 3	22(56.4%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
07MAY2020 03:21

Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
血小板数減少	Any Grade	26(66.7%)
	Grade 1	5(12.8%)
	Grade 2	6(15.4%)
	Grade 3	9(23.1%)
	Grade 4	6(15.4%)
	Grade 5	0(0.0%)
	>=Grade 3	15(38.5%)
血小板減少症	Any Grade	9(23.1%)
	Grade 1	1(2.6%)
	Grade 2	1(2.6%)
	Grade 3	5(12.8%)
	Grade 4	2(5.1%)
	Grade 5	0(0.0%)
	>=Grade 3	7(17.9%)
「トルサード　ド　ポアント／QT 延長」	Any Grade	5(12.8%)
	Grade 1	4(10.3%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
07MAY2020 03:21

Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
心電図ＱＴ延長	Any Grade	5(12.8%)
	Grade 1	4(10.3%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「ウイルス再活性化」	Any Grade	2(5.1%)
	Grade 1	1(2.6%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
サイトメガロウイルス感染	Any Grade	1(2.6%)
	Grade 1	1(2.6%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
07MAY2020 03:21

Country: Japan

Grouped Term Preferred term	Severity	40 mg (N=39) n (%)
帯状疱疹	Any Grade	1(2.6%)
	Grade 1	0(0.0%)
	Grade 2	1(2.6%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
07MAY2020 03:21

Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
Number of subjects with at least one Adverse Event of Special Interest		14(87.5%)
「貧血」	Any Grade	4(25.0%)
	Grade 1	0(0.0%)
	Grade 2	2(12.5%)
	Grade 3	2(12.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(12.5%)
貧血	Any Grade	4(25.0%)
	Grade 1	0(0.0%)
	Grade 2	2(12.5%)
	Grade 3	2(12.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(12.5%)
貧血+ヘモグロビン減少	Any Grade	4(25.0%)
	Grade 1	0(0.0%)
	Grade 2	2(12.5%)
	Grade 3	2(12.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(12.5%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
「心臓障害」	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	1(6.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
心房細動	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	1(6.3%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
「感染症」	Any Grade	4(25.0%)
	Grade 1	1(6.3%)
	Grade 2	1(6.3%)
	Grade 3	1(6.3%)
	Grade 4	0(0.0%)
	Grade 5	1(6.3%)
	>=Grade 3	2(12.5%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
上気道感染	Any Grade	2(12.5%)
	Grade 1	0(0.0%)
	Grade 2	2(12.5%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)
感染性小腸結腸炎	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(6.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(6.3%)
胃腸炎	Any Grade	1(6.3%)
	Grade 1	1(6.3%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	0(0.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
肺炎	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	0(0.0%)
	Grade 4	0(0.0%)
	Grade 5	1(6.3%)
	>=Grade 3	1(6.3%)
ブドウ球菌皮膚感染	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(6.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(6.3%)
「間質性肺疾患」	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(6.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(6.3%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
肺臓炎	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(6.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(6.3%)
「好中球減少症」	Any Grade	3(18.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	2(12.5%)
	Grade 4	1(6.3%)
	Grade 5	0(0.0%)
	>=Grade 3	3(18.8%)
好中球減少症+好中球数減少+顆粒球減少症	Any Grade	3(18.8%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	2(12.5%)
	Grade 4	1(6.3%)
	Grade 5	0(0.0%)
	>=Grade 3	3(18.8%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
好中球減少症	Any Grade	2(12.5%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(6.3%)
	Grade 4	1(6.3%)
	Grade 5	0(0.0%)
	>=Grade 3	2(12.5%)
好中球数減少	Any Grade	2(12.5%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	2(12.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(12.5%)
発熱性好中球減少症	Any Grade	1(6.3%)
	Grade 1	0(0.0%)
	Grade 2	0(0.0%)
	Grade 3	1(6.3%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	1(6.3%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
「血小板减少症」	Any Grade	11(68.8%)
	Grade 1	2(12.5%)
	Grade 2	3(18.8%)
	Grade 3	5(31.3%)
	Grade 4	1(6.3%)
	Grade 5	0(0.0%)
	>=Grade 3	6(37.5%)
血小板减少症+血小板数减少	Any Grade	11(68.8%)
	Grade 1	2(12.5%)
	Grade 2	3(18.8%)
	Grade 3	5(31.3%)
	Grade 4	1(6.3%)
	Grade 5	0(0.0%)
	>=Grade 3	6(37.5%)
血小板减少症	Any Grade	6(37.5%)
	Grade 1	0(0.0%)
	Grade 2	2(12.5%)
	Grade 3	3(18.8%)
	Grade 4	1(6.3%)
	Grade 5	0(0.0%)
	>=Grade 3	4(25.0%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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Country: Korea

Grouped Term Preferred term	Severity	40 mg (N=16) n (%)
血小板数减少	Any Grade	5(31.3%)
	Grade 1	2(12.5%)
	Grade 2	1(6.3%)
	Grade 3	2(12.5%)
	Grade 4	0(0.0%)
	Grade 5	0(0.0%)
	>=Grade 3	2(12.5%)

SOURCE: Listing 16.2.6.5 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = Number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in a subgroup in the analysis set.
Subjects with more than one TEAE are counted once in the worst severity category within the same SOC and PT.

Program: HUYA¥HBI-8000¥RXA97790¥BIOSTATISTICS¥PRODUCTION¥TABLES¥ADHOC¥T14_05_12_03_ADHOC.SAS
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表 2.7.4.7-54　血液学的検査値異常のベースライン後の Grade の概要（210 試験）（安全性解析対象集団）

Parameter	Worst Post-Baseline Grade	40 mg (N=23) n (%)
Anemia	Any Grade	20 (87.0%)
	Grade 3, 4	5 (21.7%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)
White blood cell decreased	Any Grade	13 (56.5%)
	Grade 3, 4	7 (30.4%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)
Lymphocyte count decreased	Any Grade	17 (73.9%)
	Grade 3, 4	11 (47.8%)
	Grade 4	2 (8.7%)
	Missing	1 (4.3%)
Lymphocyte count increased	Any Grade	2 (8.7%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)
Neutrophil count decreased	Any Grade	16 (69.6%)
	Grade 3, 4	9 (39.1%)
	Grade 4	3 (13.0%)
	Missing	1 (4.3%)
Platelet count decreased	Any Grade	22 (95.7%)
	Grade 3, 4	12 (52.2%)
	Grade 4	6 (26.1%)
	Missing	1 (4.3%)

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

表 2.7.4.7-55　血液学的検査値異常のベースラインの Grade と投与後の Grade のシフトテーブル（210 試験）（安全性解析対象集団）

		40 mg (N=23)						
		Worst Post-Baseline Grade						
Parameter	Baseline Grade	Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Anemia	Grade 0	2	2	1	0	0	0	5
	Grade 1	0	6	4	2	0	0	12
	Grade 2	0	0	2	3	0	1	6
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	2	8	7	5	0	1	23
White blood cell decreased	Grade 0	9	1	5	2	0	1	18
	Grade 1	0	0	0	3	0	0	3
	Grade 2	0	0	0	2	0	0	2
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	9	1	5	7	0	1	23
Lymphocyte count decreased	Grade 0	4	0	2	3	0	0	9
	Grade 1	0	1	1	1	0	0	3
	Grade 2	0	1	1	2	0	0	4
	Grade 3	1	0	0	2	1	1	5
	Grade 4	0	0	0	1	1	0	2
	Missing	0	0	0	0	0	0	0
	Overall	5	2	4	9	2	1	23

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.

n = number of subjects.

Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count or lymphocyte count, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased' or 'Lymphocyte count decreased', respectively.

Parameter	Baseline Grade	40 mg (N=23)						
		Worst Post-Baseline Grade						
		Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lymphocyte count increased	Grade 0	20	0	1	0	0	1	22
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	20	0	2	0	0	1	23
Neutrophil count decreased	Grade 0	6	1	6	5	2	1	21
	Grade 1	0	0	0	1	1	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	6	1	6	6	3	1	23
Platelet count decreased	Grade 0	0	4	3	3	2	1	13
	Grade 1	0	1	2	3	4	0	10
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	0	5	5	6	6	1	23

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count or lymphocyte count, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased' or 'Lymphocyte count decreased', respectively.

表 2.7.4.7-56　血液学的検査値異常のベースライン後の Grade の概要（201 試験）（安全性解析対象集団）

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Anemia	Any Grade	7 (100.0%)	5 (71.4%)	12 (85.7%)
	Grade 3, 4	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
White blood cell decreased	Any Grade	5 (71.4%)	5 (71.4%)	10 (71.4%)
	Grade 3, 4	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lymphocyte count decreased	Any Grade	5 (71.4%)	4 (57.1%)	9 (64.3%)
	Grade 3, 4	3 (42.9%)	3 (42.9%)	6 (42.9%)
	Grade 4	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lymphocyte count increased	Any Grade	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Neutrophil count decreased	Any Grade	6 (85.7%)	5 (71.4%)	11 (78.6%)
	Grade 3, 4	3 (42.9%)	2 (28.6%)	5 (35.7%)
	Grade 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet count decreased	Any Grade	7 (100.0%)	7 (100.0%)	14 (100.0%)
	Grade 3, 4	0 (0.0%)	3 (42.9%)	3 (21.4%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

表 2.7.4.7-57　血液学的検査値異常のベースラインの Grade と投与後の Grade のシフトテーブル（201 試験）（安全性解析対象集団）

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Anemia	Grade 0	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	3 (42.9%)
	Grade 1	0 (0.0%)	1 (14.3%)	2 (28.6%)	1 (14.3%)	-	0 (0.0%)	4 (57.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	4 (57.1%)	2 (28.6%)	1 (14.3%)	-	0 (0.0%)	7 (100.0%)
White blood cell decreased	Grade 0	2 (28.6%)	1 (14.3%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	1 (14.3%)	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Lymphocyte count decreased	Grade 0	2 (28.6%)	2 (28.6%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	2 (28.6%)	0 (0.0%)	2 (28.6%)	1 (14.3%)	0 (0.0%)	7 (100.0%)
Lymphocyte count increased	Grade 0	7 (100.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	7 (100.0%)
	Grade 1	-	-	-	-	-	-	-
	Grade 2	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Neutrophil count decreased	Grade 0	1 (14.3%)	2 (28.6%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	1 (14.3%)	3 (42.9%)	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Platelet count decreased	Grade 0	0 (0.0%)	2 (28.6%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	2 (28.6%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Anemia	Grade 0	2 (28.6%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	4 (57.1%)
	Grade 1	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	1 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	2 (28.6%)	3 (42.9%)	0 (0.0%)	-	0 (0.0%)	7 (100.0%)
White blood cell decreased	Grade 0	2 (28.6%)	1 (14.3%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	1 (14.3%)	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Lymphocyte count decreased	Grade 0	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (57.1%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	1 (14.3%)	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Lymphocyte count increased	Grade 0	6 (85.7%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	6 (85.7%)
	Grade 1	-	-	-	-	-	-	-
	Grade 2	0 (0.0%)	-	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	1 (14.3%)
	Grade 3	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	6 (85.7%)	-	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Neutrophil count decreased	Grade 0	2 (28.6%)	1 (14.3%)	2 (28.6%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	1 (14.3%)	2 (28.6%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	7 (100.0%)
Platelet count decreased	Grade 0	0 (0.0%)	1 (14.3%)	3 (42.9%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	1 (14.3%)	3 (42.9%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Anemia	Grade 0	2 (14.3%)	4 (28.6%)	1 (7.1%)	0 (0.0%)	-	0 (0.0%)	7 (50.0%)
	Grade 1	0 (0.0%)	2 (14.3%)	3 (21.4%)	1 (7.1%)	-	0 (0.0%)	6 (42.9%)
	Grade 2	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	-	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	2 (14.3%)	6 (42.9%)	5 (35.7%)	1 (7.1%)	-	0 (0.0%)	14 (100.0%)
White blood cell decreased	Grade 0	4 (28.6%)	2 (14.3%)	5 (35.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (78.6%)
	Grade 1	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (28.6%)	2 (14.3%)	6 (42.9%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Lymphocyte count decreased	Grade 0	5 (35.7%)	3 (21.4%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	9 (64.3%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	3 (21.4%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (35.7%)	3 (21.4%)	0 (0.0%)	5 (35.7%)	1 (7.1%)	0 (0.0%)	14 (100.0%)
Lymphocyte count increased	Grade 0	13 (92.9%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	13 (92.9%)
	Grade 1	-	-	-	-	-	-	-
	Grade 2	0 (0.0%)	-	1 (7.1%)	0 (0.0%)	-	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	13 (92.9%)	-	1 (7.1%)	0 (0.0%)	-	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Neutrophil count decreased	Grade 0	3 (21.4%)	3 (21.4%)	2 (14.3%)	2 (14.3%)	1 (7.1%)	0 (0.0%)	11 (78.6%)
	Grade 1	0 (0.0%)	1 (7.1%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (21.4%)	4 (28.6%)	2 (14.3%)	3 (21.4%)	2 (14.3%)	0 (0.0%)	14 (100.0%)
Platelet count decreased	Grade 0	0 (0.0%)	3 (21.4%)	7 (50.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	12 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	3 (21.4%)	8 (57.1%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.1
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

表 2.7.4.7-58　血液学的検査値異常のベースライン後の Grade の概要（203 試験）（安全性解析対象集団）

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Anemia	Any Grade	36 (92.3)	15 (93.8)	51 (92.7)
	Grade 3, 4	9 (23.1)	2 (12.5)	11 (20.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell decreased	Any Grade	33 (84.6)	8 (50.0)	41 (74.5)
	Grade 3, 4	14 (35.9)	3 (18.8)	17 (30.9)
	Grade 4	1 (2.6)	0 (0.0)	1 (1.8)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Lymphocyte count decreased	Any Grade	35 (89.7)	11 (68.8)	46 (83.6)
	Grade 3, 4	20 (51.3)	7 (43.8)	27 (49.1)
	Grade 4	6 (15.4)	0 (0.0)	6 (10.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Lymphocyte count increased	Any Grade	1 (2.6)	1 (6.3)	2 (3.6)
	Grade 3, 4	1 (2.6)	0 (0.0)	1 (1.8)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Neutrophil count decreased	Any Grade	33 (84.6)	10 (62.5)	43 (78.2)
	Grade 3, 4	19 (48.7)	4 (25.0)	23 (41.8)
	Grade 4	4 (10.3)	1 (6.3)	5 (9.1)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Platelet count decreased	Any Grade	38 (97.4)	16 (100.0)	54 (98.2)
	Grade 3, 4	22 (56.4)	5 (31.3)	27 (49.1)
	Grade 4	9 (23.1)	0 (0.0)	9 (16.4)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

表 2.7.4.7-59　血液学的検査値異常のベースラインの Grade と投与後の Grade のシフトテーブル（203 試験）（安全性解析対象集団）

Country: Japan

		40 mg (N=39)						
		Worst Post-Baseline Grade						
Parameter	Baseline Grade	Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Anemia	Grade 0	3	6	0	1	0	0	10
	Grade 1	0	11	7	2	0	0	20
	Grade 2	0	0	3	5	0	0	8
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	3	17	10	9	0	0	39
White blood cell decreased	Grade 0	6	5	11	8	0	0	30
	Grade 1	0	0	1	1	0	0	2
	Grade 2	0	1	1	3	1	0	6
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	6	6	13	13	1	0	39

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.

N = number of subjects in the Safety Analysis Set by country.

n = number of subjects.

Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.

Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in ‘Neutrophil count decreased’, ‘Lymphocyte count decreased’ or ‘white blood cell decreased’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lymphocyte count decreased	Grade 0	4	2	5	4	0	0	15
	Grade 1	0	2	2	3	1	0	8
	Grade 2	0	1	1	7	0	0	9
	Grade 3	0	0	2	0	3	0	5
	Grade 4	0	0	0	0	2	0	2
	Missing	0	0	0	0	0	0	0
	Overall	4	5	10	14	6	0	39
Lymphocyte count increased	Grade 0	38	0	0	0	0	0	38
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	38	0	0	1	0	0	39

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased', 'Lymphocyte count decreased' or 'white blood cell decreased', respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Neutrophil count decreased	Grade 0	6	2	9	11	4	0	32
	Grade 1	0	0	2	3	0	0	5
	Grade 2	0	0	0	1	0	0	1
	Grade 3	0	0	1	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	6	2	12	15	4	0	39
Platelet count decreased	Grade 0	1	8	6	7	6	0	28
	Grade 1	0	0	2	6	3	0	11
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	1	8	8	13	9	0	39

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in ‘Neutrophil count decreased’, ‘Lymphocyte count decreased’ or ‘white blood cell decreased’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Anemia	Grade 0	1	3	1	0	0	0	5
	Grade 1	0	4	3	1	0	0	8
	Grade 2	0	0	2	1	0	0	3
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	1	7	6	2	0	0	16
White blood cell decreased	Grade 0	8	1	2	1	0	0	12
	Grade 1	0	0	2	1	0	0	3
	Grade 2	0	0	0	1	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	8	1	4	3	0	0	16

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased', 'Lymphocyte count decreased' or 'white blood cell decreased', respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lymphocyte count decreased	Grade 0	5	1	1	4	0	0	11
	Grade 1	0	0	0	1	0	0	1
	Grade 2	0	0	2	0	0	0	2
	Grade 3	0	0	0	2	0	0	2
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	5	1	3	7	0	0	16
Lymphocyte count increased	Grade 0	15	0	1	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	15	0	1	0	0	0	16

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased', 'Lymphocyte count decreased' or 'white blood cell decreased', respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Neutrophil count decreased	Grade 0	6	2	4	1	1	0	14
	Grade 1	0	0	0	2	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	6	2	4	3	1	0	16
Platelet count decreased	Grade 0	0	4	3	1	0	0	8
	Grade 1	0	0	4	4	0	0	8
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	0	4	7	5	0	0	16

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased', 'Lymphocyte count decreased' or 'white blood cell decreased', respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Anemia	Grade 0	4	9	1	1	0	0	15
	Grade 1	0	15	10	3	0	0	28
	Grade 2	0	0	5	6	0	0	11
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	4	24	16	11	0	0	55
White blood cell decreased	Grade 0	14	6	13	9	0	0	42
	Grade 1	0	0	3	2	0	0	5
	Grade 2	0	1	1	4	1	0	7
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	14	7	17	16	1	0	55

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in ‘Neutrophil count decreased’, ‘Lymphocyte count decreased’ or ‘white blood cell decreased’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lymphocyte count decreased	Grade 0	9	3	6	8	0	0	26
	Grade 1	0	2	2	4	1	0	9
	Grade 2	0	1	3	7	0	0	11
	Grade 3	0	0	2	2	3	0	7
	Grade 4	0	0	0	0	2	0	2
	Missing	0	0	0	0	0	0	0
	Overall	9	6	13	21	6	0	55
Lymphocyte count increased	Grade 0	53	0	1	0	0	0	54
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	53	0	1	1	0	0	55

Source: Listing 16.2.7 1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased', 'Lymphocyte count decreased' or 'white blood cell decreased', respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Neutrophil count decreased	Grade 0	12	4	13	12	5	0	46
	Grade 1	0	0	2	5	0	0	7
	Grade 2	0	0	0	1	0	0	1
	Grade 3	0	0	1	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	12	4	16	18	5	0	55
Platelet count decreased	Grade 0	1	12	9	8	6	0	36
	Grade 1	0	0	6	10	3	0	19
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	1	12	15	18	9	0	55

Source: Listing 16 2.7.1

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For neutrophil count, lymphocyte count or leukocytes, the local reference ranges are set as the higher limits of Grade 0 in the CTCAE grading. However, at some investigational sites, the local reference ranges are lower than the upper limit of CTCAE Grade 1. In such cases, these are graded as 0 in 'Neutrophil count decreased', 'Lymphocyte count decreased' or 'white blood cell decreased', respectively.

表 2.7.4.7-60　血液生化学検査値異常のベースライン後の Grade の概要（210 試験）（安全性解析対象集団）

Parameter	Worst Post-Baseline Grade	40 mg (N=23) n (%)
Hypoalbuminemia	Any Grade	23 (100.0%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Alkaline phosphatase increased	Any Grade	10 (43.5%)
	Grade 3, 4	1 (4.3%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
ALT increased	Any Grade	6 (26.1%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Serum amylase increased	Any Grade	3 (13.0%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
AST increased	Any Grade	10 (43.5%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Blood bilirubin increased	Any Grade	1 (4.3%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	40 mg (N=23) n (%)
Lipase increased	Any Grade	9 (39.1%)
	Grade 3, 4	2 (8.7%)
	Grade 4	1 (4.3%)
	Missing	1 (4.3%)
Creatinine increased	Any Grade	21 (91.3%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Hypokalemia	Any Grade	11 (47.8%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Hyperkalemia	Any Grade	4 (17.4%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Hyponatremia	Any Grade	14 (60.9%)
	Grade 3, 4	3 (13.0%)
	Grade 4	1 (4.3%)
	Missing	0 (0.0%)
Hypernatremia	Any Grade	0 (0.0%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	40 mg (N=23) n (%)
Hypomagnesemia	Any Grade	10 (43.5%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)
Hypermagnesemia	Any Grade	4 (17.4%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)
Hypocalcemia	Any Grade	10 (43.5%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Hypercalcemia	Any Grade	8 (34.8%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)
Hypoglycemia	Any Grade	1 (4.3%)
	Grade 3, 4	0 (0.0%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)
Hyperglycemia	Any Grade	17 (73.9%)
	Grade 3, 4	1 (4.3%)
	Grade 4	0 (0.0%)
	Missing	1 (4.3%)

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	40 mg (N=23) n (%)
GGT increased	Any Grade	8 (34.8%)
	Grade 3, 4	1 (4.3%)
	Grade 4	0 (0.0%)
	Missing	0 (0.0%)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

表 2.7.4.7-61　血液生化学検査値異常のベースラインの Grade と投与後の Grade のシフトテーブル（210 試験）（安全性解析対象集団）

		40 mg (N=23)						
		Worst Post-Baseline Grade						
Parameter	Baseline Grade	Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoalbuminemia	Grade 0	0	5	1	0	0	0	6
	Grade 1	0	8	6	0	0	0	14
	Grade 2	0	0	3	0	0	0	3
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	0	13	10	0	0	0	23
Alkaline phosphatase increased	Grade 0	12	5	0	0	0	0	17
	Grade 1	1	4	0	1	0	0	6
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	13	9	0	1	0	0	23
ALT increased	Grade 0	16	4	1	0	0	0	21
	Grade 1	1	1	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	17	5	1	0	0	0	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

		40 mg (N=23)						
		Worst Post-Baseline Grade						
Parameter	Baseline Grade	Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Serum amylase increased	Grade 0	19	2	1	0	0	0	22
	Grade 1	1	0	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	20	2	1	0	0	0	23
AST increased	Grade 0	12	7	1	0	0	0	20
	Grade 1	1	2	0	0	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	13	9	1	0	0	0	23
Blood bilirubin increased	Grade 0	22	0	1	0	0	0	23
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	22	0	1	0	0	0	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Baseline Grade	40 mg (N=23) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lipase increased	Grade 0	13	3	0	0	0	0	16
	Grade 1	0	3	1	1	0	1	6
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	1	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	13	6	1	1	1	1	23
Creatinine increased	Grade 0	2	14	0	0	0	0	16
	Grade 1	0	7	0	0	0	0	7
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	2	21	0	0	0	0	23
Hypokalemia	Grade 0	12	10	0	0	0	0	22
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	1	0	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	12	11	0	0	0	0	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Baseline Grade	40 mg (N=23) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hyperkalemia	Grade 0	17	2	1	0	0	0	20
	Grade 1	2	1	0	0	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	19	3	1	0	0	0	23
Hyponatremia	Grade 0	9	8	0	0	0	0	17
	Grade 1	0	3	0	2	1	0	6
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	9	11	0	2	1	0	23
Hypernatremia	Grade 0	23	0	0	0	0	0	23
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	23	0	0	0	0	0	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Baseline Grade	40 mg (N=23) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypomagnesemia	Grade 0	12	6	0	0	0	1	19
	Grade 1	0	4	0	0	0	0	4
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	12	10	0	0	0	1	23
Hypermagnesemia	Grade 0	18	3	0	0	0	1	22
	Grade 1	0	1	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	18	4	0	0	0	1	23
Hypocalcemia	Grade 0	13	8	0	0	0	0	21
	Grade 1	0	1	1	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	13	9	1	0	0	0	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

Parameter	Baseline Grade	40 mg (N=23) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypercalcemia	Grade 0	14	5	0	0	0	0	19
	Grade 1	1	1	1	0	0	0	3
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	15	6	2	0	0	0	23
Hypoglycemia	Grade 0	21	1	0	0	0	1	23
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	21	1	0	0	0	1	23
Hyperglycemia	Grade 0	5	6	1	0	0	1	13
	Grade 1	0	3	3	1	0	0	7
	Grade 2	0	2	1	0	0	0	3
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	5	11	5	1	0	1	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

		40 mg (N=23)						
		Worst Post-Baseline Grade						
Parameter	Baseline Grade	Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
GGT increased	Grade 0	15	3	0	0	0	0	18
	Grade 1	0	3	0	1	0	0	4
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	15	6	1	1	0	0	23

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of treatment assessment visit.

表 2.7.4.7-62　血液生化学検査値異常のベースライン後の Grade の概要（201 試験）（安全性解析対象集団）

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Hypoalbuminemia	Any Grade	7 (100.0%)	7 (100.0%)	14 (100.0%)
	Grade 3, 4	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Alkaline phosphatase increased	Any Grade	3 (42.9%)	6 (85.7%)	9 (64.3%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
ALT increased	Any Grade	2 (28.6%)	4 (57.1%)	6 (42.9%)
	Grade 3, 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serum amylase increased	Any Grade	1 (14.3%)	1 (14.3%)	2 (14.3%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
AST increased	Any Grade	4 (57.1%)	6 (85.7%)	10 (71.4%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood bilirubin increased	Any Grade	3 (42.9%)	0 (0.0%)	3 (21.4%)
	Grade 3, 4	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol high	Any Grade	4 (57.1%)	4 (57.1%)	8 (57.1%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Creatinine increased	Any Grade	6 (85.7%)	6 (85.7%)	12 (85.7%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Hypokalemia	Any Grade	3 (42.9%)	2 (28.6%)	5 (35.7%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperkalemia	Any Grade	0 (0.0%)	3 (42.9%)	3 (21.4%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyponatremia	Any Grade	2 (28.6%)	3 (42.9%)	5 (35.7%)
	Grade 3, 4	1 (14.3%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypernatremia	Any Grade	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Hypomagnesemia	Any Grade	0 (0.0%)	3 (42.9%)	3 (21.4%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypermagnesemia	Any Grade	2 (28.6%)	3 (42.9%)	5 (35.7%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypocalcemia	Any Grade	5 (71.4%)	5 (71.4%)	10 (71.4%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypercalcemia	Any Grade	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Hypoglycemia	Any Grade	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperglycemia	Any Grade	5 (71.4%)	5 (71.4%)	10 (71.4%)
	Grade 3, 4	0 (0.0%)	2 (28.6%)	2 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
GGT increased	Any Grade	4 (57.1%)	3 (42.9%)	7 (50.0%)
	Grade 3, 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypophosphatemia	Any Grade	2 (28.6%)	4 (57.1%)	6 (42.9%)
	Grade 3, 4	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Worst Post-Baseline Grade	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Hypertriglyceridemia	Any Grade	4 (57.1%)	5 (71.4%)	9 (64.3%)
	Grade 3, 4	0 (0.0%)	1 (14.3%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

