Clinical trial results:
A Phase III randomized open-label multi-center study of ruxolitinib versus best available therapy in patients with corticosteroid-refractory acute graft vs. host disease after allogeneic stem cell transplantation

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies and data using 999 as data points are not accurately represented in this record. Please go to https://www.novctrd.com/CtrdWeb/home.nov for complete trial results

Summary

EudraCT number	2016-002584-33
Trial protocol	DE IT ES AT FR NO SE DK GB CZ PT HU BG PL NL GR
Global end of trial date	23 April 2021

Results information

Result version number	v1 (current)
This version publication date	08 November 2021
First version publication date	08 November 2021

Trial information

Trial identification

Sponsor protocol code	CINC424C2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02913261
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 8627788300, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 8627788300, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000901-PIP03-16

Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 March 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Japan: 30
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Saudi Arabia: 3
Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Turkey: 12

Country: Number of subjects enrolled	Australia: 24
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	Germany: 63
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Israel: 16
Worldwide total number of subjects	309
EEA total number of subjects	188

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	9
Adults (18-64 years)	243
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 310 patients with SR-aGvHD were enrolled, out of which 309 patients were included in the analysis (as one patient did not sign the study informed consent prior to receiving BAT (protocol deviation) and was excluded from all analyses).
Completed = Completed the treatment period
Not completed = Discontinued from treatment period

Pre-assignment

Screening details:

The screening period ranged from Day -28 to Day -1. Screening activities and assessment of inclusion and exclusion criteria began once the patient was diagnosed with aGvHD. Any occurrence of SR-aGvHD was monitored closely.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ruxolitinib (RUX)

Arm description:

These patients were administered Ruxolitinib orally twice per day (b.i.d) at a dose of 10 mg bid, as two 5-mg tablets. Ruxolitinib was taken without regards to food.

Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ruxolitinib was administered orally twice per day at a dose of 10 mg bid, as two 5-mg tablets. Ruxolitinib was taken without regard to food.

Arm title	Best Available Therapy (BAT)

Arm description:

These patients were administered BAT per the Investigator's best judgement based on a specific list of BAT.

Arm type	Active comparator
Investigational medicinal product name	9 different BATS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid, Tablet, Capsule, Cutaneous liquid
Routes of administration	Intravenous use, Subcutaneous use, Oral use

Dosage and administration details:

Multiform forms of BATs: anti-thymocyte globulin (ATG), extracorporeal photopheresis (ECP), mesenchymal stromal cells (MSC), low-dose methotrexate (MTX), mycophenolate mofetil (MMF), everolimus, sirolimus, etanercept, infliximab

Number of subjects in period 1	Ruxolitinib (RUX)	Best Available Therapy (BAT)
Started	154	155
Not treated	2 [1]	5 [2]
Crossover treatment at end of rand.	0 [3]	49
Entered long-term follow-up	102	51
Completed	35	20
Not completed	119	135
Adverse event, serious fatal	25	22
Physician decision	8	9
Graft loss	2	-
Adverse event, non-fatal	27	5
Technical problems	-	1
Failure to meet protocol continuation criteria	13	10
Disease relapse	8	13
Subject/guardian decision	4	6
Lack of efficacy	32	69

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These were patients who were never treated with study drug

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These were only the patients who crossed over from BAT to study drug - ruxolitinib. Patients from ruxolitinib did not cross over to BAT.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Not all patients were in the long term follow up.

Baseline characteristics

Reporting groups	
Reporting group title	Ruxolitinib (RUX)
Reporting group description:	
These patients were administered Ruxolitinib orally twice per day (b.i.d) at a dose of 10 mg bid, as two 5-mg tablets. Ruxolitinib was taken without regards to food.	
Reporting group title	Best Available Therapy (BAT)
Reporting group description:	
These patients were administered BAT per the Investigator's best judgement based on a specific list of BAT.	

Reporting group values	Ruxolitinib (RUX)	Best Available Therapy (BAT)	Total
Number of subjects	154	155	309
Age Categorical Units: Participants			
Adolescents, 12 - <18 years	5	4	9
18 - 65 years	128	126	254
>65 years	21	25	46
Age Continuous Units: years			
arithmetic mean	48.1	50.9	
standard deviation	± 16.30	± 14.97	-
Sex: Female, Male Units:			
Female	62	64	126
Male	92	91	183
Race/Ethnicity, Customized Units: Subjects			
White	111	102	213
Black or African American	0	1	1
Asian	19	29	48
Other	8	4	12
Unknown	16	19	35
Weight Units: kg			
arithmetic mean	67.5	66.2	
standard deviation	± 14.04	± 14.78	-

End points

End points reporting groups

Reporting group title	Ruxolitinib (RUX)
Reporting group description:	
These patients were administered Ruxolitinib orally twice per day (b.i.d) at a dose of 10 mg bid, as two 5-mg tablets. Ruxolitinib was taken without regards to food.	
Reporting group title	Best Available Therapy (BAT)
Reporting group description:	
These patients were administered BAT per the Investigator's best judgement based on a specific list of BAT.	
Subject analysis set title	Cross-Over
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
These were patients randomized to BAT who were eligible to cross over to Ruxolitinib between Day 28 and Week 24.	

