Clinical trial results:
A Phase 3, Randomized, Double-blind Active-controlled Study Evaluating Momelotinib vs. Ruxolitinib in Subjects with Primary Myelofibrosis (PMF) or Post-Polycythemia Vera or Post-Essential Thrombocythemia Myelofibrosis (Post-PV/ET MF)

Summary

EudraCT number	2013-002707-33
Trial protocol	CZ DE BE GB AT SE ES HU NL DK BG RO PL FR
Global end of trial date	02 May 2019

Results information

Result version number	v1 (current)
This version publication date	12 August 2021
First version publication date	12 August 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-352-0101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01969838
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sierra Oncology, Inc.
Sponsor organisation address	46701 Commerce Center Drive, Plymouth, MI, United States, 48170
Public contact	Martha Bond, Sierra Oncology, Inc., +1 4165287431, mbond@sierraoncology.com
Scientific contact	Martha Bond, Sierra Oncology, Inc., +1 4165287431, mbond@sierraoncology.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of momelotinib compared with ruxolitinib as measured by splenic response rate at Week 24 (SRR24).

Protection of trial subjects:

The protocol, protocol amendments, consent forms, and study subject information sheets were submitted by each investigator to a duly constituted independent ethics committee (IEC) or institutional review board (IRB) for review and approval before study initiation. Protocol amendments and all revisions to the consent form or study subject information sheet after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

Study GS-US-352-0101 was conducted under a United States (US) investigational new drug (IND) application and in accordance with recognized international scientific and ethical standards, including but not limited to the International Council for Harmonisation (ICH) guideline for Good Clinical Practice (GCP) and the original principles embodied in the Declaration of Helsinki. These standards are consistent with the requirements of the US Code of Federal Regulations (CFR) Title 21, Part 312 (21CFR312), and the European Community Directive 2001/20/EC, as well as other local legislation.

Investigators (or designee[s]) were responsible for obtaining written informed consent from each individual who participated in this study after adequate explanation of the aims, methods, objectives, and potential hazards of the study and before undertaking any study related procedures. Subjects were informed that they were completely free to refuse to enter the study or to withdraw from it at any time for any reason.

Background therapy: -

Evidence for comparator:

Ruxolitinib (RUX) was the only approved JAK inhibitor indicated for the treatment of intermediate or high-risk MF in adults at the time of this study’s initiation, and therefore was chosen as the control for this trial. All subjects were allowed to continue or switch to open-label momelotinib (MMB) treatment after the double-blind treatment phase, which allowed subjects to continue to receive treatment benefit and for the collection of long-term treatment data. Subjects were not allowed to receive RUX in the open-label treatment phase.

Actual start date of recruitment	06 December 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Poland: 71

Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Bulgaria: 22
Country: Number of subjects enrolled	Czechia: 21
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Hungary: 31
Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	Australia: 39
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Singapore: 8
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Taiwan: 5
Worldwide total number of subjects	432
EEA total number of subjects	267

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)	0
Adults (18-64 years)	185
From 65 to 84 years	245
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Study GS-US -352-0101 (SIMPLIFY-1) was designed to evaluate the efficacy and safety of MMB versus RUX in a double-blind head-to -head comparison in subjects with PMF, post-PV MF, or post-ET MF who had not received previous treatment with a JAK inhibitor.

Pre-assignment

Screening details:

The screening date was defined as the date the subject signed the Informed Consent Form (ICF). Subjects were screened within 35 days after signing the ICF to determine eligibility for participation in the study. Subjects who did not enroll within the 35-day screening window were considered screen failures.

Pre-assignment period milestones

Number of subjects started	602[1]
Number of subjects completed	432

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not meet Eligibility: 149
Reason: Number of subjects	Adverse event, non-fatal: 2
Reason: Number of subjects	Physician decision: 2
Reason: Number of subjects	Consent withdrawn by subject: 6
Reason: Number of subjects	Lost to Follow-up: 1
Reason: Number of subjects	Outside of visit window: 6
Reason: Number of subjects	Other: 4

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 602 subjects that were screened for the trial, 170 patients did not continue to baseline and were also not randomized, as describe in the subject non-completion reasons. 432 subjects completed screening, entered the baseline period and were randomized.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Momelotinib (MMB)

Arm description: -

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

Dosage and administration details:

Momelotinib was available as 100 mg, 150 mg, and 200 mg strength (as free base equivalent) tablets. In addition to the drug substance, the tablets also contained the excipients microcrystalline cellulose,

lactose monohydrate, sodium starch glycolate, silicon dioxide, magnesium stearate, propyl gallate, polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide, yellow iron oxide, and red iron oxide. Momelotinib 100-mg and 150-mg tablets were plain round, film-coated brown tablets, and MMB 200-mg tablets were plain capsule-shaped, film-coated brown tablets.

Momelotinib placebo tablets were visually identical to the MMB tablets but contained no active ingredient.

The starting dose of MMB for all subjects was 200 mg (or placebo equivalent) in a single tablet. Momelotinib was to be orally self-administered once daily in the morning, and thereafter at approximately the same time each day.

Momelotinib was not administered in the baseline period.

Arm title	Ruxolitinib (RUX)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ruxolitinib was orally self-administered twice daily as either 1 or 2 tablets per dose. The starting dose of RUX (or placebo equivalent) was determined based on screening laboratory values. Ruxolitinib doses may have been interrupted and/or reduced sequentially due to drug-related thrombocytopenia. Following improvement of platelet count to ≥ 50 × 10^9/L in the absence of platelet transfusion for at least 5 days, RUX may have been restarted. Dose adjustments and rule for withholding RUX are discussed in further detail in the protocol.