表 2.7.4.7-63　血液生化学検査値異常のベースラインの Grade と投与後の Grade のシフトテーブル（201 試験）（安全性解析対象集団）

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypoalbuminemia	Grade 0	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	2 (28.6%)
	Grade 1	0 (0.0%)	2 (28.6%)	2 (28.6%)	0 (0.0%)	-	0 (0.0%)	4 (57.1%)
	Grade 2	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	1 (14.3%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	4 (57.1%)	3 (42.9%)	0 (0.0%)	-	0 (0.0%)	7 (100.0%)
Alkaline phosphatase increased	Grade 0	4 (57.1%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	1 (14.3%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
ALT increased	Grade 0	5 (71.4%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (71.4%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Serum amylase increased	Grade 0	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
AST increased	Grade 0	3 (42.9%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Blood bilirubin increased	Grade 0	4 (57.1%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	0 (0.0%)	2 (28.6%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Cholesterol high	Grade 0	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (57.1%)
	Grade 1	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (42.9%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Creatinine increased	Grade 0	1 (14.3%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	1 (14.3%)	6 (85.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypokalemia	Grade 0	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hyperkalemia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hyponatremia	Grade 0	5 (71.4%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (71.4%)	1 (14.3%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypernatremia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypomagnesemia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypermagnesemia	Grade 0	5 (71.4%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (71.4%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypocalcemia	Grade 0	2 (28.6%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypercalcemia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypoglycemia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hyperglycemia	Grade 0	2 (28.6%)	2 (28.6%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	3 (42.9%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
GGT increased	Grade 0	3 (42.9%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypophosphatemia	Grade 0	5 (71.4%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (71.4%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	30 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypertriglyceridemia	Grade 0	3 (42.9%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypoalbuminemia	Grade 0	0 (0.0%)	5 (71.4%)	1 (14.3%)	0 (0.0%)	-	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	-	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	5 (71.4%)	1 (14.3%)	1 (14.3%)	-	0 (0.0%)	7 (100.0%)
Alkaline phosphatase increased	Grade 0	1 (14.3%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	1 (14.3%)	6 (85.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
ALT increased	Grade 0	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (57.1%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	3 (42.9%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	2 (28.6%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Serum amylase increased	Grade 0	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
AST increased	Grade 0	1 (14.3%)	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	1 (14.3%)	5 (71.4%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Blood bilirubin increased	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Cholesterol high	Grade 0	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (57.1%)
	Grade 1	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (42.9%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Creatinine increased	Grade 0	1 (14.3%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	1 (14.3%)	6 (85.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypokalemia	Grade 0	5 (71.4%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (71.4%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hyperkalemia	Grade 0	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hyponatremia	Grade 0	4 (57.1%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypernatremia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypomagnesemia	Grade 0	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypermagnesemia	Grade 0	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypocalcemia	Grade 0	2 (28.6%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypercalcemia	Grade 0	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypoglycemia	Grade 0	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hyperglycemia	Grade 0	2 (28.6%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	3 (42.9%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
GGT increased	Grade 0	4 (57.1%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (71.4%)
	Grade 1	0 (0.0%)	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (57.1%)	1 (14.3%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
Hypophosphatemia	Grade 0	3 (42.9%)	0 (0.0%)	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	3 (42.9%)	0 (0.0%)	3 (42.9%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	40 mg (N=7)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypertriglyceridemia	Grade 0	2 (28.6%)	3 (42.9%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	6 (85.7%)
	Grade 1	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (28.6%)	4 (57.1%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	7 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypoalbuminemia	Grade 0	0 (0.0%)	7 (50.0%)	1 (7.1%)	0 (0.0%)	-	0 (0.0%)	8 (57.1%)
	Grade 1	0 (0.0%)	2 (14.3%)	2 (14.3%)	1 (7.1%)	-	0 (0.0%)	5 (35.7%)
	Grade 2	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	-	0 (0.0%)	1 (7.1%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Grade 4	-	-	-	-	-	-	-
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)
	Overall	0 (0.0%)	9 (64.3%)	4 (28.6%)	1 (7.1%)	-	0 (0.0%)	14 (100.0%)
Alkaline phosphatase increased	Grade 0	5 (35.7%)	4 (28.6%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (71.4%)
	Grade 1	0 (0.0%)	3 (21.4%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (35.7%)	7 (50.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
ALT increased	Grade 0	8 (57.1%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (78.6%)
	Grade 1	0 (0.0%)	1 (7.1%)	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	3 (21.4%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	8 (57.1%)	4 (28.6%)	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Serum amylase increased	Grade 0	12 (85.7%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	12 (85.7%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
AST increased	Grade 0	4 (28.6%)	6 (42.9%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (78.6%)
	Grade 1	0 (0.0%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (21.4%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (28.6%)	9 (64.3%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Blood bilirubin increased	Grade 0	11 (78.6%)	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (92.9%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	11 (78.6%)	0 (0.0%)	2 (14.3%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Cholesterol high	Grade 0	6 (42.9%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (57.1%)
	Grade 1	0 (0.0%)	6 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (42.9%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	6 (42.9%)	8 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Creatinine increased	Grade 0	2 (14.3%)	10 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	12 (85.7%)
	Grade 1	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	2 (14.3%)	12 (85.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypokalemia	Grade 0	9 (64.3%)	5 (35.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	9 (64.3%)	5 (35.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Hyperkalemia	Grade 0	11 (78.6%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	11 (78.6%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hyponatremia	Grade 0	9 (64.3%)	2 (14.3%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	12 (85.7%)
	Grade 1	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	9 (64.3%)	4 (28.6%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Hypernatremia	Grade 0	14 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	14 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypomagnesemia	Grade 0	11 (78.6%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	11 (78.6%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Hypermagnesemia	Grade 0	9 (64.3%)	5 (35.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	9 (64.3%)	5 (35.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypocalcemia	Grade 0	4 (28.6%)	10 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (28.6%)	10 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Hypercalcemia	Grade 0	14 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	14 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypoglycemia	Grade 0	13 (92.9%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	13 (92.9%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Hyperglycemia	Grade 0	4 (28.6%)	5 (35.7%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (71.4%)
	Grade 1	0 (0.0%)	1 (7.1%)	1 (7.1%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	4 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	4 (28.6%)	6 (42.9%)	2 (14.3%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
GGT increased	Grade 0	7 (50.0%)	2 (14.3%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (71.4%)
	Grade 1	0 (0.0%)	2 (14.3%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (28.6%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	7 (50.0%)	4 (28.6%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
Hypophosphatemia	Grade 0	8 (57.1%)	0 (0.0%)	5 (35.7%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	Grade 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	8 (57.1%)	0 (0.0%)	5 (35.7%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

Category	Baseline Grade	Total (N=14)						
		Worst Post-Baseline Grade						
		Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Missing n (%)	Overall n (%)
Hypertriglyceridemia	Grade 0	5 (35.7%)	6 (42.9%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	12 (85.7%)
	Grade 1	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (14.3%)
	Grade 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Overall	5 (35.7%)	8 (57.1%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	14 (100.0%)

SOURCE: Listing 16.2.7.2
Abnormalities are graded using NCI-CTCAE Version 4.03.
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set.
Baseline is defined as pre-dose of Day 1 of Cycle 1.
Only on-treatment toxicity grades are presented.
On-treatment period is defined as date of first study drug administration and end date of study.
JCOG common reference range is used as reference range where normal range lower limit/ normal range upper limit are not available in the site.

表 2.7.4.7-64　血液生化学検査値異常のベースライン後の Grade の概要（203 試験）（安全性解析対象集団）

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Hypoalbuminemia	Any Grade	38 (97.4)	6 (37.5)	44 (80.0)
	Grade 3, 4	2 (5.1)	0 (0.0)	2 (3.6)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Alkaline Phosphatase increased	Any Grade	22 (56.4)	5 (31.3)	27 (49.1)
	Grade 3, 4	1 (2.6)	0 (0.0)	1 (1.8)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
ALT increased	Any Grade	12 (30.8)	4 (25.0)	16 (29.1)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Serum amylase increased	Any Grade	5 (12.8)	3 (18.8)	8 (14.5)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
AST increased	Any Grade	21 (53.8)	2 (12.5)	23 (41.8)
	Grade 3, 4	1 (2.6)	0 (0.0)	1 (1.8)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Blood bilirubin increased	Any Grade	6 (15.4)	1 (6.3)	7 (12.7)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Lipase increased	Any Grade	8 (20.5)	5 (31.3)	13 (23.6)
	Grade 3, 4	2 (5.1)	2 (12.5)	4 (7.3)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Creatinine increased	Any Grade	34 (87.2)	12 (75.0)	46 (83.6)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Hypokalemia	Any Grade	14 (35.9)	4 (25.0)	18 (32.7)
	Grade 3, 4	1 (2.6)	1 (6.3)	2 (3.6)
	Grade 4	1 (2.6)	1 (6.3)	2 (3.6)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkalemia	Any Grade	8 (20.5)	1 (6.3)	9 (16.4)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hyponatremia	Any Grade	15 (38.5)	6 (37.5)	21 (38.2)
	Grade 3, 4	4 (10.3)	1 (6.3)	5 (9.1)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hypernatremia	Any Grade	6 (15.4)	1 (6.3)	7 (12.7)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Hypomagnesemia	Any Grade	4 (10.3)	6 (37.5)	10 (18.2)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hypermagnesemia	Any Grade	6 (15.4)	2 (12.5)	8 (14.5)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hypocalcemia	Any Grade	34 (87.2)	13 (81.3)	47 (85.5)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hypercalcemia	Any Grade	2 (5.1)	0 (0.0)	2 (3.6)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

Parameter	Worst Post-Baseline Grade	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Hypoglycemia	Any Grade	4 (10.3)	0 (0.0)	4 (7.3)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
Hyperglycemia	Any Grade	34 (87.2)	16 (100.0)	50 (90.9)
	Grade 3, 4	0 (0.0)	0 (0.0)	0 (0.0)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)
GGT increased	Any Grade	18 (46.2)	6 (37.5)	24 (43.6)
	Grade 3, 4	4 (10.3)	0 (0.0)	4 (7.3)
	Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set;
Only on-treatment abnormalities (toxicity grade >= 1) are presented.
On-treatment period is defined as date of first study drug up till the end of treatment assessment visit.

表 2.7.4.7-65　血液生化学検査値異常のベースラインの Grade と投与後の Grade のシフトテーブル（203 試験）（安全性解析対象集団）

Country: Japan

		40 mg (N=39)						
		Worst Post-Baseline Grade						
Parameter	Baseline Grade	Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoalbuminemia	Grade 0	1	12	0	0	0	0	13
	Grade 1	0	10	11	1	0	0	22
	Grade 2	0	0	3	1	0	0	4
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	1	22	14	2	0	0	39
Alkaline Phosphatase increased	Grade 0	17	14	2	0	0	0	33
	Grade 1	0	3	2	1	0	0	6
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	17	17	4	1	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.

N = number of subjects in the Safety Analysis Set by country.

n = number of subjects.

Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.

Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
ALT increased	Grade 0	27	8	2	0	0	0	37
	Grade 1	0	2	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	27	10	2	0	0	0	39
Serum amylase increased	Grade 0	34	2	0	0	0	0	36
	Grade 1	0	2	0	0	0	0	2
	Grade 2	0	1	0	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	34	5	0	0	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
AST increased	Grade 0	18	12	2	1	0	0	33
	Grade 1	0	5	1	0	0	0	6
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	18	17	3	1	0	0	39
Blood bilirubin increased	Grade 0	33	5	1	0	0	0	39
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	33	5	1	0	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lipase increased	Grade 0	31	3	1	1	0	0	36
	Grade 1	0	0	1	1	0	0	2
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	31	3	3	2	0	0	39
Creatinine increased	Grade 0	5	22	4	0	0	0	31
	Grade 1	0	6	1	0	0	0	7
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	5	28	6	0	0	0	39

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypokalemia	Grade 0	25	12	0	0	0	0	37
	Grade 1	0	1	0	0	1	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	25	13	0	0	1	0	39
Hyperkalemia	Grade 0	29	7	1	0	0	0	37
	Grade 1	2	0	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	31	7	1	0	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for 'hypomagnesemia' and the local upper reference ranges are set as the lower limits of Grade 0 for 'hypermagnesemia'. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in 'hypomagnesemia' or 'hypermagnesemia', respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hyponatremia	Grade 0	23	10	0	2	0	0	35
	Grade 1	1	1	0	1	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	24	11	0	4	0	0	39
Hypernatremia	Grade 0	33	4	0	0	0	0	37
	Grade 1	0	2	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	33	6	0	0	0	0	39

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypomagnesemia	Grade 0	35	3	0	0	0	0	38
	Grade 1	0	1	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	35	4	0	0	0	0	39
Hypermagnesemia	Grade 0	33	5	0	0	0	0	38
	Grade 1	0	1	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	33	6	0	0	0	0	39

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypocalcemia	Grade 0	5	29	2	0	0	0	36
	Grade 1	0	3	0	0	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	5	32	2	0	0	0	39
Hypercalcemia	Grade 0	36	2	0	0	0	0	38
	Grade 1	1	0	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	37	2	0	0	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoglycemia	Grade 0	34	3	1	0	0	0	38
	Grade 1	1	0	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	35	3	1	0	0	0	39
Hyperglycemia	Grade 0	4	14	6	0	0	0	24
	Grade 1	1	8	4	0	0	0	13
	Grade 2	0	1	0	0	0	0	1
	Grade 3	0	1	0	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	5	24	10	0	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Japan

Parameter	Baseline Grade	40 mg (N=39) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
GGT increased	Grade 0	21	6	5	1	0	0	33
	Grade 1	0	1	1	3	0	0	5
	Grade 2	0	1	0	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	21	8	6	4	0	0	39

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoalbuminemia	Grade 0	10	1	1	0	0	0	12
	Grade 1	0	1	1	0	0	0	2
	Grade 2	0	0	2	0	0	0	2
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	10	2	4	0	0	0	16
Alkaline Phosphatase increased	Grade 0	11	2	0	0	0	0	13
	Grade 1	0	3	0	0	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	11	5	0	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
ALT increased	Grade 0	10	2	1	0	0	0	13
	Grade 1	2	1	0	0	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	12	3	1	0	0	0	16
Serum amylase increased	Grade 0	13	1	0	0	0	0	14
	Grade 1	0	1	1	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	13	2	1	0	0	0	16

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
AST increased	Grade 0	12	2	0	0	0	0	14
	Grade 1	2	0	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	14	2	0	0	0	0	16
Blood bilirubin increased	Grade 0	15	1	0	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	15	1	0	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lipase increased	Grade 0	10	2	1	1	0	0	14
	Grade 1	1	0	0	0	0	0	1
	Grade 2	0	0	0	1	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	11	2	1	2	0	0	16
Creatinine increased	Grade 0	4	12	0	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	4	12	0	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypokalemia	Grade 0	12	3	0	0	1	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	12	3	0	0	1	0	16
Hyperkalemia	Grade 0	15	0	1	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	15	0	1	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hyponatremia	Grade 0	10	4	0	0	0	0	14
	Grade 1	0	1	0	1	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	10	5	0	1	0	0	16
Hypernatremia	Grade 0	14	0	0	0	0	0	14
	Grade 1	1	1	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	15	1	0	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypomagnesemia	Grade 0	10	4	0	0	0	0	14
	Grade 1	0	1	0	0	0	0	1
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	10	5	1	0	0	0	16
Hypermagnesemia	Grade 0	14	2	0	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	14	2	0	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypocalcemia	Grade 0	3	10	0	0	0	0	13
	Grade 1	0	2	1	0	0	0	3
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	3	12	1	0	0	0	16
Hypercalcemia	Grade 0	16	0	0	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	16	0	0	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoglycemia	Grade 0	16	0	0	0	0	0	16
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	16	0	0	0	0	0	16
Hyperglycemia	Grade 0	0	7	1	0	0	0	8
	Grade 1	0	4	1	0	0	0	5
	Grade 2	0	0	2	0	0	0	2
	Grade 3	0	1	0	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	0	12	4	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Korea

Parameter	Baseline Grade	40 mg (N=16) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
GGT increased	Grade 0	10	2	0	0	0	0	12
	Grade 1	0	1	1	0	0	0	2
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	1	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	10	3	3	0	0	0	16

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoalbuminemia	Grade 0	11	13	1	0	0	0	25
	Grade 1	0	11	12	1	0	0	24
	Grade 2	0	0	5	1	0	0	6
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	11	24	18	2	0	0	55
Alkaline Phosphatase increased	Grade 0	28	16	2	0	0	0	46
	Grade 1	0	6	2	1	0	0	9
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	28	22	4	1	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
ALT increased	Grade 0	37	10	3	0	0	0	50
	Grade 1	2	3	0	0	0	0	5
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	39	13	3	0	0	0	55
Serum amylase increased	Grade 0	47	3	0	0	0	0	50
	Grade 1	0	3	1	0	0	0	4
	Grade 2	0	1	0	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	47	7	1	0	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
AST increased	Grade 0	30	14	2	1	0	0	47
	Grade 1	2	5	1	0	0	0	8
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	32	19	3	1	0	0	55
Blood bilirubin increased	Grade 0	48	6	1	0	0	0	55
	Grade 1	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	48	6	1	0	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Lipase increased	Grade 0	41	5	2	2	0	0	50
	Grade 1	1	0	1	1	0	0	3
	Grade 2	0	0	1	1	0	0	2
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	42	5	4	4	0	0	55
Creatinine increased	Grade 0	9	34	4	0	0	0	47
	Grade 1	0	6	1	0	0	0	7
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	9	40	6	0	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypokalemia	Grade 0	37	15	0	0	1	0	53
	Grade 1	0	1	0	0	1	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	37	16	0	0	2	0	55
Hyperkalemia	Grade 0	44	7	2	0	0	0	53
	Grade 1	2	0	0	0	0	0	2
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	46	7	2	0	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hyponatremia	Grade 0	33	14	0	2	0	0	49
	Grade 1	1	2	0	2	0	0	5
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	1	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	34	16	0	5	0	0	55
Hypernatremia	Grade 0	47	4	0	0	0	0	51
	Grade 1	1	3	0	0	0	0	4
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	48	7	0	0	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypomagnesemia	Grade 0	45	7	0	0	0	0	52
	Grade 1	0	2	0	0	0	0	2
	Grade 2	0	0	1	0	0	0	1
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	45	9	1	0	0	0	55
Hypermagnesemia	Grade 0	47	7	0	0	0	0	54
	Grade 1	0	1	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	47	8	0	0	0	0	55

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypocalcemia	Grade 0	8	39	2	0	0	0	49
	Grade 1	0	5	1	0	0	0	6
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	8	44	3	0	0	0	55
Hypercalcemia	Grade 0	52	2	0	0	0	0	54
	Grade 1	1	0	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	53	2	0	0	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
Hypoglycemia	Grade 0	50	3	1	0	0	0	54
	Grade 1	1	0	0	0	0	0	1
	Grade 2	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	51	3	1	0	0	0	55
Hyperglycemia	Grade 0	4	21	7	0	0	0	32
	Grade 1	1	12	5	0	0	0	18
	Grade 2	0	1	2	0	0	0	3
	Grade 3	0	2	0	0	0	0	2
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	5	36	14	0	0	0	55

Source: Listing 16 2.7.2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

Country: Overall

Parameter	Baseline Grade	40 mg (N=55) Worst Post-Baseline Grade Grade 0 n	Grade 1 n	Grade 2 n	Grade 3 n	Grade 4 n	Missing n	Overall n
GGT increased	Grade 0	31	8	5	1	0	0	45
	Grade 1	0	2	2	3	0	0	7
	Grade 2	0	1	1	0	0	0	2
	Grade 3	0	0	1	0	0	0	1
	Grade 4	0	0	0	0	0	0	0
	Missing	0	0	0	0	0	0	0
	Overall	31	11	9	4	0	0	55

Source: Listing 16.2.7 2

Abnormalities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by country.
n = number of subjects.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
On-treatment period is defined as date of first study drug up till the End of Treatment assessment visit.
Local reference ranges are used to set the margin for limits defined in CTCAE grading. For magnesium, the local lower reference ranges are set as the higher limits of Grade 0 for ‘hypomagnesemia’ and the local upper reference ranges are set as the lower limits of Grade 0 for ‘hypermagnesemia’. However, at some investigational sites, the local reference ranges are either lower or higher than the limit defined for CTCAE Grade 1. In such cases, these are graded as 0 in ‘hypomagnesemia’ or ‘hypermagnesemia’, respectively.

表 2.7.4.7-66　臨床的に重大なバイタルサインの異常（210 試験）（安全性解析対象集団）

Parameter	Criteria	40 mg N	40 mg n (%)
SBP	<= 90 mmHg AND change from baseline <= -20 mmHg	22	3 (13.6%)
	>= 180 mmHg AND change from baseline >= 20 mmHg	22	0 (0.0%)
DBP	<= 50 mmHg AND change from baseline <= -15 mmHg	22	5 (22.7%)
	>= 105 mmHg AND change from baseline >= 15 mmHg	22	0 (0.0%)
Pulse Rate	<= 50 bpm AND change from baseline <= -15 bpm	22	0 (0.0%)
	>= 120 bpm AND change from baseline >= 15 bpm	22	3 (13.6%)
Weight	>= 7% weight loss from baseline	22	8 (36.4%)
	>= 7% weight gained from baseline	22	1 (4.5%)

Source: Listing 16 2.9

N = number of subjects who have at least one post-baseline assessment with baseline;
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
DBP = diastolic blood pressure; SBP = systolic blood pressure; bpm = beats per minute.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

表 2.7.4.7-67　臨床的に重大なバイタルサインの異常（201 試験）（安全性解析対象集団）

Parameter	Criteria	30 mg	40 mg	Total
		N n (%)	N n (%)	N n (%)
SBP	<= 90 mmHg AND change from baseline <= -20 mmHg	7 3 (42.9%)	7 1 (14.3%)	14 4 (28.6%)
	>= 180 mmHg AND change from baseline >= 20 mmHg	7 0 (0.0%)	7 0 (0.0%)	14 0 (0.0%)
DBP	<= 50 mmHg AND change from baseline <= -15 mmHg	7 2 (28.6%)	7 1 (14.3%)	14 3 (21.4%)
	>= 105 mmHg AND change from baseline >= 15 mmHg	7 0 (0.0%)	7 0 (0.0%)	14 0 (0.0%)
Pulse Rate	<= 50 bpm AND change from baseline <= -15 bpm	7 0 (0.0%)	7 0 (0.0%)	14 0 (0.0%)
	>= 120 bpm AND change from baseline >= 15 bpm	7 0 (0.0%)	7 0 (0.0%)	14 0 (0.0%)
Temperature	>= 38.3 °C AND change from baseline >= 1.1 °C	7 0 (0.0%)	7 1 (14.3%)	14 1 (7.1%)
Weight	percentage change from baseline <= -7.0 %	6 1 (16.7%)	7 1 (14.3%)	13 2 (15.4%)
	percentage change from baseline >= 7.0 %	6 1 (16.7%)	7 0 (0.0%)	13 1 (7.7%)

SOURCE: Listing 16.2.9.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort with data.
DBP = diastolic blood pressure; SBP = systolic blood pressure; bpm = beats per minute.
Baseline is defined as pre-dose of Day 1 of Cycle 1.

表 2.7.4.7-68　臨床的に重大なバイタルサインの異常（203 試験）（安全性解析対象集団）

		Japan		Korea		Total	
Parameter	Criteria	N	n (%)	N	n (%)	N	n (%)
SBP	<= 90 mmHg AND change from baseline <= -20 mmHg	39	3 (7.7)	16	1 (6.3)	55	4 (7.3)
	>= 180 mmHg AND change from baseline >= 20 mmHg	39	0 (0.0)	16	0 (0.0)	55	0 (0.0)
DBP	<= 50 mmHg AND change from baseline <= -15 mmHg	39	4 (10.3)	16	0 (0.0)	55	4 (7.3)
	>= 105 mmHg AND change from baseline >= 15 mmHg	39	0 (0.0)	16	0 (0.0)	55	0 (0.0)
Pulse Rate	<= 50 bpm AND change from baseline <= -15 bpm	39	0 (0.0)	16	0 (0.0)	55	0 (0.0)
	>= 120 bpm AND change from baseline >= 15 bpm	39	2 (5.1)	16	2 (12.5)	55	4 (7.3)
Weight	>= 7% weight loss from baseline	39	11 (28.2)	16	2 (12.5)	55	13 (23.6)
	>= 7% weight gained from baseline	39	4 (10.3)	16	1 (6.3)	55	5 (9.1)

Source: Listing 16.2.9

N = number of subjects in a country who have at least one post-baseline assessment with baseline;
n = number of subjects who meet the category; % = percentages of subjects are calculated relative to the total number of subjects in a country with data;
DBP = diastolic blood pressure; SBP = systolic blood pressure; bpm = beats per minute.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

表 2.7.4.7-69　心電図パラメータの要約（210 試験）（安全性解析対象集団）

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Baseline	n	23
		Mean	170.36
		SD	27.53
		Median	167.33
		Minimum	110.7
		Maximum	223.7
	Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	175.81
		SD	24.61
		Median	178.33
		Minimum	124.7
		Maximum	226.0
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	5.45
		SD	12.14
		Median	5.67
		Minimum	-21.0
		Maximum	38.0
	Cycle2 Day1, Pre-dose	n	14
		Mean	177.17
		SD	24.87
		Median	177.33
		Minimum	137.3
		Maximum	236.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle2 Day1, Pre-dose	n	14
		Mean	-6.45
		SD	9.04
		Median	-8.00
		Minimum	-19.3
		Maximum	12.7
	Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	182.33
		SD	26.84
		Median	178.17
		Minimum	143.3
		Maximum	252.3
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	-3.61
		SD	12.38
		Median	-7.00
		Minimum	-16.7
		Maximum	28.7
	Cycle3 Day1	n	7
		Mean	175.57
		SD	35.92
		Median	175.00
		Minimum	132.0
		Maximum	244.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle3 Day1	n	7
		Mean	-8.10
		SD	15.13
		Median	-14.00
		Minimum	-20.7
		Maximum	20.3
	Cycle4 Day1	n	5
		Mean	167.00
		SD	35.65
		Median	164.00
		Minimum	131.0
		Maximum	210.0
	Change from Baseline at Cycle4 Day1	n	5
		Mean	-15.13
		SD	14.07
		Median	-17.67
		Minimum	-31.7
		Maximum	7.0
	Cycle5 Day1	n	3
		Mean	187.33
		SD	15.04
		Median	186.00
		Minimum	173.0
		Maximum	203.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle5 Day1	n	3
		Mean	-10.78
		SD	9.02
		Median	-8.67
		Minimum	-20.7
		Maximum	-3.0
	Cycle6 Day1	n	3
		Mean	185.00
		SD	16.52
		Median	177.00
		Minimum	174.0
		Maximum	204.0
	Change from Baseline at Cycle6 Day1	n	3
		Mean	-13.11
		SD	6.08
		Median	-12.00
		Minimum	-19.7
		Maximum	-7.7
	Cycle7 Day1	n	3
		Mean	193.67
		SD	16.74
		Median	184.00
		Minimum	184.0
		Maximum	213.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle7 Day1	n	3
		Mean	-4.44
		SD	6.52
		Median	-5.00
		Minimum	-10.7
		Maximum	2.3
	Cycle8 Day1	n	3
		Mean	179.33
		SD	15.82
		Median	183.00
		Minimum	162.0
		Maximum	193.0
	Change from Baseline at Cycle8 Day1	n	3
		Mean	-18.78
		SD	12.36
		Median	-19.67
		Minimum	-30.7
		Maximum	-6.0
	Cycle9 Day1	n	3
		Mean	177.00
		SD	15.39
		Median	173.00
		Minimum	164.0
		Maximum	194.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle9 Day1	n	3
		Mean	-21.11
		SD	7.46
		Median	-17.67
		Minimum	-29.7
		Maximum	-16.0
	Cycle10 Day1	n	2
		Mean	180.00
		SD	21.21
		Median	180.00
		Minimum	165.0
		Maximum	195.0
	Change from Baseline at Cycle10 Day1	n	2
		Mean	-22.67
		SD	8.49
		Median	-22.67
		Minimum	-28.7
		Maximum	-16.7
	Cycle11 Day1	n	1
		Mean	163.00
		SD	-
		Median	163.00
		Minimum	163.0
		Maximum	163.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle11 Day1	n	1
		Mean	-18.67
		SD	-
		Median	-18.67
		Minimum	-18.7
		Maximum	-18.7
	Cycle12 Day1	n	1
		Mean	155.00
		SD	-
		Median	155.00
		Minimum	155.0
		Maximum	155.0
	Change from Baseline at Cycle12 Day1	n	1
		Mean	-26.67
		SD	-
		Median	-26.67
		Minimum	-26.7
		Maximum	-26.7
	Cycle13 Day1	n	1
		Mean	167.00
		SD	-
		Median	167.00
		Minimum	167.0
		Maximum	167.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at Cycle13 Day1	n	1
		Mean	-14.67
		SD	-
		Median	-14.67
		Minimum	-14.7
		Maximum	-14.7
	Cycle14 Day1	n	1
		Mean	152.00
		SD	-
		Median	152.00
		Minimum	152.0
		Maximum	152.0
	Change from Baseline at Cycle14 Day1	n	1
		Mean	-29.67
		SD	-
		Median	-29.67
		Minimum	-29.7
		Maximum	-29.7
	End of Treatment	n	18
		Mean	168.50
		SD	23.56
		Median	169.50
		Minimum	122.0
		Maximum	213.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
PR Interval (msec)	Change from Baseline at End of Treatment	n	18
		Mean	-8.57
		SD	13.58
		Median	-9.33
		Minimum	-43.0
		Maximum	14.0
QRS Duration (msec)	Baseline	n	23
		Mean	87.39
		SD	6.97
		Median	87.33
		Minimum	78.7
		Maximum	105.3
	Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	88.74
		SD	6.79
		Median	91.33
		Minimum	73.7
		Maximum	100.7
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	1.35
		SD	4.31
		Median	0.67
		Minimum	-5.0
		Maximum	9.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle2 Day1, Pre-dose	n	14
		Mean	87.10
		SD	5.30
		Median	87.00
		Minimum	79.3
		Maximum	96.3
	Change from Baseline at Cycle2 Day1, Pre-dose	n	14
		Mean	-1.33
		SD	6.26
		Median	-1.67
		Minimum	-10.3
		Maximum	10.3
	Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	88.08
		SD	6.23
		Median	88.83
		Minimum	79.7
		Maximum	98.7
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	-0.50
		SD	6.99
		Median	-3.00
		Minimum	-13.0
		Maximum	12.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle3 Day1	n	7
		Mean	87.71
		SD	6.63
		Median	89.00
		Minimum	78.0
		Maximum	98.0
	Change from Baseline at Cycle3 Day1	n	7
		Mean	-0.38
		SD	6.46
		Median	-4.00
		Minimum	-7.7
		Maximum	7.7
	Cycle4 Day1	n	5
		Mean	89.20
		SD	6.02
		Median	89.00
		Minimum	82.0
		Maximum	97.0
	Change from Baseline at Cycle4 Day1	n	5
		Mean	-1.20
		SD	6.17
		Median	-1.67
		Minimum	-10.0
		Maximum	7.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle5 Day1	n	3
		Mean	94.00
		SD	5.29
		Median	92.00
		Minimum	90.0
		Maximum	100.0
	Change from Baseline at Cycle5 Day1	n	3
		Mean	4.67
		SD	6.66
		Median	6.33
		Minimum	-2.7
		Maximum	10.3
	Cycle6 Day1	n	3
		Mean	90.67
		SD	1.15
		Median	90.00
		Minimum	90.0
		Maximum	92.0
	Change from Baseline at Cycle6 Day1	n	3
		Mean	1.33
		SD	4.58
		Median	0.33
		Minimum	-2.7
		Maximum	6.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle7 Day1	n	3
		Mean	86.33
		SD	3.51
		Median	86.00
		Minimum	83.0
		Maximum	90.0
	Change from Baseline at Cycle7 Day1	n	3
		Mean	-3.00
		SD	4.73
		Median	-4.67
		Minimum	-6.7
		Maximum	2.3
	Cycle8 Day1	n	3
		Mean	89.00
		SD	6.24
		Median	87.00
		Minimum	84.0
		Maximum	96.0
	Change from Baseline at Cycle8 Day1	n	3
		Mean	-0.33
		SD	4.73
		Median	1.33
		Minimum	-5.7
		Maximum	3.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle9 Day1	n	3
		Mean	89.00
		SD	3.00
		Median	89.00
		Minimum	86.0
		Maximum	92.0
	Change from Baseline at Cycle9 Day1	n	3
		Mean	-0.33
		SD	2.52
		Median	-0.67
		Minimum	-2.7
		Maximum	2.3
	Cycle10 Day1	n	2
		Mean	86.50
		SD	9.19
		Median	86.50
		Minimum	80.0
		Maximum	93.0
	Change from Baseline at Cycle10 Day1	n	2
		Mean	-2.67
		SD	1.41
		Median	-2.67
		Minimum	-3.7
		Maximum	-1.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle11 Day1	n	1
		Mean	85.00
		SD	-
		Median	85.00
		Minimum	85.0
		Maximum	85.0
	Change from Baseline at Cycle11 Day1	n	1
		Mean	1.33
		SD	-
		Median	1.33
		Minimum	1.3
		Maximum	1.3
	Cycle12 Day1	n	1
		Mean	94.00
		SD	-
		Median	94.00
		Minimum	94.0
		Maximum	94.0
	Change from Baseline at Cycle12 Day1	n	1
		Mean	10.33
		SD	-
		Median	10.33
		Minimum	10.3
		Maximum	10.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	Cycle13 Day1	n	1
		Mean	87.00
		SD	-
		Median	87.00
		Minimum	87.0
		Maximum	87.0
	Change from Baseline at Cycle13 Day1	n	1
		Mean	3.33
		SD	-
		Median	3.33
		Minimum	3.3
		Maximum	3.3
	Cycle14 Day1	n	1
		Mean	88.00
		SD	-
		Median	88.00
		Minimum	88.0
		Maximum	88.0
	Change from Baseline at Cycle14 Day1	n	1
		Mean	4.33
		SD	-
		Median	4.33
		Minimum	4.3
		Maximum	4.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QRS Duration (msec)	End of Treatment	n	18
		Mean	86.00
		SD	6.96
		Median	87.00
		Minimum	74.0
		Maximum	102.0
	Change from Baseline at End of Treatment	n	18
		Mean	-1.20
		SD	6.14
		Median	-3.00
		Minimum	-8.7
		Maximum	12.3
QT Interval (msec)	Baseline	n	23
		Mean	381.54
		SD	44.65
		Median	382.67
		Minimum	312.3
		Maximum	484.7
	Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	380.87
		SD	42.75
		Median	392.67
		Minimum	317.0
		Maximum	487.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	-0.67
		SD	13.67
		Median	3.00
		Minimum	-31.3
		Maximum	16.0
	Cycle2 Day1, Pre-dose	n	14
		Mean	392.81
		SD	49.42
		Median	384.00
		Minimum	290.0
		Maximum	471.3
	Change from Baseline at Cycle2 Day1, Pre-dose	n	14
		Mean	-5.52
		SD	28.21
		Median	-2.00
		Minimum	-58.0
		Maximum	42.3
	Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	386.78
		SD	53.21
		Median	382.67
		Minimum	289.0
		Maximum	473.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	-17.75
		SD	30.23
		Median	-14.00
		Minimum	-64.7
		Maximum	27.0
	Cycle3 Day1	n	7
		Mean	399.29
		SD	54.02
		Median	384.00
		Minimum	335.0
		Maximum	484.0
	Change from Baseline at Cycle3 Day1	n	7
		Mean	-6.00
		SD	30.87
		Median	1.33
		Minimum	-53.0
		Maximum	39.3
	Cycle4 Day1	n	5
		Mean	407.60
		SD	63.86
		Median	375.00
		Minimum	342.0
		Maximum	488.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle4 Day1	n	5
		Mean	0.53
		SD	32.87
		Median	7.00
		Minimum	-46.0
		Maximum	43.3
	Cycle5 Day1	n	3
		Mean	431.33
		SD	46.20
		Median	457.00
		Minimum	378.0
		Maximum	459.0
	Change from Baseline at Cycle5 Day1	n	3
		Mean	9.78
		SD	5.93
		Median	12.33
		Minimum	3.0
		Maximum	14.0
	Cycle6 Day1	n	3
		Mean	421.67
		SD	54.60
		Median	431.00
		Minimum	363.0
		Maximum	471.0