Primary: Overall response rate (ORR) at Day 28

End point title	Overall response rate (ORR) at Day 28
End point description:	
Overall response rate at Day 28 after randomization was defined as the percentage participants in each arm demonstrating a complete response (CR) or partial response (PR), based on investigator assessment & according to standard criteria, without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. Scoring of response was relative to the organ stage at the time of randomization. CR was defined as a score of 0 for the aGvHD grading in all evaluable organs that indicates complete resolution of all signs & symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of aGvHD. PR was defined as improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response or non-response of aGvHD.	
End point type	Primary
End point timeframe:	
Day 28	

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)	62.3 (54.2 to 70.0)	39.4 (31.6 to 47.5)		

Statistical analyses

Statistical analysis title	ORR at Day 28
Comparison groups	Ruxolitinib (RUX) v Best Available Therapy (BAT)

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	4.22

Secondary: Durable overall response rate (DORR) (Key Secondary endpoint) at Day 56

End point title	Durable overall response rate (DORR) (Key Secondary endpoint) at Day 56

End point description:

Percentage of all participants in each arm who achieved a complete response (CR) or partial response (PR) at Day 28 (primary endpoint) AND maintained a CR or PR at Day 56 based on investigator assessment and according to standard criteria.
CR was defined as a score of 0 for the aGvHD grading in all evaluable organs that indicates complete resolution of all signs and symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of aGvHD.
PR was defined as improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response
or non-response of aGvHD.

End point type	Secondary

End point timeframe:

Day 56

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)	39.6 (31.8 to 47.8)	21.9 (15.7 to 29.3)		

Statistical analyses

Statistical analysis title	DORR at Day 56
Comparison groups	Ruxolitinib (RUX) v Best Available Therapy (BAT)

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0005
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	3.94

Secondary: Overall response rate (ORR) at Day 14

End point title	Overall response rate (ORR) at Day 14

End point description:

ORR at Da4 14 is the percentage of participants who achieved overall response (CR+PR) at Day 14 based on investigator assessment and according to standard criteria.
CR was defined as a score of 0 for the aGvHD grading in all evaluable organs that indicates complete resolution of all signs and symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of aGvHD.
PR was defined as improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response
or non-response of aGvHD.

End point type	Secondary

End point timeframe:

Day 14

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)	63.0 (54.8 to 70.6)	47.1 (39.0 to 55.3)		

Statistical analyses

Statistical analysis title	ORR at Day 14
Comparison groups	Ruxolitinib (RUX) v Best Available Therapy (BAT)

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0029
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	3.17

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

Duration of response was defined for patients who had a CR or PR at Day 28. This was the interval between the date of first documented response of CR or PR (i.e., the start date of response), till the date of progression or addition of systemic therapies for aGvHD on or after Day 28. Death without prior observation of aGvHD progression and onset of chronic GvHD were considered. Duration of response was censored at the last response assessment prior to or at the analysis cut-off date, if no events/competing risk occurred before or at the cut-off date.

End point type	Secondary

End point timeframe:

Up to 24 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	62		
Units: Days				
median (full range (min-max))	167.0 (22.0 to 677.0)	106.0 (10.0 to 526.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative steroid dosing until Day 56

End point title	Cumulative steroid dosing until Day 56

End point description:

Weekly cumulative steroid dose for each participant up to Day 56 or discontinuation of randomized treatment. Participants should have undergone tapering of steroids if it had been required. Tapering the immunosuppression therapy was performed in 2 steps: Taper of corticosteroids: initiated not earlier than Day 7, and performed as per institutional guidelines.

End point type	Secondary

End point timeframe:

up to Day 56

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: mg				
median (full range (min-max))				
By Week 1 (n = 151, 154)	962.5 (140.0 to 2337.5)	923.6 (140.0 to 6093.8)		
By Week 2 (n = 150, 150)	1740.0 (280.0 to 3500.0)	1725.0 (280.0 to 7173.3)		
By Week 3 (n = 143, 141)	2375.0 (350.0 to 5250.0)	2340.0 (370.0 to 8000.0)		
By Week 4 (n = 132, 136)	2866.9 (420.0 to 7000.0)	2816.3 (420.0 to 9050.0)		
By Week 5 (n = 124, 106)	3268.1 (455.0 to 8750.0)	3290.6 (420.0 to 9825.0)		
By Week 6 (n = 115, 84)	3606.3 (490.0 to 10500.0)	3543.8 (420.0 to 10435.0)		
By Week 7 (n = 107, 75)	3850.0 (495.0 to 11250.0)	3706.3 (420.0 to 10955.0)		
By Week 8 (n = 87, 67)	4000.0 (857.5 to 9475.0)	4006.3 (420.0 to 11875.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Reported Outcomes (PROs): Change from Baseline in Functional Assessment of Cancer Therapy-Bone Marrow Transplantation (FACT-BMT) Total score

End point title	Patient Reported Outcomes (PROs): Change from Baseline in Functional Assessment of Cancer Therapy-Bone Marrow Transplantation (FACT-BMT) Total score

End point description:

The Functional assessment of Cancer Therapy – Bone Marrow Transplant (FACT-BMT) is a 50-item self-report questionnaire that measures the effect of a therapy on domains including physical, functional, social/family and emotional well-being, together with additional concerns relevant for bone marrow transplantation patients. Patients are requested to indicate their response on a scale of 0 to 4 on each statement. Depending on the statement, 0 or 4 may mean the best or worst feeling. Descriptive statistics (mean, standard deviation, median, Q1, Q3, minimum, and maximum) were calculated based on the scored scales at each scheduled assessment time point. Additionally, change from baseline in the scores at the time of each assessment were also calculated. Missing items data in a scale were handled based on each instrument manual. No imputation were applied if the total or subscale scores are missing at a visit.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: scores on a scale				
median (full range (min-max))				
Baseline (n = 106, 94)	89.00 (41.0 to 138.0)	81.00 (29.0 to 129.0)		
Week (W) 24 (n = 36, 13)	108.50 (67.0 to 139.0)	86.00 (21.0 to 124.0)		
Change from Baseline to W24 (n = 29, 12)	9.00 (-40.0 to 44.0)	4.50 (-29.0 to 41.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Reported Outcomes (PROs): Change from Baseline in EuroQol-5D-5L UK Score

End point title	Patient Reported Outcomes (PROs): Change from Baseline in EuroQol-5D-5L UK Score

End point description:

The EQ-5D descriptive classification consists of five dimensions of health: mobility, self-care, usual activities, anxiety/depression and pain/discomfort. Patients are requested to select the statement which best describes their condition on that day for each dimension. For overall health that day, the EuroQoL-5D-5L scale is numbered from 0 to 100, with 100 being the best health you can imagine and 0 being the worst health you can imagine. Descriptive statistics (mean, standard deviation, median, Q1, Q3, minimum, and maximum) were calculated based on the scored scales at each scheduled assessment time point. In order to measure Quality-of-Life (QoL) among aGvHD patients, and potential changes over time, change from baseline in EuroQol-5D-5L scores at the time of each assessment were also calculated. Missing items data in a scale will be handled based on each instrument manual. No imputation will be applied if the total or subscale scores are missing at a visit.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: scores on a scale				
median (full range (min-max))				
Baseline (n= 122, 118)	0.60 (-0.6 to 1.0)	0.54 (-0.6 to 1.0)		
W24 (n = 36, 14)	0.78 (0.4 to 1.0)	0.68 (-0.1 to 1.0)		
Change from Baseline (n = 32, 12)	0.12 (-0.3 to 1.1)	0.12 (-0.2 to 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: Area Under the Curve (AUC) (AUCinf, AUClast, AUCtau) of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: Area Under the Curve (AUC) (AUCinf, AUClast, AUCtau) of Ruxolitinib[1]

End point description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (tlast) (mass x time x volume-1)
AUCinf: The AUC from time zero to infinity (mass x time x volume-1)
AUCtau: The AUC calculated to the end of a dosing interval (tau) at steady-state (amount x time x volume-1).
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients was assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Week 1 Day 1 AUCinf (n = 11)	529.6 (± 55.2)			
Week 1 Day 1 AUClast (n = 26)	522.9 (± 89.6)			
Week 1 Day 1 AUCtau (n = 20)	578.9 (± 97.5)			
Week 1 Day 7 AUCinf (n = 9)	440.9 (± 91.5)			
Week 1 Day 7 AUClast (n = 22)	597.3 (± 73.2)			
Week 1 Day 7 AUCtau (n = 18)	651.9 (± 86.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: Plasma concentration at peak (Cmax) of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: Plasma concentration at peak (Cmax) of Ruxolitinib[2]

End point description:

Cmax is the maximum (peak) observed plasma, blood, serum, or other body fluid drug concentration after single dose administration (mass X volume-1).
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients was assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Week 1 Day 1	118 (± 70.4)			
Week 1 Day 7 (n = 22)	129.3 (± 76.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: CL/F of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: CL/F of Ruxolitinib[3]

End point description:

CL/F is the total body clearance of ruxolitinib from the plasma after a single dose and at steady state.
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients was assayed for Ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: L/hr				
geometric mean (geometric coefficient of variation)				

Week 1 Day 1 CL/F (n = 11)	18.88 (± 55.2)			
Week 1 Day 7 CL/F (n = 9)	23.31 (± 89.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: VzF of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: VzF of Ruxolitinib[4]

End point description:

VzF is the apparent volume of distribution during terminal phase after a single dose and at steady state. Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients will be assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: Liters (L)				
geometric mean (geometric coefficient of variation)				
Week 1 Day 1 (n = 11)	52.57 (± 46.4)			
Week 1 Day 7 (n = 9)	66.76 (± 71.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: Lambda_z of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: Lambda_z of Ruxolitinib[5]

End point description:

Lambda_z is the smallest (slowest) disposition (hybrid) rate constant (hr-1) may also be used for terminal elimination rate constant (hr-1).
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients will be assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: 1/hr				
geometric mean (geometric coefficient of variation)				
Week 1 Day 1 (n = 11)	0.3592 (± 34.2)			
Week 1 Day 7 (n = 9)	0.3492 (± 31.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: T1/2 of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: T1/2 of Ruxolitinib[6]

End point description:

T1/2 is the elimination half-life associated with the terminal slope of a semi logarithmic concentration-time curve (hr).
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients will be assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: hour (hr)				
geometric mean (geometric coefficient of variation)				
Week 1 Day 1 (n = 11)	1.93 (± 34.2)			
Week 1 Day 7 (n = 9)	1.985 (± 31.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: Tmax of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: Tmax of Ruxolitinib[7]

End point description:

Tmax is the time to reach maximum (peak) plasma, blood, serum, or other body fluid drug concentration after single dose and repeated dose administration (hr).
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients will be assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: hour (hr)				
median (full range (min-max))				
Week 1 Day 1 (n = 26)	1.767 (0.5167 to 8.917)			
Week 1 Day 7 (n = 22)	1.542 (0.5 to 4.083)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: Racc of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: Racc of Ruxolitinib[8]

End point description:

Racc is the accumulation ratio (AUC at steady state/AUC Day 1).
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients was be assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS).

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 1.5, 2, 4, 6, 9 hrs post-dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: ratio				
geometric mean (geometric coefficient of variation)	1.145 (± 27.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) parameter: Ctrough of Ruxolitinib

End point title	Pharmacokinetic (PK) parameter: Ctrough of Ruxolitinib[9]

End point description:

Minimum concentration (Ctrough) of ruxolitinib and at steady state in corticosteroid refractory acute GVHD patients.
Plasma samples for PK was taken at Day 1 (start of treatment), at Day 7 (week 1) to characterize the PK after first dose, and at steady state by non-compartmental analysis.
The plasma samples from all patients will be assayed for ruxolitinib concentrations using validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS)

End point type	Secondary

End point timeframe:

pre-dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	17.22 (± 187.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence rate of Failure-Free survival (FFS)

End point title	Cumulative Incidence rate of Failure-Free survival (FFS)

End point description:

FFS was defined as the time from the date of randomization to date of hematologic disease relapse/progression, non-relapse mortality, or addition of new systemic aGvHD treatment.
Incidence rate for FFS with 95% CIs are presented for each treatment group, accounting for onset of chronic GvHD as the competing risk.