Ruxolitinib was not administered during baseline.

Number of subjects in period 1	Momelotinib (MMB)	Ruxolitinib (RUX)
Started	215	217
Completed	215	217

Period 2

Period 2 title	Double-blind Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

During the double-blind (DB) phase, study drug was administered in a DB fashion. The identity of the study drug was concealed by central blinding of study drug assignments. DB treatment assignments remained blinded until all subjects had completed Week 24 and the study was unblinded for the purpose of the final efficacy analysis. Blinding was accomplished through use of placebos that were well-matched to the study drugs in appearance, packaging, labeling, and schedule of administration.

Arms	
Are arms mutually exclusive?	Yes
Arm title	Momelotinib (MMB)

Arm description: -

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

Dosage and administration details:

Momelotinib was available as 100 mg, 150 mg, and 200 mg strength (as free base equivalent) tablets. In addition to the drug substance, the tablets also contained the excipients microcrystalline cellulose, lactose monohydrate, sodium starch glycolate, silicon dioxide, magnesium stearate, propyl gallate, polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide, yellow iron oxide, and red iron oxide. Momelotinib 100-mg and 150-mg tablets were plain round, film-coated brown tablets, and MMB 200-mg tablets were plain capsule-shaped, film-coated brown tablets.

Momelotinib placebo tablets were visually identical to the MMB tablets but contained no active ingredient.

The starting dose of MMB for all subjects was 200 mg (or placebo equivalent) in a single tablet. Momelotinib was to be orally self-administered once daily in the morning, and thereafter at approximately the same time each day.

Arm title	Ruxolitinib (RUX)

Arm description: -

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

Dosage and administration details:

Ruxolitinib was orally self-administered twice daily as either 1 or 2 tablets per dose. The starting dose of RUX (or placebo equivalent) was determined based on screening laboratory values. Ruxolitinib doses may have been interrupted and/or reduced sequentially due to drug-related thrombocytopenia. Following improvement of platelet count to ≥ 50 × 10^9/L in the absence of platelet transfusion for at least 5 days, RUX may have been restarted. Dose adjustments and rule for withholding RUX are discussed in further detail in the protocol.

Number of subjects in period 2	Momelotinib (MMB)	Ruxolitinib (RUX)
Started	215	217
Completed	188	208
Not completed	27	9
Adverse event, serious fatal	-	1
Physician decision	5	1
Disease progression	2	-
Adverse event, non-fatal	10	3
Subject decision	4	2

Death	5	2
Symptomatic spleen growth	1	-

Period 3

Period 3 title	Open-label Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MMB to MMB

Arm description: -

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

Dosage and administration details:

Momelotinib was available as 100 mg, 150 mg, and 200 mg strength (as free base equivalent) tablets. In addition to the drug substance, the tablets also contained the excipients microcrystalline cellulose, lactose monohydrate, sodium starch glycolate, silicon dioxide, magnesium stearate, propyl gallate, polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide, yellow iron oxide, and red iron oxide. Momelotinib 100-mg and 150-mg tablets were plain round, film-coated brown tablets, and MMB 200-mg tablets were plain capsule-shaped, film-coated brown tablets.

Momelotinib was to be orally self-administered once daily in the morning, and thereafter at approximately the same time each day.

Arm title	RUX to MMB

Arm description: -

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

Dosage and administration details:

Momelotinib was available as 100 mg, 150 mg, and 200 mg strength (as free base equivalent) tablets. In addition to the drug substance, the tablets also contained the excipients microcrystalline cellulose, lactose monohydrate, sodium starch glycolate, silicon dioxide, magnesium stearate, propyl gallate, polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide, yellow iron oxide, and red iron oxide. Momelotinib 100-mg and 150-mg tablets were plain round, film-coated brown tablets, and MMB 200-mg tablets were plain capsule-shaped, film-coated brown tablets.

Momelotinib was to be orally self-administered once daily in the morning, and thereafter at approximately the same time each day.

Number of subjects in period 3[2]	MMB to MMB	RUX to MMB
Started	171	197
Completed	1	0
Not completed	170	197
Adverse event, serious fatal	1	1
Transferred to study SRA-MMB-4365	52	62
Physician decision	9	14
Disease progression	26	27
Subject decision	14	15
Adverse event, non-fatal	36	48
Death	13	11
Non compliance with study drug	2	-
Lack of efficacy	17	19

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all subjects that completed the double-blind period entered the open-label phase. Of 188 subjects in the MMB group that completed the double-blind phase, 171 entered open-label MMB. Of the 208 subjects in the RUX group that completed the double-blind phase, 197 entered open-label MMB.