Source: Listing 16 2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle6 Day1	n	3
		Mean	0.11
		SD	14.37
		Median	-1.00
		Minimum	-13.7
		Maximum	15.0
	Cycle7 Day1	n	3
		Mean	443.33
		SD	30.55
		Median	450.00
		Minimum	410.0
		Maximum	470.0
	Change from Baseline at Cycle7 Day1	n	3
		Mean	21.78
		SD	21.42
		Median	14.00
		Minimum	5.3
		Maximum	46.0
	Cycle8 Day1	n	3
		Mean	420.67
		SD	41.88
		Median	433.00
		Minimum	374.0
		Maximum	455.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle8 Day1	n	3
		Mean	-0.89
		SD	10.83
		Median	-1.00
		Minimum	-11.7
		Maximum	10.0
	Cycle9 Day1	n	3
		Mean	427.67
		SD	46.49
		Median	445.00
		Minimum	375.0
		Maximum	463.0
	Change from Baseline at Cycle9 Day1	n	3
		Mean	6.11
		SD	5.39
		Median	7.00
		Minimum	0.3
		Maximum	11.0
	Cycle10 Day1	n	2
		Mean	405.50
		SD	67.18
		Median	405.50
		Minimum	358.0
		Maximum	453.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle10 Day1	n	2
		Mean	-4.50
		SD	2.12
		Median	-4.50
		Minimum	-6.0
		Maximum	-3.0
	Cycle11 Day1	n	1
		Mean	368.00
		SD	-
		Median	368.00
		Minimum	368.0
		Maximum	368.0
	Change from Baseline at Cycle11 Day1	n	1
		Mean	4.00
		SD	-
		Median	4.00
		Minimum	4.0
		Maximum	4.0
	Cycle12 Day1	n	1
		Mean	382.00
		SD	-
		Median	382.00
		Minimum	382.0
		Maximum	382.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle12 Day1	n	1
		Mean	18.00
		SD	-
		Median	18.00
		Minimum	18.0
		Maximum	18.0
	Cycle13 Day1	n	1
		Mean	405.00
		SD	-
		Median	405.00
		Minimum	405.0
		Maximum	405.0
	Change from Baseline at Cycle13 Day1	n	1
		Mean	41.00
		SD	-
		Median	41.00
		Minimum	41.0
		Maximum	41.0
	Cycle14 Day1	n	1
		Mean	391.00
		SD	-
		Median	391.00
		Minimum	391.0
		Maximum	391.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QT Interval (msec)	Change from Baseline at Cycle14 Day1	n	1
		Mean	27.00
		SD	-
		Median	27.00
		Minimum	27.0
		Maximum	27.0
	End of Treatment	n	18
		Mean	369.89
		SD	46.54
		Median	362.50
		Minimum	294.0
		Maximum	453.0
	Change from Baseline at End of Treatment	n	18
		Mean	-18.48
		SD	25.32
		Median	-16.83
		Minimum	-71.0
		Maximum	36.3
QTcB Interval (msec)	Baseline	n	23
		Mean	424.74
		SD	22.12
		Median	425.33
		Minimum	384.3
		Maximum	464.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	423.36
		SD	23.48
		Median	427.00
		Minimum	378.3
		Maximum	481.0
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	-1.38
		SD	16.14
		Median	-4.67
		Minimum	-34.7
		Maximum	35.7
	Cycle2 Day1, Pre-dose	n	14
		Mean	416.95
		SD	23.07
		Median	418.83
		Minimum	365.0
		Maximum	452.0
	Change from Baseline at Cycle2 Day1, Pre-dose	n	14
		Mean	-5.43
		SD	16.44
		Median	-7.33
		Minimum	-27.7
		Maximum	29.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	413.42
		SD	25.89
		Median	410.17
		Minimum	362.3
		Maximum	456.3
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	-5.56
		SD	20.05
		Median	-14.17
		Minimum	-26.0
		Maximum	34.7
	Cycle3 Day1	n	7
		Mean	420.86
		SD	16.46
		Median	426.00
		Minimum	397.0
		Maximum	446.0
	Change from Baseline at Cycle3 Day1	n	7
		Mean	4.24
		SD	21.13
		Median	9.00
		Minimum	-20.7
		Maximum	26.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle4 Day1	n	5
		Mean	416.40
		SD	19.62
		Median	411.00
		Minimum	393.0
		Maximum	445.0
	Change from Baseline at Cycle4 Day1	n	5
		Mean	0.80
		SD	16.33
		Median	-1.67
		Minimum	-14.7
		Maximum	24.7
	Cycle5 Day1	n	3
		Mean	410.00
		SD	24.88
		Median	415.00
		Minimum	383.0
		Maximum	432.0
	Change from Baseline at Cycle5 Day1	n	3
		Mean	6.56
		SD	19.41
		Median	-1.33
		Minimum	-7.7
		Maximum	28.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle6 Day1	n	3
		Mean	392.33
		SD	37.21
		Median	384.00
		Minimum	360.0
		Maximum	433.0
	Change from Baseline at Cycle6 Day1	n	3
		Mean	-11.11
		SD	11.65
		Median	-6.67
		Minimum	-24.3
		Maximum	-2.3
	Cycle7 Day1	n	3
		Mean	428.67
		SD	43.09
		Median	451.00
		Minimum	379.0
		Maximum	456.0
	Change from Baseline at Cycle7 Day1	n	3
		Mean	25.22
		SD	35.84
		Median	16.33
		Minimum	-5.3
		Maximum	64.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle8 Day1	n	3
		Mean	416.67
		SD	10.02
		Median	416.00
		Minimum	407.0
		Maximum	427.0
	Change from Baseline at Cycle8 Day1	n	3
		Mean	13.22
		SD	22.69
		Median	22.67
		Minimum	-12.7
		Maximum	29.7
	Cycle9 Day1	n	3
		Mean	418.33
		SD	17.04
		Median	417.00
		Minimum	402.0
		Maximum	436.0
	Change from Baseline at Cycle9 Day1	n	3
		Mean	14.89
		SD	18.18
		Median	15.67
		Minimum	-3.7
		Maximum	32.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle10 Day1	n	2
		Mean	419.50
		SD	26.16
		Median	419.50
		Minimum	401.0
		Maximum	438.0
	Change from Baseline at Cycle10 Day1	n	2
		Mean	6.50
		SD	11.55
		Median	6.50
		Minimum	-1.7
		Maximum	14.7
	Cycle11 Day1	n	1
		Mean	399.00
		SD	-
		Median	399.00
		Minimum	399.0
		Maximum	399.0
	Change from Baseline at Cycle11 Day1	n	1
		Mean	12.67
		SD	-
		Median	12.67
		Minimum	12.7
		Maximum	12.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle12 Day1	n	1
		Mean	420.00
		SD	-
		Median	420.00
		Minimum	420.0
		Maximum	420.0
	Change from Baseline at Cycle12 Day1	n	1
		Mean	33.67
		SD	-
		Median	33.67
		Minimum	33.7
		Maximum	33.7
	Cycle13 Day1	n	1
		Mean	434.00
		SD	-
		Median	434.00
		Minimum	434.0
		Maximum	434.0
	Change from Baseline at Cycle13 Day1	n	1
		Mean	47.67
		SD	-
		Median	47.67
		Minimum	47.7
		Maximum	47.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcB Interval (msec)	Cycle14 Day1	n	1
		Mean	459.00
		SD	-
		Median	459.00
		Minimum	459.0
		Maximum	459.0
	Change from Baseline at Cycle14 Day1	n	1
		Mean	72.67
		SD	-
		Median	72.67
		Minimum	72.7
		Maximum	72.7
	End of Treatment	n	18
		Mean	422.22
		SD	20.10
		Median	421.50
		Minimum	383.0
		Maximum	454.0
	Change from Baseline at End of Treatment	n	18
		Mean	-3.91
		SD	27.23
		Median	-11.83
		Minimum	-35.3
		Maximum	67.7

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Baseline	n	23
		Mean	409.09
		SD	21.69
		Median	409.67
		Minimum	366.0
		Maximum	458.0
	Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	408.03
		SD	23.70
		Median	410.00
		Minimum	359.0
		Maximum	483.0
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	23
		Mean	-1.06
		SD	12.21
		Median	-2.00
		Minimum	-31.0
		Maximum	25.0
	Cycle2 Day1, Pre-dose	n	14
		Mean	408.12
		SD	25.34
		Median	413.17
		Minimum	338.3
		Maximum	436.3

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle2 Day1, Pre-dose	n	14
		Mean	-5.52
		SD	18.49
		Median	-6.50
		Minimum	-35.0
		Maximum	27.7
	Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	403.64
		SD	29.02
		Median	410.50
		Minimum	335.7
		Maximum	435.3
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	12
		Mean	-10.00
		SD	19.45
		Median	-13.50
		Minimum	-37.0
		Maximum	23.0
	Cycle3 Day1	n	7
		Mean	413.00
		SD	20.49
		Median	412.00
		Minimum	388.0
		Maximum	440.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle3 Day1	n	7
		Mean	0.67
		SD	20.06
		Median	-5.00
		Minimum	-25.3
		Maximum	30.7
	Cycle4 Day1	n	5
		Mean	412.40
		SD	20.44
		Median	419.00
		Minimum	385.0
		Maximum	437.0
	Change from Baseline at Cycle4 Day1	n	5
		Mean	0.27
		SD	19.21
		Median	-5.33
		Minimum	-24.7
		Maximum	20.7
	Cycle5 Day1	n	3
		Mean	416.33
		SD	21.46
		Median	406.00
		Minimum	402.0
		Maximum	441.0

Source: Listing 16 2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle5 Day1	n	3
		Mean	7.44
		SD	14.44
		Median	2.67
		Minimum	-4.0
		Maximum	23.7
	Cycle6 Day1	n	3
		Mean	401.33
		SD	37.90
		Median	382.00
		Minimum	377.0
		Maximum	445.0
	Change from Baseline at Cycle6 Day1	n	3
		Mean	-7.56
		SD	11.95
		Median	-1.33
		Minimum	-21.3
		Maximum	0.0
	Cycle7 Day1	n	3
		Mean	433.00
		SD	30.20
		Median	437.00
		Minimum	401.0
		Maximum	461.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle7 Day1	n	3
		Mean	24.11
		SD	31.30
		Median	16.00
		Minimum	-2.3
		Maximum	58.7
	Cycle8 Day1	n	3
		Mean	418.00
		SD	17.09
		Median	416.00
		Minimum	402.0
		Maximum	436.0
	Change from Baseline at Cycle8 Day1	n	3
		Mean	9.11
		SD	16.62
		Median	12.67
		Minimum	-9.0
		Maximum	23.7
	Cycle9 Day1	n	3
		Mean	421.33
		SD	26.31
		Median	426.00
		Minimum	393.0
		Maximum	445.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle9 Day1	n	3
		Mean	12.44
		SD	11.50
		Median	14.67
		Minimum	0.0
		Maximum	22.7
	Cycle10 Day1	n	2
		Mean	414.50
		SD	40.31
		Median	414.50
		Minimum	386.0
		Maximum	443.0
	Change from Baseline at Cycle10 Day1	n	2
		Mean	2.83
		SD	6.84
		Median	2.83
		Minimum	-2.0
		Maximum	7.7
	Cycle11 Day1	n	1
		Mean	389.00
		SD	-
		Median	389.00
		Minimum	389.0
		Maximum	389.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle11 Day1	n	1
		Mean	10.67
		SD	-
		Median	10.67
		Minimum	10.7
		Maximum	10.7
	Cycle12 Day1	n	1
		Mean	407.00
		SD	-
		Median	407.00
		Minimum	407.0
		Maximum	407.0
	Change from Baseline at Cycle12 Day1	n	1
		Mean	28.67
		SD	-
		Median	28.67
		Minimum	28.7
		Maximum	28.7
	Cycle13 Day1	n	1
		Mean	424.00
		SD	-
		Median	424.00
		Minimum	424.0
		Maximum	424.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at Cycle13 Day1	n	1
		Mean	45.67
		SD	-
		Median	45.67
		Minimum	45.7
		Maximum	45.7
	Cycle14 Day1	n	1
		Mean	435.00
		SD	-
		Median	435.00
		Minimum	435.0
		Maximum	435.0
	Change from Baseline at Cycle14 Day1	n	1
		Mean	56.67
		SD	-
		Median	56.67
		Minimum	56.7
		Maximum	56.7
	End of Treatment	n	18
		Mean	403.28
		SD	24.45
		Median	404.00
		Minimum	351.0
		Maximum	448.0

Source: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=23)
QTcF Interval (msec)	Change from Baseline at End of Treatment	n	18
		Mean	-9.15
		SD	19.84
		Median	-13.67
		Minimum	-33.3
		Maximum	47.7

Source: Listing 16 2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

表 2.7.4.7-70　臨床的に重大な心電図の異常（210 試験）（安全性解析対象集団）

Description	Category	40 mg (N=23) n (%)
Number of patients with baseline and at least one post-baseline result of QTcF		23
Absolute QTcF (msec)	> 450 msec	3 (13.0%)
	> 480 msec	1 (4.3%)
	> 500 msec	0 (0.0%)
Change from Baseline for QTcF	> 30 msec increase from baseline	2 (8.7%)
	> 60 msec increase from baseline	0 (0.0%)

Source: Listing 16.2.8

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
ECG = electrocardiogram; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
Abnormal ECG results of average triplicate measurements are included in this analysis.
Absolute QTcF measurements only included post baseline measurements.

表 2.7.4.7-71　臨床的に重大な心電図の異常（201 試験）（安全性解析対象集団）

Description	Category	30 mg (N=7) n (%)	40 mg (N=7) n (%)	Total (N=14) n (%)
Number of patients with at least one post-baseline result of QTcF		7	7	14
Absolute QTcF (msec)	> 450 msec	3 (42.9%)	2 (28.6%)	5 (35.7%)
	> 480 msec	0 (0.0%)	1 (14.3%)	1 (7.1%)
	> 500 msec	0 (0.0%)	0 (0.0%)	0 (0.0%)
Change from Baseline for QTcF	> 30 msec increase from baseline	1 (14.3%)	3 (42.9%)	4 (28.6%)
	> 60 msec increase from baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.8.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort of the analysis set with data.
ECG = electrocardiogram; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as pre-dose of Day 1 of Cycle 1.