End point type	Secondary

End point timeframe:

1, 2, 6, 12, 18, & 24 Months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)				
1 Month	17.92 (12.26 to 24.46)	49.13 (40.94 to 56.80)		
2 Months	35.39 (27.79 to 43.07)	61.32 (53.00 to 68.61)		
6 Months	53.67 (45.28 to 61.34)	80.17 (72.52 to 85.89)		
12 Months	58.64 (50.18 to 66.16)	80.91 (73.32 to 86.54)		
18 Months	59.35 (50.88 to 66.84)	80.91 (73.32 to 86.54)		
24 Months	61.48 (53.01 to 68.88)	81.66 (74.12 to 87.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence rate of Non Relapse Mortality (NRM)

End point title	Cumulative Incidence rate of Non Relapse Mortality (NRM)

End point description:

NRM was defined as the time from date of randomization to date of death not preceded by hematologic disease relapse/progression. Hematologic disease relapse/progression was considered a competing risk for NRM with the date of hematologic disease relapse/progression being the earlier of documented hematologic disease relapse/progression or institution of therapy to treat potential hematologic disease relapse/progression. If a patient was not known to have died or to have relapsed/progressed, then NRM was censored at the latest date the patient was known to be alive (on or before the cut-off date). Data is provided based on incidence of hematologic disease relapse/progression.

End point type	Secondary

End point timeframe:

1, 2, 6, 12, 18 & 24 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)				
1 Month	9.96 (5.83 to 15.39)	14.52 (9.45 to 20.64)		

2 Months	20.71 (14.61 to 27.54)	23.54 (17.04 to 30.65)		
6 Months	37.59 (29.81 to 45.33)	42.42 (34.18 to 50.41)		
12 Months	43.91 (35.75 to 51.77)	46.11 (37.68 to 54.12)		
18 Months	46.03 (37.77 to 53.89)	49.21 (40.63 to 57.22)		
24 Months	49.53 (40.91 to 57.55)	49.99 (41.38 to 57.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence rate of Malignancy Relapse/Progression (MR)

End point title	Cumulative Incidence rate of Malignancy Relapse/Progression (MR)

End point description:

MR was defined as the time from date of randomization to hematologic malignancy relapse/progression. Deaths not preceded by hematologic malignancy relapse/progression were considered competing risks. If a patient was not known to have event or competing risks, then MR was censored at the latest date the patient was known to be alive (on or before the cut-off date). Calculated for patients with underlying hematologic malignant disease.

End point type	Secondary

End point timeframe:

1, 2, 6, 12 , 18 & 24 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	147		
Units: Percentage of participants				
number (confidence interval 95%)				
1 Month	0.69 (0.06 to 3.51)	2.80 (0.92 to 6.54)		
2 Months	4.21 (1.73 to 8.46)	4.29 (1.75 to 8.60)		
6 Months	8.46 (4.60 to 13.79)	13.49 (8.32 to 19.91)		
12 Months	10.68 (6.24 to 16.47)	15.06 (9.56 to 21.71)		
18 Months	12.91 (7.96 to 19.09)	16.72 (10.89 to 23.64)		
24 Months	14.75 (9.32 to 21.37)	18.81 (12.46 to 26.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence rate of chronic Graft versus Host Disease (cGvHD)

End point title	Cumulative Incidence rate of chronic Graft versus Host Disease (cGvHD)

End point description:

Incidence of cGvHD was the time from date of randomization to onset of cGvHD is the diagnosis of any cGvHD including mild, moderate, severe. Deaths without prior onset of cGvHD and hematologic disease relapse/progression were competing
risks. If a patient was not known to have event or competing risks, then the incidence of cGvHD was censored at the latest date the patient was known to be alive (on or before the cut-off date). Calculated for patients with underlying hematologic malignant disease and the participants with incidence has been provided.

End point type	Secondary

End point timeframe:

1, 2, 6, 12, 18 & 24 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)				
1 Month	0 (-999 to 999)	1.33 (0.26 to 4.34)		
2 Months	1.34 (0.26 to 4.39)	2.03 (0.55 to 5.41)		
6 Months	15.60 (10.26 to 21.96)	12.19 (7.40 to 18.25)		
12 Months	29.66 (22.41 to 37.25)	20.24 (13.98 to 27.34)		
18 Months	32.48 (24.96 to 40.20)	23.36 (16.62 to 30.76)		
24 Months	36.00 (28.20 to 43.84)	24.95 (18.00 to 32.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-efficacy relationship of ruxolitinib in corticosteroid refractory aGvHD: PK-Overall Response Rate

End point title	Exposure-efficacy relationship of ruxolitinib in corticosteroid refractory aGvHD: PK-Overall Response Rate[10]

End point description:

Exposure-efficacy relationship of ruxolitinib in terms of concentration-effect and dose-effect.
ORR was defined as the percentage of participants with a best overall response defined as complete response (CR) or partial response (PR) as assessed by local investigators. CR was defined as a score of 0 for the Acute Graft vs. Host Disease (aGvHD) grading in all evaluable organs that indicates complete resolution of all signs and symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of aGvHD. PR was defined as improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms

without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response or non-response of aGvHD.

End point type	Secondary

End point timeframe:

Day 28

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Percentage of participants				
number (not applicable)	82.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-efficacy relationship of ruxolitinib in corticosteroid refractory aGvHD: PK- Durable Overall Response Rate (DORR)

End point title	Exposure-efficacy relationship of ruxolitinib in corticosteroid refractory aGvHD: PK- Durable Overall Response Rate (DORR)[11]

End point description:

Exposure-efficacy relationship of ruxolitinib in terms of concentration-effect and dose-effect.
DORR is the percentage of all participants in each arm who achieved a complete response (CR) or partial response (PR) at Day 28 (primary endpoint) AND maintained a CR or PR at Day 56.
CR was defined as a score of 0 for the aGvHD grading in all evaluable organs that indicates complete resolution of all signs and symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of aGvHD.
PR was defined as improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response
or non-response of aGvHD.