Baseline characteristics

Reporting groups	
Reporting group title	Momelotinib (MMB)
Reporting group description: -	
Reporting group title	Ruxolitinib (RUX)
Reporting group description: -	

Reporting group values	Momelotinib (MMB)	Ruxolitinib (RUX)	Total
Number of subjects	215	217	432
Age categorical Units: Subjects			
< 65	90	95	185
>= 65	125	122	247
Age continuous Units: years			
median	67.0	66.0	
full range (min-max)	28.0 to 85.0	25.0 to 86.0	-
Gender categorical Units: Subjects			
Female	91	97	188
Male	124	120	244
Race Units: Subjects			
White	179	178	357
Black or African American	2	2	4
Asian	17	20	37
Not Permitted	15	16	31
Other	2	1	3
Ethnicity Units: Subjects			
Hispanic or Latino	6	4	10
Not Hispanic or Latino	191	194	385
Not Permitted	18	19	37
Transfusion Dependent Units: Subjects			
Yes	53	52	105
No	162	165	327
Platelet Count (10^9/L) Units: Subjects			
< 100	18	23	41
>= 100 and <= 200	66	63	129
> 200	131	131	262
Weight Units: kg			
median	69.3	71.4	
inter-quartile range (Q1-Q3)	62.9 to 80.0	62.5 to 83.4	-
Height Units: cm			

median	170.0	170.0	
inter-quartile range (Q1-Q3)	163.0 to 176.0	162.0 to 177.0	-
BMI			
Units: kg/m^2			
median	24.6	24.9	
inter-quartile range (Q1-Q3)	22.0 to 26.7	22.3 to 27.5	-
Hemoglobin			
Units: g/dL			
median	10.5	10.3	
inter-quartile range (Q1-Q3)	9.1 to 12.0	9.2 to 11.9	-

Subject analysis sets

Subject analysis set title	Intent-to-Treat Analysis Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Analysis Set included all subjects who were randomized in the study. Subjects were grouped within the ITT Analysis Set by the treatment group to which they were randomized. This is the primary analysis set for efficacy analyses and for demographic and baseline characteristics. For the secondary efficacy endpoint of TSS response rate at Week 24, the analysis was performed on subjects in the ITT Analysis Set who had a baseline TSS > 0 or who had a baseline TSS = 0 but a nonzero or missing TSS at Week 24.

Reporting group values	Intent-to-Treat Analysis Set		
Number of subjects	432		
Age categorical			
Units: Subjects			
< 65	185		
>= 65	247		
Age continuous			
Units: years			
median	66.0		
full range (min-max)	25.0 to 86.0		
Gender categorical			
Units: Subjects			
Female	188		
Male	244		
Race			
Units: Subjects			
White	357		
Black or African American	4		
Asian	37		
Not Permitted	31		
Other	3		
Ethnicity			
Units: Subjects			
Hispanic or Latino	10		
Not Hispanic or Latino	385		
Not Permitted	37		
Transfusion Dependent			
Units: Subjects			
Yes	105		

No	327		
Platelet Count (10^9/L) Units: Subjects			
< 100	41		
>= 100 and <= 200	129		
> 200	262		
Weight Units: kg			
median	70.0		
inter-quartile range (Q1-Q3)	62.8 to 82.0		
Height Units: cm			
median	170.0		
inter-quartile range (Q1-Q3)	162.5 to 176.0		
BMI Units: kg/m^2			
median	24.6		
inter-quartile range (Q1-Q3)	22.2 to 27.2		
Hemoglobin Units: g/dL			
median	10.4		
inter-quartile range (Q1-Q3)	9.1 to 12.0		

End points

End points reporting groups

Reporting group title	Momelotinib (MMB)
Reporting group description: -	
Reporting group title	Ruxolitinib (RUX)
Reporting group description: -	
Reporting group title	Momelotinib (MMB)
Reporting group description: -	
Reporting group title	Ruxolitinib (RUX)
Reporting group description: -	
Reporting group title	MMB to MMB
Reporting group description: -	
Reporting group title	RUX to MMB
Reporting group description: -	
Subject analysis set title	Intent-to-Treat Analysis Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Analysis Set included all subjects who were randomized in the study. Subjects were grouped within the ITT Analysis Set by the treatment group to which they were randomized. This is the primary analysis set for efficacy analyses and for demographic and baseline characteristics. For the secondary efficacy endpoint of TSS response rate at Week 24, the analysis was performed on subjects in the ITT Analysis Set who had a baseline TSS > 0 or who had a baseline TSS = 0 but a nonzero or missing TSS at Week 24.

Primary: Splenic Response Rate at Week 24

End point title	Splenic Response Rate at Week 24

End point description:

The primary endpoint of the study, splenic response rate at Week 24, was defined as the proportion of subjects who achieved a spleen volume reduction of ≥ 35% from baseline at the Week 24 assessment as measured by MRI or CT scans. A similar proportion of subjects achieved a response in the MMB group (57 of 215 subjects, 26.5%) as in the RUX group (64 of 217 subjects, 29.5%) in the ITT population. The non-inferiority proportion difference in response rates was statistically significant by stratified CMH method (0.09 [95% CI: 0.02, 0.16]; p = 0.014). Because the lower bound of the 2-sided 95% CI was greater than 0, the MMB group met the primary endpoint of noninferiority on splenic response rate over the RUX group. An additional 101 subjects (47.0%) in the MMB group and 112 subjects (51.6%) in the RUX group achieved a reduction of spleen volume that was insufficient to meet the response definition (< 35% spleen volume reduction and not more than a 0% spleen volume increase at Week 24).