表 2.7.4.7-72　心電図パラメータの要約（203 試験）（安全性解析対象集団）

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Baseline	n	54
		Mean	164.64
		SD	22.53
		Median	165.50
		Minimum	123.0
		Maximum	216.0
	Cycle1 Day1, 3.5hrs Post-dose	n	54
		Mean	167.27
		SD	22.84
		Median	167.00
		Minimum	124.7
		Maximum	226.7
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	54
		Mean	2.63
		SD	8.13
		Median	1.67
		Minimum	-26.3
		Maximum	27.3
	Cycle2 Day1, Pre-dose	n	44
		Mean	163.90
		SD	20.22
		Median	165.33
		Minimum	124.3
		Maximum	205.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle2 Day1, Pre-dose	Mean	44
		SD	-3.12
		Median	10.92
		Minimum	-4.17
		Maximum	-29.3
		Mean	18.7
	Cycle2 Day1, 3.5hrs Post-dose	Mean	40
		SD	164.99
		Median	21.05
		Minimum	163.50
		Maximum	124.3
		Mean	211.3
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	Mean	40
		SD	-1.64
		Median	11.12
		Minimum	-0.83
		Maximum	-27.0
		Mean	29.7
	Cycle3 Day1	Mean	33
		SD	164.27
		Median	22.58
		Minimum	163.00
		Maximum	128.0
		Mean	207.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle3 Day1	n	33
		Mean	-3.12
		SD	10.73
		Median	-4.33
		Minimum	-28.7
		Maximum	16.3
	Cycle4 Day1	n	26
		Mean	161.88
		SD	27.33
		Median	164.50
		Minimum	115.0
		Maximum	226.0
	Change from Baseline at Cycle4 Day1	n	26
		Mean	-3.97
		SD	11.78
		Median	-5.50
		Minimum	-30.7
		Maximum	23.7
	Cycle5 Day1	n	20
		Mean	164.80
		SD	20.90
		Median	162.50
		Minimum	136.0
		Maximum	211.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle5 Day1	n	20
		Mean	-5.13
		SD	10.89
		Median	-5.33
		Minimum	-21.7
		Maximum	15.3
	Cycle6 Day1	n	14
		Mean	164.93
		SD	23.41
		Median	161.50
		Minimum	131.0
		Maximum	212.0
	Change from Baseline at Cycle6 Day1	n	14
		Mean	-3.17
		SD	8.04
		Median	-3.50
		Minimum	-20.3
		Maximum	8.7
	Cycle7 Day1	n	14
		Mean	163.36
		SD	19.04
		Median	167.50
		Minimum	124.0
		Maximum	193.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle7 Day1	n	14
		Mean	-2.52
		SD	12.87
		Median	-2.17
		Minimum	-21.7
		Maximum	15.3
	Cycle8 Day1	n	12
		Mean	158.75
		SD	16.77
		Median	159.50
		Minimum	135.0
		Maximum	181.0
	Change from Baseline at Cycle8 Day1	n	12
		Mean	-7.08
		SD	15.02
		Median	-9.50
		Minimum	-30.3
		Maximum	29.7
	Cycle9 Day1	n	11
		Mean	158.82
		SD	23.20
		Median	163.00
		Minimum	108.0
		Maximum	193.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle9 Day1	n	11
		Mean	-5.00
		SD	15.90
		Median	-1.00
		Minimum	-33.7
		Maximum	24.7
	Cycle10 Day1	n	7
		Mean	159.00
		SD	23.35
		Median	153.00
		Minimum	132.0
		Maximum	194.0
	Change from Baseline at Cycle10 Day1	n	7
		Mean	-0.33
		SD	10.24
		Median	-3.00
		Minimum	-12.3
		Maximum	14.3
	Cycle11 Day1	n	7
		Mean	156.00
		SD	25.37
		Median	168.00
		Minimum	116.0
		Maximum	179.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle11 Day1	n	7
		Mean	-3.33
		SD	16.02
		Median	-8.33
		Minimum	-27.3
		Maximum	15.7
	Cycle12 Day1	n	5
		Mean	174.40
		SD	18.50
		Median	167.00
		Minimum	152.0
		Maximum	196.0
	Change from Baseline at Cycle12 Day1	n	5
		Mean	4.53
		SD	8.41
		Median	8.00
		Minimum	-10.3
		Maximum	10.3
	Cycle13 Day1	n	3
		Mean	171.00
		SD	27.87
		Median	158.00
		Minimum	152.0
		Maximum	203.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle13 Day1	n	3
		Mean	1.11
		SD	6.05
		Median	-1.33
		Minimum	-3.3
		Maximum	8.0
	Cycle14 Day1	n	3
		Mean	169.00
		SD	25.16
		Median	156.00
		Minimum	153.0
		Maximum	198.0
	Change from Baseline at Cycle14 Day1	n	3
		Mean	-0.89
		SD	8.92
		Median	-3.33
		Minimum	-8.3
		Maximum	9.0
	Cycle15 Day1	n	3
		Mean	161.67
		SD	16.50
		Median	162.00
		Minimum	145.0
		Maximum	178.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle15 Day1	n	3
		Mean	-8.22
		SD	17.44
		Median	1.00
		Minimum	-28.3
		Maximum	2.7
	Cycle16 Day1	n	3
		Mean	165.33
		SD	27.23
		Median	156.00
		Minimum	144.0
		Maximum	196.0
	Change from Baseline at Cycle16 Day1	n	3
		Mean	-4.56
		SD	5.27
		Median	-3.33
		Minimum	-10.3
		Maximum	0.0
	Cycle17 Day1	n	3
		Mean	167.00
		SD	11.53
		Median	163.00
		Minimum	158.0
		Maximum	180.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle17 Day1	n	3
		Mean	-2.89
		SD	22.71
		Median	-1.33
		Minimum	-26.3
		Maximum	19.0
	Cycle18 Day1	n	2
		Mean	182.00
		SD	21.21
		Median	182.00
		Minimum	167.0
		Maximum	197.0
	Change from Baseline at Cycle18 Day1	n	2
		Mean	-0.83
		SD	12.02
		Median	-0.83
		Minimum	-9.3
		Maximum	7.7
	Cycle19 Day1	n	2
		Mean	184.00
		SD	28.28
		Median	184.00
		Minimum	164.0
		Maximum	204.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle19 Day1	n	2
		Mean	1.17
		SD	4.95
		Median	1.17
		Minimum	-2.3
		Maximum	4.7
	Cycle20 Day1	n	1
		Mean	155.00
		SD	-
		Median	155.00
		Minimum	155.0
		Maximum	155.0
	Change from Baseline at Cycle20 Day1	n	1
		Mean	-4.33
		SD	-
		Median	-4.33
		Minimum	-4.3
		Maximum	-4.3
	Cycle21 Day1	n	1
		Mean	155.00
		SD	-
		Median	155.00
		Minimum	155.0
		Maximum	155.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
PR Interval (msec)	Change from Baseline at Cycle21 Day1	n	1
		Mean	-4.33
		SD	-
		Median	-4.33
		Minimum	-4.3
		Maximum	-4.3
	End of Treatment	n	33
		Mean	159.52
		SD	25.61
		Median	163.00
		Minimum	122.0
		Maximum	225.0
	Change from Baseline at End of Treatment	n	33
		Mean	-4.47
		SD	15.12
		Median	-3.00
		Minimum	-48.3
		Maximum	28.7
QRS Duration (msec)	Baseline	n	55
		Mean	92.13
		SD	16.81
		Median	89.67
		Minimum	73.3
		Maximum	186.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	91.44
		SD	14.82
		Median	89.33
		Minimum	73.7
		Maximum	164.7
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	-0.68
		SD	4.66
		Median	-0.33
		Minimum	-22.0
		Maximum	7.0
	Cycle2 Day1, Pre-dose	n	45
		Mean	90.50
		SD	11.67
		Median	88.67
		Minimum	78.7
		Maximum	155.3
	Change from Baseline at Cycle2 Day1, Pre-dose	n	45
		Mean	-0.56
		SD	7.65
		Median	-1.67
		Minimum	-31.3
		Maximum	23.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle2 Day1, 3.5hrs Post-dose	n	41
		Mean	89.89
		SD	6.13
		Median	89.67
		Minimum	77.0
		Maximum	104.0
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	41
		Mean	1.00
		SD	5.51
		Median	0.67
		Minimum	-9.0
		Maximum	16.7
	Cycle3 Day1	n	34
		Mean	89.94
		SD	7.93
		Median	90.00
		Minimum	73.0
		Maximum	106.0
	Change from Baseline at Cycle3 Day1	n	34
		Mean	1.13
		SD	5.36
		Median	2.50
		Minimum	-14.0
		Maximum	10.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle4 Day1	n	26
		Mean	89.73
		SD	8.67
		Median	88.00
		Minimum	69.0
		Maximum	106.0
	Change from Baseline at Cycle4 Day1	n	26
		Mean	-0.23
		SD	7.27
		Median	-0.17
		Minimum	-14.3
		Maximum	14.3
	Cycle5 Day1	n	20
		Mean	90.40
		SD	9.41
		Median	90.00
		Minimum	73.0
		Maximum	107.0
	Change from Baseline at Cycle5 Day1	n	20
		Mean	0.03
		SD	8.42
		Median	-0.83
		Minimum	-15.0
		Maximum	17.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle6 Day1	n	15
		Mean	89.67
		SD	7.44
		Median	90.00
		Minimum	72.0
		Maximum	102.0
	Change from Baseline at Cycle6 Day1	n	15
		Mean	-2.78
		SD	5.13
		Median	-3.00
		Minimum	-13.7
		Maximum	5.7
	Cycle7 Day1	n	14
		Mean	90.07
		SD	8.04
		Median	88.00
		Minimum	74.0
		Maximum	104.0
	Change from Baseline at Cycle7 Day1	n	14
		Mean	-1.71
		SD	5.55
		Median	-1.17
		Minimum	-11.3
		Maximum	6.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle8 Day1	n	12
		Mean	89.25
		SD	10.23
		Median	89.50
		Minimum	70.0
		Maximum	105.0
	Change from Baseline at Cycle8 Day1	n	12
		Mean	-2.11
		SD	4.68
		Median	-1.33
		Minimum	-9.0
		Maximum	6.3
	Cycle9 Day1	n	11
		Mean	91.27
		SD	7.14
		Median	94.00
		Minimum	77.0
		Maximum	103.0
	Change from Baseline at Cycle9 Day1	n	11
		Mean	1.03
		SD	5.50
		Median	-0.67
		Minimum	-5.7
		Maximum	13.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle10 Day1	n	7
		Mean	88.29
		SD	8.75
		Median	85.00
		Minimum	79.0
		Maximum	101.0
	Change from Baseline at Cycle10 Day1	n	7
		Mean	-2.95
		SD	5.57
		Median	-3.67
		Minimum	-8.0
		Maximum	8.7
	Cycle11 Day1	n	7
		Mean	91.00
		SD	8.35
		Median	91.00
		Minimum	79.0
		Maximum	105.0
	Change from Baseline at Cycle11 Day1	n	7
		Mean	-0.24
		SD	3.02
		Median	-1.67
		Minimum	-3.0
		Maximum	5.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle12 Day1	n	5
		Mean	93.20
		SD	7.89
		Median	91.00
		Minimum	87.0
		Maximum	106.0
	Change from Baseline at Cycle12 Day1	n	5
		Mean	-1.00
		SD	3.95
		Median	-1.67
		Minimum	-4.7
		Maximum	5.7
	Cycle13 Day1	n	3
		Mean	84.67
		SD	6.66
		Median	83.00
		Minimum	79.0
		Maximum	92.0
	Change from Baseline at Cycle13 Day1	n	3
		Mean	-6.67
		SD	3.84
		Median	-5.33
		Minimum	-11.0
		Maximum	-3.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle14 Day1	n	3
		Mean	89.00
		SD	5.29
		Median	91.00
		Minimum	83.0
		Maximum	93.0
	Change from Baseline at Cycle14 Day1	n	3
		Mean	-2.33
		SD	4.84
		Median	-2.67
		Minimum	-7.0
		Maximum	2.7
	Cycle15 Day1	n	3
		Mean	85.67
		SD	5.51
		Median	86.00
		Minimum	80.0
		Maximum	91.0
	Change from Baseline at Cycle15 Day1	n	3
		Mean	-5.67
		SD	2.33
		Median	-4.67
		Minimum	-8.3
		Maximum	-4.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle16 Day1	n	3
		Mean	88.67
		SD	3.06
		Median	88.00
		Minimum	86.0
		Maximum	92.0
	Change from Baseline at Cycle16 Day1	n	3
		Mean	-2.67
		SD	5.78
		Median	-4.00
		Minimum	-7.7
		Maximum	3.7
	Cycle17 Day1	n	3
		Mean	86.67
		SD	2.08
		Median	86.00
		Minimum	85.0
		Maximum	89.0
	Change from Baseline at Cycle17 Day1	n	3
		Mean	-4.67
		SD	1.76
		Median	-4.00
		Minimum	-6.7
		Maximum	-3.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle18 Day1	n	2
		Mean	87.00
		SD	8.49
		Median	87.00
		Minimum	81.0
		Maximum	93.0
	Change from Baseline at Cycle18 Day1	n	2
		Mean	-5.00
		SD	3.30
		Median	-5.00
		Minimum	-7.3
		Maximum	-2.7
	Cycle19 Day1	n	2
		Mean	91.00
		SD	4.24
		Median	91.00
		Minimum	88.0
		Maximum	94.0
	Change from Baseline at Cycle19 Day1	n	2
		Mean	-1.00
		SD	9.43
		Median	-1.00
		Minimum	-7.7
		Maximum	5.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	Cycle20 Day1	n	1
		Mean	96.00
		SD	-
		Median	96.00
		Minimum	96.0
		Maximum	96.0
	Change from Baseline at Cycle20 Day1	n	1
		Mean	0.33
		SD	-
		Median	0.33
		Minimum	0.3
		Maximum	0.3
	Cycle21 Day1	n	1
		Mean	95.00
		SD	-
		Median	95.00
		Minimum	95.0
		Maximum	95.0
	Change from Baseline at Cycle21 Day1	n	1
		Mean	-0.67
		SD	-
		Median	-0.67
		Minimum	-0.7
		Maximum	-0.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QRS Duration (msec)	End of Treatment	n	34
		Mean	94.03
		SD	16.45
		Median	90.50
		Minimum	73.0
		Maximum	166.0
	Change from Baseline at End of Treatment	n	34
		Mean	-0.53
		SD	7.54
		Median	-0.50
		Minimum	-20.7
		Maximum	12.0
QT Interval (msec)	Baseline	n	55
		Mean	380.10
		SD	32.38
		Median	379.00
		Minimum	317.0
		Maximum	459.7
	Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	381.13
		SD	33.40
		Median	379.33
		Minimum	306.0
		Maximum	464.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	1.04
		SD	13.49
		Median	2.00
		Minimum	-24.7
		Maximum	43.7
	Cycle2 Day1, Pre-dose	n	45
		Mean	380.24
		SD	32.57
		Median	381.33
		Minimum	302.7
		Maximum	461.7
	Change from Baseline at Cycle2 Day1, Pre-dose	n	45
		Mean	-4.07
		SD	22.64
		Median	0.00
		Minimum	-76.0
		Maximum	52.0
	Cycle2 Day1, 3.5hrs Post-dose	n	40
		Mean	372.70
		SD	30.75
		Median	369.33
		Minimum	293.7
		Maximum	443.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	40
		Mean	-12.09
		SD	29.60
		Median	-13.50
		Minimum	-88.0
		Maximum	45.3
	Cycle3 Day1	n	34
		Mean	386.59
		SD	30.36
		Median	390.00
		Minimum	316.0
		Maximum	444.0
	Change from Baseline at Cycle3 Day1	n	34
		Mean	-2.02
		SD	24.42
		Median	-2.83
		Minimum	-60.7
		Maximum	44.7
	Cycle4 Day1	n	26
		Mean	386.42
		SD	32.77
		Median	384.00
		Minimum	304.0
		Maximum	460.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle4 Day1	n	26
		Mean	-1.81
		SD	17.40
		Median	-3.00
		Minimum	-36.7
		Maximum	41.7
	Cycle5 Day1	n	20
		Mean	391.60
		SD	28.50
		Median	386.00
		Minimum	359.0
		Maximum	457.0
	Change from Baseline at Cycle5 Day1	n	20
		Mean	1.17
		SD	21.41
		Median	10.17
		Minimum	-32.3
		Maximum	34.3
	Cycle6 Day1	n	15
		Mean	381.67
		SD	25.98
		Median	381.00
		Minimum	357.0
		Maximum	465.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle6 Day1	n	15
		Mean	-4.40
		SD	33.13
		Median	-5.67
		Minimum	-96.7
		Maximum	44.3
	Cycle7 Day1	n	14
		Mean	388.43
		SD	41.35
		Median	381.50
		Minimum	323.0
		Maximum	494.0
	Change from Baseline at Cycle7 Day1	n	14
		Mean	-0.17
		SD	29.98
		Median	9.83
		Minimum	-47.7
		Maximum	54.0
	Cycle8 Day1	n	12
		Mean	399.00
		SD	32.99
		Median	389.00
		Minimum	360.0
		Maximum	488.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle8 Day1	n	12
		Mean	8.22
		SD	28.65
		Median	15.33
		Minimum	-44.7
		Maximum	52.0
	Cycle9 Day1	n	11
		Mean	393.09
		SD	29.70
		Median	387.00
		Minimum	354.0
		Maximum	449.0
	Change from Baseline at Cycle9 Day1	n	11
		Mean	6.79
		SD	23.90
		Median	2.67
		Minimum	-26.7
		Maximum	45.0
	Cycle10 Day1	n	7
		Mean	393.29
		SD	11.76
		Median	393.00
		Minimum	379.0
		Maximum	410.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle10 Day1	n	7
		Mean	14.33
		SD	22.33
		Median	19.00
		Minimum	-16.3
		Maximum	43.0
	Cycle11 Day1	n	7
		Mean	407.86
		SD	11.28
		Median	405.00
		Minimum	396.0
		Maximum	424.0
	Change from Baseline at Cycle11 Day1	n	7
		Mean	28.90
		SD	14.33
		Median	30.33
		Minimum	6.3
		Maximum	50.0
	Cycle12 Day1	n	5
		Mean	394.60
		SD	25.84
		Median	397.00
		Minimum	356.0
		Maximum	424.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle12 Day1	n	5
		Mean	16.80
		SD	35.77
		Median	31.67
		Minimum	-30.7
		Maximum	57.0
	Cycle13 Day1	n	3
		Mean	406.67
		SD	26.39
		Median	394.00
		Minimum	389.0
		Maximum	437.0
	Change from Baseline at Cycle13 Day1	n	3
		Mean	33.67
		SD	32.51
		Median	23.67
		Minimum	7.3
		Maximum	70.0
	Cycle14 Day1	n	3
		Mean	395.33
		SD	7.64
		Median	397.00
		Minimum	387.0
		Maximum	402.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle14 Day1	n	3
		Mean	22.33
		SD	12.35
		Median	21.67
		Minimum	10.3
		Maximum	35.0
	Cycle15 Day1	n	3
		Mean	400.33
		SD	15.01
		Median	401.00
		Minimum	385.0
		Maximum	415.0
	Change from Baseline at Cycle15 Day1	n	3
		Mean	27.33
		SD	18.10
		Median	19.67
		Minimum	14.3
		Maximum	48.0
	Cycle16 Day1	n	3
		Mean	376.00
		SD	25.51
		Median	366.00
		Minimum	357.0
		Maximum	405.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle16 Day1	n	3
		Mean	3.00
		SD	30.93
		Median	-8.33
		Minimum	-20.7
		Maximum	38.0
	Cycle17 Day1	n	3
		Mean	396.67
		SD	27.61
		Median	390.00
		Minimum	373.0
		Maximum	427.0
	Change from Baseline at Cycle17 Day1	n	3
		Mean	23.67
		SD	31.54
		Median	7.67
		Minimum	3.3
		Maximum	60.0
	Cycle18 Day1	n	2
		Mean	380.00
		SD	11.31
		Median	380.00
		Minimum	372.0
		Maximum	388.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle18 Day1	n	2
		Mean	4.00
		SD	3.77
		Median	4.00
		Minimum	1.3
		Maximum	6.7
	Cycle19 Day1	n	2
		Mean	393.00
		SD	8.49
		Median	393.00
		Minimum	387.0
		Maximum	399.0
	Change from Baseline at Cycle19 Day1	n	2
		Mean	17.00
		SD	6.60
		Median	17.00
		Minimum	12.3
		Maximum	21.7
	Cycle20 Day1	n	1
		Mean	382.00
		SD	-
		Median	382.00
		Minimum	382.0
		Maximum	382.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at Cycle20 Day1	n	1
		Mean	-4.67
		SD	-
		Median	-4.67
		Minimum	-4.7
		Maximum	-4.7
	Cycle21 Day1	n	1
		Mean	405.00
		SD	-
		Median	405.00
		Minimum	405.0
		Maximum	405.0
	Change from Baseline at Cycle21 Day1	n	1
		Mean	18.33
		SD	-
		Median	18.33
		Minimum	18.3
		Maximum	18.3
	End of Treatment	n	34
		Mean	384.21
		SD	41.35
		Median	376.50
		Minimum	306.0
		Maximum	472.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QT Interval (msec)	Change from Baseline at End of Treatment	n	34
		Mean	-1.30
		SD	32.15
		Median	-1.33
		Minimum	-72.0
		Maximum	62.7
QTcB Interval (msec)	Baseline	n	55
		Mean	424.58
		SD	23.67
		Median	423.00
		Minimum	369.3
		Maximum	490.0
	Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	423.40
		SD	22.34
		Median	420.67
		Minimum	378.0
		Maximum	468.7
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	-1.18
		SD	12.77
		Median	1.00
		Minimum	-39.3
		Maximum	26.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle2 Day1, Pre-dose	n	45
		Mean	431.01
		SD	25.56
		Median	432.33
		Minimum	384.3
		Maximum	492.0
	Change from Baseline at Cycle2 Day1, Pre-dose	n	45
		Mean	7.01
		SD	22.55
		Median	10.00
		Minimum	-54.3
		Maximum	63.0
	Cycle2 Day1, 3.5hrs Post-dose	n	40
		Mean	426.97
		SD	22.36
		Median	427.83
		Minimum	378.3
		Maximum	465.3
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	40
		Mean	4.63
		SD	23.45
		Median	6.00
		Minimum	-61.0
		Maximum	53.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle3 Day1	n	34
		Mean	433.71
		SD	24.17
		Median	430.50
		Minimum	385.0
		Maximum	486.0
	Change from Baseline at Cycle3 Day1	n	34
		Mean	11.91
		SD	14.89
		Median	10.83
		Minimum	-11.7
		Maximum	41.7
	Cycle4 Day1	n	26
		Mean	430.88
		SD	23.03
		Median	428.50
		Minimum	378.0
		Maximum	469.0
	Change from Baseline at Cycle4 Day1	n	26
		Mean	12.94
		SD	15.77
		Median	12.17
		Minimum	-27.7
		Maximum	41.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle5 Day1	n	20
		Mean	431.35
		SD	22.77
		Median	430.00
		Minimum	398.0
		Maximum	479.0
	Change from Baseline at Cycle5 Day1	n	20
		Mean	16.50
		SD	17.46
		Median	14.33
		Minimum	-7.7
		Maximum	72.0
	Cycle6 Day1	n	15
		Mean	431.00
		SD	18.58
		Median	427.00
		Minimum	412.0
		Maximum	476.0
	Change from Baseline at Cycle6 Day1	n	15
		Mean	11.29
		SD	12.81
		Median	10.67
		Minimum	-14.0
		Maximum	31.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle7 Day1	n	14
		Mean	437.36
		SD	24.53
		Median	436.50
		Minimum	404.0
		Maximum	496.0
	Change from Baseline at Cycle7 Day1	n	14
		Mean	16.64
		SD	18.48
		Median	14.83
		Minimum	-7.0
		Maximum	56.7
	Cycle8 Day1	n	12
		Mean	440.25
		SD	21.19
		Median	435.50
		Minimum	407.0
		Maximum	480.0
	Change from Baseline at Cycle8 Day1	n	12
		Mean	16.86
		SD	21.01
		Median	17.33
		Minimum	-9.0
		Maximum	49.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle9 Day1	n	11
		Mean	442.00
		SD	22.84
		Median	436.00
		Minimum	416.0
		Maximum	495.0
	Change from Baseline at Cycle9 Day1	n	11
		Mean	20.06
		SD	17.14
		Median	16.00
		Minimum	-11.0
		Maximum	54.0
	Cycle10 Day1	n	7
		Mean	436.14
		SD	14.09
		Median	431.00
		Minimum	424.0
		Maximum	460.0
	Change from Baseline at Cycle10 Day1	n	7
		Mean	12.57
		SD	19.24
		Median	6.67
		Minimum	-12.0
		Maximum	44.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle11 Day1	n	7
		Mean	435.29
		SD	17.53
		Median	433.00
		Minimum	410.0
		Maximum	458.0
	Change from Baseline at Cycle11 Day1	n	7
		Mean	11.71
		SD	16.24
		Median	13.67
		Minimum	-18.0
		Maximum	34.7
	Cycle12 Day1	n	5
		Mean	435.20
		SD	12.50
		Median	433.00
		Minimum	423.0
		Maximum	456.0
	Change from Baseline at Cycle12 Day1	n	5
		Mean	16.80
		SD	6.43
		Median	13.67
		Minimum	10.0
		Maximum	26.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle13 Day1	n	3
		Mean	439.33
		SD	12.86
		Median	434.00
		Minimum	430.0
		Maximum	454.0
	Change from Baseline at Cycle13 Day1	n	3
		Mean	24.78
		SD	17.51
		Median	14.67
		Minimum	14.7
		Maximum	45.0
	Cycle14 Day1	n	3
		Mean	429.67
		SD	10.97
		Median	426.00
		Minimum	421.0
		Maximum	442.0
	Change from Baseline at Cycle14 Day1	n	3
		Mean	15.11
		SD	10.36
		Median	12.00
		Minimum	6.7
		Maximum	26.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle15 Day1	n	3
		Mean	437.33
		SD	15.01
		Median	438.00
		Minimum	422.0
		Maximum	452.0
	Change from Baseline at Cycle15 Day1	n	3
		Mean	22.78
		SD	17.83
		Median	29.00
		Minimum	2.7
		Maximum	36.7
	Cycle16 Day1	n	3
		Mean	415.33
		SD	8.33
		Median	418.00
		Minimum	406.0
		Maximum	422.0
	Change from Baseline at Cycle16 Day1	n	3
		Mean	0.78
		SD	9.31
		Median	2.67
		Minimum	-9.3
		Maximum	9.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle17 Day1	n	3
		Mean	430.67
		SD	21.36
		Median	422.00
		Minimum	415.0
		Maximum	455.0
	Change from Baseline at Cycle17 Day1	n	3
		Mean	16.11
		SD	26.46
		Median	6.67
		Minimum	-4.3
		Maximum	46.0
	Cycle18 Day1	n	2
		Mean	427.50
		SD	2.12
		Median	427.50
		Minimum	426.0
		Maximum	429.0
	Change from Baseline at Cycle18 Day1	n	2
		Mean	10.17
		SD	0.71
		Median	10.17
		Minimum	9.7
		Maximum	10.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle19 Day1	n	2
		Mean	428.50
		SD	10.61
		Median	428.50
		Minimum	421.0
		Maximum	436.0
	Change from Baseline at Cycle19 Day1	n	2
		Mean	11.17
		SD	13.44
		Median	11.17
		Minimum	1.7
		Maximum	20.7
	Cycle20 Day1	n	1
		Mean	398.00
		SD	-
		Median	398.00
		Minimum	398.0
		Maximum	398.0
	Change from Baseline at Cycle20 Day1	n	1
		Mean	-17.33
		SD	-
		Median	-17.33
		Minimum	-17.3
		Maximum	-17.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcB Interval (msec)	Cycle21 Day1	n	1
		Mean	443.00
		SD	-
		Median	443.00
		Minimum	443.0
		Maximum	443.0
	Change from Baseline at Cycle21 Day1	n	1
		Mean	27.67
		SD	-
		Median	27.67
		Minimum	27.7
		Maximum	27.7
	End of Treatment	n	34
		Mean	432.03
		SD	21.67
		Median	428.50
		Minimum	383.0
		Maximum	478.0
	Change from Baseline at End of Treatment	n	34
		Mean	3.75
		SD	19.79
		Median	6.17
		Minimum	-36.0
		Maximum	43.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Baseline	n	55
		Mean	408.77
		SD	20.23
		Median	407.33
		Minimum	374.0
		Maximum	446.7
	Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	408.33
		SD	19.93
		Median	408.67
		Minimum	358.3
		Maximum	448.3
	Change from Baseline at Cycle1 Day1, 3.5hrs Post-dose	n	55
		Mean	-0.44
		SD	9.49
		Median	-0.33
		Minimum	-22.7
		Maximum	23.7
	Cycle2 Day1, Pre-dose	n	45
		Mean	412.95
		SD	20.88
		Median	413.33
		Minimum	370.7
		Maximum	456.3

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle2 Day1, Pre-dose	n	45
		Mean	3.05
		SD	19.18
		Median	3.33
		Minimum	-54.0
		Maximum	48.0
	Cycle2 Day1, 3.5hrs Post-dose	n	40
		Mean	407.73
		SD	20.03
		Median	410.33
		Minimum	366.3
		Maximum	439.3
	Change from Baseline at Cycle2 Day1, 3.5hrs Post-dose	n	40
		Mean	-1.29
		SD	22.71
		Median	1.67
		Minimum	-70.0
		Maximum	47.7
	Cycle3 Day1	n	34
		Mean	417.09
		SD	21.89
		Median	415.50
		Minimum	371.0
		Maximum	471.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle3 Day1	n	34
		Mean	6.95
		SD	11.44
		Median	5.17
		Minimum	-22.3
		Maximum	29.3
	Cycle4 Day1	n	26
		Mean	415.27
		SD	21.75
		Median	412.00
		Minimum	371.0
		Maximum	466.0
	Change from Baseline at Cycle4 Day1	n	26
		Mean	7.78
		SD	12.28
		Median	10.33
		Minimum	-15.3
		Maximum	28.3
	Cycle5 Day1	n	20
		Mean	417.45
		SD	20.39
		Median	411.50
		Minimum	391.0
		Maximum	460.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle5 Day1	n	20
		Mean	11.25
		SD	13.24
		Median	11.33
		Minimum	-11.3
		Maximum	52.7
	Cycle6 Day1	n	15
		Mean	413.67
		SD	18.77
		Median	410.00
		Minimum	395.0
		Maximum	465.0
	Change from Baseline at Cycle6 Day1	n	15
		Mean	5.71
		SD	16.23
		Median	9.00
		Minimum	-33.3
		Maximum	25.7
	Cycle7 Day1	n	14
		Mean	420.14
		SD	28.38
		Median	417.00
		Minimum	375.0
		Maximum	495.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett's correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle7 Day1	n	14
		Mean	10.64
		SD	15.72
		Median	7.83
		Minimum	-11.7
		Maximum	55.7
	Cycle8 Day1	n	12
		Mean	425.83
		SD	19.81
		Median	423.00
		Minimum	391.0
		Maximum	470.0
	Change from Baseline at Cycle8 Day1	n	12
		Mean	13.83
		SD	18.83
		Median	20.00
		Minimum	-18.3
		Maximum	39.3
	Cycle9 Day1	n	11
		Mean	424.91
		SD	22.13
		Median	415.00
		Minimum	401.0
		Maximum	479.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle9 Day1	n	11
		Mean	15.39
		SD	15.92
		Median	13.67
		Minimum	-15.0
		Maximum	46.0
	Cycle10 Day1	n	7
		Mean	421.00
		SD	7.12
		Median	420.00
		Minimum	413.0
		Maximum	433.0
	Change from Baseline at Cycle10 Day1	n	7
		Mean	12.90
		SD	16.06
		Median	14.67
		Minimum	-10.0
		Maximum	29.7
	Cycle11 Day1	n	7
		Mean	425.86
		SD	11.51
		Median	421.00
		Minimum	414.0
		Maximum	446.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle11 Day1	n	7
		Mean	17.76
		SD	9.49
		Median	20.67
		Minimum	4.0
		Maximum	28.3
	Cycle12 Day1	n	5
		Mean	421.00
		SD	11.49
		Median	421.00
		Minimum	403.0
		Maximum	431.0
	Change from Baseline at Cycle12 Day1	n	5
		Mean	16.67
		SD	16.50
		Median	20.67
		Minimum	-2.7
		Maximum	36.7
	Cycle13 Day1	n	3
		Mean	427.67
		SD	17.62
		Median	418.00
		Minimum	417.0
		Maximum	448.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle13 Day1	n	3
		Mean	27.56
		SD	22.83
		Median	17.67
		Minimum	11.3
		Maximum	53.7
	Cycle14 Day1	n	3
		Mean	418.00
		SD	7.00
		Median	415.00
		Minimum	413.0
		Maximum	426.0
	Change from Baseline at Cycle14 Day1	n	3
		Mean	17.89
		SD	4.53
		Median	20.33
		Minimum	12.7
		Maximum	20.7
	Cycle15 Day1	n	3
		Mean	424.67
		SD	12.86
		Median	430.00
		Minimum	410.0
		Maximum	434.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle15 Day1	n	3
		Mean	24.56
		SD	13.41
		Median	28.33
		Minimum	9.7
		Maximum	35.7
	Cycle16 Day1	n	3
		Mean	401.33
		SD	10.69
		Median	399.00
		Minimum	392.0
		Maximum	413.0
	Change from Baseline at Cycle16 Day1	n	3
		Mean	1.22
		SD	16.32
		Median	-1.33
		Minimum	-13.7
		Maximum	18.7
	Cycle17 Day1	n	3
		Mean	419.33
		SD	23.63
		Median	411.00
		Minimum	401.0
		Maximum	446.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle17 Day1	n	3
		Mean	19.22
		SD	28.19
		Median	5.33
		Minimum	0.7
		Maximum	51.7
	Cycle18 Day1	n	2
		Mean	411.00
		SD	2.83
		Median	411.00
		Minimum	409.0
		Maximum	413.0
	Change from Baseline at Cycle18 Day1	n	2
		Mean	8.00
		SD	0.94
		Median	8.00
		Minimum	7.3
		Maximum	8.7
	Cycle19 Day1	n	2
		Mean	417.00
		SD	9.90
		Median	417.00
		Minimum	410.0
		Maximum	424.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle19 Day1	n	2
		Mean	14.00
		SD	6.13
		Median	14.00
		Minimum	9.7
		Maximum	18.3
	Cycle20 Day1	n	1
		Mean	393.00
		SD	-
		Median	393.00
		Minimum	393.0
		Maximum	393.0
	Change from Baseline at Cycle20 Day1	n	1
		Mean	-12.67
		SD	-
		Median	-12.67
		Minimum	-12.7
		Maximum	-12.7
	Cycle21 Day1	n	1
		Mean	430.00
		SD	-
		Median	430.00
		Minimum	430.0
		Maximum	430.0

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Parameter (unit)	Visit	Statistic	40 mg (N=55)
QTcF Interval (msec)	Change from Baseline at Cycle21 Day1	n	1
		Mean	24.33
		SD	-
		Median	24.33
		Minimum	24.3
		Maximum	24.3
	End of Treatment	n	34
		Mean	414.97
		SD	24.28
		Median	411.50
		Minimum	368.0
		Maximum	460.0
	Change from Baseline at End of Treatment	n	34
		Mean	1.95
		SD	16.51
		Median	2.83
		Minimum	-49.7
		Maximum	27.7

SOURCE: Listing 16.2.8

ECG = electrocardiogram; QTcB = QT interval using Bazett’s correction formula; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

表 2.7.4.7-73　臨床的に重大な心電図の異常（203 試験）（安全性解析対象集団）

Description	Category	Japan (N=39) n (%)	Korea (N=16) n (%)	Total (N=55) n (%)
Number of patients with baseline and at least one post-baseline result of QTcF		39	16	55
Absolute QTcF (msec)	> 450 msec	5 (12.8)	0 (0.0)	5 (9.1)
	> 480 msec	1 (2.6)	0 (0.0)	1 (1.8)
	> 500 msec	0 (0.0)	0 (0.0)	0 (0.0)
Change from Baseline for QTcF	> 30 msec increase from baseline	5 (12.8)	3 (18.8)	8 (14.5)
	> 60 msec increase from baseline	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.8

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECG = electrocardiogram; QTcF = QT interval using Fridericia's correction formula.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).
Abnormal ECG results of average triplicate measurements are included in this analysis.
Absolute QTcF measurements only included post baseline measurements.

表 2.7.4.7-74　ECOG PS の評価（210 試験）（安全性解析対象集団）

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle2 Day1	Total	10 (71.4%)	3 (21.4%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	14 (100.0%)
	0	7 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (50.0%)
	1	3 (21.4%)	3 (21.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (42.9%)
	2	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle3 Day1	Total	7 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (100.0%)
	0	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (42.9%)
	1	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (57.1%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle4 Day1	Total	5 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (100.0%)
	0	2 (40.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	1	2 (40.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	2	1 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle5 Day1	Total	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
	0	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (66.7%)
	1	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.11.1

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle6 Day1	Total	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
	0	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)
	1	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (66.7%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle7 Day1	Total	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
	0	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (66.7%)
	1	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle8 Day1	Total	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
	0	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (66.7%)
	1	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle9 Day1	Total	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
	0	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (66.7%)
	1	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16.2.11.1

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle10 Day1	Total	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)
	0	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)
	1	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle11 Day1	Total	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle12 Day1	Total	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle13 Day1	Total	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Source: Listing 16 2 11.1

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle14 Day1	Total	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
End of Treatment	Total	11 (52.4%)	9 (42.9%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	21 (100.0%)
	0	4 (19.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (19.0%)
	1	4 (19.0%)	3 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (33.3%)
	2	3 (14.3%)	3 (14.3%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	7 (33.3%)
	3	0 (0.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
	4	0 (0.0%)	2 (9.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)

Source: Listing 16.2.11.1

n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

表 2.7.4.7-75　ECOG PS の評価（201 試験）（安全性解析対象集団）

Visit	ECOG Performance Status Assessment	30 mg	40 mg	Total
		n (%)	n (%)	n (%)
Screening	N	7	7	14
	0	4 (57.1%)	4 (57.1%)	8 (57.1%)
	1	3 (42.9%)	3 (42.9%)	6 (42.9%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)
Baseline	N	7	7	14
	0	4 (57.1%)	5 (71.4%)	9 (64.3%)
	1	3 (42.9%)	2 (28.6%)	5 (35.7%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle2 Day1 Pre-dose	N	4	6	10
	0	2 (50.0%)	5 (83.3%)	7 (70.0%)
	1	2 (50.0%)	1 (16.7%)	3 (30.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort with data.
ECOG = Eastern Cooperative Oncology Group
Baseline is defined as pre-dose of Day 1 of Cycle 1.

Visit	ECOG Performance Status Assessment	30 mg	40 mg	Total
		n (%)	n (%)	n (%)
Cycle3 Day1 Pre-dose	N	2	3	5
	0	1 (50.0%)	2 (66.7%)	3 (60.0%)
	1	1 (50.0%)	1 (33.3%)	2 (40.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle4 Day1 Pre-dose	N	2	3	5
	0	1 (50.0%)	2 (66.7%)	3 (60.0%)
	1	1 (50.0%)	1 (33.3%)	2 (40.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cycle5 Day1 Pre-dose	N	1	2	3
	0	1 (100.0%)	1 (50.0%)	2 (66.7%)
	1	0 (0.0%)	1 (50.0%)	1 (33.3%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	0 (0.0%)	0 (0.0%)	0 (0.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort with data.
ECOG = Eastern Cooperative Oncology Group
Baseline is defined as pre-dose of Day 1 of Cycle 1.

Visit	ECOG Performance Status Assessment	30 mg	40 mg	Total
		n (%)	n (%)	n (%)
Cycle6 Day1 Pre-dose	N	0	2	2
	0	-	2 (100.0%)	2 (100.0%)
	1	-	0 (0.0%)	0 (0.0%)
	2	-	0 (0.0%)	0 (0.0%)
	3	-	0 (0.0%)	0 (0.0%)
	4	-	0 (0.0%)	0 (0.0%)
Cycle7 Day1 Pre-dose	N	0	1	1
	0	-	0 (0.0%)	0 (0.0%)
	1	-	1 (100.0%)	1 (100.0%)
	2	-	0 (0.0%)	0 (0.0%)
	3	-	0 (0.0%)	0 (0.0%)
	4	-	0 (0.0%)	0 (0.0%)
End-of-Study	N	4	6	10
	0	3 (75.0%)	4 (66.7%)	7 (70.0%)
	1	0 (0.0%)	2 (33.3%)	2 (20.0%)
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)
	3	1 (25.0%)	0 (0.0%)	1 (10.0%)
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)

SOURCE: Listing 16.2.13.1
n = number of patients; % = percentage of patients calculated relative to the total number of patients in each cohort with data.
ECOG = Eastern Cooperative Oncology Group
Baseline is defined as pre-dose of Day 1 of Cycle 1.