End point type	Secondary

End point timeframe:

Day 56

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	67			
Units: Percentage of participants				
number (not applicable)	91.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-efficacy relationship of ruxolitinib in corticosteroid refractory aGvHD: PK-Overall Survival

End point title	Exposure-efficacy relationship of ruxolitinib in corticosteroid refractory aGvHD: PK-Overall Survival[12]

End point description:

Exposure-efficacy relationship of ruxolitinib in terms of concentration-effect and dose-effect.
Overall survival (OS) was defined as the time from the date of randomization to If a patient was not known to have died, then OS was censored at the latest date the patient was known to be alive (on or before the cut-off date).the date of death due to any cause.

End point type	Secondary

End point timeframe:

up to 24 months

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistics was planned for this endpoint

End point values	Ruxolitinib (RUX)			
Subject group type	Reporting group			
Number of subjects analysed	150			
Units: Percentage of participants				
number (not applicable)	80.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS was defined as the time from the date of randomization to date of death due to any cause. If a patient was not known to have died, then OS was censored at the latest date the patient was known to be alive (on or before the cut-off date). Results are based on Kaplan Meier (KM) estimates.

End point type	Secondary

End point timeframe:

1, 2, 6, 12, 18 & 24 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: months				
number (confidence interval 95%)				
KM median estimates: 0 - <1 Month	90.04 (84.02 to 93.87)	85.48 (78.79 to 90.19)		
KM median estimates: 1 - <2 Months	77.95 (70.42 to 83.79)	75.69 (67.92 to 81.83)		
KM median estimates: 2 - <6 Months	58.38 (50.03 to 65.82)	49.42 (40.89 to 57.37)		
KM median estimates: 6 - <12 Months	49.27 (40.96 to 57.05)	42.71 (34.39 to 50.75)		
KM median estimates: 12 - <18 Months	42.94 (34.82 to 50.79)	37.97 (29.86 to 46.03)		
KM median estimates: 18 - <24 Months	38.65 (30.50 to 46.72)	35.55 (27.57 to 43.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free survival

End point title	Event-free survival

End point description:

Event-free survival was defined as the time from the date of randomization to the date of hematologic disease relapse/progression, graft failure, or death due to any cause. If a patient was not known to have any event, then EFS was censored at the latest date the patient was known to be alive (on or before the cut-off date). Results are based on Kaplan Meier (KM) estimates.

End point type	Secondary

End point timeframe:

1, 2, 6, 12, 18 & 24 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Days				
median (confidence interval 95%)				
KM median estimates: 0 - <1 Month	89.38 (83.24 to 93.35)	82.83 (75.81 to 87.97)		
KM median estimates: 1 - <2 Months	74.60 (66.82 to 80.82)	71.72 (63.71 to 78.26)		
KM median estimates: 2- <6 Months	53.68 (45.34 to 61.30)	44.14 (35.82 to 52.13)		
KM median estimates: 6- <12 Months	44.53 (36.36 to 52.36)	39.98 (30.90 to 46.96)		
KM median estimates: 12- <18 Months	40.29 (32.30 to 48.12)	35.09 (27.23 to 43.04)		
KM median estimates: 18- <24 Months	34.98 (27.01 to 43.04)	32.38 (24.61 to 40.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response rate (BOR)

End point title	Best overall response rate (BOR)

End point description:

Percentage of participants who achieved overall response (OR) (CR+PR) at any time point up to and including Day 28 and before the start of additional systemic therapy for aGvHD.
CR was defined as a score of 0 for the Acute Graft vs. Host Disease (aGvHD) grading in all evaluable organs that indicates complete resolution of all signs and symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of aGvHD.
PR was defined as improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response or non-response of aGvHD.

End point type	Secondary

End point timeframe:

up to Day 28

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	155		
Units: Percentage of participants				
number (confidence interval 95%)	81.8 (74.8 to 87.6)	60.6 (52.5 to 68.4)		

Statistical analyses

Statistical analysis title	BOR
Comparison groups	Ruxolitinib (RUX) v Best Available Therapy (BAT)
Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.25

Post-hoc: All Collected Deaths

End point title	All Collected Deaths

End point description:

On treatment deaths were collected from the start of treatment up to 30 days after study drug discontinuation, for a maximum duration of 708 days (treatment duration ranged from 6.0 to 678.0) for the RUX arm and 218 days (treatment duration ranged from 1.0 to 188.0 days) for the BAT arm. Deaths post treatment survival follow up were collected after the on- treatment period, up to approx. 49 months. Patients who didn't die during the on-treatment period and had not stopped study participation at the time of data cut-off (end of study) were censored.

End point type	Post-hoc

End point timeframe:

approx. 708 days, approx. 49 months

End point values	Ruxolitinib (RUX)	Best Available Therapy (BAT)	Cross-Over	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	152	150	49	
Units: Participants				
Total Deaths	89	89	29	
Deaths on-treatment	43	36	19	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On treatment deaths were collected from the start of treatment up to 30 days after study drug discontinuation, for a maximum duration of 708 days for the RUX arm and 218 days for the BAT arm.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Ruxolitinib (RUX) (Experimental)

Reporting group description:

These patients were administered Ruxolitinib orally twice per day (b.i.d) at a dose of 10 mg bid, as two 5-mg tablets. Ruxolitinib was taken without regards to food.

Reporting group title	Cross-Over

Reporting group description:

These were patients randomized to BAT who were eligible to cross over to Ruxolitinib between Day 28 and Week 24.