End point type	Primary

End point timeframe:

Week 24

End point values	Momelotinib (MMB)	Ruxolitinib (RUX)	Intent-to-Treat Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	215	217	432	
Units: Subjects				
Responder	57	64	121	
Nonresponder	158	153	311	

Attachments (see zip file)	15.12.1.1 t-srr24.pdf

Statistical analyses

Statistical analysis title	Analysis of Splenic Response Rate

Statistical analysis description:

The primary endpoint was splenic response rate at Week 24, defined as the proportion of subjects who achieved a ≥ 35% reduction in spleen volume at Week 24 versus baseline as measured by MRI or CT. The primary hypothesis is that MMB is non-inferior to RUX in splenic response rate at Week 24. Noninferiority of MMB was evaluated by comparing the difference in response rate at Week 24 (Pa − 0.60 Pc) and 0 at a 2-sided 0.05 level, using the CMH approach to adjust for the stratification factors.

Comparison groups	Momelotinib (MMB) v Ruxolitinib (RUX)
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.014
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference - Stratified CMH
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.16

Secondary: Total Symptom Score (TSS) Response Rate at Week 24

End point title	Total Symptom Score (TSS) Response Rate at Week 24

End point description:

Response rate in TSS, a prespecified secondary endpoint, was defined as the proportion of subjects who achieved a ≥ 50% reduction in TSS at Week 24 versus baseline as measured by the modified MPN-SAF TSS v2.0 diary. Response rate was calculated using the average of the daily TSS from a consecutive 28-day period prior to Week 24, which had ≥ 20 daily TSS available. Response rate was evaluated for subjects in the ITT analysis set who had a baseline TSS > 0 or had a baseline TSS = 0 but nonzero or missing TSS at Week 24. In the MMB group, 60 (28.4%) of the 211 subjects at Week 24 had a TSS reduction of ≥ 50% from baseline compared to 89 (42.2%) of the 211 evaluable subjects in the RUX group. The noninferior proportion difference by stratified CMH method (95% CI) was 0.00 (-0.08, 0.08); this difference was not statistically significant (p = 0.98). Because the lower bound of the 2-sided 95% CI was not greater than 0, noninferiority of the MMB group to the RUX group was not met.

End point type	Secondary

End point timeframe:

Week 24

End point values	Momelotinib (MMB)	Ruxolitinib (RUX)	Intent-to-Treat Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	211	211	422	
Units: Subjects				
Responder	60	89	149	
Nonresponder	151	122	273	

Attachments (see zip file)	15.12.2.1_t-tss24.pdf

Statistical analyses

Statistical analysis title	Analysis of Response Rate in TSS at Week 24

Statistical analysis description:

Response rate in TSS from baseline to Week 24 is defined as the proportion of subjects who achieved a ≥ 50% reduction from baseline in TSS at Week 24 as measured by the modified MPN SAF TSS v2.0 diary. Noninferiority of MMB was evaluated by comparing the difference in response rate of total symptom score at Week 24 (Pa − 0.67 Pc) and 0 at a 2-sided 0.05 level, using the CMH approach to adjust for the stratification factors.

Comparison groups	Ruxolitinib (RUX) v Momelotinib (MMB)
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.98
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference - Stratified CMH
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.08

Secondary: Rate of Red Blood Cell Transfusions in the DB Phase

End point title	Rate of Red Blood Cell Transfusions in the DB Phase

End point description:

The rate of RBC transfusions in the double-blind phase was a prespecified secondary endpoint, defined as the average number of RBC units transfused not associated with clinically overt bleeding per subject-month during the double-blind phase. For the ITT analysis set, the rate of RBC transfusion was nominally significantly lower in the MMB group with transfusion rate ratio of 0.28 (95% CI=0.19 to 0.43) and p-value < 0.001 per negative binomial model adjusted for strata. The median (Q1, Q3) rate of RBC transfusion was lower in the MMB group (0.0 [0.0, 0.2] units/month) compared with the RUX group (0.4 [0.0, 1.5] units/month) through Week 24. The median (Q1, Q3) total number of RBC transfusion units in the double-blind phase was lower in the MMB group (0.0 [0.0, 1.0]) compared with the RUX group (2.0 [0.0, 8.0]).

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Momelotinib (MMB)	Ruxolitinib (RUX)	Intent-to-Treat Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	215	217	432	
Units: units/month				
median (inter-quartile range (Q1-Q3))				
Rate of RBC Transfusion	0.0 (0.0 to 0.2)	0.4 (0.0 to 1.5)	0.0 (0.0 to 0.9)	

Attachments (see zip file)	15.12.3.1 t-rbc24.pdf

Statistical analyses

Statistical analysis title	Analysis of Rate of RBC Transfusion in the RT

Statistical analysis description:

Rate of RBC transfusion in the RT phase is defined as the average number of RBC units transfused that was not associated with clinically overt bleeding per subject month during the double-blind phase

Comparison groups	Momelotinib (MMB) v Ruxolitinib (RUX)
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative Binomial Model, Adjusted
Parameter estimate	Rate ratio of RBC transfusion
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.43

Secondary: RBC Transfusion Independence Rate at Week 24

End point title	RBC Transfusion Independence Rate at Week 24

End point description:

Transfusion independent response at Week 24 was defined as the absence of RBC transfusion and no hemoglobin level < 8 g/dL in the 12 weeks prior to Week 24, excluding cases associated with clinically overt bleeding. A greater proportion of subjects in the MMB group was TI at Week 24: 66.5% (143 subjects) compared with the RUX group 49.3% (107 subjects). The difference was nominally statistically significant (p < 0.001).