表 2.7.4.7-76　ECOG PS の評価（203 試験）（安全性解析対象集団）

Country: Japan (N=39)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle2 Day1	Total	22 (64.7)	12 (35.3)	0 (0.0)	0 (0.0)	0 (0.0)	34 (100.0)
	0	22 (64.7)	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	24 (70.6)
	1	0 (0.0)	8 (23.5)	0 (0.0)	0 (0.0)	0 (0.0)	8 (23.5)
	2	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)
	3	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle3 Day1	Total	17 (65.4)	9 (34.6)	0 (0.0)	0 (0.0)	0 (0.0)	26 (100.0)
	0	16 (61.5)	4 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	20 (76.9)
	1	1 (3.8)	5 (19.2)	0 (0.0)	0 (0.0)	0 (0.0)	6 (23.1)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle4 Day1	Total	16 (76.2)	5 (23.8)	0 (0.0)	0 (0.0)	0 (0.0)	21 (100.0)
	0	15 (71.4)	3 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	18 (85.7)
	1	1 (4.8)	2 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (14.3)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle5 Day1	Total	14 (82.4)	3 (17.6)	0 (0.0)	0 (0.0)	0 (0.0)	17 (100.0)
	0	14 (82.4)	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	15 (88.2)
	1	0 (0.0)	2 (11.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (11.8)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Japan (N=39)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle6 Day1	Total	10 (83.3)	2 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	12 (100.0)
	0	10 (83.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (83.3)
	1	0 (0.0)	2 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle7 Day1	Total	9 (81.8)	2 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	11 (100.0)
	0	8 (72.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (72.7)
	1	1 (9.1)	2 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (27.3)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle8 Day1	Total	7 (77.8)	2 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)	9 (100.0)
	0	6 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (66.7)
	1	1 (11.1)	2 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (33.3)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle9 Day1	Total	6 (75.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (100.0)
	0	5 (62.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (62.5)
	1	1 (12.5)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (37.5)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Japan (N=39)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle10 Day1	Total	4 (80.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)
	0	3 (60.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (60.0)
	1	1 (20.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (40.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle11 Day1	Total	4 (80.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)
	0	4 (80.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (80.0)
	1	0 (0.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle12 Day1	Total	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle13 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Japan (N=39)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle14 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle15 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle16 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle17 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Japan (N=39)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle18 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle19 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle20 Day1	Total	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle21 Day1	Total	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Japan (N=39)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
End of Treatment	Total	19 (65.5)	10 (34.5)	0 (0.0)	0 (0.0)	0 (0.0)	29 (100.0)
	0	14 (48.3)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)	16 (55.2)
	1	4 (13.8)	4 (13.8)	0 (0.0)	0 (0.0)	0 (0.0)	8 (27.6)
	2	1 (3.4)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (6.9)
	3	0 (0.0)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (6.9)
	4	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.4)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Korea (N=16)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle2 Day1	Total	2 (16.7)	9 (75.0)	1 (8.3)	0 (0.0)	0 (0.0)	12 (100.0)
	0	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
	1	2 (16.7)	8 (66.7)	1 (8.3)	0 (0.0)	0 (0.0)	11 (91.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle3 Day1	Total	1 (12.5)	7 (87.5)	0 (0.0)	0 (0.0)	0 (0.0)	8 (100.0)
	0	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)
	1	1 (12.5)	6 (75.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (87.5)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle4 Day1	Total	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)
	0	0 (0.0)	2 (40.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (40.0)
	1	1 (20.0)	2 (40.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (60.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle5 Day1	Total	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
	1	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Korea (N=16)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle6 Day1	Total	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
	1	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle7 Day1	Total	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
	1	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle8 Day1	Total	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
	1	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle9 Day1	Total	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
	1	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Korea (N=16)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle10 Day1	Total	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)
	1	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle11 Day1	Total	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)
	1	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle12 Day1	Total	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)
	1	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle13 Day1	Total	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Korea (N=16)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle14 Day1	Total	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle15 Day1	Total	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle16 Day1	Total	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle17 Day1	Total	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Korea (N=16)

Visit		ECOG Performance Status Assessment at Baseline n (%) 0	1	2	3	4	Total
End of Treatment	Total	1 (12.5)	6 (75.0)	1 (12.5)	0 (0.0)	0 (0.0)	8 (100.0)
	0	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)
	1	1 (12.5)	5 (62.5)	1 (12.5)	0 (0.0)	0 (0.0)	7 (87.5)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Overall (N=55)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle2 Day1	Total	24 (52.2)	21 (45.7)	1 (2.2)	0 (0.0)	0 (0.0)	46 (100.0)
	0	22 (47.8)	3 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	25 (54.3)
	1	2 (4.3)	16 (34.8)	1 (2.2)	0 (0.0)	0 (0.0)	19 (41.3)
	2	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)
	3	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle3 Day1	Total	18 (52.9)	16 (47.1)	0 (0.0)	0 (0.0)	0 (0.0)	34 (100.0)
	0	16 (47.1)	5 (14.7)	0 (0.0)	0 (0.0)	0 (0.0)	21 (61.8)
	1	2 (5.9)	11 (32.4)	0 (0.0)	0 (0.0)	0 (0.0)	13 (38.2)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle4 Day1	Total	17 (65.4)	9 (34.6)	0 (0.0)	0 (0.0)	0 (0.0)	26 (100.0)
	0	15 (57.7)	5 (19.2)	0 (0.0)	0 (0.0)	0 (0.0)	20 (76.9)
	1	2 (7.7)	4 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	6 (23.1)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle5 Day1	Total	15 (75.0)	5 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	20 (100.0)
	0	14 (70.0)	2 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	16 (80.0)
	1	1 (5.0)	3 (15.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (20.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Overall (N=55)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle6 Day1	Total	11 (73.3)	4 (26.7)	0 (0.0)	0 (0.0)	0 (0.0)	15 (100.0)
	0	10 (66.7)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	11 (73.3)
	1	1 (6.7)	3 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (26.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle7 Day1	Total	10 (71.4)	4 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	14 (100.0)
	0	8 (57.1)	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	9 (64.3)
	1	2 (14.3)	3 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)	5 (35.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle8 Day1	Total	8 (66.7)	4 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	12 (100.0)
	0	6 (50.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	7 (58.3)
	1	2 (16.7)	3 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (41.7)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle9 Day1	Total	7 (63.6)	4 (36.4)	0 (0.0)	0 (0.0)	0 (0.0)	11 (100.0)
	0	5 (45.5)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	6 (54.5)
	1	2 (18.2)	3 (27.3)	0 (0.0)	0 (0.0)	0 (0.0)	5 (45.5)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Overall (N=55)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle10 Day1	Total	5 (71.4)	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	7 (100.0)
	0	3 (42.9)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (57.1)
	1	2 (28.6)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (42.9)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle11 Day1	Total	5 (71.4)	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	7 (100.0)
	0	4 (57.1)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	5 (71.4)
	1	1 (14.3)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle12 Day1	Total	4 (80.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)
	0	3 (60.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (80.0)
	1	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle13 Day1	Total	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Overall (N=55)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle14 Day1	Total	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle15 Day1	Total	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle16 Day1	Total	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle17 Day1	Total	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	0	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Overall (N=55)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
Cycle18 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle19 Day1	Total	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	0	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle20 Day1	Total	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cycle21 Day1	Total	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	0	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

Country: Overall (N=55)

Visit		ECOG Performance Status Assessment at Baseline n (%)					
		0	1	2	3	4	Total
End of Treatment	Total	20 (54.1)	16 (43.2)	1 (2.7)	0 (0.0)	0 (0.0)	37 (100.0)
	0	14 (37.8)	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)	17 (45.9)
	1	5 (13.5)	9 (24.3)	1 (2.7)	0 (0.0)	0 (0.0)	15 (40.5)
	2	1 (2.7)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.4)
	3	0 (0.0)	2 (5.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.4)
	4	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.7)

Source: Listing 16.2.11.1

N = number of subjects in the Safety Analysis Set by country.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a country in the analysis set with data;
ECOG = Eastern Cooperative Oncology Group.
Baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments).

表 2.7.4.7-77　性別（男性、女性）の有害事象の概要（210 試験）（安全性解析対象集団）

Sex: Female

Description	40 mg (N=8) n (%)
Number of subjects with	
At least one TEAE	8 (100.0%)
At least one TEAE related to the study drug	8 (100.0%)
At least one serious TEAE	6 (75.0%)
At least one serious TEAE related to the study drug	5 (62.5%)
At least one TEAE leading to dose reduction or interruption	7 (87.5%)
At least one TEAE leading to study drug discontinuation	5 (62.5%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	8 (100.0%)
At least one TEAE with grade 3 or higher and related to the study drug	8 (100.0%)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Sex: Male

Description	40 mg (N=15) n (%)
Number of subjects with	
At least one TEAE	15 (100.0%)
At least one TEAE related to the study drug	15 (100.0%)
At least one serious TEAE	1 (6.7%)
At least one serious TEAE related to the study drug	1 (6.7%)
At least one TEAE leading to dose reduction or interruption	9 (60.0%)
At least one TEAE leading to study drug discontinuation	4 (26.7%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	10 (66.7%)
At least one TEAE with grade 3 or higher and related to the study drug	10 (66.7%)

Source: Listing 16.2.6.1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-78　性別（男性、女性）の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	Female (N=8) n (%)	Male (N=15) n (%)
Number of subjects with at least one TEAE	8(100.0%)	15(100.0%)
血液およびリンパ系障害	7(87.5%)	12(80.0%)
貧血*	3(37.5%)	6(40.0%)
好酸球増加症	1(12.5%)	0
発熱性好中球減少症	0	1(6.7%)
白血球減少症*	3(37.5%)	7(46.7%)
リンパ球減少症*	1(12.5%)	1(6.7%)
好中球減少症*	5(62.5%)	7(46.7%)
血小板減少症*	6(75.0%)	12(80.0%)
心臓障害	2(25.0%)	0
第一度房室ブロック	1(12.5%)	0
動悸	1(12.5%)	0
眼障害	1(12.5%)	0
ドライアイ	1(12.5%)	0
胃腸障害	4(50.0%)	5(33.3%)
腹痛	0	3(20.0%)
下痢	3(37.5%)	3(20.0%)
悪心	2(25.0%)	1(6.7%)
口内炎	1(12.5%)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Female (N=8) n (%)	Male (N=15) n (%)
一般・全身障害および投与部位の状態	6(75.0%)	7(46.7%)
悪寒	0	1(6.7%)
疲労	2(25.0%)	1(6.7%)
倦怠感	3(37.5%)	4(26.7%)
非心臓性胸痛	0	1(6.7%)
末梢性浮腫	1(12.5%)	0
発熱	2(25.0%)	1(6.7%)
感染症および寄生虫症	3(37.5%)	4(26.7%)
細菌感染	0	1(6.7%)
サイトメガロウイルス感染	0	1(6.7%)
医療機器関連感染	0	1(6.7%)
麦粒腫	1(12.5%)	0
口腔カンジダ症	1(12.5%)	0
ニューモシスチス・イロベチイ肺炎	1(12.5%)	0
皮膚感染	0	1(6.7%)
扁桃炎	0	1(6.7%)
上気道感染	1(12.5%)	0
尿路感染	1(12.5%)	0
傷害、中毒および処置合併症	1(12.5%)	0
挫傷	1(12.5%)	0

Source: Listing 16 2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Female (N=8) n (%)	Male (N=15) n (%)
臨床検査	4(50.0%)	6(40.0%)
アラニンアミノトランスフェラーゼ増加	0	1(6.7%)
アスパラギン酸アミノトランスフェラーゼ増加	0	2(13.3%)
血中アルカリホスファターゼ増加	1(12.5%)	0
血中乳酸脱水素酵素増加	0	1(6.7%)
脳性ナトリウム利尿ペプチド増加	1(12.5%)	0
好酸球数増加	1(12.5%)	0
γ－グルタミルトランスフェラーゼ増加	1(12.5%)	1(6.7%)
リパーゼ増加	0	1(6.7%)
体重減少	1(12.5%)	3(20.0%)
代謝および栄養障害	5(62.5%)	8(53.3%)
食欲減退	4(50.0%)	4(26.7%)
高カルシウム血症	0	1(6.7%)
低アルブミン血症	0	3(20.0%)
低カリウム血症	1(12.5%)	0
低ナトリウム血症	0	2(13.3%)
低リン酸血症	1(12.5%)	0
筋骨格系および結合組織障害	5(62.5%)	2(13.3%)
関節痛	0	1(6.7%)
背部痛	3(37.5%)	1(6.7%)
脊椎すべり症	1(12.5%)	0
尺骨突き上げ症候群	1(12.5%)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Female (N=8) n (%)	Male (N=15) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1(6.7%)
腫瘍疼痛	0	1(6.7%)
神経系障害	4(50.0%)	5(33.3%)
味覚消失	0	1(6.7%)
認知障害	0	1(6.7%)
浮動性めまい	1(12.5%)	0
味覚異常	2(25.0%)	2(13.3%)
頭痛	1(12.5%)	1(6.7%)
傾眠	1(12.5%)	0
腎および尿路障害	0	1(6.7%)
尿瘻	0	1(6.7%)

Source: Listing 16.2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Female (N=8) n (%)	Male (N=15) n (%)
呼吸器、胸郭および縦隔障害	3(37.5%)	1(6.7%)
急性呼吸不全	1(12.5%)	0
鼻出血	1(12.5%)	0
間質性肺疾患	0	1(6.7%)
口腔咽頭痛	1(12.5%)	0
皮膚および皮下組織障害	5(62.5%)	3(20.0%)
接触皮膚炎	0	1(6.7%)
湿疹	1(12.5%)	0
紅斑	1(12.5%)	0
多形紅斑	1(12.5%)	0
光線過敏性反応	1(12.5%)	0
そう痒症	1(12.5%)	0
発疹	1(12.5%)	0
皮膚剥脱	0	1(6.7%)
皮膚潰瘍	0	1(6.7%)
血管障害	0	1(6.7%)
高血圧	0	1(6.7%)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-79　性別（男性、女性）の有害事象の概要（203 試験）（安全性解析対象集団）

Sex: Male

Description	40 mg (N=35)
	n (%)
Number of subjects with	
At least one TEAE	35 (100.0)
At least one TEAE related to the study drug	33 (94.3)
At least one serious TEAE	12 (34.3)
At least one serious TEAE related to the study drug	9 (25.7)
At least one TEAE leading to dose reduction or interruption	27 (77.1)
At least one TEAE leading to study drug discontinuation	11 (31.4)
At least one TEAE leading to death	1 (2.9)
At least one TEAE with grade 3 or higher	28 (80.0)
At least one TEAE with grade 3 or higher and related to the study drug	26 (74.3)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Sex: Female

Description	40 mg (N=20) n (%)
Number of subjects with	
At least one TEAE	20 (100.0)
At least one TEAE related to the study drug	18 (90.0)
At least one serious TEAE	2 (10.0)
At least one serious TEAE related to the study drug	1 (5.0)
At least one TEAE leading to dose reduction or interruption	13 (65.0)
At least one TEAE leading to study drug discontinuation	7 (35.0)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	18 (90.0)
At least one TEAE with grade 3 or higher and related to the study drug	16 (80.0)

Source: Listing 16 2.6.1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-80　性別（男性、女性）の有害事象の発現割合（203 試験）（安全性解析対象集団）

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
Number of subjects with at least one TEAE	35(100.0)	20(100.0)
血液およびリンパ系障害	33(94.3)	19(95.0)
貧血*	8(22.9)	10(50.0)
再生不良性貧血	0	1(5.0)
好酸球増加症	1(2.9)	0
発熱性好中球減少症	3(8.6)	0
白血球減少症*	13(37.1)	11(55.0)
リンパ球減少症*	10(28.6)	6(30.0)
好中球減少症*	19(54.3)	12(60.0)
血小板減少症*	30(85.7)	16(80.0)
心臓障害	5(14.3)	2(10.0)
不安定狭心症	1(2.9)	0
不整脈	1(2.9)	0
心房細動	2(5.7)	0
動悸	2(5.7)	1(5.0)
心嚢液貯留	0	1(5.0)
耳および迷路障害	2(5.7)	0
耳痛	1(2.9)	0
回転性めまい	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
眼障害	3(8.6)	2(10.0)
白内障	1(2.9)	0
結膜出血	0	1(5.0)
ドライアイ	1(2.9)	0
角膜炎	1(2.9)	0
霧視	0	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
胃腸障害	21(60.0)	11(55.0)
腹部不快感	1(2.9)	0
腹痛	3(8.6)	0
上腹部痛	1(2.9)	1(5.0)
肛門出血	0	1(5.0)
便秘	1(2.9)	0
齲歯	2(5.7)	0
下痢	12(34.3)	5(25.0)
消化不良	1(2.9)	0
心窩部不快感	1(2.9)	0
胃潰瘍	1(2.9)	0
胃炎	0	1(5.0)
痔出血	1(2.9)	0
悪心	7(20.0)	5(25.0)
口腔粘膜血腫	1(2.9)	0
口内炎	1(2.9)	1(5.0)
歯痛	0	1(5.0)
嘔吐	1(2.9)	2(10.0)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
一般・全身障害および投与部位の状態	16(45.7)	11(55.0)
無力症	1(2.9)	1(5.0)
カテーテル留置部位腫脹	0	1(5.0)
胸部不快感	0	1(5.0)
胸痛	1(2.9)	0
溢出	1(2.9)	0
疲労	3(8.6)	3(15.0)
歩行障害	0	1(5.0)
インフルエンザ様疾患	0	2(10.0)
倦怠感	6(17.1)	2(10.0)
末梢性浮腫	3(8.6)	1(5.0)
発熱	7(20.0)	4(20.0)
口渇	0	1(5.0)
免疫系障害	1(2.9)	0
薬物過敏症	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
感染症および寄生虫症	15(42.9)	4(20.0)
気管支炎	2(5.7)	0
結膜炎	1(2.9)	1(5.0)
膀胱炎	0	1(5.0)
サイトメガロウイルス感染	1(2.9)	0
感染性小腸結腸炎	1(2.9)	0
胃腸炎	1(2.9)	0
帯状疱疹	1(2.9)	0
膿痂疹	1(2.9)	0
インフルエンザ	2(5.7)	0
上咽頭炎	2(5.7)	0
咽頭炎	2(5.7)	1(5.0)
ニューモシスチス・イロベチイ肺炎	1(2.9)	0
肺炎	1(2.9)	0
鼻炎	0	1(5.0)
ブドウ球菌皮膚感染	1(2.9)	0
上気道感染	3(8.6)	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
傷害、中毒および処置合併症	2(5.7)	1(5.0)
胃瘻管部合併症	1(2.9)	0
爪損傷	1(2.9)	0
処置による疼痛	0	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
臨床検査	18(51.4)	7(35.0)
アラニンアミノトランスフェラーゼ増加	4(11.4)	1(5.0)
アスパラギン酸アミノトランスフェラーゼ増加	6(17.1)	1(5.0)
血中アルカリホスファターゼ増加	7(20.0)	1(5.0)
血中コレステロール増加	0	1(5.0)
血中クレアチンホスホキナーゼＭＢ増加	1(2.9)	0
血中クレアチンホスホキナーゼ増加	0	1(5.0)
血中クレアチニン増加	1(2.9)	1(5.0)
血中免疫グロブリンＡ減少	1(2.9)	0
尿中血陽性	1(2.9)	0
脳性ナトリウム利尿ペプチド増加	2(5.7)	0
Ｃ－反応性蛋白増加	3(8.6)	0
心胸郭比増加	1(2.9)	0
心電図ＱＴ延長	3(8.6)	2(10.0)
心電図Ｔ波逆転	1(2.9)	0
好酸球数増加	2(5.7)	0
γ－グルタミルトランスフェラーゼ増加	6(17.1)	2(10.0)
リパーゼ増加	1(2.9)	0
体重減少	4(11.4)	2(10.0)
体重増加	0	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
代謝および栄養障害	15(42.9)	10(50.0)
食欲減退	7(20.0)	6(30.0)
糖尿病	1(2.9)	0
高カリウム血症	1(2.9)	0
高マグネシウム血症	1(2.9)	0
高トリグリセリド血症	0	1(5.0)
低アルブミン血症	5(14.3)	0
低カルシウム血症	2(5.7)	1(5.0)
低カリウム血症	3(8.6)	2(10.0)
低ナトリウム血症	1(2.9)	1(5.0)
低蛋白血症	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4 1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
筋骨格系および結合組織障害	13(37.1)	6(30.0)
関節痛	1(2.9)	0
関節炎	0	1(5.0)
背部痛	2(5.7)	3(15.0)
出血性関節症	1(2.9)	0
関節腫脹	1(2.9)	0
筋肉疲労	1(2.9)	1(5.0)
筋痙縮	3(8.6)	2(10.0)
筋力低下	1(2.9)	0
筋骨格硬直	1(2.9)	0
筋肉痛	2(5.7)	0
頚部痛	1(2.9)	0
四肢痛	0	1(5.0)
肩回旋筋腱板症候群	0	1(5.0)
腱炎	1(2.9)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3(8.6)	1(5.0)
末梢性Ｔ細胞性リンパ腫、組織型不明	1(2.9)	0
皮膚乳頭腫	0	1(5.0)
腫瘍疼痛	2(5.7)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
神経系障害	7(20.0)	2(10.0)
浮動性めまい	1(2.9)	0
味覚異常	1(2.9)	1(5.0)
頭痛	5(14.3)	1(5.0)
感覚鈍麻	1(2.9)	0
末梢性感覚ニューロパチー	1(2.9)	0
失神寸前の状態	1(2.9)	0
精神障害	3(8.6)	2(10.0)
譫妄	1(2.9)	1(5.0)
不眠症	3(8.6)	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4 1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
腎および尿路障害	2(5.7)	0
急性腎障害	1(2.9)	0
血尿	1(2.9)	0
蛋白尿	1(2.9)	0
生殖系および乳房障害	1(2.9)	0
陰嚢浮腫	1(2.9)	0
呼吸器、胸郭および縦隔障害	9(25.7)	12(60.0)
咳嗽	3(8.6)	3(15.0)
咽頭知覚不全	0	1(5.0)
発声障害	0	1(5.0)
呼吸困難	0	4(20.0)
労作性呼吸困難	0	1(5.0)
鼻出血	1(2.9)	1(5.0)
しゃっくり	1(2.9)	0
間質性肺疾患	1(2.9)	0
口腔咽頭痛	0	3(15.0)
胸水	1(2.9)	1(5.0)
肺臓炎	2(5.7)	2(10.0)
湿性咳嗽	1(2.9)	0
アレルギー性鼻炎	0	1(5.0)
鼻漏	0	1(5.0)
上気道の炎症	0	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Male (N=35) n (%)	Female (N=20) n (%)
皮膚および皮下組織障害	14(40.0)	9(45.0)
褥瘡性潰瘍	0	1(5.0)
ざ瘡様皮膚炎	1(2.9)	0
全身性剥脱性皮膚炎	1(2.9)	0
皮膚乾燥	1(2.9)	0
皮脂欠乏性湿疹	0	1(5.0)
紅斑	2(5.7)	0
多形紅斑	1(2.9)	0
全身紅斑	1(2.9)	0
皮膚疼痛	1(2.9)	0
点状出血	1(2.9)	0
色素沈着障害	0	1(5.0)
全身性そう痒症	1(2.9)	1(5.0)
紫斑	0	2(10.0)
発疹	3(8.6)	2(10.0)
斑状丘疹状皮疹	2(5.7)	0
そう痒性皮疹	1(2.9)	0
蕁麻疹	2(5.7)	3(15.0)
血管障害	2(5.7)	1(5.0)
深部静脈血栓症	0	1(5.0)
低血圧	1(2.9)	0
末梢動脈閉塞性疾患	1(2.9)	0

Source: Listing 16 2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by sex.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-81　年齢別（65 歳未満、65 歳以上 75 歳未満、75 歳以上）の有害事象の概要（210 試験）（安全性解析対象集団）

Age group: <65

Description	40 mg (N=1)
	n (%)
Number of subjects with	
At least one TEAE	1 (100.0%)
At least one TEAE related to the study drug	1 (100.0%)
At least one serious TEAE	0 (0.0%)
At least one serious TEAE related to the study drug	0 (0.0%)
At least one TEAE leading to dose reduction or interruption	1 (100.0%)
At least one TEAE leading to study drug discontinuation	1 (100.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	1 (100.0%)
At least one TEAE with grade 3 or higher and related to the study drug	1 (100.0%)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Age group: >=65 to <75

Description	40 mg (N=13) n (%)
Number of subjects with	
At least one TEAE	13 (100.0%)
At least one TEAE related to the study drug	13 (100.0%)
At least one serious TEAE	5 (38.5%)
At least one serious TEAE related to the study drug	4 (30.8%)
At least one TEAE leading to dose reduction or interruption	9 (69.2%)
At least one TEAE leading to study drug discontinuation	5 (38.5%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	11 (84.6%)
At least one TEAE with grade 3 or higher and related to the study drug	11 (84.6%)

Source: Listing 16.2.6 1 and 16.2.4 1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Age group: >=75

Description	40 mg (N=9) n (%)
Number of subjects with	
At least one TEAE	9 (100.0%)
At least one TEAE related to the study drug	9 (100.0%)
At least one serious TEAE	2 (22.2%)
At least one serious TEAE related to the study drug	2 (22.2%)
At least one TEAE leading to dose reduction or interruption	6 (66.7%)
At least one TEAE leading to study drug discontinuation	3 (33.3%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	6 (66.7%)
At least one TEAE with grade 3 or higher and related to the study drug	6 (66.7%)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-82　年齢別（65 歳未満、65 歳以上 75 歳未満、75 歳以上）の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	<65 (N=1) n (%)	>=65 to <75 (N=13) n (%)	>=75 (N=9) n (%)
Number of subjects with at least one TEAE	1(100.0%)	13(100.0%)	9 (100.0%)
血液およびリンパ系障害	1(100.0%)	11(84.6%)	7 (77.8%)
貧血*	0	6(46.2%)	3 (33.3%)
好酸球増加症	0	0	1 (11.1%)
発熱性好中球減少症	0	1(7.7%)	0
白血球減少症*	1(100.0%)	7(53.8%)	2 (22.2%)
リンパ球減少症*	1(100.0%)	1(7.7%)	0
好中球減少症*	1(100.0%)	8(61.5%)	3 (33.3%)
血小板減少症*	0	11(84.6%)	7 (77.8%)
心臓障害	0	1(7.7%)	1 (11.1%)
第一度房室ブロック	0	0	1 (11.1%)
動悸	0	1(7.7%)	0
眼障害	0	0	1 (11.1%)
ドライアイ	0	0	1 (11.1%)
胃腸障害	0	4(30.8%)	5 (55.6%)
腹痛	0	1(7.7%)	2 (22.2%)
下痢	0	3(23.1%)	3 (33.3%)
悪心	0	2(15.4%)	1 (11.1%)
口内炎	0	0	1 (11.1%)

Source: Listing 16 2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=1) n (%)	>=65 to <75 (N=13) n (%)	>=75 (N=9) n (%)
一般・全身障害および投与部位の状態	0	7(53.8%)	6 (66.7%)
悪寒	0	1(7.7%)	0
疲労	0	0	3 (33.3%)
倦怠感	0	3(23.1%)	4 (44.4%)
非心臓性胸痛	0	1(7.7%)	0
末梢性浮腫	0	0	1 (11.1%)
発熱	0	3(23.1%)	0
感染症および寄生虫症	0	4(30.8%)	3 (33.3%)
細菌感染	0	1(7.7%)	0
サイトメガロウイルス感染	0	1(7.7%)	0
医療機器関連感染	0	1(7.7%)	0
麦粒腫	0	0	1 (11.1%)
口腔カンジダ症	0	0	1 (11.1%)
ニューモシスチス・イロベチイ肺炎	0	1(7.7%)	0
皮膚感染	0	1(7.7%)	0
扁桃炎	0	0	1 (11.1%)
上気道感染	0	1(7.7%)	0
尿路感染	0	0	1 (11.1%)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=1) n (%)	>=65 to <75 (N=13) n (%)	>=75 (N=9) n (%)
傷害、中毒および処置合併症	0	0	1 (11.1%)
挫傷	0	0	1 (11.1%)
臨床検査	0	7(53.8%)	3 (33.3%)
アラニンアミノトランスフェラーゼ増加	0	1(7.7%)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2(15.4%)	0
血中アルカリホスファターゼ増加	0	1(7.7%)	0
血中乳酸脱水素酵素増加	0	1(7.7%)	0
脳性ナトリウム利尿ペプチド増加	0	0	1 (11.1%)
好酸球数増加	0	0	1 (11.1%)
γーグルタミルトランスフェラーゼ増加	0	2(15.4%)	0
リパーゼ増加	0	1(7.7%)	0
体重減少	0	3(23.1%)	1 (11.1%)

Source: Listing 16 2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=1) n (%)	>=65 to <75 (N=13) n (%)	>=75 (N=9) n (%)
代謝および栄養障害	0	7(53.8%)	6 (66.7%)
食欲減退	0	4(30.8%)	4 (44.4%)
高カルシウム血症	0	1(7.7%)	0
低アルブミン血症	0	1(7.7%)	2 (22.2%)
低カリウム血症	0	1(7.7%)	0
低ナトリウム血症	0	1(7.7%)	1 (11.1%)
低リン酸血症	0	1(7.7%)	0
筋骨格系および結合組織障害	0	5(38.5%)	2 (22.2%)
関節痛	0	1(7.7%)	0
背部痛	0	3(23.1%)	1 (11.1%)
脊椎すべり症	0	0	1 (11.1%)
尺骨突き上げ症候群	0	1(7.7%)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=1)	>=65 to <75 (N=13)	>=75 (N=9)
	n (%)	n (%)	n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (11.1%)
腫瘍疼痛	0	0	1 (11.1%)
神経系障害	0	4(30.8%)	5 (55.6%)
味覚消失	0	1(7.7%)	0
認知障害	0	0	1 (11.1%)
浮動性めまい	0	0	1 (11.1%)
味覚異常	0	3(23.1%)	1 (11.1%)
頭痛	0	0	2 (22.2%)
傾眠	0	0	1 (11.1%)
腎および尿路障害	0	1(7.7%)	0
尿瘻	0	1(7.7%)	0
呼吸器、胸郭および縦隔障害	0	3(23.1%)	1 (11.1%)
急性呼吸不全	0	1(7.7%)	0
鼻出血	0	1(7.7%)	0
間質性肺疾患	0	1(7.7%)	0
口腔咽頭痛	0	0	1 (11.1%)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=1) n (%)	>=65 to <75 (N=13) n (%)	>=75 (N=9) n (%)
皮膚および皮下組織障害	0	5(38.5%)	3 (33.3%)
接触皮膚炎	0	1(7.7%)	0
湿疹	0	1(7.7%)	0
紅斑	0	1(7.7%)	0
多形紅斑	0	0	1 (11.1%)
光線過敏性反応	0	0	1 (11.1%)
そう痒症	0	0	1 (11.1%)
発疹	0	1(7.7%)	0
皮膚剥脱	0	0	1 (11.1%)
皮膚潰瘍	0	1(7.7%)	0
血管障害	0	1(7.7%)	0
高血圧	0	1(7.7%)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-83　年齢別（65 歳未満、65 歳以上 75 歳未満、75 歳以上）の有害事象の概要（203 試験）（安全性解析対象集団）

Age group: <65

Description	40 mg (N=15)
	n (%)
Number of subjects with	
At least one TEAE	15 (100.0)
At least one TEAE related to the study drug	13 (86.7)
At least one serious TEAE	1 (6.7)
At least one serious TEAE related to the study drug	0 (0.0)
At least one TEAE leading to dose reduction or interruption	10 (66.7)
At least one TEAE leading to study drug discontinuation	6 (40.0)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	11 (73.3)
At least one TEAE with grade 3 or higher and related to the study drug	10 (66.7)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Age group: >=65 to <75

Description	40 mg (N=23) n (%)
Number of subjects with	
At least one TEAE	23 (100.0)
At least one TEAE related to the study drug	21 (91.3)
At least one serious TEAE	7 (30.4)
At least one serious TEAE related to the study drug	6 (26.1)
At least one TEAE leading to dose reduction or interruption	15 (65.2)
At least one TEAE leading to study drug discontinuation	8 (34.8)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	19 (82.6)
At least one TEAE with grade 3 or higher and related to the study drug	16 (69.6)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Age group: >=75

Description	40 mg (N=17) n (%)
Number of subjects with	
At least one TEAE	17 (100.0)
At least one TEAE related to the study drug	17 (100.0)
At least one serious TEAE	6 (35.3)
At least one serious TEAE related to the study drug	4 (23.5)
At least one TEAE leading to dose reduction or interruption	15 (88.2)
At least one TEAE leading to study drug discontinuation	4 (23.5)
At least one TEAE leading to death	1 (5.9)
At least one TEAE with grade 3 or higher	16 (94.1)
At least one TEAE with grade 3 or higher and related to the study drug	16 (94.1)

Source: Listing 16.2.6 1 and 16.2.4.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-84　年齢別（65 歳未満、65 歳以上 75 歳未満、75 歳以上）の有害事象の発現割合（203 試験）（安全性解析対象集団）

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
Number of subjects with at least one TEAE	15(100.0)	23(100.0)	17 (100.0)
血液およびリンパ系障害	14(93.3)	21(91.3)	17 (100.0)
貧血*	3(20.0)	10(43.5)	5 (29.4)
再生不良性貧血	0	1(4.3)	0
好酸球増加症	0	1(4.3)	0
発熱性好中球減少症	0	2(8.7)	1 (5.9)
白血球減少症*	5(33.3)	11(47.8)	8 (47.1)
リンパ球減少症*	5(33.3)	9(39.1)	2 (11.8)
好中球減少症*	8(53.3)	14(60.9)	9 (52.9)
血小板減少症*	14(93.3)	16(69.6)	16 (94.1)
心臓障害	1(6.7)	3(13.0)	3 (17.6)
不安定狭心症	0	1(4.3)	0
不整脈	0	0	1 (5.9)
心房細動	0	0	2 (11.8)
動悸	1(6.7)	2(8.7)	0
心嚢液貯留	0	0	1 (5.9)
耳および迷路障害	0	1(4.3)	1 (5.9)
耳痛	0	1(4.3)	0
回転性めまい	0	0	1 (5.9)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
眼障害	1(6.7)	3(13.0)	1 (5.9)
白内障	0	1(4.3)	0
結膜出血	0	1(4.3)	0
ドライアイ	0	0	1 (5.9)
角膜炎	1(6.7)	0	0
霧視	0	1(4.3)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by age category.

n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
胃腸障害	11(73.3)	11(47.8)	10 (58.8)
腹部不快感	0	0	1 (5.9)
腹痛	2(13.3)	0	1 (5.9)
上腹部痛	1(6.7)	1(4.3)	0
肛門出血	0	1(4.3)	0
便秘	1(6.7)	0	0
齲歯	2(13.3)	0	0
下痢	6(40.0)	4(17.4)	7 (41.2)
消化不良	0	1(4.3)	0
心窩部不快感	0	1(4.3)	0
胃潰瘍	1(6.7)	0	0
胃炎	1(6.7)	0	0
痔出血	1(6.7)	0	0
悪心	3(20.0)	4(17.4)	5 (29.4)
口腔粘膜血腫	0	1(4.3)	0
口内炎	0	1(4.3)	1 (5.9)
歯痛	0	1(4.3)	0
嘔吐	1(6.7)	1(4.3)	1 (5.9)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
一般・全身障害および投与部位の状態	6(40.0)	11(47.8)	10 (58.8)
無力症	1(6.7)	1(4.3)	0
カテーテル留置部位腫脹	0	1(4.3)	0
胸部不快感	0	1(4.3)	0
胸痛	0	1(4.3)	0
溢出	1(6.7)	0	0
疲労	0	4(17.4)	2 (11.8)
歩行障害	0	1(4.3)	0
インフルエンザ様疾患	0	2(8.7)	0
倦怠感	2(13.3)	1(4.3)	5 (29.4)
末梢性浮腫	1(6.7)	2(8.7)	1 (5.9)
発熱	2(13.3)	4(17.4)	5 (29.4)
口渇	0	1(4.3)	0
免疫系障害	0	1(4.3)	0
薬物過敏症	0	1(4.3)	0

Source: Listing 16.2.6 1 and 16.2.4 1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
感染症および寄生虫症	7(46.7)	8(34.8)	4 (23.5)
気管支炎	0	2(8.7)	0
結膜炎	1(6.7)	1(4.3)	0
膀胱炎	1(6.7)	0	0
サイトメガロウイルス感染	0	1(4.3)	0
感染性小腸結腸炎	1(6.7)	0	0
胃腸炎	1(6.7)	0	0
帯状疱疹	0	0	1 (5.9)
膿痂疹	0	0	1 (5.9)
インフルエンザ	1(6.7)	1(4.3)	0
上咽頭炎	1(6.7)	1(4.3)	0
咽頭炎	1(6.7)	2(8.7)	0
ニューモシスチス・イロベチイ肺炎	0	1(4.3)	0
肺炎	0	0	1 (5.9)
鼻炎	0	1(4.3)	0
ブドウ球菌皮膚感染	1(6.7)	0	0
上気道感染	1(6.7)	1(4.3)	2 (11.8)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
傷害、中毒および処置合併症	2(13.3)	0	1 (5.9)
胃瘻管部合併症	1(6.7)	0	0
爪損傷	1(6.7)	0	0
処置による疼痛	0	0	1 (5.9)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
臨床検査	3(20.0)	13(56.5)	9 (52.9)
アラニンアミノトランスフェラーゼ増加	0	2(8.7)	3 (17.6)
アスパラギン酸アミノトランスフェラーゼ増加	1(6.7)	2(8.7)	4 (23.5)
血中アルカリホスファターゼ増加	0	4(17.4)	4 (23.5)
血中コレステロール増加	0	1(4.3)	0
血中クレアチンホスホキナーゼＭＢ増加	1(6.7)	0	0
血中クレアチンホスホキナーゼ増加	0	1(4.3)	0
血中クレアチニン増加	0	2(8.7)	0
血中免疫グロブリンＡ減少	0	1(4.3)	0
尿中血陽性	0	1(4.3)	0
脳性ナトリウム利尿ペプチド増加	0	2(8.7)	0
Ｃ－反応性蛋白増加	0	1(4.3)	2 (11.8)
心胸郭比増加	0	1(4.3)	0
心電図ＱＴ延長	1(6.7)	2(8.7)	2 (11.8)
心電図Ｔ波逆転	0	1(4.3)	0
好酸球数増加	0	1(4.3)	1 (5.9)
γ－グルタミルトランスフェラーゼ増加	1(6.7)	3(13.0)	4 (23.5)
リパーゼ増加	0	1(4.3)	0
体重減少	0	2(8.7)	4 (23.5)
体重増加	0	1(4.3)	0

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
代謝および栄養障害	3(20.0)	11(47.8)	11 (64.7)
食欲減退	2(13.3)	4(17.4)	7 (41.2)
糖尿病	0	1(4.3)	0
高カリウム血症	0	0	1 (5.9)
高マグネシウム血症	0	0	1 (5.9)
高トリグリセリド血症	0	1(4.3)	0
低アルブミン血症	0	1(4.3)	4 (23.5)
低カルシウム血症	0	1(4.3)	2 (11.8)
低カリウム血症	1(6.7)	4(17.4)	0
低ナトリウム血症	0	0	2 (11.8)
低蛋白血症	0	0	1 (5.9)

Source: Listing 16.2.6 1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
筋骨格系および結合組織障害	3(20.0)	9(39.1)	7 (41.2)
関節痛	0	1(4.3)	0
関節炎	0	1(4.3)	0
背部痛	1(6.7)	2(8.7)	2 (11.8)
出血性関節症	0	0	1 (5.9)
関節腫脹	0	1(4.3)	0
筋肉疲労	0	1(4.3)	1 (5.9)
筋痙縮	2(13.3)	2(8.7)	1 (5.9)
筋力低下	0	1(4.3)	0
筋骨格硬直	0	0	1 (5.9)
筋肉痛	1(6.7)	0	1 (5.9)
頚部痛	0	0	1 (5.9)
四肢痛	0	1(4.3)	0
肩回旋筋腱板症候群	0	1(4.3)	0
腱炎	0	1(4.3)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1(6.7)	3(13.0)	0
末梢性Ｔ細胞性リンパ腫、組織型不明	0	1(4.3)	0
皮膚乳頭腫	0	1(4.3)	0
腫瘍疼痛	1(6.7)	1(4.3)	0

Source: Listing 16.2.6 1 and 16.2.4 1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
神経系障害	3(20.0)	4(17.4)	2 (11.8)
浮動性めまい	1(6.7)	0	0
味覚異常	0	1(4.3)	1 (5.9)
頭痛	3(20.0)	2(8.7)	1 (5.9)
感覚鈍麻	1(6.7)	0	0
末梢性感覚ニューロパチー	0	0	1 (5.9)
失神寸前の状態	0	1(4.3)	0
精神障害	0	4(17.4)	1 (5.9)
譫妄	0	1(4.3)	1 (5.9)
不眠症	0	4(17.4)	0

Source: Listing 16 2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
腎および尿路障害	0	0	2 (11.8)
急性腎障害	0	0	1 (5.9)
血尿	0	0	1 (5.9)
蛋白尿	0	0	1 (5.9)
生殖系および乳房障害	1(6.7)	0	0
陰嚢浮腫	1(6.7)	0	0
呼吸器、胸郭および縦隔障害	4(26.7)	11(47.8)	6 (35.3)
咳嗽	1(6.7)	2(8.7)	3 (17.6)
咽頭知覚不全	0	1(4.3)	0
発声障害	0	1(4.3)	0
呼吸困難	1(6.7)	2(8.7)	1 (5.9)
労作性呼吸困難	0	0	1 (5.9)
鼻出血	0	2(8.7)	0
しゃっくり	0	1(4.3)	0
間質性肺疾患	0	1(4.3)	0
口腔咽頭痛	3(20.0)	0	0
胸水	0	0	2 (11.8)
肺臓炎	1(6.7)	3(13.0)	0
湿性咳嗽	0	1(4.3)	0
アレルギー性鼻炎	0	0	1 (5.9)
鼻漏	0	0	1 (5.9)
上気道の炎症	0	0	1 (5.9)

Source: Listing 16.2.6.1 and 16.2.4.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<65 (N=15) n (%)	>=65 to <75 (N=23) n (%)	>=75 (N=17) n (%)
皮膚および皮下組織障害	6(40.0)	12(52.2)	5 (29.4)
褥瘡性潰瘍	0	0	1 (5.9)
ざ瘡様皮膚炎	0	1(4.3)	0
全身性剥脱性皮膚炎	0	0	1 (5.9)
皮膚乾燥	0	0	1 (5.9)
皮脂欠乏性湿疹	1(6.7)	0	0
紅斑	0	2(8.7)	0
多形紅斑	0	0	1 (5.9)
全身紅斑	0	1(4.3)	0
皮膚疼痛	0	1(4.3)	0
点状出血	0	1(4.3)	0
色素沈着障害	0	1(4.3)	0
全身性そう痒症	1(6.7)	1(4.3)	0
紫斑	0	2(8.7)	0
発疹	1(6.7)	3(13.0)	1 (5.9)
斑状丘疹状皮疹	0	2(8.7)	0
そう痒性皮疹	1(6.7)	0	0
蕁麻疹	2(13.3)	3(13.0)	0
血管障害	0	0	3 (17.6)
深部静脈血栓症	0	0	1 (5.9)
低血圧	0	0	1 (5.9)
末梢動脈閉塞性疾患	0	0	1 (5.9)

Source: Listing 16.2.6 1 and 16.2.4 1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by age category.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-85　ATL サブセット別（再発、再燃、難治性）の有害事象の概要（210 試験）（安全性解析対象集団）

ATL status: Refractory

Description	40 mg (N=5)
	n (%)
Number of subjects with	
At least one TEAE	5 (100.0%)
At least one TEAE related to the study drug	5 (100.0%)
At least one serious TEAE	1 (20.0%)
At least one serious TEAE related to the study drug	0 (0.0%)
At least one TEAE leading to dose reduction or interruption	2 (40.0%)
At least one TEAE leading to study drug discontinuation	2 (40.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	3 (60.0%)
At least one TEAE with grade 3 or higher and related to the study drug	3 (60.0%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL; n = number of subjects;
% = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

ATL status: Recurrent

Description	40 mg (N=13) n (%)
Number of subjects with	
At least one TEAE	13 (100.0%)
At least one TEAE related to the study drug	13 (100.0%)
At least one serious TEAE	3 (23.1%)
At least one serious TEAE related to the study drug	3 (23.1%)
At least one TEAE leading to dose reduction or interruption	9 (69.2%)
At least one TEAE leading to study drug discontinuation	4 (30.8%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	10 (76.9%)
At least one TEAE with grade 3 or higher and related to the study drug	10 (76.9%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL; n = number of subjects;
% = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

ATL status: Relapsed

Description	40 mg (N=5) n (%)
Number of subjects with	
At least one TEAE	5 (100.0%)
At least one TEAE related to the study drug	5 (100.0%)
At least one serious TEAE	3 (60.0%)
At least one serious TEAE related to the study drug	3 (60.0%)
At least one TEAE leading to dose reduction or interruption	5 (100.0%)
At least one TEAE leading to study drug discontinuation	3 (60.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	5 (100.0%)
At least one TEAE with grade 3 or higher and related to the study drug	5 (100.0%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL; n = number of subjects;
% = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-86　ATL サブセット別（再発、再燃、難治性）の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	Relapsed (N=5) n (%)	Recurrent (N=13) n (%)	Refractory (N=5) n (%)
Number of subjects with at least one TEAE	5(100.0%)	13(100.0%)	5(100.0%)
血液およびリンパ系障害	5(100.0%)	11(84.6%)	3(60.0%)
貧血*	2(40.0%)	5(38.5%)	2(40.0%)
好酸球増加症	0	1(7.7%)	0
発熱性好中球減少症	0	1(7.7%)	0
白血球減少症*	3(60.0%)	6(46.2%)	1(20.0%)
リンパ球減少症*	0	1(7.7%)	1(20.0%)
好中球減少症*	5(100.0%)	5(38.5%)	2(40.0%)
血小板減少症*	5(100.0%)	10(76.9%)	3(60.0%)
心臓障害	1(20.0%)	1(7.7%)	0
第一度房室ブロック	0	1(7.7%)	0
動悸	1(20.0%)	0	0
眼障害	0	1(7.7%)	0
ドライアイ	0	1(7.7%)	0
胃腸障害	2(40.0%)	4(30.8%)	3(60.0%)
腹痛	1(20.0%)	1(7.7%)	1(20.0%)
下痢	1(20.0%)	2(15.4%)	3(60.0%)
悪心	0	1(7.7%)	2(40.0%)
口内炎	0	1(7.7%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Relapsed (N=5)	Recurrent (N=13)	Refractory (N=5)
	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	3(60.0%)	7(53.8%)	3(60.0%)
悪寒	0	0	1(20.0%)
疲労	0	3(23.1%)	0
倦怠感	2(40.0%)	3(23.1%)	2(40.0%)
非心臓性胸痛	0	1(7.7%)	0
末梢性浮腫	0	1(7.7%)	0
発熱	1(20.0%)	1(7.7%)	1(20.0%)
感染症および寄生虫症	1(20.0%)	5(38.5%)	1(20.0%)
細菌感染	0	1(7.7%)	0
サイトメガロウイルス感染	0	1(7.7%)	0
医療機器関連感染	0	1(7.7%)	0
麦粒腫	0	1(7.7%)	0
口腔カンジダ症	0	1(7.7%)	0
ニューモシスチス・イロベチイ肺炎	1(20.0%)	0	0
皮膚感染	0	1(7.7%)	0
扁桃炎	0	0	1(20.0%)
上気道感染	1(20.0%)	0	0
尿路感染	0	1(7.7%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Relapsed (N=5) n (%)	Recurrent (N=13) n (%)	Refractory (N=5) n (%)
傷害、中毒および処置合併症	0	1(7.7%)	0
挫傷	0	1(7.7%)	0
臨床検査	4(80.0%)	4(30.8%)	2(40.0%)
アラニンアミノトランスフェラーゼ増加	0	0	1(20.0%)
アスパラギン酸アミノトランスフェラーゼ増加	1(20.0%)	0	1(20.0%)
血中アルカリホスファターゼ増加	1(20.0%)	0	0
血中乳酸脱水素酵素増加	0	1(7.7%)	0
脳性ナトリウム利尿ペプチド増加	0	1(7.7%)	0
好酸球数増加	0	1(7.7%)	0
γ－グルタミルトランスフェラーゼ増加	2(40.0%)	0	0
リパーゼ増加	0	1(7.7%)	0
体重減少	3(60.0%)	0	1(20.0%)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Relapsed (N=5) n (%)	Recurrent (N=13) n (%)	Refractory (N=5) n (%)
代謝および栄養障害	4(80.0%)	6(46.2%)	3(60.0%)
食欲減退	3(60.0%)	3(23.1%)	2(40.0%)
高カルシウム血症	0	1(7.7%)	0
低アルブミン血症	0	3(23.1%)	0
低カリウム血症	1(20.0%)	0	0
低ナトリウム血症	0	1(7.7%)	1(20.0%)
低リン酸血症	1(20.0%)	0	0
筋骨格系および結合組織障害	2(40.0%)	4(30.8%)	1(20.0%)
関節痛	0	1(7.7%)	0
背部痛	1(20.0%)	2(15.4%)	1(20.0%)
脊椎すべり症	0	1(7.7%)	0
尺骨突き上げ症候群	1(20.0%)	0	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Relapsed (N=5) n (%)	Recurrent (N=13) n (%)	Refractory (N=5) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1(20.0%)
腫瘍疼痛	0	0	1(20.0%)
神経系障害	1(20.0%)	4(30.8%)	4(80.0%)
味覚消失	0	1(7.7%)	0
認知障害	0	0	1(20.0%)
浮動性めまい	0	1(7.7%)	0
味覚異常	1(20.0%)	1(7.7%)	2(40.0%)
頭痛	0	1(7.7%)	1(20.0%)
傾眠	0	1(7.7%)	0
腎および尿路障害	0	0	1(20.0%)
尿瘻	0	0	1(20.0%)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Relapsed (N=5) n (%)	Recurrent (N=13) n (%)	Refractory (N=5) n (%)
呼吸器、胸郭および縦隔障害	1(20.0%)	2(15.4%)	1(20.0%)
急性呼吸不全	0	0	1(20.0%)
鼻出血	1(20.0%)	0	0
間質性肺疾患	0	1(7.7%)	0
口腔咽頭痛	0	1(7.7%)	0
皮膚および皮下組織障害	2(40.0%)	5(38.5%)	1(20.0%)
接触皮膚炎	0	1(7.7%)	0
湿疹	1(20.0%)	0	0
紅斑	0	0	1(20.0%)
多形紅斑	0	1(7.7%)	0
光線過敏性反応	0	1(7.7%)	0
そう痒症	0	1(7.7%)	0
発疹	1(20.0%)	0	0
皮膚剥脱	0	1(7.7%)	0
皮膚潰瘍	0	1(7.7%)	0
血管障害	0	1(7.7%)	0
高血圧	0	1(7.7%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by refractory, recurrent or relapsed ATL.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Subjects with refractory, recurrent and relapsed ATL are confirmed by Medical Expert.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-87　ECOG PS 別（0、1、2）の有害事象の概要（210 試験）（安全性解析対象集団）

ECOG performance status: 0

Description	40 mg (N=12)
	n (%)
Number of subjects with	
At least one TEAE	12 (100.0%)
At least one TEAE related to the study drug	12 (100.0%)
At least one serious TEAE	5 (41.7%)
At least one serious TEAE related to the study drug	5 (41.7%)
At least one TEAE leading to dose reduction or interruption	11 (91.7%)
At least one TEAE leading to study drug discontinuation	7 (58.3%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	11 (91.7%)
At least one TEAE with grade 3 or higher and related to the study drug	11 (91.7%)

Source: Listing 16 2.6.1 and 16.2.11.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

ECOG performance status: 1

Description	40 mg (N=10) n (%)
Number of subjects with	
At least one TEAE	10 (100.0%)
At least one TEAE related to the study drug	10 (100.0%)
At least one serious TEAE	2 (20.0%)
At least one serious TEAE related to the study drug	1 (10.0%)
At least one TEAE leading to dose reduction or interruption	4 (40.0%)
At least one TEAE leading to study drug discontinuation	2 (20.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	6 (60.0%)
At least one TEAE with grade 3 or higher and related to the study drug	6 (60.0%)

Source: Listing 16.2.6 1 and 16.2.11.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

ECOG performance status: 2

Description	40 mg (N=1) n (%)
Number of subjects with	
At least one TEAE	1 (100.0%)
At least one TEAE related to the study drug	1 (100.0%)
At least one serious TEAE	0 (0.0%)
At least one serious TEAE related to the study drug	0 (0.0%)
At least one TEAE leading to dose reduction or interruption	1 (100.0%)
At least one TEAE leading to study drug discontinuation	0 (0.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	1 (100.0%)
At least one TEAE with grade 3 or higher and related to the study drug	1 (100.0%)

Source: Listing 16 2.6.1 and 16.2.11.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-88　ECOG PS 別（0、1、2）の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	ECOG Status: 0 (N=12) n (%)	ECOG Status: 1 (N=10) n (%)	ECOG Status: 2 (N=1) n (%)
Number of subjects with at least one TEAE	12(100.0%)	10(100.0%)	1(100.0%)
血液およびリンパ系障害	10(83.3%)	8(80.0%)	1(100.0%)
貧血*	6(50.0%)	3(30.0%)	0
好酸球増加症	1(8.3%)	0	0
発熱性好中球減少症	1(8.3%)	0	0
白血球減少症*	7(58.3%)	2(20.0%)	1(100.0%)
リンパ球減少症*	2(16.7%)	0	0
好中球減少症*	9(75.0%)	3(30.0%)	0
血小板減少症*	9(75.0%)	8(80.0%)	1(100.0%)
心臓障害	1(8.3%)	1(10.0%)	0
第一度房室ブロック	0	1(10.0%)	0
動悸	1(8.3%)	0	0
眼障害	0	1(10.0%)	0
ドライアイ	0	1(10.0%)	0
胃腸障害	4(33.3%)	5(50.0%)	0
腹痛	1(8.3%)	2(20.0%)	0
下痢	3(25.0%)	3(30.0%)	0
悪心	1(8.3%)	2(20.0%)	0
口内炎	0	1(10.0%)	0

Source: Listing 16 2.6.1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=12)	ECOG Status: 1 (N=10)	ECOG Status: 2 (N=1)
	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	7(58.3%)	5(50.0%)	1(100.0%)
悪寒	1(8.3%)	0	0
疲労	2(16.7%)	1(10.0%)	0
倦怠感	4(33.3%)	3(30.0%)	0
非心臓性胸痛	0	0	1(100.0%)
末梢性浮腫	0	1(10.0%)	0
発熱	2(16.7%)	1(10.0%)	0
感染症および寄生虫症	4(33.3%)	3(30.0%)	0
細菌感染	0	1(10.0%)	0
サイトメガロウイルス感染	1(8.3%)	0	0
医療機器関連感染	1(8.3%)	0	0
麦粒腫	1(8.3%)	0	0
口腔カンジダ症	0	1(10.0%)	0
ニューモシスチス・イロベチイ肺炎	1(8.3%)	0	0
皮膚感染	1(8.3%)	0	0
扁桃炎	0	1(10.0%)	0
上気道感染	1(8.3%)	0	0
尿路感染	1(8.3%)	0	0
傷害、中毒および処置合併症	0	1(10.0%)	0
挫傷	0	1(10.0%)	0

Source: Listing 16 2.6.1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=12)	ECOG Status: 1 (N=10)	ECOG Status: 2 (N=1)
	n (%)	n (%)	n (%)
臨床検査	6(50.0%)	4(40.0%)	0
アラニンアミノトランスフェラーゼ増加	1(8.3%)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1(8.3%)	1(10.0%)	0
血中アルカリホスファターゼ増加	1(8.3%)	0	0
血中乳酸脱水素酵素増加	0	1(10.0%)	0
脳性ナトリウム利尿ペプチド増加	1(8.3%)	0	0
好酸球数増加	0	1(10.0%)	0
γ－グルタミルトランスフェラーゼ増加	1(8.3%)	1(10.0%)	0
リパーゼ増加	0	1(10.0%)	0
体重減少	3(25.0%)	1(10.0%)	0
代謝および栄養障害	6(50.0%)	7(70.0%)	0
食欲減退	4(33.3%)	4(40.0%)	0
高カルシウム血症	0	1(10.0%)	0
低アルブミン血症	1(8.3%)	2(20.0%)	0
低カリウム血症	1(8.3%)	0	0
低ナトリウム血症	1(8.3%)	1(10.0%)	0
低リン酸血症	1(8.3%)	0	0
筋骨格系および結合組織障害	4(33.3%)	3(30.0%)	0
関節痛	1(8.3%)	0	0
背部痛	2(16.7%)	2(20.0%)	0
脊椎すべり症	0	1(10.0%)	0
尺骨突き上げ症候群	1(8.3%)	0	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=12)	ECOG Status: 1 (N=10)	ECOG Status: 2 (N=1)
	n (%)	n (%)	n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1(10.0%)	0
腫瘍疼痛	0	1(10.0%)	0
神経系障害	3(25.0%)	6(60.0%)	0
味覚消失	0	1(10.0%)	0
認知障害	0	1(10.0%)	0
浮動性めまい	0	1(10.0%)	0
味覚異常	1(8.3%)	3(30.0%)	0
頭痛	1(8.3%)	1(10.0%)	0
傾眠	1(8.3%)	0	0
腎および尿路障害	1(8.3%)	0	0
尿瘻	1(8.3%)	0	0
呼吸器、胸郭および縦隔障害	2(16.7%)	2(20.0%)	0
急性呼吸不全	0	1(10.0%)	0
鼻出血	1(8.3%)	0	0
間質性肺疾患	1(8.3%)	0	0
口腔咽頭痛	0	1(10.0%)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=12)	ECOG Status: 1 (N=10)	ECOG Status: 2 (N=1)
	n (%)	n (%)	n (%)
皮膚および皮下組織障害	4(33.3%)	3(30.0%)	1(100.0%)
接触皮膚炎	0	0	1(100.0%)
湿疹	1(8.3%)	0	0
紅斑	0	1(10.0%)	0
多形紅斑	0	1(10.0%)	0
光線過敏性反応	0	1(10.0%)	0
そう痒症	1(8.3%)	0	0
発疹	1(8.3%)	0	0
皮膚剥脱	0	1(10.0%)	0
皮膚潰瘍	1(8.3%)	0	0
血管障害	1(8.3%)	0	0
高血圧	1(8.3%)	0	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.

n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

表 2.7.4.7-89　ECOG PS 別（0、1、2）の有害事象の概要（203 試験）（安全性解析対象集団）

ECOG performance status: 0

Description	40 mg (N=28) n (%)
Number of subjects with	
At least one TEAE	28 (100.0)
At least one TEAE related to the study drug	27 (96.4)
At least one serious TEAE	6 (21.4)
At least one serious TEAE related to the study drug	4 (14.3)
At least one TEAE leading to dose reduction or interruption	23 (82.1)
At least one TEAE leading to study drug discontinuation	8 (28.6)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	25 (89.3)
At least one TEAE with grade 3 or higher and related to the study drug	23 (82.1)

Source: Listing 16.2.6 1 and 16.2.11.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE.　For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

ECOG performance status: 1

Description	40 mg (N=25) n (%)
Number of subjects with	
At least one TEAE	25 (100.0)
At least one TEAE related to the study drug	22 (88.0)
At least one serious TEAE	7 (28.0)
At least one serious TEAE related to the study drug	5 (20.0)
At least one TEAE leading to dose reduction or interruption	15 (60.0)
At least one TEAE leading to study drug discontinuation	10 (40.0)
At least one TEAE leading to death	1 (4.0)
At least one TEAE with grade 3 or higher	19 (76.0)
At least one TEAE with grade 3 or higher and related to the study drug	17 (68.0)

Source: Listing 16.2.6 1 and 16.2.11.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

ECOG performance status: 2

Description	40 mg (N=2) n (%)
Number of subjects with	
At least one TEAE	2 (100.0)
At least one TEAE related to the study drug	2 (100.0)
At least one serious TEAE	1 (50.0)
At least one serious TEAE related to the study drug	1 (50.0)
At least one TEAE leading to dose reduction or interruption	2 (100.0)
At least one TEAE leading to study drug discontinuation	0 (0.0)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	2 (100.0)
At least one TEAE with grade 3 or higher and related to the study drug	2 (100.0)

Source: Listing 16.2.6 1 and 16.2.11.1

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-90　ECOG PS 別（0、1、2）の有害事象の発現割合（203 試験）（安全性解析対象集団）

System organ class Preferred term	ECOG Status: 0 (N=28) n (%)	ECOG Status: 1 (N=25) n (%)	ECOG Status: 2 (N=2) n (%)
Number of subjects with at least one TEAE	28(100.0)	25(100.0)	2(100.0)
血液およびリンパ系障害	28(100.0)	22(88.0)	2(100.0)
貧血*	9(32.1)	9(36.0)	0
再生不良性貧血	1(3.6)	0	0
好酸球増加症	0	0	1(50.0)
発熱性好中球減少症	0	2(8.0)	1(50.0)
白血球減少症*	17(60.7)	6(24.0)	1(50.0)
リンパ球減少症*	14(50.0)	2(8.0)	0
好中球減少症*	20(71.4)	10(40.0)	1(50.0)
血小板減少症*	27(96.4)	18(72.0)	1(50.0)
心臓障害	5(17.9)	1(4.0)	1(50.0)
不安定狭心症	1(3.6)	0	0
不整脈	1(3.6)	0	0
心房細動	1(3.6)	1(4.0)	0
動悸	3(10.7)	0	0
心嚢液貯留	0	0	1(50.0)
耳および迷路障害	0	1(4.0)	1(50.0)
耳痛	0	0	1(50.0)
回転性めまい	0	1(4.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
眼障害	4(14.3)	1(4.0)	0
白内障	0	1(4.0)	0
結膜出血	1(3.6)	0	0
ドライアイ	1(3.6)	0	0
角膜炎	1(3.6)	0	0
霧視	1(3.6)	0	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.

n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28) n (%)	ECOG Status: 1 (N=25) n (%)	ECOG Status: 2 (N=2) n (%)
胃腸障害	19(67.9)	11(44.0)	2(100.0)
腹部不快感	1(3.6)	0	0
腹痛	2(7.1)	1(4.0)	0
上腹部痛	2(7.1)	0	0
肛門出血	1(3.6)	0	0
便秘	1(3.6)	0	0
齲歯	2(7.1)	0	0
下痢	9(32.1)	6(24.0)	2(100.0)
消化不良	0	1(4.0)	0
心窩部不快感	1(3.6)	0	0
胃潰瘍	1(3.6)	0	0
胃炎	0	1(4.0)	0
痔出血	1(3.6)	0	0
悪心	6(21.4)	4(16.0)	2(100.0)
口腔粘膜血腫	0	1(4.0)	0
口内炎	0	1(4.0)	1(50.0)
歯痛	1(3.6)	0	0
嘔吐	1(3.6)	1(4.0)	1(50.0)

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28) n (%)	ECOG Status: 1 (N=25) n (%)	ECOG Status: 2 (N=2) n (%)
一般・全身障害および投与部位の状態	16(57.1)	9(36.0)	2(100.0)
無力症	0	1(4.0)	1(50.0)
カテーテル留置部位腫脹	1(3.6)	0	0
胸部不快感	1(3.6)	0	0
胸痛	1(3.6)	0	0
溢出	1(3.6)	0	0
疲労	3(10.7)	3(12.0)	0
歩行障害	1(3.6)	0	0
インフルエンザ様疾患	1(3.6)	1(4.0)	0
倦怠感	6(21.4)	1(4.0)	1(50.0)
末梢性浮腫	2(7.1)	1(4.0)	1(50.0)
発熱	5(17.9)	5(20.0)	1(50.0)
口渇	1(3.6)	0	0
免疫系障害	0	1(4.0)	0
薬物過敏症	0	1(4.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
感染症および寄生虫症	11(39.3)	8(32.0)	0
気管支炎	1(3.6)	1(4.0)	0
結膜炎	2(7.1)	0	0
膀胱炎	0	1(4.0)	0
サイトメガロウイルス感染	0	1(4.0)	0
感染性小腸結腸炎	0	1(4.0)	0
胃腸炎	1(3.6)	0	0
帯状疱疹	0	1(4.0)	0
膿痂疹	1(3.6)	0	0
インフルエンザ	1(3.6)	1(4.0)	0
上咽頭炎	2(7.1)	0	0
咽頭炎	2(7.1)	1(4.0)	0
ニューモシスチス・イロベチイ肺炎	0	1(4.0)	0
肺炎	0	1(4.0)	0
鼻炎	1(3.6)	0	0
ブドウ球菌皮膚感染	0	1(4.0)	0
上気道感染	2(7.1)	2(8.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
傷害、中毒および処置合併症	1(3.6)	2(8.0)	0
胃瘻管部合併症	0	1(4.0)	0
爪損傷	1(3.6)	0	0
処置による疼痛	0	1(4.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
臨床検査	15(53.6)	9(36.0)	1(50.0)
アラニンアミノトランスフェラーゼ増加	2(7.1)	2(8.0)	1(50.0)
アスパラギン酸アミノトランスフェラーゼ増加	5(17.9)	1(4.0)	1(50.0)
血中アルカリホスファターゼ増加	5(17.9)	3(12.0)	0
血中コレステロール増加	1(3.6)	0	0
血中クレアチンホスホキナーゼＭＢ増加	1(3.6)	0	0
血中クレアチンホスホキナーゼ増加	1(3.6)	0	0
血中クレアチニン増加	1(3.6)	1(4.0)	0
血中免疫グロブリンＡ減少	1(3.6)	0	0
尿中血陽性	1(3.6)	0	0
脳性ナトリウム利尿ペプチド増加	2(7.1)	0	0
Ｃ－反応性蛋白増加	2(7.1)	1(4.0)	0
心胸郭比増加	1(3.6)	0	0
心電図ＱＴ延長	2(7.1)	3(12.0)	0
心電図Ｔ波逆転	1(3.6)	0	0
好酸球数増加	0	2(8.0)	0
γ－グルタミルトランスフェラーゼ増加	4(14.3)	3(12.0)	1(50.0)
リパーゼ増加	1(3.6)	0	0
体重減少	5(17.9)	1(4.0)	0
体重増加	1(3.6)	0	0

Source: Listing 16 2.6.1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.

n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28) n (%)	ECOG Status: 1 (N=25) n (%)	ECOG Status: 2 (N=2) n (%)
代謝および栄養障害	12(42.9)	11(44.0)	2(100.0)
食欲減退	6(21.4)	6(24.0)	1(50.0)
糖尿病	0	1(4.0)	0
高カリウム血症	0	1(4.0)	0
高マグネシウム血症	0	1(4.0)	0
高トリグリセリド血症	1(3.6)	0	0
低アルブミン血症	2(7.1)	2(8.0)	1(50.0)
低カルシウム血症	1(3.6)	2(8.0)	0
低カリウム血症	3(10.7)	2(8.0)	0
低ナトリウム血症	1(3.6)	0	1(50.0)
低蛋白血症	0	1(4.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28) n (%)	ECOG Status: 1 (N=25) n (%)	ECOG Status: 2 (N=2) n (%)
筋骨格系および結合組織障害	12(42.9)	6(24.0)	1(50.0)
関節痛	0	1(4.0)	0
関節炎	1(3.6)	0	0
背部痛	3(10.7)	1(4.0)	1(50.0)
出血性関節症	1(3.6)	0	0
関節腫脹	1(3.6)	0	0
筋肉疲労	1(3.6)	1(4.0)	0
筋痙縮	5(17.9)	0	0
筋力低下	0	1(4.0)	0
筋骨格硬直	1(3.6)	0	0
筋肉痛	2(7.1)	0	0
頚部痛	0	1(4.0)	0
四肢痛	1(3.6)	0	0
肩回旋筋腱板症候群	1(3.6)	0	0
腱炎	0	1(4.0)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3(10.7)	1(4.0)	0
末梢性Ｔ細胞性リンパ腫、組織型不明	1(3.6)	0	0
皮膚乳頭腫	1(3.6)	0	0
腫瘍疼痛	1(3.6)	1(4.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
神経系障害	6(21.4)	2(8.0)	1(50.0)
浮動性めまい	1(3.6)	0	0
味覚異常	1(3.6)	1(4.0)	0
頭痛	5(17.9)	0	1(50.0)
感覚鈍麻	1(3.6)	0	0
末梢性感覚ニューロパチー	0	1(4.0)	0
失神寸前の状態	1(3.6)	0	0
精神障害	1(3.6)	3(12.0)	1(50.0)
譫妄	0	1(4.0)	1(50.0)
不眠症	1(3.6)	3(12.0)	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
腎および尿路障害	1(3.6)	1(4.0)	0
急性腎障害	0	1(4.0)	0
血尿	1(3.6)	0	0
蛋白尿	1(3.6)	0	0
生殖系および乳房障害	0	1(4.0)	0
陰嚢浮腫	0	1(4.0)	0
呼吸器、胸郭および縦隔障害	8(28.6)	11(44.0)	2(100.0)
咳嗽	2(7.1)	3(12.0)	1(50.0)
咽頭知覚不全	1(3.6)	0	0
発声障害	1(3.6)	0	0
呼吸困難	2(7.1)	1(4.0)	1(50.0)
労作性呼吸困難	0	1(4.0)	0
鼻出血	1(3.6)	1(4.0)	0
しゃっくり	0	1(4.0)	0
間質性肺疾患	0	1(4.0)	0
口腔咽頭痛	1(3.6)	2(8.0)	0
胸水	0	1(4.0)	1(50.0)
肺臓炎	1(3.6)	3(12.0)	0
湿性咳嗽	0	0	1(50.0)
アレルギー性鼻炎	0	1(4.0)	0
鼻漏	0	1(4.0)	0
上気道の炎症	1(3.6)	0	0

Source: Listing 16.2.6 1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	ECOG Status: 0 (N=28)	ECOG Status: 1 (N=25)	ECOG Status: 2 (N=2)
	n (%)	n (%)	n (%)
皮膚および皮下組織障害	12(42.9)	9(36.0)	2(100.0)
褥瘡性潰瘍	0	0	1(50.0)
ざ瘡様皮膚炎	1(3.6)	0	0
全身性剥脱性皮膚炎	1(3.6)	0	0
皮膚乾燥	0	1(4.0)	0
皮脂欠乏性湿疹	1(3.6)	0	0
紅斑	1(3.6)	1(4.0)	0
多形紅斑	0	1(4.0)	0
全身紅斑	1(3.6)	0	0
皮膚疼痛	0	1(4.0)	0
点状出血	0	1(4.0)	0
色素沈着障害	1(3.6)	0	0
全身性そう痒症	2(7.1)	0	0
紫斑	2(7.1)	0	0
発疹	1(3.6)	4(16.0)	0
斑状丘疹状皮疹	2(7.1)	0	0
そう痒性皮疹	1(3.6)	0	0
蕁麻疹	1(3.6)	3(12.0)	1(50.0)
血管障害	0	3(12.0)	0
深部静脈血栓症	0	1(4.0)	0
低血圧	0	1(4.0)	0
末梢動脈閉塞性疾患	0	1(4.0)	0

Source: Listing 16 2.6.1 and 16.2.11.1

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by ECOG performance status at baseline.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-91　前治療のレジメン数別（3 レジメン未満、3 レジメン以上）の有害事象の概要（210 試験）（安全性解析対象集団）

Number of Regimens Before the Study Treatment: Less than 3 regimens

Description	40 mg (N=11)
	n (%)
Number of subjects with	
At least one TEAE	11 (100.0%)
At least one TEAE related to the study drug	11 (100.0%)
At least one serious TEAE	5 (45.5%)
At least one serious TEAE related to the study drug	5 (45.5%)
At least one TEAE leading to dose reduction or interruption	7 (63.6%)
At least one TEAE leading to study drug discontinuation	3 (27.3%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	8 (72.7%)
At least one TEAE with grade 3 or higher and related to the study drug	8 (72.7%)

Source: Listing 16 2.6.1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Number of Regimens Before the Study Treatment: 3 or more regimens

Description	40 mg (N=12) n (%)
Number of subjects with	
At least one TEAE	12 (100.0%)
At least one TEAE related to the study drug	12 (100.0%)
At least one serious TEAE	2 (16.7%)
At least one serious TEAE related to the study drug	1 (8.3%)
At least one TEAE leading to dose reduction or interruption	9 (75.0%)
At least one TEAE leading to study drug discontinuation	6 (50.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	10 (83.3%)
At least one TEAE with grade 3 or higher and related to the study drug	10 (83.3%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-92　前治療のレジメン数別（3 レジメン未満、3 レジメン以上）の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	Less than 3 regimens (N=11) n (%)	3 or more regimens (N=12) n (%)
Number of subjects with at least one TEAE	11(100.0%)	12(100.0%)
血液およびリンパ系障害	8(72.7%)	11(91.7%)
貧血*	2(18.2%)	7(58.3%)
好酸球増加症	1(9.1%)	0
発熱性好中球減少症	0	1(8.3%)
白血球減少症*	3(27.3%)	7(58.3%)
リンパ球減少症*	0	2(16.7%)
好中球減少症*	5(45.5%)	7(58.3%)
血小板減少症*	8(72.7%)	10(83.3%)
心臓障害	2(18.2%)	0
第一度房室ブロック	1(9.1%)	0
動悸	1(9.1%)	0
眼障害	1(9.1%)	0
ドライアイ	1(9.1%)	0
胃腸障害	4(36.4%)	5(41.7%)
腹痛	1(9.1%)	2(16.7%)
下痢	2(18.2%)	4(33.3%)
悪心	1(9.1%)	2(16.7%)
口内炎	1(9.1%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=11)	3 or more regimens (N=12)
	n (%)	n (%)
一般・全身障害および投与部位の状態	6(54.5%)	7(58.3%)
悪寒	0	1(8.3%)
疲労	2(18.2%)	1(8.3%)
倦怠感	4(36.4%)	3(25.0%)
非心臓性胸痛	0	1(8.3%)
末梢性浮腫	1(9.1%)	0
発熱	1(9.1%)	2(16.7%)
感染症および寄生虫症	4(36.4%)	3(25.0%)
細菌感染	1(9.1%)	0
サイトメガロウイルス感染	0	1(8.3%)
医療機器関連感染	0	1(8.3%)
麦粒腫	1(9.1%)	0
口腔カンジダ症	1(9.1%)	0
ニューモシスチス・イロベチイ肺炎	1(9.1%)	0
皮膚感染	0	1(8.3%)
扁桃炎	0	1(8.3%)
上気道感染	1(9.1%)	0
尿路感染	1(9.1%)	0
傷害、中毒および処置合併症	1(9.1%)	0
挫傷	1(9.1%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=11) n (%)	3 or more regimens (N=12) n (%)
臨床検査	8(72.7%)	2(16.7%)
アラニンアミノトランスフェラーゼ増加	1(9.1%)	0
アスパラギン酸アミノトランスフェラーゼ増加	2(18.2%)	0
血中アルカリホスファターゼ増加	1(9.1%)	0
血中乳酸脱水素酵素増加	1(9.1%)	0
脳性ナトリウム利尿ペプチド増加	1(9.1%)	0
好酸球数増加	1(9.1%)	0
γ－グルタミルトランスフェラーゼ増加	2(18.2%)	0
リパーゼ増加	1(9.1%)	0
体重減少	2(18.2%)	2(16.7%)
代謝および栄養障害	7(63.6%)	6(50.0%)
食欲減退	5(45.5%)	3(25.0%)
高カルシウム血症	1(9.1%)	0
低アルブミン血症	1(9.1%)	2(16.7%)
低カリウム血症	1(9.1%)	0
低ナトリウム血症	0	2(16.7%)
低リン酸血症	1(9.1%)	0
筋骨格系および結合組織障害	5(45.5%)	2(16.7%)
関節痛	0	1(8.3%)
背部痛	3(27.3%)	1(8.3%)
脊椎すべり症	1(9.1%)	0
尺骨突き上げ症候群	1(9.1%)	0

Source: Listing 16 2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=11)	3 or more regimens (N=12)
	n (%)	n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1(8.3%)
腫瘍疼痛	0	1(8.3%)
神経系障害	5(45.5%)	4(33.3%)
味覚消失	1(9.1%)	0
認知障害	0	1(8.3%)
浮動性めまい	1(9.1%)	0
味覚異常	2(18.2%)	2(16.7%)
頭痛	1(9.1%)	1(8.3%)
傾眠	1(9.1%)	0
腎および尿路障害	0	1(8.3%)
尿瘻	0	1(8.3%)
呼吸器、胸郭および縦隔障害	2(18.2%)	2(16.7%)
急性呼吸不全	0	1(8.3%)
鼻出血	1(9.1%)	0
間質性肺疾患	0	1(8.3%)
口腔咽頭痛	1(9.1%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.

n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=11)	3 or more regimens (N=12)
	n (%)	n (%)
皮膚および皮下組織障害	4(36.4%)	4(33.3%)
接触皮膚炎	0	1(8.3%)
湿疹	1(9.1%)	0
紅斑	0	1(8.3%)
多形紅斑	1(9.1%)	0
光線過敏性反応	1(9.1%)	0
そう痒症	1(9.1%)	0
発疹	1(9.1%)	0
皮膚剥脱	0	1(8.3%)
皮膚潰瘍	0	1(8.3%)
血管障害	0	1(8.3%)
高血圧	0	1(8.3%)

Source: Listing 16 2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-93　前治療のレジメン数別（3 レジメン未満、3 レジメン以上）の有害事象の概要（203 試験）（安全性解析対象集団）

Number of Regimens Before the Study Treatment: Less than 3 regimens

Description	40 mg (N=35)
	n (%)
Number of subjects with	
At least one TEAE	35 (100.0)
At least one TEAE related to the study drug	32 (91.4)
At least one serious TEAE	10 (28.6)
At least one serious TEAE related to the study drug	7 (20.0)
At least one TEAE leading to dose reduction or interruption	25 (71.4)
At least one TEAE leading to study drug discontinuation	8 (22.9)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	31 (88.6)
At least one TEAE with grade 3 or higher and related to the study drug	28 (80.0)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Number of Regimens Before the Study Treatment: 3 or more regimens

Description	40 mg (N=20) n (%)
Number of subjects with	
At least one TEAE	20 (100.0)
At least one TEAE related to the study drug	19 (95.0)
At least one serious TEAE	4 (20.0)
At least one serious TEAE related to the study drug	3 (15.0)
At least one TEAE leading to dose reduction or interruption	15 (75.0)
At least one TEAE leading to study drug discontinuation	10 (50.0)
At least one TEAE leading to death	1 (5.0)
At least one TEAE with grade 3 or higher	15 (75.0)
At least one TEAE with grade 3 or higher and related to the study drug	14 (70.0)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-94　前治療のレジメン数別（3 レジメン未満、3 レジメン以上）の有害事象の発現割合（203 試験）（安全性解析対象集団）

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
Number of subjects with at least one TEAE	35(100.0)	20(100.0)
血液およびリンパ系障害	34(97.1)	18(90.0)
貧血*	13(37.1)	5(25.0)
再生不良性貧血	0	1(5.0)
好酸球増加症	1(2.9)	0
発熱性好中球減少症	2(5.7)	1(5.0)
白血球減少症*	15(42.9)	9(45.0)
リンパ球減少症*	11(31.4)	5(25.0)
好中球減少症*	20(57.1)	11(55.0)
血小板減少症*	29(82.9)	17(85.0)
心臓障害	3(8.6)	4(20.0)
不安定狭心症	0	1(5.0)
不整脈	0	1(5.0)
心房細動	0	2(10.0)
動悸	2(5.7)	1(5.0)
心嚢液貯留	1(2.9)	0
耳および迷路障害	1(2.9)	1(5.0)
耳痛	1(2.9)	0
回転性めまい	0	1(5.0)

Source: Listing 16 2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
眼障害	4(11.4)	1(5.0)
白内障	1(2.9)	0
結膜出血	0	1(5.0)
ドライアイ	1(2.9)	0
角膜炎	1(2.9)	0
霧視	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.

n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
胃腸障害	23(65.7)	9(45.0)
腹部不快感	0	1(5.0)
腹痛	2(5.7)	1(5.0)
上腹部痛	1(2.9)	1(5.0)
肛門出血	1(2.9)	0
便秘	1(2.9)	0
齲歯	2(5.7)	0
下痢	13(37.1)	4(20.0)
消化不良	1(2.9)	0
心窩部不快感	1(2.9)	0
胃潰瘍	1(2.9)	0
胃炎	0	1(5.0)
痔出血	0	1(5.0)
悪心	8(22.9)	4(20.0)
口腔粘膜血腫	1(2.9)	0
口内炎	2(5.7)	0
歯痛	1(2.9)	0
嘔吐	2(5.7)	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
一般・全身障害および投与部位の状態	17(48.6)	10(50.0)
無力症	1(2.9)	1(5.0)
カテーテル留置部位腫脹	1(2.9)	0
胸部不快感	1(2.9)	0
胸痛	0	1(5.0)
溢出	1(2.9)	0
疲労	2(5.7)	4(20.0)
歩行障害	1(2.9)	0
インフルエンザ様疾患	2(5.7)	0
倦怠感	5(14.3)	3(15.0)
末梢性浮腫	4(11.4)	0
発熱	7(20.0)	4(20.0)
口渇	1(2.9)	0
免疫系障害	1(2.9)	0
薬物過敏症	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35)	3 or more regimens (N=20)
	n (%)	n (%)
感染症および寄生虫症	15(42.9)	4(20.0)
気管支炎	2(5.7)	0
結膜炎	2(5.7)	0
膀胱炎	1(2.9)	0
サイトメガロウイルス感染	1(2.9)	0
感染性小腸結腸炎	0	1(5.0)
胃腸炎	1(2.9)	0
帯状疱疹	1(2.9)	0
膿痂疹	1(2.9)	0
インフルエンザ	1(2.9)	1(5.0)
上咽頭炎	1(2.9)	1(5.0)
咽頭炎	3(8.6)	0
ニューモシスチス・イロベチイ肺炎	1(2.9)	0
肺炎	0	1(5.0)
鼻炎	1(2.9)	0
ブドウ球菌皮膚感染	0	1(5.0)
上気道感染	2(5.7)	2(10.0)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
傷害、中毒および処置合併症	2(5.7)	1(5.0)
胃瘻管部合併症	0	1(5.0)
爪損傷	1(2.9)	0
処置による疼痛	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
臨床検査	17(48.6)	8(40.0)
アラニンアミノトランスフェラーゼ増加	4(11.4)	1(5.0)
アスパラギン酸アミノトランスフェラーゼ増加	7(20.0)	0
血中アルカリホスファターゼ増加	5(14.3)	3(15.0)
血中コレステロール増加	1(2.9)	0
血中クレアチンホスホキナーゼＭＢ増加	1(2.9)	0
血中クレアチンホスホキナーゼ増加	1(2.9)	0
血中クレアチニン増加	2(5.7)	0
血中免疫グロブリンＡ減少	0	1(5.0)
尿中血陽性	1(2.9)	0
脳性ナトリウム利尿ペプチド増加	0	2(10.0)
Ｃ－反応性蛋白増加	2(5.7)	1(5.0)
心胸郭比増加	0	1(5.0)
心電図ＱＴ延長	3(8.6)	2(10.0)
心電図Ｔ波逆転	1(2.9)	0
好酸球数増加	1(2.9)	1(5.0)
γ－グルタミルトランスフェラーゼ増加	6(17.1)	2(10.0)
リパーゼ増加	0	1(5.0)
体重減少	5(14.3)	1(5.0)
体重増加	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
代謝および栄養障害	17(48.6)	8(40.0)
食欲減退	10(28.6)	3(15.0)
糖尿病	1(2.9)	0
高カリウム血症	0	1(5.0)
高マグネシウム血症	0	1(5.0)
高トリグリセリド血症	1(2.9)	0
低アルブミン血症	3(8.6)	2(10.0)
低カルシウム血症	2(5.7)	1(5.0)
低カリウム血症	2(5.7)	3(15.0)
低ナトリウム血症	2(5.7)	0
低蛋白血症	0	1(5.0)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
筋骨格系および結合組織障害	14(40.0)	5(25.0)
関節痛	1(2.9)	0
関節炎	1(2.9)	0
背部痛	3(8.6)	2(10.0)
出血性関節症	1(2.9)	0
関節腫脹	1(2.9)	0
筋肉疲労	1(2.9)	1(5.0)
筋痙縮	4(11.4)	1(5.0)
筋力低下	1(2.9)	0
筋骨格硬直	1(2.9)	0
筋肉痛	1(2.9)	1(5.0)
頚部痛	1(2.9)	0
四肢痛	1(2.9)	0
肩回旋筋腱板症候群	1(2.9)	0
腱炎	1(2.9)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4(11.4)	0
末梢性Ｔ細胞性リンパ腫、組織型不明	1(2.9)	0
皮膚乳頭腫	1(2.9)	0
腫瘍疼痛	2(5.7)	0

Source: Listing 16.2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
神経系障害	6(17.1)	3(15.0)
浮動性めまい	0	1(5.0)
味覚異常	1(2.9)	1(5.0)
頭痛	5(14.3)	1(5.0)
感覚鈍麻	0	1(5.0)
末梢性感覚ニューロパチー	1(2.9)	0
失神寸前の状態	0	1(5.0)
精神障害	4(11.4)	1(5.0)
譫妄	2(5.7)	0
不眠症	3(8.6)	1(5.0)

Source: Listing 16.2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35) n (%)	3 or more regimens (N=20) n (%)
腎および尿路障害	1(2.9)	1(5.0)
急性腎障害	0	1(5.0)
血尿	1(2.9)	0
蛋白尿	1(2.9)	0
生殖系および乳房障害	0	1(5.0)
陰嚢浮腫	0	1(5.0)
呼吸器、胸郭および縦隔障害	18(51.4)	3(15.0)
咳嗽	6(17.1)	0
咽頭知覚不全	1(2.9)	0
発声障害	1(2.9)	0
呼吸困難	3(8.6)	1(5.0)
労作性呼吸困難	1(2.9)	0
鼻出血	2(5.7)	0
しゃっくり	1(2.9)	0
間質性肺疾患	1(2.9)	0
口腔咽頭痛	2(5.7)	1(5.0)
胸水	1(2.9)	1(5.0)
肺臓炎	2(5.7)	2(10.0)
湿性咳嗽	1(2.9)	0
アレルギー性鼻炎	1(2.9)	0
鼻漏	1(2.9)	0
上気道の炎症	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

System organ class Preferred term	Less than 3 regimens (N=35)	3 or more regimens (N=20)
	n (%)	n (%)
皮膚および皮下組織障害	17(48.6)	6(30.0)
褥瘡性潰瘍	1(2.9)	0
ざ瘡様皮膚炎	1(2.9)	0
全身性剥脱性皮膚炎	1(2.9)	0
皮膚乾燥	0	1(5.0)
皮脂欠乏性湿疹	1(2.9)	0
紅斑	2(5.7)	0
多形紅斑	0	1(5.0)
全身紅斑	0	1(5.0)
皮膚疼痛	1(2.9)	0
点状出血	1(2.9)	0
色素沈着障害	1(2.9)	0
全身性そう痒症	2(5.7)	0
紫斑	2(5.7)	0
発疹	5(14.3)	0
斑状丘疹状皮疹	1(2.9)	1(5.0)
そう痒性皮疹	0	1(5.0)
蕁麻疹	4(11.4)	1(5.0)
血管障害	2(5.7)	1(5.0)
深部静脈血栓症	1(2.9)	0
低血圧	0	1(5.0)
末梢動脈閉塞性疾患	1(2.9)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the number of regimens before the start of study treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.

表 2.7.4.7-95　直近のがん治療の種類別［化学療法（モガムリズマブ及びレナリドミドを除く）、モガムリズマブの併用療法、モガムリズマブの単独療法、レナリドミドの単独療法］の有害事象の概要（210 試験）（安全性解析対象集団）

Last Immediate Prior Cancer Therapy: Chemotherapy (excluding mogamulizumab and lenalidomide)

Description	40 mg (N=6) n (%)
Number of subjects with	
At least one TEAE	6 (100.0%)
At least one TEAE related to the study drug	6 (100.0%)
At least one serious TEAE	1 (16.7%)
At least one serious TEAE related to the study drug	1 (16.7%)
At least one TEAE leading to dose reduction or interruption	6 (100.0%)
At least one TEAE leading to study drug discontinuation	3 (50.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	6 (100.0%)
At least one TEAE with grade 3 or higher and related to the study drug	6 (100.0%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Last Immediate Prior Cancer Therapy: mogamulizumab monotherapy

Description	40 mg (N=6) n (%)
Number of subjects with	
At least one TEAE	6 (100.0%)
At least one TEAE related to the study drug	6 (100.0%)
At least one serious TEAE	0 (0.0%)
At least one serious TEAE related to the study drug	0 (0.0%)
At least one TEAE leading to dose reduction or interruption	3 (50.0%)
At least one TEAE leading to study drug discontinuation	1 (16.7%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	4 (66.7%)
At least one TEAE with grade 3 or higher and related to the study drug	4 (66.7%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Last Immediate Prior Cancer Therapy: mogamulizumab combination therapy

Description	40 mg (N=8) n (%)
Number of subjects with	
At least one TEAE	8 (100.0%)
At least one TEAE related to the study drug	8 (100.0%)
At least one serious TEAE	6 (75.0%)
At least one serious TEAE related to the study drug	5 (62.5%)
At least one TEAE leading to dose reduction or interruption	5 (62.5%)
At least one TEAE leading to study drug discontinuation	4 (50.0%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	6 (75.0%)
At least one TEAE with grade 3 or higher and related to the study drug	6 (75.0%)

Source: Listing 16.2.6.1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Last Immediate Prior Cancer Therapy: lenalidomide monotherapy

Description	40 mg (N=3) n (%)
Number of subjects with	
At least one TEAE	3 (100.0%)
At least one TEAE related to the study drug	3 (100.0%)
At least one serious TEAE	0 (0.0%)
At least one serious TEAE related to the study drug	0 (0.0%)
At least one TEAE leading to dose reduction or interruption	2 (66.7%)
At least one TEAE leading to study drug discontinuation	1 (33.3%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	2 (66.7%)
At least one TEAE with grade 3 or higher and related to the study drug	2 (66.7%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy.
n = number of subjects; % = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-96　直近のがん治療の種類別［化学療法（モガムリズマブ及びレナリドミドを除く）、モガムリズマブの併用療法、モガムリズマブの単独療法、レナリドミドの単独療法］の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	Chemo Ex Mo Le (N=6)	Chemo Mo Mono (N=6)	Chemo Mo Comb (N=8)	Chemo Lena (N=3)
	n (%)	n (%)	n (%)	n (%)
Number of subjects with at least one TEAE	6(100.0%)	6(100.0%)	8(100.0%)	3(100.0%)
血液およびリンパ系障害	6(100.0%)	4(66.7%)	7(87.5%)	2(66.7%)
貧血*	3(50.0%)	2(33.3%)	3(37.5%)	1(33.3%)
好酸球増加症	0	0	1(12.5%)	0
発熱性好中球減少症	1(16.7%)	0	0	0
白血球減少症*	5(83.3%)	2(33.3%)	2(25.0%)	1(33.3%)
リンパ球減少症*	0	1(16.7%)	0	1(33.3%)
好中球減少症*	4(66.7%)	2(33.3%)	4(50.0%)	2(66.7%)
血小板減少症*	6(100.0%)	3(50.0%)	7(87.5%)	2(66.7%)
心臓障害	0	0	2(25.0%)	0
第一度房室ブロック	0	0	1(12.5%)	0
動悸	0	0	1(12.5%)	0
眼障害	0	0	1(12.5%)	0
ドライアイ	0	0	1(12.5%)	0
胃腸障害	1(16.7%)	1(16.7%)	5(62.5%)	2(66.7%)
腹痛	1(16.7%)	0	1(12.5%)	1(33.3%)
下痢	0	1(16.7%)	3(37.5%)	2(66.7%)
悪心	0	0	2(25.0%)	1(33.3%)
口内炎	0	0	1(12.5%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy; n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

Chemo Ex Mo Le = Chemotherapy (excluding mogamulizumab and lenalidomide); Chemo Mo Mono = mogamulizumab monotherapy; Chemo Mo Comb = mogamulizumab combination therapy; Chemo Lena = lenalidomide.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Chemo Ex Mo Le (N=6) n (%)	Chemo Mo Mono (N=6) n (%)	Chemo Mo Comb (N=8) n (%)	Chemo Lena (N=3) n (%)
一般・全身障害および投与部位の状態	3(50.0%)	2(33.3%)	6(75.0%)	2(66.7%)
悪寒	0	0	0	1(33.3%)
疲労	0	2(33.3%)	1(12.5%)	0
倦怠感	1(16.7%)	1(16.7%)	3(37.5%)	2(66.7%)
非心臓性胸痛	1(16.7%)	0	0	0
末梢性浮腫	0	0	1(12.5%)	0
発熱	1(16.7%)	0	2(25.0%)	0
感染症および寄生虫症	2(33.3%)	1(16.7%)	3(37.5%)	1(33.3%)
細菌感染	0	1(16.7%)	0	0
サイトメガロウイルス感染	1(16.7%)	0	0	0
医療機器関連感染	1(16.7%)	0	0	0
麦粒腫	0	0	1(12.5%)	0
口腔カンジダ症	0	0	1(12.5%)	0
ニューモシスチス・イロベチイ肺炎	0	0	1(12.5%)	0
皮膚感染	1(16.7%)	0	0	0
扁桃炎	0	0	0	1(33.3%)
上気道感染	0	0	1(12.5%)	0
尿路感染	0	0	1(12.5%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy; n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

Chemo Ex Mo Le = Chemotherapy (excluding mogamulizumab and lenalidomide); Chemo Mo Mono = mogamulizumab monotherapy; Chemo Mo Comb = mogamulizumab combination therapy; Chemo Lena = lenalidomide.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Chemo Ex Mo Le (N=6)	Chemo Mo Mono (N=6)	Chemo Mo Comb (N=8)	Chemo Lena (N=3)
	n (%)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症	0	0	1(12.5%)	0
挫傷	0	0	1(12.5%)	0
臨床検査	2(33.3%)	1(16.7%)	6(75.0%)	1(33.3%)
アラニンアミノトランスフェラーゼ増加	0	0	1(12.5%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1(16.7%)	0	1(12.5%)	0
血中アルカリホスファターゼ増加	0	0	1(12.5%)	0
血中乳酸脱水素酵素増加	0	0	1(12.5%)	0
脳性ナトリウム利尿ペプチド増加	0	0	1(12.5%)	0
好酸球数増加	0	0	1(12.5%)	0
γーグルタミルトランスフェラーゼ増加	1(16.7%)	0	1(12.5%)	0
リパーゼ増加	0	1(16.7%)	0	0
体重減少	2(33.3%)	0	1(12.5%)	1(33.3%)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy; n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

Chemo Ex Mo Le = Chemotherapy (excluding mogamulizumab and lenalidomide); Chemo Mo Mono = mogamulizumab monotherapy; Chemo Mo Comb = mogamulizumab combination therapy; Chemo Lena = lenalidomide.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Chemo Ex Mo Le (N=6)	Chemo Mo Mono (N=6)	Chemo Mo Comb (N=8)	Chemo Lena (N=3)
	n (%)	n (%)	n (%)	n (%)
代謝および栄養障害	3(50.0%)	3(50.0%)	5(62.5%)	2(66.7%)
食欲減退	2(33.3%)	2(33.3%)	3(37.5%)	1(33.3%)
高カルシウム血症	0	0	1(12.5%)	0
低アルブミン血症	1(16.7%)	2(33.3%)	0	0
低カリウム血症	0	0	1(12.5%)	0
低ナトリウム血症	1(16.7%)	0	0	1(33.3%)
低リン酸血症	0	0	1(12.5%)	0
筋骨格系および結合組織障害	0	1(16.7%)	6(75.0%)	0
関節痛	0	1(16.7%)	0	0
背部痛	0	0	4(50.0%)	0
脊椎すべり症	0	0	1(12.5%)	0
尺骨突き上げ症候群	0	0	1(12.5%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	1(33.3%)
腫瘍疼痛	0	0	0	1(33.3%)

Source: Listing 16 2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy; n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

Chemo Ex Mo Le = Chemotherapy (excluding mogamulizumab and lenalidomide); Chemo Mo Mono = mogamulizumab monotherapy; Chemo Mo Comb = mogamulizumab combination therapy; Chemo Lena = lenalidomide.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Chemo Ex Mo Le (N=6)	Chemo Mo Mono (N=6)	Chemo Mo Comb (N=8)	Chemo Lena (N=3)
	n (%)	n (%)	n (%)	n (%)
神経系障害	1(16.7%)	1(16.7%)	4(50.0%)	3(100.0%)
味覚消失	0	0	1(12.5%)	0
認知障害	0	0	0	1(33.3%)
浮動性めまい	0	0	1(12.5%)	0
味覚異常	1(16.7%)	0	2(25.0%)	1(33.3%)
頭痛	0	0	1(12.5%)	1(33.3%)
傾眠	0	1(16.7%)	0	0
腎および尿路障害	0	0	0	1(33.3%)
尿瘻	0	0	0	1(33.3%)
呼吸器、胸郭および縦隔障害	1(16.7%)	0	3(37.5%)	0
急性呼吸不全	0	0	1(12.5%)	0
鼻出血	0	0	1(12.5%)	0
間質性肺疾患	1(16.7%)	0	0	0
口腔咽頭痛	0	0	1(12.5%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy; n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

Chemo Ex Mo Le = Chemotherapy (excluding mogamulizumab and lenalidomide); Chemo Mo Mono = mogamulizumab monotherapy; Chemo Mo Comb = mogamulizumab combination therapy; Chemo Lena = lenalidomide.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

System organ class Preferred term	Chemo Ex Mo Le (N=6) n (%)	Chemo Mo Mono (N=6) n (%)	Chemo Mo Comb (N=8) n (%)	Chemo Lena (N=3) n (%)
皮膚および皮下組織障害	2(33.3%)	1(16.7%)	5(62.5%)	0
接触皮膚炎	1(16.7%)	0	0	0
湿疹	0	0	1(12.5%)	0
紅斑	0	0	1(12.5%)	0
多形紅斑	0	0	1(12.5%)	0
光線過敏性反応	0	0	1(12.5%)	0
そう痒症	0	0	1(12.5%)	0
発疹	0	0	1(12.5%)	0
皮膚剥脱	0	1(16.7%)	0	0
皮膚潰瘍	1(16.7%)	0	0	0
血管障害	1(16.7%)	0	0	0
高血圧	1(16.7%)	0	0	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.

N = number of subjects in the Safety Analysis Set by last immediate prior cancer therapy; n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.

TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.

Chemo Ex Mo Le = Chemotherapy (excluding mogamulizumab and lenalidomide); Chemo Mo Mono = mogamulizumab monotherapy; Chemo Mo Comb = mogamulizumab combination therapy; Chemo Lena = lenalidomide.

* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.

TEAE of overdose is not included in this analysis.

表 2.7.4.7-97　直近のがん治療からの期間別（3 ヵ月未満、3 ヵ月以上）の有害事象の概要（210 試験）（安全性解析対象集団）

Days from End of the Last Immediate Previous Treatment: < 3 months

Description	40 mg (N=12)
	n (%)
Number of subjects with	
At least one TEAE	12 (100.0%)
At least one TEAE related to the study drug	12 (100.0%)
At least one serious TEAE	3 (25.0%)
At least one serious TEAE related to the study drug	2 (16.7%)
At least one TEAE leading to dose reduction or interruption	7 (58.3%)
At least one TEAE leading to study drug discontinuation	4 (33.3%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	9 (75.0%)
At least one TEAE with grade 3 or higher and related to the study drug	9 (75.0%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment; n = number of subjects;
% = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

Days from End of the Last Immediate Previous Treatment: >=3 months

Description	40 mg (N=11) n (%)
Number of subjects with	
At least one TEAE	11 (100.0%)
At least one TEAE related to the study drug	11 (100.0%)
At least one serious TEAE	4 (36.4%)
At least one serious TEAE related to the study drug	4 (36.4%)
At least one TEAE leading to dose reduction or interruption	9 (81.8%)
At least one TEAE leading to study drug discontinuation	5 (45.5%)
At least one TEAE leading to death	0 (0.0%)
At least one TEAE with grade 3 or higher	9 (81.8%)
At least one TEAE with grade 3 or higher and related to the study drug	9 (81.8%)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment; n = number of subjects;
% = percentages of subjects are calculated relative to the total number of subjects in a subgroup in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.

表 2.7.4.7-98　直近のがん治療からの期間別（3 ヵ月未満、3 ヵ月以上）の有害事象の発現割合（210 試験）（安全性解析対象集団）

System organ class Preferred term	<3months (N=12) n (%)	>= 3months (N=11) n (%)
Number of subjects with at least one TEAE	12(100.0%)	11(100.0%)
血液およびリンパ系障害	9(75.0%)	10(90.9%)
貧血*	5(41.7%)	4(36.4%)
好酸球増加症	0	1(9.1%)
発熱性好中球減少症	1(8.3%)	0
白血球減少症*	5(41.7%)	5(45.5%)
リンパ球減少症*	1(8.3%)	1(9.1%)
好中球減少症*	5(41.7%)	7(63.6%)
血小板減少症*	9(75.0%)	9(81.8%)
心臓障害	1(8.3%)	1(9.1%)
第一度房室ブロック	1(8.3%)	0
動悸	0	1(9.1%)
眼障害	1(8.3%)	0
ドライアイ	1(8.3%)	0
胃腸障害	5(41.7%)	4(36.4%)
腹痛	2(16.7%)	1(9.1%)
下痢	3(25.0%)	3(27.3%)
悪心	3(25.0%)	0
口内炎	1(8.3%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<3months (N=12) n (%)	>= 3months (N=11) n (%)
一般・全身障害および投与部位の状態	7(58.3%)	6(54.5%)
悪寒	1(8.3%)	0
疲労	0	3(27.3%)
倦怠感	4(33.3%)	3(27.3%)
非心臓性胸痛	1(8.3%)	0
末梢性浮腫	1(8.3%)	0
発熱	2(16.7%)	1(9.1%)
感染症および寄生虫症	5(41.7%)	2(18.2%)
細菌感染	1(8.3%)	0
サイトメガロウイルス感染	1(8.3%)	0
医療機器関連感染	1(8.3%)	0
麦粒腫	0	1(9.1%)
口腔カンジダ症	1(8.3%)	0
ニューモシスチス・イロベチイ肺炎	0	1(9.1%)
皮膚感染	1(8.3%)	0
扁桃炎	1(8.3%)	0
上気道感染	0	1(9.1%)
尿路感染	0	1(9.1%)

Source: Listing 16.2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<3months (N=12) n (%)	>= 3months (N=11) n (%)
傷害、中毒および処置合併症	1(8.3%)	0
挫傷	1(8.3%)	0
臨床検査	5(41.7%)	5(45.5%)
アラニンアミノトランスフェラーゼ増加	1(8.3%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1(8.3%)	1(9.1%)
血中アルカリホスファターゼ増加	0	1(9.1%)
血中乳酸脱水素酵素増加	1(8.3%)	0
脳性ナトリウム利尿ペプチド増加	0	1(9.1%)
好酸球数増加	1(8.3%)	0
γーグルタミルトランスフェラーゼ増加	0	2(18.2%)
リパーゼ増加	1(8.3%)	0
体重減少	1(8.3%)	3(27.3%)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<3months (N=12) n (%)	>= 3months (N=11) n (%)
代謝および栄養障害	6(50.0%)	7(63.6%)
食欲減退	3(25.0%)	5(45.5%)
高カルシウム血症	1(8.3%)	0
低アルブミン血症	1(8.3%)	2(18.2%)
低カリウム血症	0	1(9.1%)
低ナトリウム血症	2(16.7%)	0
低リン酸血症	0	1(9.1%)
筋骨格系および結合組織障害	3(25.0%)	4(36.4%)
関節痛	0	1(9.1%)
背部痛	2(16.7%)	2(18.2%)
脊椎すべり症	1(8.3%)	0
尺骨突き上げ症候群	0	1(9.1%)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<3months (N=12) n (%)	>= 3months (N=11) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1(8.3%)	0
腫瘍疼痛	1(8.3%)	0
神経系障害	6(50.0%)	3(27.3%)
味覚消失	1(8.3%)	0
認知障害	1(8.3%)	0
浮動性めまい	1(8.3%)	0
味覚異常	3(25.0%)	1(9.1%)
頭痛	1(8.3%)	1(9.1%)
傾眠	0	1(9.1%)
腎および尿路障害	1(8.3%)	0
尿瘻	1(8.3%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.

System organ class Preferred term	<3months (N=12) n (%)	>= 3months (N=11) n (%)
呼吸器、胸郭および縦隔障害	3(25.0%)	1(9.1%)
急性呼吸不全	1(8.3%)	0
鼻出血	0	1(9.1%)
間質性肺疾患	1(8.3%)	0
口腔咽頭痛	1(8.3%)	0
皮膚および皮下組織障害	4(33.3%)	4(36.4%)
接触皮膚炎	1(8.3%)	0
湿疹	0	1(9.1%)
紅斑	1(8.3%)	0
多形紅斑	1(8.3%)	0
光線過敏性反応	1(8.3%)	0
そう痒症	0	1(9.1%)
発疹	0	1(9.1%)
皮膚剥脱	0	1(9.1%)
皮膚潰瘍	1(8.3%)	0
血管障害	1(8.3%)	0
高血圧	1(8.3%)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects in each subtype in the analysis set.
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375
TEAE of overdose is not included in this analysis.

表 2.7.4.7-99　直近のがん治療からの期間別（3 ヵ月未満、3 ヵ月以上）の有害事象の概要（203 試験）（安全性解析対象集団）

Days from End of the Last Immediate Previous Treatment: < 3 months

Description	40 mg (N=27)
	n (%)
Number of subjects with	
At least one TEAE	27 (100.0)
At least one TEAE related to the study drug	25 (92.6)
At least one serious TEAE	5 (18.5)
At least one serious TEAE related to the study drug	4 (14.8)
At least one TEAE leading to dose reduction or interruption	18 (66.7)
At least one TEAE leading to study drug discontinuation	7 (25.9)
At least one TEAE leading to death	0 (0.0)
At least one TEAE with grade 3 or higher	20 (74.1)
At least one TEAE with grade 3 or higher and related to the study drug	19 (70.4)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment; n = number of subjects;
% = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

Days from End of the Last Immediate Previous Treatment: >=3 months

Description	40 mg (N=28) n (%)
Number of subjects with	
At least one TEAE	28 (100.0)
At least one TEAE related to the study drug	26 (92.9)
At least one serious TEAE	9 (32.1)
At least one serious TEAE related to the study drug	6 (21.4)
At least one TEAE leading to dose reduction or interruption	22 (78.6)
At least one TEAE leading to study drug discontinuation	11 (39.3)
At least one TEAE leading to death	1 (3.6)
At least one TEAE with grade 3 or higher	26 (92.9)
At least one TEAE with grade 3 or higher and related to the study drug	23 (82.1)

Source: Listing 16.2.6 1 and 16.2.4.4

Severities are graded using NCI-CTCAE Version 4.03.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment; n = number of subjects;
% = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
Subjects with more than one TEAE are counted once in the worst severity or strongest relationship category.
TEAE related to study drug is defined as a TEAE with a relationship of possible, probable or definite to study drug.
TEAE of overdose is not included in this analysis.
For TEAE leading to dose reduction or interruption, the worst action taken is considered for a derived TEAE. For example, if the actions taken for a derived AE consisted of dose reduction/interruption and study drug discontinuation, the worst action taken of TEAE leading to study drug discontinuation will be considered, and dose reduction/interruption will not be counted for this derived AE.
If TEAE leading to dose reduction/interruption and AE leading to study drug discontinuation occurred to different derived TEAEs, these actions taken will be counted separately.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

表 2.7.4.7-100　直近のがん治療からの期間別（3 ヵ月未満、3 ヵ月以上）の有害事象の発現割合（203 試験）（安全性解析対象集団）

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
Number of subjects with at least one TEAE	27(100.0)	28(100.0)
血液およびリンパ系障害	25(92.6)	27(96.4)
貧血*	9(33.3)	9(32.1)
再生不良性貧血	1(3.7)	0
好酸球増加症	1(3.7)	0
発熱性好中球減少症	3(11.1)	0
白血球減少症*	13(48.1)	11(39.3)
リンパ球減少症*	7(25.9)	9(32.1)
好中球減少症*	15(55.6)	16(57.1)
血小板減少症*	22(81.5)	24(85.7)
心臓障害	4(14.8)	3(10.7)
不安定狭心症	0	1(3.6)
不整脈	1(3.7)	0
心房細動	1(3.7)	1(3.6)
動悸	2(7.4)	1(3.6)
心嚢液貯留	1(3.7)	0
耳および迷路障害	2(7.4)	0
耳痛	1(3.7)	0
回転性めまい	1(3.7)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
眼障害	3(11.1)	2(7.1)
白内障	1(3.7)	0
結膜出血	1(3.7)	0
ドライアイ	0	1(3.6)
角膜炎	0	1(3.6)
霧視	1(3.7)	0

Source: Listing 16.2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
胃腸障害	16(59.3)	16(57.1)
腹部不快感	1(3.7)	0
腹痛	1(3.7)	2(7.1)
上腹部痛	1(3.7)	1(3.6)
肛門出血	1(3.7)	0
便秘	0	1(3.6)
齲歯	0	2(7.1)
下痢	10(37.0)	7(25.0)
消化不良	0	1(3.6)
心窩部不快感	0	1(3.6)
胃潰瘍	0	1(3.6)
胃炎	1(3.7)	0
痔出血	1(3.7)	0
悪心	7(25.9)	5(17.9)
口腔粘膜血腫	0	1(3.6)
口内炎	1(3.7)	1(3.6)
歯痛	1(3.7)	0
嘔吐	2(7.4)	1(3.6)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
一般・全身障害および投与部位の状態	15(55.6)	12(42.9)
無力症	2(7.4)	0
カテーテル留置部位腫脹	0	1(3.6)
胸部不快感	0	1(3.6)
胸痛	0	1(3.6)
溢出	0	1(3.6)
疲労	3(11.1)	3(10.7)
歩行障害	1(3.7)	0
インフルエンザ様疾患	0	2(7.1)
倦怠感	5(18.5)	3(10.7)
末梢性浮腫	1(3.7)	3(10.7)
発熱	6(22.2)	5(17.9)
口渇	1(3.7)	0
免疫系障害	1(3.7)	0
薬物過敏症	1(3.7)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
感染症および寄生虫症	4(14.8)	15(53.6)
気管支炎	0	2(7.1)
結膜炎	1(3.7)	1(3.6)
膀胱炎	1(3.7)	0
サイトメガロウイルス感染	1(3.7)	0
感染性小腸結腸炎	0	1(3.6)
胃腸炎	0	1(3.6)
帯状疱疹	0	1(3.6)
膿痂疹	0	1(3.6)
インフルエンザ	2(7.4)	0
上咽頭炎	1(3.7)	1(3.6)
咽頭炎	0	3(10.7)
ニューモシスチス・イロベチイ肺炎	0	1(3.6)
肺炎	0	1(3.6)
鼻炎	0	1(3.6)
ブドウ球菌皮膚感染	0	1(3.6)
上気道感染	0	4(14.3)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
傷害、中毒および処置合併症	0	3(10.7)
胃瘻管部合併症	0	1(3.6)
爪損傷	0	1(3.6)
処置による疼痛	0	1(3.6)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
臨床検査	11(40.7)	14(50.0)
アラニンアミノトランスフェラーゼ増加	3(11.1)	2(7.1)
アスパラギン酸アミノトランスフェラーゼ増加	3(11.1)	4(14.3)
血中アルカリホスファターゼ増加	2(7.4)	6(21.4)
血中コレステロール増加	1(3.7)	0
血中クレアチンホスホキナーゼＭＢ増加	0	1(3.6)
血中クレアチンホスホキナーゼ増加	0	1(3.6)
血中クレアチニン増加	1(3.7)	1(3.6)
血中免疫グロブリンＡ減少	1(3.7)	0
尿中血陽性	0	1(3.6)
脳性ナトリウム利尿ペプチド増加	1(3.7)	1(3.6)
Ｃ－反応性蛋白増加	1(3.7)	2(7.1)
心胸郭比増加	1(3.7)	0
心電図ＱＴ延長	2(7.4)	3(10.7)
心電図Ｔ波逆転	0	1(3.6)
好酸球数増加	1(3.7)	1(3.6)
γ－グルタミルトランスフェラーゼ増加	4(14.8)	4(14.3)
リパーゼ増加	0	1(3.6)
体重減少	2(7.4)	4(14.3)
体重増加	1(3.7)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
代謝および栄養障害	14(51.9)	11(39.3)
食欲減退	8(29.6)	5(17.9)
糖尿病	0	1(3.6)
高カリウム血症	1(3.7)	0
高マグネシウム血症	1(3.7)	0
高トリグリセリド血症	1(3.7)	0
低アルブミン血症	4(14.8)	1(3.6)
低カルシウム血症	1(3.7)	2(7.1)
低カリウム血症	3(11.1)	2(7.1)
低ナトリウム血症	1(3.7)	1(3.6)
低蛋白血症	1(3.7)	0

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
筋骨格系および結合組織障害	8(29.6)	11(39.3)
関節痛	0	1(3.6)
関節炎	1(3.7)	0
背部痛	4(14.8)	1(3.6)
出血性関節症	0	1(3.6)
関節腫脹	0	1(3.6)
筋肉疲労	1(3.7)	1(3.6)
筋痙縮	2(7.4)	3(10.7)
筋力低下	1(3.7)	0
筋骨格硬直	0	1(3.6)
筋肉痛	1(3.7)	1(3.6)
頚部痛	0	1(3.6)
四肢痛	0	1(3.6)
肩回旋筋腱板症候群	0	1(3.6)
腱炎	0	1(3.6)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2(7.4)	2(7.1)
末梢性Ｔ細胞性リンパ腫、組織型不明	0	1(3.6)
皮膚乳頭腫	1(3.7)	0
腫瘍疼痛	1(3.7)	1(3.6)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
神経系障害	5(18.5)	4(14.3)
浮動性めまい	1(3.7)	0
味覚異常	1(3.7)	1(3.6)
頭痛	4(14.8)	2(7.1)
感覚鈍麻	1(3.7)	0
末梢性感覚ニューロパチー	0	1(3.6)
失神寸前の状態	0	1(3.6)
精神障害	4(14.8)	1(3.6)
譫妄	1(3.7)	1(3.6)
不眠症	3(11.1)	1(3.6)
腎および尿路障害	1(3.7)	1(3.6)
急性腎障害	1(3.7)	0
血尿	0	1(3.6)
蛋白尿	0	1(3.6)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
生殖系および乳房障害	1(3.7)	0
陰嚢浮腫	1(3.7)	0
呼吸器、胸郭および縦隔障害	10(37.0)	11(39.3)
咳嗽	1(3.7)	5(17.9)
咽頭知覚不全	1(3.7)	0
発声障害	0	1(3.6)
呼吸困難	2(7.4)	2(7.1)
労作性呼吸困難	0	1(3.6)
鼻出血	1(3.7)	1(3.6)
しゃっくり	1(3.7)	0
間質性肺疾患	0	1(3.6)
口腔咽頭痛	2(7.4)	1(3.6)
胸水	2(7.4)	0
肺臓炎	3(11.1)	1(3.6)
湿性咳嗽	1(3.7)	0
アレルギー性鼻炎	0	1(3.6)
鼻漏	0	1(3.6)
上気道の炎症	0	1(3.6)

Source: Listing 16 2.6.1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

System organ class Preferred term	< 3months (N=27) n (%)	>= 3months (N=28) n (%)
皮膚および皮下組織障害	10(37.0)	13(46.4)
褥瘡性潰瘍	1(3.7)	0
ざ瘡様皮膚炎	0	1(3.6)
全身性剥脱性皮膚炎	0	1(3.6)
皮膚乾燥	1(3.7)	0
皮脂欠乏性湿疹	0	1(3.6)
紅斑	1(3.7)	1(3.6)
多形紅斑	1(3.7)	0
全身紅斑	0	1(3.6)
皮膚疼痛	0	1(3.6)
点状出血	0	1(3.6)
色素沈着障害	1(3.7)	0
全身性そう痒症	0	2(7.1)
紫斑	2(7.4)	0
発疹	1(3.7)	4(14.3)
斑状丘疹状皮疹	0	2(7.1)
そう痒性皮疹	1(3.7)	0
蕁麻疹	3(11.1)	2(7.1)
血管障害	1(3.7)	2(7.1)
深部静脈血栓症	0	1(3.6)
低血圧	1(3.7)	0
末梢動脈閉塞性疾患	0	1(3.6)

Source: Listing 16.2.6 1 and 16.2.4.4

MedDRA Version 21.1 was used to code adverse events.
N = number of subjects in the Safety Analysis Set by the duration from end of last immediate previous treatment.
n = number of subjects; % = percentages of subjects are calculated relative to the number of subjects within a subgroup in the analysis set;
TEAE = treatment-emergent adverse event is defined as AEs that started or worsened in severity on or after the first study drug administration.
* Hematological adverse events are defined as grouped AEs where anemia is combined with haemoglobin decreased; thrombocytopenia is combined with platelet count decreased; leukopenia is combined with white blood cell count decreased; lymphopenia is combined with lymphocyte count decreased; neutropenia is combined with neutrophil count decreased and granulocytopenia.
TEAE of overdose is not included in this analysis.
Days from end of the last immediate previous treatment (months) = (date of first study drug - end date of the last immediate previous treatment +1)/ 30.4375.

ツシジノスタット
ハイヤスタ錠 10mg

第 2 部 CTD の概要

2.7 臨床概要
2.7.5 参考文献

Huya Japan 合同会社

2.7.5 参考文献

2.7.5.1 2.7.1 生物薬剤学及び関連する分析法の概要で引用した参考文献

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2.7.5.3 2.7.3 臨床的有効性で引用した参考文献

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2.7.5.4 2.7.4 臨床的安全性で引用した文献

該当なし