Reporting group title	Best Available Therapy (BAT)

Reporting group description:

These patients were administered BAT per the Investigator's best judgement based on a specific list of BAT.

Serious adverse events	Ruxolitinib (RUX) (Experimental)	Cross-Over	Best Available Therapy (BAT)
Total subjects affected by serious adverse events			
subjects affected / exposed	101 / 152 (66.45%)	38 / 49 (77.55%)	80 / 150 (53.33%)
number of deaths (all causes)	89	29	89
number of deaths resulting from adverse events	10	4	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute erythroid leukaemia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia recurrent			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Anogenital warts			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lymphoma			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma multiforme			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukaemia recurrent			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microangiopathy			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Disease recurrence			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	1 / 3
Pyrexia			
subjects affected / exposed	10 / 152 (6.58%)	0 / 49 (0.00%)	6 / 150 (4.00%)
occurrences causally related to treatment / all	2 / 10	0 / 0	4 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Acute graft versus host disease in intestine			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Allergy to immunoglobulin therapy			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serum sickness			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Perineal ulceration			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute lung injury			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchial fistula			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoxia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic pneumonia syndrome			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Interstitial lung disease			

subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung consolidation			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	2 / 152 (1.32%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 152 (0.00%)	2 / 49 (4.08%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 152 (1.32%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory disorder			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	2 / 152 (1.32%)	2 / 49 (4.08%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	6 / 152 (3.95%)	6 / 49 (12.24%)	6 / 150 (4.00%)
occurrences causally related to treatment / all	0 / 6	3 / 7	0 / 6
deaths causally related to treatment / all	0 / 1	2 / 4	0 / 4
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental disorder			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Bacterial test positive			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			

subjects affected / exposed	3 / 152 (1.97%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus test positive			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Influenza B virus test positive			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft loss			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous haematoma			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplantation complication			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 152 (1.32%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			

subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiopulmonary failure			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Basal ganglia haemorrhage			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebrovascular accident			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chorea			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Depressed level of consciousness			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Epilepsy			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mononeuropathy			

subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stupor			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	3 / 152 (1.97%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelosuppression			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	3 / 152 (1.97%)	0 / 49 (0.00%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	3 / 152 (1.97%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 152 (1.32%)	2 / 49 (4.08%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal haemorrhage			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Diarrhoea			
subjects affected / exposed	8 / 152 (5.26%)	0 / 49 (0.00%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	1 / 8	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 152 (1.32%)	2 / 49 (4.08%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal perforation			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal stenosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 152 (0.66%)	2 / 49 (4.08%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intestinal obstruction			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hepatic function abnormal			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Petechiae			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 152 (1.97%)	2 / 49 (4.08%)	5 / 150 (3.33%)
occurrences causally related to treatment / all	2 / 4	0 / 2	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cystitis haemorrhagic			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal impairment			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Renal tubular necrosis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Bone pain			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myopathy			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Anal abscess			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspergillus infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	4 / 150 (2.67%)
occurrences causally related to treatment / all	0 / 1	1 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial disease carrier			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral aspergillosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial sepsis			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis viral			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis			
subjects affected / exposed	3 / 152 (1.97%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus enteritis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	3 / 152 (1.97%)	1 / 49 (2.04%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection reactivation			
subjects affected / exposed	3 / 152 (1.97%)	2 / 49 (4.08%)	6 / 150 (4.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 152 (0.66%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter sepsis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal sepsis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human herpesvirus 6 infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal sepsis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection fungal			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis enterococcal			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucormycosis			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	7 / 152 (4.61%)	2 / 49 (4.08%)	8 / 150 (5.33%)
occurrences causally related to treatment / all	3 / 10	0 / 2	1 / 8
deaths causally related to treatment / all	1 / 2	0 / 0	1 / 4
Pneumonia bacterial			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			

subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	3 / 152 (1.97%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Respiratory tract infection			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection bacterial			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	12 / 152 (7.89%)	7 / 49 (14.29%)	10 / 150 (6.67%)
occurrences causally related to treatment / all	6 / 14	2 / 7	1 / 10
deaths causally related to treatment / all	3 / 8	1 / 2	1 / 4
Septic shock			
subjects affected / exposed	10 / 152 (6.58%)	3 / 49 (6.12%)	8 / 150 (5.33%)
occurrences causally related to treatment / all	2 / 10	0 / 4	1 / 8
deaths causally related to treatment / all	2 / 7	0 / 0	1 / 4
Staphylococcal infection			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal sepsis			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic candida			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection viral			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral diarrhoea			
subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	2 / 152 (1.32%)	0 / 49 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	2 / 152 (1.32%)	1 / 49 (2.04%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			