End point type	Secondary

End point timeframe:

Week 24

End point values	Momelotinib (MMB)	Ruxolitinib (RUX)	Intent-to-Treat Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	215	217	432	
Units: Subjects				
Responder	143	107	250	
Nonresponder	72	110	182	

Attachments (see zip file)	15.12.4.1 t-rbcti24.pdf

Statistical analyses

Statistical analysis title	Analysis of RBC TI Rate at Week 24

Statistical analysis description:

Response rate for TI at Week 24 is defined as the proportion of subjects who were TI at Week 24, where TI was defined as absence of RBC transfusion and no hemoglobin level below 8 g/dL in the prior 12 weeks, excluding cases associated with clinically overt bleeding.

Comparison groups	Momelotinib (MMB) v Ruxolitinib (RUX)
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference - Stratified CMH
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.26

Secondary: RBC Transfusion Dependence Rate at Week 24

End point title	RBC Transfusion Dependence Rate at Week 24

End point description:

Red blood cell TD rate at Week 24 for the ITT population was a prespecified secondary endpoint, defined as having had at least 4 units of RBC transfusion or a hemoglobin level below 8 g/dL in the prior 8 weeks ending with Week 24 (excluding cases associated with clinically overt bleeding). Subjects with the last double-blind phase participation date prior to Day 162 (ie. missing at Week 24) were considered TD at Week 24. A smaller proportion of subjects in the MMB group were TD at Week 24 (30.2%, 65 subjects) compared with the RUX group (40.1%, 87 subjects). The difference was nominally statistically significant (p = 0.019).

End point type	Secondary

End point timeframe:

Week 24

End point values	Momelotinib (MMB)	Ruxolitinib (RUX)	Intent-to-Treat Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	215	217	432	
Units: Subjects				
Dependent	65	87	152	
Nondependent	150	130	280	

Attachments (see zip file)	15.12.5.1 t-rbctd24.pdf

Statistical analyses

Statistical analysis title	Analysis of RBC TD Rate at Week 24
Comparison groups	Momelotinib (MMB) v Ruxolitinib (RUX)
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference - Stratified CMH
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	-0.02

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded that occurred from initiation of investigational product (IP) until 30 days after the last administration of IP regardless of cause or relationship.

Adverse event reporting additional description:

All adverse events were recorded in the eCRF database. Serious adverse events needed to be reported within 24 hours of investigator being aware. Severity of AEs were graded using the CTCAE, Version 4.03, per AE (episode) the highest severity grade attained should be reported. All AEs were followed up until resolution when possible.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Momelotinib (MMB)
Reporting group description: -	
Reporting group title	Ruxolitinib (RUX)
Reporting group description: -	
Reporting group title	MMB to MMB
Reporting group description: -	
Reporting group title	RUX to MMB
Reporting group description: -	

Serious adverse events	Momelotinib (MMB)	Ruxolitinib (RUX)	MMB to MMB
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 214 (22.90%)	39 / 216 (18.06%)	79 / 171 (46.20%)
number of deaths (all causes)	8	7	44
number of deaths resulting from adverse events	7	7	18
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Ovarian clear cell carcinoma			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Splenic marginal zone lymphoma			

subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Uterine cancer			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Malignant melanoma			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Mantle cell lymphoma recurrent			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Myelofibrosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinonasal papilloma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma recurrent			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Langerhans cell sarcoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Primary myelofibrosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seminoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Aortic thrombosis			

subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Hypertension			
subjects affected / exposed	1 / 214 (0.47%)	1 / 216 (0.46%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Aortic stenosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 214 (0.93%)	3 / 216 (1.39%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			

subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Sudden death			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Catheter site haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Chest pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Mucosal haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Oedema peripheral			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
General physical health deterioration			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Breast hyperplasia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Hypoxia			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute respiratory failure			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Pulmonary oedema			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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 arrest			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Blood creatinine increased			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Blood bilirubin increased			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Limb injury			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Abdominal injury			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Head injury			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Post procedural haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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

Tendon rupture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural inflammation			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic rupture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	4 / 214 (1.87%)	1 / 216 (0.46%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	2 / 5	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	2 / 214 (0.93%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 214 (0.93%)	0 / 216 (0.00%)	5 / 171 (2.92%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Angina unstable			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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 failure congestive			
subjects affected / exposed	1 / 214 (0.47%)	1 / 216 (0.46%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pericardial effusion			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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 failure acute			
subjects affected / exposed	0 / 214 (0.00%)	2 / 216 (0.93%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive heart disease			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Sinus bradycardia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial flutter			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Left ventricular failure			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Syncope			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Dizziness			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			

subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord paralysis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar stroke			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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 venous thrombosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular insufficiency			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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			
Anaemia			
subjects affected / exposed	4 / 214 (1.87%)	8 / 216 (3.70%)	7 / 171 (4.09%)
occurrences causally related to treatment / all	3 / 7	16 / 18	12 / 26
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microangiopathic haemolytic anaemia			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Splenic infarction			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytosis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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	0 / 214 (0.00%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Splenic haematoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 214 (0.00%)	3 / 216 (1.39%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic thrombosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 214 (0.00%)	2 / 216 (0.93%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Cataract nuclear			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vision blurred			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 214 (1.87%)	1 / 216 (0.46%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 214 (0.47%)	1 / 216 (0.46%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Inguinal hernia			

subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Melaena			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Nausea			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			

subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Gastric haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal haemorrhage			

subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Subileus			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Vomiting			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Colitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal infarction			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visceral venous thrombosis			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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 and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 214 (0.47%)	1 / 216 (0.46%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 1	0 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nephrolithiasis			
subjects affected / exposed	1 / 214 (0.47%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urinary bladder polyp			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Urinary retention			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Haematuria			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Renal colic			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive nephropathy			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Chest wall haematoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 214 (1.87%)	3 / 216 (1.39%)	16 / 171 (9.36%)
occurrences causally related to treatment / all	1 / 5	0 / 3	4 / 19
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Cystitis			
subjects affected / exposed	2 / 214 (0.93%)	0 / 216 (0.00%)	0 / 171 (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
Sepsis			
subjects affected / exposed	2 / 214 (0.93%)	1 / 216 (0.46%)	6 / 171 (3.51%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Anal abscess			

subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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 sepsis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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 bacterial			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Skin infection			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Streptococcal sepsis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Bronchitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Lung infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	3 / 171 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Peritonitis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Postoperative wound infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			

subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Urinary tract infection			
subjects affected / exposed	0 / 214 (0.00%)	2 / 216 (0.93%)	2 / 171 (1.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal sepsis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neuroborreliosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serratia bacteraemia			

subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tetanus			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
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	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 214 (0.47%)	0 / 216 (0.00%)	0 / 171 (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
Hyperkalaemia			
subjects affected / exposed	1 / 214 (0.47%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			

subjects affected / exposed	0 / 214 (0.00%)	1 / 216 (0.46%)	0 / 171 (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
Hypoglycaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 214 (0.00%)	0 / 216 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RUX to MMB		
Total subjects affected by serious			

adverse events				
subjects affected / exposed	79 / 197 (40.10%)			
number of deaths (all causes)	54			
number of deaths resulting from adverse events	17			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Bladder transitional cell carcinoma				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian clear cell carcinoma				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Splenic marginal zone lymphoma				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine cancer				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Mantle cell lymphoma recurrent				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelofibrosis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinonasal papilloma				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myeloid leukaemia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bladder transitional cell carcinoma recurrent				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic myeloid leukaemia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Langerhans cell sarcoma				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Primary myelofibrosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seminoma				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the tongue				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic dissection				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic thrombosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Sudden death				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Catheter site haemorrhage				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mucosal haemorrhage				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Breast hyperplasia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute respiratory failure				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				

subjects affected / exposed	4 / 197 (2.03%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute pulmonary oedema				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Mental status changes				

subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Abdominal injury				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Post procedural inflammation				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Splenic rupture				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haemorrhage				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound secretion				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Angina unstable				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pericardial effusion				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertensive heart disease				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular failure				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral ischaemia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coma				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral sensorimotor neuropathy				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vocal cord paralysis				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebellar stroke				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral venous thrombosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular insufficiency				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Microangiopathic haemolytic anaemia				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Splenic infarction				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic haematoma				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Thrombocytopenia				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Haemolytic anaemia				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Splenic thrombosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cataract nuclear				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye haemorrhage				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye pain				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vision blurred				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cataract				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				

Diarrhoea			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Melaena			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varices oesophageal			

subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal pain			

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal varices haemorrhage				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritoneal haemorrhage				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematemesis				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal infarction				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Visceral venous thrombosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic failure				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver disorder				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Portal vein thrombosis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				

Dermatitis allergic				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis exfoliative generalised				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 1			
Chronic kidney disease				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary bladder polyp				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive nephropathy				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nephropathy				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Gouty arthritis				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest wall haematoma				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteolysis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle haemorrhage				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				

subjects affected / exposed	9 / 197 (4.57%)			
occurrences causally related to treatment / all	2 / 12			
deaths causally related to treatment / all	0 / 1			
Cystitis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcal sepsis				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	5 / 197 (2.54%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal sepsis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuroborreliosis				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				

subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Serratia bacteraemia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tetanus				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vestibular neuronitis				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Gout				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypervolaemia				
subjects affected / exposed	0 / 197 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypomagnesaemia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus inadequate control				

subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperuricaemia			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	0 / 197 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Momelotinib (MMB)	Ruxolitinib (RUX)	MMB to MMB
Total subjects affected by non-serious adverse events			
subjects affected / exposed	197 / 214 (92.06%)	206 / 216 (95.37%)	153 / 171 (89.47%)
Vascular disorders			
Hypotension			
subjects affected / exposed	18 / 214 (8.41%)	1 / 216 (0.46%)	6 / 171 (3.51%)
occurrences (all)	19	1	7
Flushing			
subjects affected / exposed	13 / 214 (6.07%)	1 / 216 (0.46%)	1 / 171 (0.58%)
occurrences (all)	14	1	1
Hypertension			
subjects affected / exposed	9 / 214 (4.21%)	19 / 216 (8.80%)	10 / 171 (5.85%)
occurrences (all)	11	20	10
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	31 / 214 (14.49%)	26 / 216 (12.04%)	17 / 171 (9.94%)
occurrences (all)	36	35	24
Asthenia			
subjects affected / exposed	12 / 214 (5.61%)	16 / 216 (7.41%)	13 / 171 (7.60%)
occurrences (all)	13	29	16
Pyrexia			