subjects affected / exposed	1 / 152 (0.66%)	0 / 49 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Ruxolitinib (RUX) (Experimental)	Cross-Over	Best Available Therapy (BAT)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 152 (94.74%)	43 / 49 (87.76%)	136 / 150 (90.67%)
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 152 (13.82%)	6 / 49 (12.24%)	18 / 150 (12.00%)
occurrences (all)	22	7	20
Hypotension			
subjects affected / exposed	15 / 152 (9.87%)	1 / 49 (2.04%)	10 / 150 (6.67%)
occurrences (all)	17	1	10
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 152 (7.24%)	3 / 49 (6.12%)	6 / 150 (4.00%)
occurrences (all)	13	3	6
Generalised oedema			
subjects affected / exposed	5 / 152 (3.29%)	0 / 49 (0.00%)	8 / 150 (5.33%)
occurrences (all)	5	0	8
Oedema peripheral			
subjects affected / exposed	37 / 152 (24.34%)	5 / 49 (10.20%)	32 / 150 (21.33%)
occurrences (all)	45	6	39
Pyrexia			
subjects affected / exposed	29 / 152 (19.08%)	9 / 49 (18.37%)	21 / 150 (14.00%)
occurrences (all)	38	12	29
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	14 / 152 (9.21%)	3 / 49 (6.12%)	7 / 150 (4.67%)
occurrences (all)	15	3	8
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	16 / 152 (10.53%)	2 / 49 (4.08%)	12 / 150 (8.00%)
occurrences (all)	16	2	15
Dyspnoea			
subjects affected / exposed	8 / 152 (5.26%)	3 / 49 (6.12%)	6 / 150 (4.00%)
occurrences (all)	9	3	6
Epistaxis			
subjects affected / exposed	8 / 152 (5.26%)	2 / 49 (4.08%)	6 / 150 (4.00%)
occurrences (all)	9	2	6
Pleural effusion			
subjects affected / exposed	4 / 152 (2.63%)	0 / 49 (0.00%)	8 / 150 (5.33%)
occurrences (all)	4	0	9
Psychiatric disorders			
Depression			
subjects affected / exposed	9 / 152 (5.92%)	1 / 49 (2.04%)	4 / 150 (2.67%)
occurrences (all)	9	1	4
Insomnia			
subjects affected / exposed	9 / 152 (5.92%)	2 / 49 (4.08%)	8 / 150 (5.33%)
occurrences (all)	10	2	8
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	16 / 152 (10.53%)	2 / 49 (4.08%)	11 / 150 (7.33%)
occurrences (all)	20	3	13
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 152 (5.92%)	1 / 49 (2.04%)	9 / 150 (6.00%)
occurrences (all)	15	4	11
Blood bilirubin increased			
subjects affected / exposed	7 / 152 (4.61%)	3 / 49 (6.12%)	15 / 150 (10.00%)
occurrences (all)	9	3	19
Blood creatinine increased			
subjects affected / exposed	8 / 152 (5.26%)	3 / 49 (6.12%)	10 / 150 (6.67%)
occurrences (all)	11	6	11
C-reactive protein increased			
subjects affected / exposed	4 / 152 (2.63%)	3 / 49 (6.12%)	5 / 150 (3.33%)
occurrences (all)	4	3	6
Gamma-glutamyltransferase increased			

subjects affected / exposed	14 / 152 (9.21%)	2 / 49 (4.08%)	12 / 150 (8.00%)
occurrences (all)	17	2	13
Neutrophil count decreased			
subjects affected / exposed	19 / 152 (12.50%)	4 / 49 (8.16%)	16 / 150 (10.67%)
occurrences (all)	36	7	30
Platelet count decreased			
subjects affected / exposed	31 / 152 (20.39%)	6 / 49 (12.24%)	24 / 150 (16.00%)
occurrences (all)	38	7	39
Weight decreased			
subjects affected / exposed	7 / 152 (4.61%)	3 / 49 (6.12%)	5 / 150 (3.33%)
occurrences (all)	7	3	6
White blood cell count decreased			
subjects affected / exposed	21 / 152 (13.82%)	2 / 49 (4.08%)	16 / 150 (10.67%)
occurrences (all)	38	2	35
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	12 / 152 (7.89%)	2 / 49 (4.08%)	3 / 150 (2.00%)
occurrences (all)	13	2	3
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 152 (1.97%)	2 / 49 (4.08%)	9 / 150 (6.00%)
occurrences (all)	3	2	12
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 152 (8.55%)	2 / 49 (4.08%)	5 / 150 (3.33%)
occurrences (all)	25	2	5
Tremor			
subjects affected / exposed	6 / 152 (3.95%)	3 / 49 (6.12%)	5 / 150 (3.33%)
occurrences (all)	16	3	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	61 / 152 (40.13%)	16 / 49 (32.65%)	47 / 150 (31.33%)
occurrences (all)	107	38	93
Leukopenia			
subjects affected / exposed	14 / 152 (9.21%)	3 / 49 (6.12%)	2 / 150 (1.33%)
occurrences (all)	21	3	2