subjects affected / exposed	12 / 214 (5.61%)	14 / 216 (6.48%)	15 / 171 (8.77%)
occurrences (all)	12	15	18
Oedema peripheral			
subjects affected / exposed	10 / 214 (4.67%)	13 / 216 (6.02%)	16 / 171 (9.36%)
occurrences (all)	10	13	20
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	19 / 214 (8.88%)	17 / 216 (7.87%)	14 / 171 (8.19%)
occurrences (all)	19	21	15
Cough			
subjects affected / exposed	18 / 214 (8.41%)	17 / 216 (7.87%)	23 / 171 (13.45%)
occurrences (all)	21	23	30
Epistaxis			
subjects affected / exposed	9 / 214 (4.21%)	14 / 216 (6.48%)	8 / 171 (4.68%)
occurrences (all)	10	14	10
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 214 (1.87%)	6 / 216 (2.78%)	11 / 171 (6.43%)
occurrences (all)	4	7	11
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 214 (4.67%)	10 / 216 (4.63%)	5 / 171 (2.92%)
occurrences (all)	15	10	6
Blood creatinine increased			
subjects affected / exposed	9 / 214 (4.21%)	2 / 216 (0.93%)	10 / 171 (5.85%)
occurrences (all)	11	2	14
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 214 (3.27%)	5 / 216 (2.31%)	3 / 171 (1.75%)
occurrences (all)	10	5	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	16 / 214 (7.48%)	10 / 216 (4.63%)	9 / 171 (5.26%)
occurrences (all)	22	11	16
Fall			

subjects affected / exposed	6 / 214 (2.80%)	4 / 216 (1.85%)	9 / 171 (5.26%)
occurrences (all)	6	4	11
Nervous system disorders			
Headache			
subjects affected / exposed	38 / 214 (17.76%)	43 / 216 (19.91%)	13 / 171 (7.60%)
occurrences (all)	49	52	14
Dizziness			
subjects affected / exposed	34 / 214 (15.89%)	25 / 216 (11.57%)	17 / 171 (9.94%)
occurrences (all)	44	28	19
Peripheral sensory neuropathy			
subjects affected / exposed	20 / 214 (9.35%)	12 / 216 (5.56%)	15 / 171 (8.77%)
occurrences (all)	31	13	15
Paraesthesia			
subjects affected / exposed	15 / 214 (7.01%)	7 / 216 (3.24%)	6 / 171 (3.51%)
occurrences (all)	15	8	7
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	40 / 214 (18.69%)	62 / 216 (28.70%)	29 / 171 (16.96%)
occurrences (all)	99	109	58
Anaemia			
subjects affected / exposed	30 / 214 (14.02%)	79 / 216 (36.57%)	38 / 171 (22.22%)
occurrences (all)	57	184	80
Neutropenia			
subjects affected / exposed	9 / 214 (4.21%)	14 / 216 (6.48%)	7 / 171 (4.09%)
occurrences (all)	26	35	15
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	36 / 214 (16.82%)	42 / 216 (19.44%)	30 / 171 (17.54%)
occurrences (all)	48	57	32
Nausea			
subjects affected / exposed	33 / 214 (15.42%)	8 / 216 (3.70%)	16 / 171 (9.36%)
occurrences (all)	45	11	18
Abdominal pain			
subjects affected / exposed	21 / 214 (9.81%)	24 / 216 (11.11%)	13 / 171 (7.60%)
occurrences (all)	28	28	14
Constipation			

subjects affected / exposed	21 / 214 (9.81%)	15 / 216 (6.94%)	13 / 171 (7.60%)
occurrences (all)	22	15	14
Vomiting			
subjects affected / exposed	20 / 214 (9.35%)	7 / 216 (3.24%)	8 / 171 (4.68%)
occurrences (all)	25	8	9
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 214 (2.80%)	3 / 216 (1.39%)	4 / 171 (2.34%)
occurrences (all)	7	3	4
Abdominal pain upper			
subjects affected / exposed	10 / 214 (4.67%)	10 / 216 (4.63%)	6 / 171 (3.51%)
occurrences (all)	11	13	6
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	10 / 214 (4.67%)	11 / 216 (5.09%)	12 / 171 (7.02%)
occurrences (all)	13	12	12
Night sweats			
subjects affected / exposed	8 / 214 (3.74%)	9 / 216 (4.17%)	12 / 171 (7.02%)
occurrences (all)	9	12	14
Rash			
subjects affected / exposed	9 / 214 (4.21%)	5 / 216 (2.31%)	10 / 171 (5.85%)
occurrences (all)	9	5	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	15 / 214 (7.01%)	10 / 216 (4.63%)	10 / 171 (5.85%)
occurrences (all)	19	13	12
Pain in extremity			
subjects affected / exposed	14 / 214 (6.54%)	18 / 216 (8.33%)	11 / 171 (6.43%)
occurrences (all)	18	19	13
Muscle spasms			
subjects affected / exposed	8 / 214 (3.74%)	11 / 216 (5.09%)	1 / 171 (0.58%)
occurrences (all)	8	12	1
Bone pain			
subjects affected / exposed	3 / 214 (1.40%)	15 / 216 (6.94%)	4 / 171 (2.34%)
occurrences (all)	3	17	6
Back pain			

subjects affected / exposed	10 / 214 (4.67%)	10 / 216 (4.63%)	10 / 171 (5.85%)
occurrences (all)	10	13	12
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	12 / 214 (5.61%)	14 / 216 (6.48%)	18 / 171 (10.53%)
occurrences (all)	13	17	21
Nasopharyngitis			
subjects affected / exposed	9 / 214 (4.21%)	16 / 216 (7.41%)	7 / 171 (4.09%)
occurrences (all)	9	17	10
Urinary tract infection			
subjects affected / exposed	10 / 214 (4.67%)	9 / 216 (4.17%)	19 / 171 (11.11%)
occurrences (all)	12	10	23
Bronchitis			
subjects affected / exposed	4 / 214 (1.87%)	5 / 216 (2.31%)	8 / 171 (4.68%)
occurrences (all)	4	5	10
Pneumonia			
subjects affected / exposed	1 / 214 (0.47%)	4 / 216 (1.85%)	4 / 171 (2.34%)
occurrences (all)	1	4	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 214 (5.14%)	13 / 216 (6.02%)	15 / 171 (8.77%)
occurrences (all)	11	16	16
Vitamin B1 deficiency			
subjects affected / exposed	7 / 214 (3.27%)	12 / 216 (5.56%)	8 / 171 (4.68%)
occurrences (all)	7	12	10
Hyperuricaemia			
subjects affected / exposed	10 / 214 (4.67%)	7 / 216 (3.24%)	11 / 171 (6.43%)
occurrences (all)	11	7	12
Hyperkalaemia			
subjects affected / exposed	6 / 214 (2.80%)	4 / 216 (1.85%)	9 / 171 (5.26%)
occurrences (all)	13	4	11

Non-serious adverse events	RUX to MMB		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	188 / 197 (95.43%)		
Vascular disorders			

Hypotension			
subjects affected / exposed	9 / 197 (4.57%)		
occurrences (all)	9		
Flushing			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Hypertension			
subjects affected / exposed	18 / 197 (9.14%)		
occurrences (all)	22		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	38 / 197 (19.29%)		
occurrences (all)	44		
Asthenia			
subjects affected / exposed	12 / 197 (6.09%)		
occurrences (all)	20		
Pyrexia			
subjects affected / exposed	14 / 197 (7.11%)		
occurrences (all)	18		
Oedema peripheral			
subjects affected / exposed	10 / 197 (5.08%)		
occurrences (all)	14		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	16 / 197 (8.12%)		
occurrences (all)	23		
Cough			
subjects affected / exposed	34 / 197 (17.26%)		
occurrences (all)	38		
Epistaxis			
subjects affected / exposed	12 / 197 (6.09%)		
occurrences (all)	13		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 197 (3.05%)		
occurrences (all)	6		

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	16		
Blood creatinine increased			
subjects affected / exposed	10 / 197 (5.08%)		
occurrences (all)	12		
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 197 (5.08%)		
occurrences (all)	13		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	5 / 197 (2.54%)		
occurrences (all)	6		
Fall			
subjects affected / exposed	8 / 197 (4.06%)		
occurrences (all)	9		
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 197 (12.18%)		
occurrences (all)	42		
Dizziness			
subjects affected / exposed	25 / 197 (12.69%)		
occurrences (all)	30		
Peripheral sensory neuropathy			
subjects affected / exposed	28 / 197 (14.21%)		
occurrences (all)	38		
Paraesthesia			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	13		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	39 / 197 (19.80%)		
occurrences (all)	102		
Anaemia			

subjects affected / exposed	29 / 197 (14.72%)		
occurrences (all)	70		
Neutropenia			
subjects affected / exposed	7 / 197 (3.55%)		
occurrences (all)	11		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	37 / 197 (18.78%)		
occurrences (all)	49		
Nausea			
subjects affected / exposed	39 / 197 (19.80%)		
occurrences (all)	51		
Abdominal pain			
subjects affected / exposed	26 / 197 (13.20%)		
occurrences (all)	37		
Constipation			
subjects affected / exposed	18 / 197 (9.14%)		
occurrences (all)	20		
Vomiting			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	15		
Gastrooesophageal reflux disease			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	14		
Abdominal pain upper			
subjects affected / exposed	7 / 197 (3.55%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	20 / 197 (10.15%)		
occurrences (all)	21		
Night sweats			
subjects affected / exposed	17 / 197 (8.63%)		
occurrences (all)	19		
Rash			

subjects affected / exposed	12 / 197 (6.09%)		
occurrences (all)	16		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 197 (6.60%)		
occurrences (all)	18		
Pain in extremity			
subjects affected / exposed	19 / 197 (9.64%)		
occurrences (all)	23		
Muscle spasms			
subjects affected / exposed	5 / 197 (2.54%)		
occurrences (all)	7		
Bone pain			
subjects affected / exposed	12 / 197 (6.09%)		
occurrences (all)	12		
Back pain			
subjects affected / exposed	19 / 197 (9.64%)		
occurrences (all)	25		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 197 (9.14%)		
occurrences (all)	23		
Nasopharyngitis			
subjects affected / exposed	14 / 197 (7.11%)		
occurrences (all)	22		
Urinary tract infection			
subjects affected / exposed	19 / 197 (9.64%)		
occurrences (all)	28		
Bronchitis			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	14		
Pneumonia			
subjects affected / exposed	12 / 197 (6.09%)		
occurrences (all)	14		
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	15 / 197 (7.61%) 19		
Vitamin B1 deficiency subjects affected / exposed occurrences (all)	11 / 197 (5.58%) 12		
Hyperuricaemia subjects affected / exposed occurrences (all)	14 / 197 (7.11%) 16		
Hyperkalaemia subjects affected / exposed occurrences (all)	2 / 197 (1.02%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28930494