Neutropenia			
subjects affected / exposed	36 / 152 (23.68%)	10 / 49 (20.41%)	19 / 150 (12.67%)
occurrences (all)	64	20	39
Thrombocytopenia			
subjects affected / exposed	56 / 152 (36.84%)	14 / 49 (28.57%)	30 / 150 (20.00%)
occurrences (all)	85	27	57
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 152 (1.32%)	3 / 49 (6.12%)	1 / 150 (0.67%)
occurrences (all)	2	3	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	20 / 152 (13.16%)	4 / 49 (8.16%)	11 / 150 (7.33%)
occurrences (all)	23	4	14
Constipation			
subjects affected / exposed	9 / 152 (5.92%)	2 / 49 (4.08%)	6 / 150 (4.00%)
occurrences (all)	9	2	6
Diarrhoea			
subjects affected / exposed	18 / 152 (11.84%)	4 / 49 (8.16%)	20 / 150 (13.33%)
occurrences (all)	28	5	28
Nausea			
subjects affected / exposed	30 / 152 (19.74%)	3 / 49 (6.12%)	16 / 150 (10.67%)
occurrences (all)	43	4	19
Stomatitis			
subjects affected / exposed	6 / 152 (3.95%)	3 / 49 (6.12%)	5 / 150 (3.33%)
occurrences (all)	7	3	5
Vomiting			
subjects affected / exposed	25 / 152 (16.45%)	5 / 49 (10.20%)	16 / 150 (10.67%)
occurrences (all)	39	5	22
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 152 (4.61%)	0 / 49 (0.00%)	8 / 150 (5.33%)
occurrences (all)	8	0	8
Purpura			
subjects affected / exposed	0 / 152 (0.00%)	3 / 49 (6.12%)	0 / 150 (0.00%)
occurrences (all)	0	3	0
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	8 / 152 (5.26%)	0 / 49 (0.00%)	6 / 150 (4.00%)
occurrences (all)	9	0	6
Acute kidney injury			
subjects affected / exposed	18 / 152 (11.84%)	2 / 49 (4.08%)	7 / 150 (4.67%)
occurrences (all)	20	2	7
Haematuria			
subjects affected / exposed	12 / 152 (7.89%)	1 / 49 (2.04%)	6 / 150 (4.00%)
occurrences (all)	14	1	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 152 (8.55%)	3 / 49 (6.12%)	6 / 150 (4.00%)
occurrences (all)	15	5	8
Back pain			
subjects affected / exposed	8 / 152 (5.26%)	4 / 49 (8.16%)	7 / 150 (4.67%)
occurrences (all)	8	4	8
Myopathy			
subjects affected / exposed	7 / 152 (4.61%)	3 / 49 (6.12%)	9 / 150 (6.00%)
occurrences (all)	7	3	9
Pain in extremity			
subjects affected / exposed	9 / 152 (5.92%)	0 / 49 (0.00%)	10 / 150 (6.67%)
occurrences (all)	12	0	11
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	11 / 152 (7.24%)	1 / 49 (2.04%)	9 / 150 (6.00%)
occurrences (all)	15	1	9
Cytomegalovirus infection reactivation			
subjects affected / exposed	38 / 152 (25.00%)	8 / 49 (16.33%)	30 / 150 (20.00%)
occurrences (all)	55	9	39
Device related infection			
subjects affected / exposed	13 / 152 (8.55%)	1 / 49 (2.04%)	5 / 150 (3.33%)
occurrences (all)	14	1	5
Epstein-Barr virus infection reactivation			
subjects affected / exposed	8 / 152 (5.26%)	1 / 49 (2.04%)	6 / 150 (4.00%)
occurrences (all)	8	1	6

Pneumonia			
subjects affected / exposed	10 / 152 (6.58%)	3 / 49 (6.12%)	6 / 150 (4.00%)
occurrences (all)	10	3	6
Sepsis			
subjects affected / exposed	5 / 152 (3.29%)	3 / 49 (6.12%)	9 / 150 (6.00%)
occurrences (all)	7	5	9
Urinary tract infection			
subjects affected / exposed	15 / 152 (9.87%)	1 / 49 (2.04%)	9 / 150 (6.00%)
occurrences (all)	21	1	13
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 152 (4.61%)	1 / 49 (2.04%)	8 / 150 (5.33%)
occurrences (all)	7	1	9
Hyperglycaemia			
subjects affected / exposed	10 / 152 (6.58%)	1 / 49 (2.04%)	15 / 150 (10.00%)
occurrences (all)	10	1	18
Hyperkalaemia			
subjects affected / exposed	9 / 152 (5.92%)	2 / 49 (4.08%)	9 / 150 (6.00%)
occurrences (all)	11	2	10
Hypertriglyceridaemia			
subjects affected / exposed	9 / 152 (5.92%)	4 / 49 (8.16%)	4 / 150 (2.67%)
occurrences (all)	9	4	5
Hypoalbuminaemia			
subjects affected / exposed	18 / 152 (11.84%)	2 / 49 (4.08%)	20 / 150 (13.33%)
occurrences (all)	30	2	22
Hypocalcaemia			
subjects affected / exposed	15 / 152 (9.87%)	4 / 49 (8.16%)	16 / 150 (10.67%)
occurrences (all)	19	5	31
Hypokalaemia			
subjects affected / exposed	34 / 152 (22.37%)	10 / 49 (20.41%)	28 / 150 (18.67%)
occurrences (all)	51	12	67
Hypomagnesaemia			
subjects affected / exposed	23 / 152 (15.13%)	6 / 49 (12.24%)	23 / 150 (15.33%)
occurrences (all)	34	7	42
Hyponatraemia			

subjects affected / exposed	5 / 152 (3.29%)	3 / 49 (6.12%)	6 / 150 (4.00%)
occurrences (all)	6	3	10
Hypophosphataemia			
subjects affected / exposed	15 / 152 (9.87%)	4 / 49 (8.16%)	15 / 150 (10.00%)
occurrences (all)	21	6	31

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2017	The main purpose of the amendment was to clarify exclusion criterion #5 and other eligibility criteria to follow standard medical practice. The revision of exclusion criterion #5 was to follow standard medical practice in determining the presence of active viral infection. This determination was based on the treating physician's clinical assessment according to local institutional guidelines at the time of randomization including but not limited to vital signs, physical examination, laboratory and relevant radiologic studies and viral load testing results when available.
21 June 2018	The main purpose of the amendment was to allow for more flexibility in the tapering of corticosteroids, calcineurin inhibitors (CNI) and ruxolitinib; and if needed, for this taper to be completed safely beyond Week 24. This change included clarification that institutional guidelines for the tapering of corticosteroids and CNI could be followed. Additionally, the physician could tailor the tapering strategy to each patient's condition, including stopping ruxolitinib more slowly in case of an acute Graft vs. Host Disease (aGvHD) flare or other safety concerns which may prevent the taper from being completed by Week 24. • Patients who met the protocol criteria for treatment discontinuation were not eligible to continue receiving ruxolitinib within the study. However, as part of Novartis "Posttrial access" commitment, patients who met all of the following criteria : • responded to ruxolitinib at Day 28 (or Crossover Day 28), • met study discontinuation criteria, other than safety reasons, • are assessed by the Investigator to still be deriving clinical benefit from ruxolitinib, were given the possibility to continue ruxolitinib outside the study, where permitted by and in accordance to local laws and regulations, if requested; they would then not enter the Long-Term Follow-Up period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies and data using 999 as data points are not accurately represented in this record. Please go to https://www.novctrd.com/CtrdWeb/home.nov for complete trial results

Notes: