Clinical trial results:
Controlled Myelofibrosis Study With Oral Janus-associated Kinase (JAK) Inhibitor Treatment-II: The COMFORT-II Trial

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2009-009858-24
Trial protocol	BE GB SE FR DE AT ES NL IT
Global end of trial date	04 March 2015

Results information

Result version number	v1 (current)
This version publication date	07 July 2018
First version publication date	07 July 2018

Trial information

Trial identification

Sponsor protocol code	CINC424A2352

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00934544
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH 4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Clinical Disclosure Office, 41 613241111,
Scientific contact	Clinical Disclosure Office, Clinical Disclosure Office, 41 613241111,

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	04 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy, safety and tolerability of INC424 given twice daily compared to the best-available therapy, in subjects with primary myelofibrosis (PMF), post polycythemia vera myelofibrosis (PPV-MF) and post essential thrombocythemia myelofibrosis (PET-MF).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Austria: 15
Country: Number of subjects enrolled	Belgium: 36
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 47
Country: Number of subjects enrolled	Italy: 47
Worldwide total number of subjects	219
EEA total number of subjects	219

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	93
From 65 to 84 years	124
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Following the acquisition of the development rights for ruxolitinib by Novartis , Incyte Corporation transferred the responsibilities of the Sponsor to Novartis on 15-Mar-2010. At the time of transfer the study was fully enrolled. The data management, safety and administrative sections were aligned to the Novartis processes and procedures.

Pre-assignment

Screening details:

Enrollment was planned for 150. Due to an unforeseen increase in screening activity coupled with a strict protocol adherence by the participating sites, the total enrollment for the study was 219 patients.The protocol was amended after the primary analysis to allow all patients to receive ruxolitinib and move into the extension phase.

Period 1

Period 1 title	Primary Endpoint Analysis (Interim)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	INC424/INCB018424

Arm description:

Starting dose of 15 mg BID or 20 mg BID were selected with starting dose based on baseline platelet count. Dose titration ranging from 5 mg BID to a maximum dose of 25 mg BID was permitted during the study based on safety and efficacy. Tablets were to be taken 12 hours apart. Administration instructions were provided at study visits.

Arm type	Experimental
Investigational medicinal product name	INC424
Investigational medicinal product code	
Other name	Ruxolitinib phosphate, INCB018424
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Five milligram tablets were orally administered without regard to food in an outpatient setting in accordance with the specified dosing schedule. Administration instructions for the investigational treatment were provided at study visits.

Arm title	Best Available Therapy (BAT)

Arm description:

Best-available Investigator-selected therapy included a combination of available agents to treat the disease and/or its symptoms, and was selected by the investigator for each subject. Therapy could change at different times during the treatment phase. No experimental agents (e.g. those not approved for the treatment of any indication) were allowed. BAT also included the option of no treatment.

Arm type	Active comparator
Investigational medicinal product name	Best available therapy (BAT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In the control arm, commercially available BAT was administered according to manufacturer’s

instructions and Investigator discretion.

Number of subjects in period 1	INC424/INCB018424	Best Available Therapy (BAT)
Started	146	73
Completed	91	31
Not completed	55	42
Consent withdrawn by subject	2	9
Disease progression	1	3
Other unspecified	7	7
Adverse event, non-fatal	12	4
Protocol violation	2	-
Non-compliance with study medication	2	-
Entered extension phase INC424	29	18
Non-compliance with study procedures	-	1

Period 2	
Period 2 title	Overall Disposition at 5 year follow-up
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	No
Arm title	Ruxolitinib

Arm description:

Starting dose of 15 mg BID or 20 mg BID were selected with starting dose based on baseline platelet count. Dose titration ranging from 5 mg BID to a maximum dose of 25 mg BID was permitted during the study based on safety and efficacy. Tablets were to be taken 12 hours apart. Administration instructions were provided at study visits.

Arm type	Experimental
Investigational medicinal product name	INC424
Investigational medicinal product code	
Other name	Ruxolitinib phosphate, INCB018424
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Five milligram tablets were orally administered without regard to food in an outpatient setting in accordance with the specified dosing schedule. Administration instructions for the investigational treatment were provided at study visits.

Arm title	Best Available Therapy (BAT)

Arm description:

Best-available Investigator-selected therapy included a combination of available agents to treat the disease and/or its symptoms, and was selected by the investigator for each subject. Therapy could change at different times during the treatment phase. No experimental agents (e.g. those not approved for the treatment of any indication) were allowed. BAT also included the option of no treatment.

Arm type	Active comparator
Investigational medicinal product name	Best available therapy (BAT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In the control arm, commercially available BAT was administered according to manufacturer's instructions and Investigator discretion.

Arm title	Rux after cross-over from BAT

Arm description: -

Arm type	Experimental
Investigational medicinal product name	INC424
Investigational medicinal product code	
Other name	Ruxolitinib phosphate, INCB018424
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Five milligram tablets were orally administered without regard to food in an outpatient setting in accordance with the specified dosing schedule. Administration instructions for the investigational treatment were provided at study visits.

Number of subjects in period 2	Ruxolitinib	Best Available Therapy (BAT)	Rux after cross-over from BAT
Started	146	28	45
Completed	39	0	11
Not completed	107	28	34
Other, including stem cell transplantation	16	9	6
Consent withdrawn by subject	10	9	-
Disease progression	32	4	7
Adverse event, non-fatal	35	5	10
Protocol violation	2	-	5
Non-compliance with study medication	4	-	1
Lack of efficacy	8	-	5
Non-compliance with study procedures	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	INC424/INCB018424

Reporting group description:

Starting dose of 15 mg BID or 20 mg BID were selected with starting dose based on baseline platelet count. Dose titration ranging from 5 mg BID to a maximum dose of 25 mg BID was permitted during the study based on safety and efficacy. Tablets were to be taken 12 hours apart. Administration instructions were provided at study visits.

Reporting group title	Best Available Therapy (BAT)

Reporting group description:

Best-available Investigator-selected therapy included a combination of available agents to treat the disease and/or its symptoms, and was selected by the investigator for each subject. Therapy could change at different times during the treatment phase. No experimental agents (e.g. those not approved for the treatment of any indication) were allowed. BAT also included the option of no treatment.

Reporting group values	INC424/INCB018424	Best Available Therapy (BAT)	Total
Number of subjects	146	73	219
Age categorical Units: Subjects			
Adults (18-64 years)	60	33	93
From 65-84 years	86	38	124
85 years and over	0	2	2
Age continuous Units: years			
arithmetic mean	65.1	65.2	
standard deviation	± 9.74	± 10.27	-
Gender categorical Units: Subjects			
Female	63	31	94
Male	83	42	125

End points

End points reporting groups

Reporting group title	INC424/INCB018424

Reporting group description:

Starting dose of 15 mg BID or 20 mg BID were selected with starting dose based on baseline platelet count. Dose titration ranging from 5 mg BID to a maximum dose of 25 mg BID was permitted during the study based on safety and efficacy. Tablets were to be taken 12 hours apart. Administration instructions were provided at study visits.

Reporting group title	Best Available Therapy (BAT)

Reporting group description:

Best-available Investigator-selected therapy included a combination of available agents to treat the disease and/or its symptoms, and was selected by the investigator for each subject. Therapy could change at different times during the treatment phase. No experimental agents (e.g. those not approved for the treatment of any indication) were allowed. BAT also included the option of no treatment.

Reporting group title	Ruxolitinib

Reporting group description:

Starting dose of 15 mg BID or 20 mg BID were selected with starting dose based on baseline platelet count. Dose titration ranging from 5 mg BID to a maximum dose of 25 mg BID was permitted during the study based on safety and efficacy. Tablets were to be taken 12 hours apart. Administration instructions were provided at study visits.

Reporting group title	Best Available Therapy (BAT)

Reporting group description:

Best-available Investigator-selected therapy included a combination of available agents to treat the disease and/or its symptoms, and was selected by the investigator for each subject. Therapy could change at different times during the treatment phase. No experimental agents (e.g. those not approved for the treatment of any indication) were allowed. BAT also included the option of no treatment.

Reporting group title	Rux after cross-over from BAT

Reporting group description: -

Primary: Percentage of Participants With at Least 35% Reduction in Spleen Volume From Baseline at Week 48

End point title	Percentage of Participants With at Least 35% Reduction in Spleen Volume From Baseline at Week 48

End point description:

The change in spleen volume from baseline to week 48 was measured by magnetic resonance imaging (MRI) (or by computer tomography (CT) for participants unable to undergo MRI) and was calculated only for participants who had an evaluable spleen volume at baseline. The percentage of participants achieving a greater than or equal to 35% reduction in spleen volume from baseline to week 48 was then calculated by treatment group.

End point type	Primary

End point timeframe:

Baseline, Week 48

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	72		
Units: percent				
number (confidence interval 95%)	28.5 (21.3 to 36.6)	0 (0 to 5)		

Statistical analyses

Statistical analysis title	35% reduction in spleen volume week 48
Comparison groups	INC424/INCB018424 v Best Available Therapy (BAT)
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Confidence interval	
level	95 %

Notes:

[1] - P-value is calculated using CMH test stratified by baseline prognostic category. If the proportion for the control group is less than 4% then p-value is obtained from exact CMH test.

Secondary: Percentage of Participants With at Least 35% Reduction in Spleen Volume From Baseline at Week 24

End point title	Percentage of Participants With at Least 35% Reduction in Spleen Volume From Baseline at Week 24

End point description:

The change in spleen volume from baseline to week 24 was measured by magnetic resonance imaging (MRI) (or by computer tomography (CT) for participants unable to undergo MRI) and was calculated only for participants who had an evaluable spleen volume at baseline. The percentage of participants achieving a greater than or equal to 35% reduction in spleen volume from baseline to week 24 was then calculated by treatment group.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	72		
Units: percent				
number (confidence interval 95%)	31.9 (24.4 to 40.2)	0 (0 to 5)		

Statistical analyses

Statistical analysis title	35% reduction in spleen volume week 24
Comparison groups	INC424/INCB018424 v Best Available Therapy (BAT)
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.0001 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[2] - P-value is calculated using CMH test. If the proportion for the control group is less then 4% then p-value is obtained from exact CMH test.

Secondary: Duration of Maintenance of at Least 35% Reduction in Spleen Volume (DoMSR) From Baseline

End point title	Duration of Maintenance of at Least 35% Reduction in Spleen Volume (DoMSR) From Baseline

End point description:

Defined as the interval between the first spleen volume measurement that was ≥ 35% reduction from baseline and the date of first scan that was no longer equal to 35% reduction and that was a >25% increase over nadir, regardless of the occurrence of a subsequent spleen progressive disease.

End point type	Secondary

End point timeframe:

Baseline, every 12 weeks until 25% progression from baseline

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78[3]	1[4]		
Units: years				
median (confidence interval 95%)	3.22 (1.65 to 999.99)	999.99 (999.99 to 999.99)		

Notes:

[3] - 999.99 = fewer than 50% of patients had loss of spleen response

[4] - No summary is provided-there was only one patient who achieved at least 35% spleen volume reduction.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First at Least 35% Reduction in Spleen Volume From Baseline by Treatment

End point title	Time to First at Least 35% Reduction in Spleen Volume From Baseline by Treatment

End point description:

Defined as an interval between randomization and date of the first MRI showing a 35% reduction from baseline in spleen volume. The analysis was done on patients who achieve a 35% reduction in spleen volume except BAT patients who achieved first 35% reduction or more in spleen volume only after crossover to ruxolitinib.

End point type	Secondary

End point timeframe:

Baseline, every 12 weeks until first 35% reduction in spleen is achieved

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	1[5]		
Units: weeks				
median (confidence interval 95%)	12.29 (12.14 to 14.43)	15.43 (9.99 to 999.99)		

Notes:

[5] - 9.99/999.99= Not available; only one patient evaluated

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Bone Marrow Histomorphology at Week 48

End point title	Percentage of Participants With Bone Marrow Histomorphology at Week 48

End point description:

This was noted as fibrosis density and was tabulated by fibrosis grade at baseline and at week 48 (post-baseline). Descriptive statistics (participant percentages) were used.

End point type	Secondary

End point timeframe:

48 weeks

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	73		
Units: percent				
number (not applicable)				
Baseline Grade 0	2.1	2.7		
Baseline Grade 1	14.4	4.1		
Baseline Grade 2	37.7	37		
Baseline Grade 3	40.4	46.6		
Baseline Missing	5.5	9.6		
48 Weeks Grade 0	2.7	0		
48 Weeks Grade 1	7.5	2.7		
48 Weeks Grade 2	8.9	6.8		
48 Weeks Grade 3	24	15.1		
48 Weeks Missing	56.8	75.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) by Treatment

End point title	Progression Free Survival (PFS) by Treatment

End point description:

PFS was defined as the interval between randomization and the earliest of either increase in spleen volume ≥ 25% from on-study nadir, splenic irradiation, splenectomy, leukemic transformation or death.

End point type	Secondary

End point timeframe:

Every three months after End of Study (EOS) until end of extension phase (96 weeks LPLV for the primary endpoint)

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	73		
Units: years				
median (confidence interval 95%)	1.6 (1.2 to 2.3)	1.4 (1.1 to 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Leukemia-free Survival (LFS)

End point title	Leukemia-free Survival (LFS)

End point description:

Defined as time to leukemic transformation has been defined as the interval between randomization and the date of bone marrow blast count of 20% or greater OR the date of the first peripheral blast count of 20% or greater that is subsequently confirmed to have been sustained for at least 8 weeks.

End point type	Secondary

End point timeframe:

Every three months after EOS until end of extension phase (96 weeks Last patient last visit (LPLV) for the primary end)

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146[6]	73[7]		
Units: years				
median (confidence interval 95%)	999.99 (999.99 to 999.99)	4.1 (2.4 to 999.99)		

Notes:

[6] - 999.99 = N/A

[7] - 999.99 = N/A

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) by Treatment at 5 years

End point title	Overall Survival (OS) by Treatment at 5 years

End point description:

Defined as the interval between randomization and death from any cause.

End point type	Secondary

End point timeframe:

Every three months after EOS until end of extension phase (96 weeks LPLV for the primary end)

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146[8]	73[9]		
Units: years				
median (confidence interval 95%)	999.99 (999.99 to 999.99)	4.1 (2.4 to 888.88)		

Notes:

[8] - 999.99 = NA, a median was not reached

[9] - 888.88 = NA; upper limit not available with crossover of patients to Ruxolitinib arm

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier estimates (95% CI) of duration of maintenance of at least 35 percent reduction in spleen volume

End point title	Kaplan-Meier estimates (95% CI) of duration of maintenance of at least 35 percent reduction in spleen volume

End point description:

End point type	Secondary

End point timeframe:

Baseline, every 6 months up to 5 years

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	1[10]		
Units: year				
arithmetic mean (confidence interval 95%)				
1.0 year	0.72 (0.6 to 0.81)	999.99 (999.99 to 999.99)		

1.5 years	0.67 (0.55 to 0.77)	999.99 (999.99 to 999.99)		
2.0 years	0.63 (0.5 to 0.73)	999.99 (999.99 to 999.99)		
2.5 years	0.54 (0.41 to 0.65)	999.99 (999.99 to 999.99)		
3.0 years	0.51 (0.38 to 0.62)	999.99 (999.99 to 999.99)		
3.5 years	0.48 (0.35 to 0.6)	999.99 (999.99 to 999.99)		
4.0 years	0.48 (0.35 to 0.6)	999.99 (999.99 to 999.99)		
4.5 years	0.48 (0.35 to 0.6)	999.99 (999.99 to 999.99)		
5.0 years	0.48 (0.35 to 0.6)	999.99 (999.99 to 999.99)		

Notes:

[10] - 999.99=NA; Only one BAT patient responder no consecutive readings to determine duration of response

Statistical analyses

No statistical analyses for this end point

Secondary: Analysis of overall survival (OS) at 5 years

End point title	Analysis of overall survival (OS) at 5 years

End point description:

End point type	Secondary

End point timeframe:

Every three months after EOS until end of extension phase (96 weeks LPLV for the primary end)

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	73		
Units: percent				
number (not applicable)				
Number of events	40.4	47.9		
Number censored	59.6	52.1		

Statistical analyses

Statistical analysis title	Analysis of overall survival at 5 years
Comparison groups	INC424/INCB018424 v Best Available Therapy (BAT)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.062 [11]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.02

Notes:

[11] - descriptive

Secondary: Kaplan-Meier estimates (95% CI) of overall survival by treatment at 5 years

End point title	Kaplan-Meier estimates (95% CI) of overall survival by treatment at 5 years

End point description:

End point type	Secondary

End point timeframe:

Baseline, every 6 months up to 5.5 years

End point values	INC424/INCB018424	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	73[12]		
Units: years				
arithmetic mean (confidence interval 95%)				
1.0 year	0.95 (0.9 to 0.98)	0.93 (0.83 to 0.97)		
1.5 years	0.88 (0.81 to 0.92)	0.86 (0.75 to 0.93)		
2.0 years	0.85 (0.77 to 0.9)	0.77 (0.64 to 0.85)		
2.5 years	0.82 (0.75 to 0.88)	0.61 (0.48 to 0.72)		
3.0 years	0.78 (0.7 to 0.84)	0.58 (0.44 to 0.69)		
3.5 years	0.71 (0.63 to 0.78)	0.54 (0.41 to 0.66)		
4.0 years	0.69 (0.6 to 0.76)	0.51 (0.38 to 0.63)		
4.5 years	0.62 (0.53 to 0.7)	0.46 (0.33 to 0.58)		
5.0 years	0.56 (0.47 to 0.64)	0.44 (0.31 to 0.56)		

5.5 years	0.52 (0.4 to 0.62)	999.99 (999.99 to 999.99)		

Notes:

[12] - 999.99= Not available

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All other adverse events are monitored from First Patient First Treatment until Last Patient Last Visit .

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Ruxolitinib Randomized + Extension Phase
Reporting group description:	
Ruxolitinib Randomized + Extension Phase	
Reporting group title	Ruxolitinib Randomized
Reporting group description:	
Ruxolitinib Randomized	
Reporting group title	Ruxolitinib cross-over
Reporting group description:	
Ruxolitinib cross-over	
Reporting group title	Total Ruxolitinib (INC both + BAT ext)
Reporting group description:	
Total Ruxolitinib (INC both + BAT ext)	
Reporting group title	BAT Randomized
Reporting group description:	
BAT Randomized	

Serious adverse events	Ruxolitinib Randomized + Extension Phase	Ruxolitinib Randomized	Ruxolitinib cross-over
Total subjects affected by serious adverse events			
subjects affected / exposed	85 / 146 (58.22%)	51 / 146 (34.93%)	20 / 45 (44.44%)
number of deaths (all causes)	17	8	4
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Basal cell carcinoma			

subjects affected / exposed	4 / 146 (2.74%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Bronchial carcinoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Carcinoma in situ			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesteatoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Gastric cancer			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Glioblastoma multiforme			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma recurrent			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Malignant melanoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Metastases to lymph nodes			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Metastases to peritoneum			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Metastases to spine			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Metastatic squamous cell carcinoma			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelofibrosis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Prostate cancer			

subjects affected / exposed	4 / 146 (2.74%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	5 / 146 (3.42%)	3 / 146 (2.05%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Aortic thrombosis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Arterial stenosis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haematoma			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Thrombosis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
General physical health deterioration			
subjects affected / exposed	4 / 146 (2.74%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Multi-organ failure			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Oedema peripheral			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Pyrexia			
subjects affected / exposed	5 / 146 (3.42%)	4 / 146 (2.74%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	4 / 8	4 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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 prolapse			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Cough			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	4 / 146 (2.74%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Lung disorder			
subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	0 / 45 (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
Lung infiltration			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Pleural effusion			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Productive cough			

subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	4 / 146 (2.74%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Pulmonary oedema			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory distress			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Respiratory failure			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Tachypnoea			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Confusional state			

subjects affected / exposed	3 / 146 (2.05%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Depression			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Blood creatinine increased			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Haemoglobin decreased			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight increased			

subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Ear injury			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Femur fracture			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Hip fracture			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			

subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	0 / 45 (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
Post procedural haemorrhage			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic pain			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative fever			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Postoperative respiratory distress			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Procedural pain			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Seroma			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Traumatic fracture			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Atrial fibrillation			
subjects affected / exposed	4 / 146 (2.74%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			

subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
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 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
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 arrest			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	5 / 146 (3.42%)	3 / 146 (2.05%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 6	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Cardiopulmonary failure			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Congestive cardiomyopathy			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Hypertensive heart disease			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Sick sinus syndrome			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Stress cardiomyopathy			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Supraventricular tachycardia			
subjects affected / exposed	3 / 146 (2.05%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Cerebral haemorrhage			

subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cerebrovascular accident			
subjects affected / exposed	4 / 146 (2.74%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Coma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Convulsion			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Depressed level of consciousness			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Encephalopathy			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Epilepsy			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Hepatic encephalopathy			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Paraesthesia			

subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Pseudoradicular syndrome			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Somnolence			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 146 (6.85%)	8 / 146 (5.48%)	2 / 45 (4.44%)
occurrences causally related to treatment / all	11 / 14	10 / 12	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia of chronic disease			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Coagulopathy			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Febrile neutropenia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Leukocytosis			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Lymphadenopathy			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paratracheal lymphadenopathy			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Splenic infarction			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenomegaly			
subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	4 / 45 (8.89%)
occurrences causally related to treatment / all	1 / 2	1 / 1	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			

subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular vascular disorder			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual impairment			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 146 (4.11%)	3 / 146 (2.05%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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

Anal fistula			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Constipation			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Diarrhoea			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Enterocolitis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric varices			

subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis haemorrhagic			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal ulcer			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Haematemesis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Incarcerated umbilical hernia			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Inguinal hernia			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Intestinal perforation			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Oesophageal haemorrhage			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Peritoneal haemorrhage			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 haemorrhage			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			

subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Small intestinal perforation			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Subileus			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Umbilical hernia			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 3	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	4 / 146 (2.74%)	3 / 146 (2.05%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Hepatic failure			

subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Hepatomegaly			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Portal hypertension			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 failure			

subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	4 / 146 (2.74%)	3 / 146 (2.05%)	3 / 45 (6.67%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Renal failure chronic			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 infarct			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Urinary retention			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			

subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Groin pain			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Osteitis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Osteonecrosis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 146 (2.74%)	3 / 146 (2.05%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Campylobacter infection			

subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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
Cellulitis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Cystitis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Endocarditis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Enterococcal sepsis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Escherichia infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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 urinary tract infection			

subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	2 / 45 (4.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Gastroenteritis			
subjects affected / exposed	3 / 146 (2.05%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	0 / 45 (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 norovirus			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Genital infection female			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	3 / 146 (2.05%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Klebsiella sepsis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung infection			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningoencephalitis herpetic			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Oesophageal infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Peritonitis			

subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	11 / 146 (7.53%)	2 / 146 (1.37%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	1 / 16	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Postoperative abscess			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Pseudomonal sepsis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Pyelonephritis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Respiratory tract infection			
subjects affected / exposed	3 / 146 (2.05%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis syndrome			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Septic shock			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Skin infection			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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
Staphylococcal infection			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular abscess			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			

subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 146 (1.37%)	1 / 146 (0.68%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	3 / 5	3 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	3 / 146 (2.05%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Fluid retention			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	0 / 45 (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
Hyperkalaemia			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	1 / 45 (2.22%)
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	3 / 146 (2.05%)	0 / 146 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	0 / 45 (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

Serious adverse events	Total Ruxolitinib (INC both + BAT ext)	BAT Randomized	
Total subjects affected by serious adverse events			
subjects affected / exposed	105 / 191 (54.97%)	22 / 73 (30.14%)	
number of deaths (all causes)	21	4	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	4 / 191 (2.09%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma in situ			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholesteatoma			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma recurrent			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 191 (0.52%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to spine			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	4 / 191 (2.09%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	5 / 191 (2.62%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	1 / 6	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haematoma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 191 (0.52%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			

subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General physical health deterioration			
subjects affected / exposed	4 / 191 (2.09%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Oedema peripheral			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			

subjects affected / exposed	6 / 191 (3.14%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	4 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cough			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	4 / 191 (2.09%)	3 / 73 (4.11%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lung infiltration			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 191 (1.05%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	4 / 191 (2.09%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 191 (0.52%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory distress			

subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 191 (0.52%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Tachypnoea			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusion			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear injury			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic pain			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative fever			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative respiratory distress			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	4 / 191 (2.09%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			

subjects affected / exposed	6 / 191 (3.14%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiopulmonary failure			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Right ventricular failure			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sick sinus syndrome			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	3 / 191 (1.57%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	4 / 191 (2.09%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudoradicular syndrome			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	12 / 191 (6.28%)	4 / 73 (5.48%)	
occurrences causally related to treatment / all	12 / 16	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of chronic disease			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paratracheal lymphadenopathy			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenomegaly			
subjects affected / exposed	3 / 191 (1.57%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	6 / 191 (3.14%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	4 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular vascular disorder			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 191 (3.66%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 191 (0.52%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colitis ischaemic			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faeces discoloured			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric varices			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 191 (1.05%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			

subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	0 / 191 (0.00%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	5 / 191 (2.62%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatomegaly			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	2 / 191 (1.05%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Skin and subcutaneous tissue disorders			

Actinic keratosis			
subjects affected / exposed	0 / 191 (0.00%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	7 / 191 (3.66%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Renal failure chronic			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal infarct			

subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 191 (2.09%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter infection			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	0 / 191 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital infection female			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	4 / 191 (2.09%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung infection			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis herpetic			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	12 / 191 (6.28%)	4 / 73 (5.48%)	
occurrences causally related to treatment / all	1 / 18	1 / 5	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis syndrome			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin infection			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Soft tissue infection			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular abscess			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	3 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	2 / 191 (1.05%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Fluid retention			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	3 / 191 (1.57%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 191 (0.52%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ruxolitinib Randomized + Extension Phase	Ruxolitinib Randomized	Ruxolitinib cross-over
Total subjects affected by non-serious adverse events			
subjects affected / exposed	145 / 146 (99.32%)	145 / 146 (99.32%)	42 / 45 (93.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	11 / 146 (7.53%)	5 / 146 (3.42%)	1 / 45 (2.22%)
occurrences (all)	15	5	1
Squamous cell carcinoma of skin			
subjects affected / exposed	10 / 146 (6.85%)	3 / 146 (2.05%)	0 / 45 (0.00%)
occurrences (all)	17	3	0
Vascular disorders			

Haematoma			
subjects affected / exposed	22 / 146 (15.07%)	15 / 146 (10.27%)	4 / 45 (8.89%)
occurrences (all)	33	21	6
Hypertension			
subjects affected / exposed	19 / 146 (13.01%)	8 / 146 (5.48%)	2 / 45 (4.44%)
occurrences (all)	20	8	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	38 / 146 (26.03%)	28 / 146 (19.18%)	10 / 45 (22.22%)
occurrences (all)	47	31	11
Chest pain			
subjects affected / exposed	0 / 146 (0.00%)	0 / 146 (0.00%)	4 / 45 (8.89%)
occurrences (all)	0	0	6
Chills			
subjects affected / exposed	8 / 146 (5.48%)	4 / 146 (2.74%)	0 / 45 (0.00%)
occurrences (all)	8	4	0
Fatigue			
subjects affected / exposed	36 / 146 (24.66%)	23 / 146 (15.75%)	8 / 45 (17.78%)
occurrences (all)	44	23	9
General physical health deterioration			
subjects affected / exposed	7 / 146 (4.79%)	3 / 146 (2.05%)	3 / 45 (6.67%)
occurrences (all)	9	4	3
Oedema peripheral			
subjects affected / exposed	55 / 146 (37.67%)	33 / 146 (22.60%)	8 / 45 (17.78%)
occurrences (all)	94	47	10
Peripheral swelling			
subjects affected / exposed	7 / 146 (4.79%)	3 / 146 (2.05%)	3 / 45 (6.67%)
occurrences (all)	7	3	4
Pyrexia			
subjects affected / exposed	36 / 146 (24.66%)	20 / 146 (13.70%)	7 / 45 (15.56%)
occurrences (all)	76	29	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	38 / 146 (26.03%)	22 / 146 (15.07%)	9 / 45 (20.00%)
occurrences (all)	47	23	11
Dyspnoea			

subjects affected / exposed	35 / 146 (23.97%)	22 / 146 (15.07%)	12 / 45 (26.67%)
occurrences (all)	48	26	15
Dyspnoea exertional			
subjects affected / exposed	13 / 146 (8.90%)	11 / 146 (7.53%)	1 / 45 (2.22%)
occurrences (all)	18	14	1
Epistaxis			
subjects affected / exposed	18 / 146 (12.33%)	13 / 146 (8.90%)	6 / 45 (13.33%)
occurrences (all)	28	18	6
Oropharyngeal pain			
subjects affected / exposed	8 / 146 (5.48%)	4 / 146 (2.74%)	2 / 45 (4.44%)
occurrences (all)	10	5	2
Rales			
subjects affected / exposed	8 / 146 (5.48%)	6 / 146 (4.11%)	2 / 45 (4.44%)
occurrences (all)	9	7	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	9 / 146 (6.16%)	5 / 146 (3.42%)	1 / 45 (2.22%)
occurrences (all)	10	6	1
Insomnia			
subjects affected / exposed	13 / 146 (8.90%)	9 / 146 (6.16%)	5 / 45 (11.11%)
occurrences (all)	15	11	5
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 146 (2.05%)	2 / 146 (1.37%)	3 / 45 (6.67%)
occurrences (all)	3	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 146 (2.05%)	1 / 146 (0.68%)	3 / 45 (6.67%)
occurrences (all)	3	1	4
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 146 (2.05%)	3 / 146 (2.05%)	3 / 45 (6.67%)
occurrences (all)	4	3	4
Cardiac murmur			
subjects affected / exposed	8 / 146 (5.48%)	6 / 146 (4.11%)	3 / 45 (6.67%)
occurrences (all)	10	7	4
Gamma-glutamyltransferase increased			

subjects affected / exposed	11 / 146 (7.53%)	7 / 146 (4.79%)	1 / 45 (2.22%)
occurrences (all)	11	7	1
Haemoglobin decreased			
subjects affected / exposed	6 / 146 (4.11%)	4 / 146 (2.74%)	4 / 45 (8.89%)
occurrences (all)	11	9	5
Platelet count decreased			
subjects affected / exposed	12 / 146 (8.22%)	11 / 146 (7.53%)	9 / 45 (20.00%)
occurrences (all)	23	16	13
Weight decreased			
subjects affected / exposed	8 / 146 (5.48%)	3 / 146 (2.05%)	2 / 45 (4.44%)
occurrences (all)	9	3	2
Weight increased			
subjects affected / exposed	29 / 146 (19.86%)	23 / 146 (15.75%)	5 / 45 (11.11%)
occurrences (all)	33	23	5
White blood cell count increased			
subjects affected / exposed	4 / 146 (2.74%)	3 / 146 (2.05%)	4 / 45 (8.89%)
occurrences (all)	4	3	5
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 146 (5.48%)	4 / 146 (2.74%)	1 / 45 (2.22%)
occurrences (all)	11	5	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	8 / 146 (5.48%)	5 / 146 (3.42%)	2 / 45 (4.44%)
occurrences (all)	13	7	2
Atrial fibrillation			
subjects affected / exposed	11 / 146 (7.53%)	2 / 146 (1.37%)	1 / 45 (2.22%)
occurrences (all)	13	2	1
Palpitations			
subjects affected / exposed	12 / 146 (8.22%)	8 / 146 (5.48%)	2 / 45 (4.44%)
occurrences (all)	15	10	2
Tachycardia			
subjects affected / exposed	8 / 146 (5.48%)	4 / 146 (2.74%)	1 / 45 (2.22%)
occurrences (all)	12	4	1
Nervous system disorders			

Dizziness			
subjects affected / exposed	20 / 146 (13.70%)	12 / 146 (8.22%)	6 / 45 (13.33%)
occurrences (all)	22	13	6
Headache			
subjects affected / exposed	23 / 146 (15.75%)	18 / 146 (12.33%)	8 / 45 (17.78%)
occurrences (all)	28	22	14
Paraesthesia			
subjects affected / exposed	16 / 146 (10.96%)	10 / 146 (6.85%)	4 / 45 (8.89%)
occurrences (all)	17	10	4
Sciatica			
subjects affected / exposed	9 / 146 (6.16%)	5 / 146 (3.42%)	0 / 45 (0.00%)
occurrences (all)	12	6	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	71 / 146 (48.63%)	61 / 146 (41.78%)	19 / 45 (42.22%)
occurrences (all)	115	80	22
Leukocytosis			
subjects affected / exposed	8 / 146 (5.48%)	7 / 146 (4.79%)	2 / 45 (4.44%)
occurrences (all)	9	8	2
Thrombocytopenia			
subjects affected / exposed	77 / 146 (52.74%)	67 / 146 (45.89%)	21 / 45 (46.67%)
occurrences (all)	165	110	35
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	9 / 146 (6.16%)	5 / 146 (3.42%)	1 / 45 (2.22%)
occurrences (all)	12	6	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	11 / 146 (7.53%)	7 / 146 (4.79%)	3 / 45 (6.67%)
occurrences (all)	14	7	3
Abdominal pain			
subjects affected / exposed	21 / 146 (14.38%)	14 / 146 (9.59%)	3 / 45 (6.67%)
occurrences (all)	30	17	4
Abdominal pain upper			
subjects affected / exposed	16 / 146 (10.96%)	12 / 146 (8.22%)	5 / 45 (11.11%)
occurrences (all)	23	16	5
Ascites			

subjects affected / exposed	6 / 146 (4.11%)	4 / 146 (2.74%)	3 / 45 (6.67%)
occurrences (all)	6	4	3
Constipation			
subjects affected / exposed	19 / 146 (13.01%)	12 / 146 (8.22%)	2 / 45 (4.44%)
occurrences (all)	21	12	2
Diarrhoea			
subjects affected / exposed	55 / 146 (37.67%)	36 / 146 (24.66%)	12 / 45 (26.67%)
occurrences (all)	91	54	16
Dyspepsia			
subjects affected / exposed	10 / 146 (6.85%)	7 / 146 (4.79%)	3 / 45 (6.67%)
occurrences (all)	10	7	4
Gastrooesophageal reflux disease			
subjects affected / exposed	10 / 146 (6.85%)	4 / 146 (2.74%)	2 / 45 (4.44%)
occurrences (all)	10	4	2
Nausea			
subjects affected / exposed	30 / 146 (20.55%)	21 / 146 (14.38%)	5 / 45 (11.11%)
occurrences (all)	37	23	5
Vomiting			
subjects affected / exposed	27 / 146 (18.49%)	16 / 146 (10.96%)	4 / 45 (8.89%)
occurrences (all)	38	17	4
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	8 / 146 (5.48%)	3 / 146 (2.05%)	4 / 45 (8.89%)
occurrences (all)	14	4	4
Eczema			
subjects affected / exposed	3 / 146 (2.05%)	1 / 146 (0.68%)	4 / 45 (8.89%)
occurrences (all)	3	1	5
Hyperhidrosis			
subjects affected / exposed	11 / 146 (7.53%)	3 / 146 (2.05%)	1 / 45 (2.22%)
occurrences (all)	11	3	1
Night sweats			
subjects affected / exposed	27 / 146 (18.49%)	14 / 146 (9.59%)	4 / 45 (8.89%)
occurrences (all)	33	14	4
Pruritus			
subjects affected / exposed	17 / 146 (11.64%)	9 / 146 (6.16%)	4 / 45 (8.89%)
occurrences (all)	30	12	7

Rash			
subjects affected / exposed	12 / 146 (8.22%)	8 / 146 (5.48%)	2 / 45 (4.44%)
occurrences (all)	14	9	2
Rosacea			
subjects affected / exposed	4 / 146 (2.74%)	2 / 146 (1.37%)	3 / 45 (6.67%)
occurrences (all)	7	2	3
Skin lesion			
subjects affected / exposed	12 / 146 (8.22%)	2 / 146 (1.37%)	2 / 45 (4.44%)
occurrences (all)	17	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	30 / 146 (20.55%)	19 / 146 (13.01%)	7 / 45 (15.56%)
occurrences (all)	40	26	12
Back pain			
subjects affected / exposed	24 / 146 (16.44%)	18 / 146 (12.33%)	3 / 45 (6.67%)
occurrences (all)	30	20	3
Bone pain			
subjects affected / exposed	9 / 146 (6.16%)	9 / 146 (6.16%)	2 / 45 (4.44%)
occurrences (all)	9	9	3
Muscle spasms			
subjects affected / exposed	28 / 146 (19.18%)	15 / 146 (10.27%)	4 / 45 (8.89%)
occurrences (all)	33	17	6
Musculoskeletal chest pain			
subjects affected / exposed	8 / 146 (5.48%)	4 / 146 (2.74%)	3 / 45 (6.67%)
occurrences (all)	8	4	3
Musculoskeletal pain			
subjects affected / exposed	11 / 146 (7.53%)	7 / 146 (4.79%)	1 / 45 (2.22%)
occurrences (all)	12	8	1
Osteoarthritis			
subjects affected / exposed	9 / 146 (6.16%)	3 / 146 (2.05%)	1 / 45 (2.22%)
occurrences (all)	12	3	1
Pain in extremity			
subjects affected / exposed	24 / 146 (16.44%)	18 / 146 (12.33%)	11 / 45 (24.44%)
occurrences (all)	33	22	17
Infections and infestations			

Bronchitis			
subjects affected / exposed	37 / 146 (25.34%)	15 / 146 (10.27%)	3 / 45 (6.67%)
occurrences (all)	53	18	4
Cystitis			
subjects affected / exposed	15 / 146 (10.27%)	9 / 146 (6.16%)	1 / 45 (2.22%)
occurrences (all)	23	10	1
Gastroenteritis			
subjects affected / exposed	14 / 146 (9.59%)	9 / 146 (6.16%)	1 / 45 (2.22%)
occurrences (all)	18	11	1
Herpes zoster			
subjects affected / exposed	16 / 146 (10.96%)	9 / 146 (6.16%)	5 / 45 (11.11%)
occurrences (all)	18	10	6
Lower respiratory tract infection			
subjects affected / exposed	2 / 146 (1.37%)	2 / 146 (1.37%)	3 / 45 (6.67%)
occurrences (all)	4	2	3
Nasopharyngitis			
subjects affected / exposed	40 / 146 (27.40%)	27 / 146 (18.49%)	4 / 45 (8.89%)
occurrences (all)	79	36	7
Respiratory tract infection			
subjects affected / exposed	9 / 146 (6.16%)	6 / 146 (4.11%)	2 / 45 (4.44%)
occurrences (all)	11	6	2
Rhinitis			
subjects affected / exposed	9 / 146 (6.16%)	7 / 146 (4.79%)	1 / 45 (2.22%)
occurrences (all)	10	8	1
Upper respiratory tract infection			
subjects affected / exposed	9 / 146 (6.16%)	6 / 146 (4.11%)	2 / 45 (4.44%)
occurrences (all)	13	7	4
Urinary tract infection			
subjects affected / exposed	19 / 146 (13.01%)	11 / 146 (7.53%)	6 / 45 (13.33%)
occurrences (all)	36	14	8
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	20 / 146 (13.70%)	6 / 146 (4.11%)	4 / 45 (8.89%)
occurrences (all)	22	7	4
Gout			

subjects affected / exposed	6 / 146 (4.11%)	1 / 146 (0.68%)	3 / 45 (6.67%)
occurrences (all)	10	1	4
Hyperuricaemia			
subjects affected / exposed	8 / 146 (5.48%)	1 / 146 (0.68%)	0 / 45 (0.00%)
occurrences (all)	12	1	0
Iron overload			
subjects affected / exposed	5 / 146 (3.42%)	2 / 146 (1.37%)	3 / 45 (6.67%)
occurrences (all)	5	2	3

Non-serious adverse events	Total Ruxolitinib (INC both + BAT ext)	BAT Randomized	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	187 / 191 (97.91%)	64 / 73 (87.67%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	12 / 191 (6.28%)	1 / 73 (1.37%)	
occurrences (all)	16	1	
Squamous cell carcinoma of skin			
subjects affected / exposed	10 / 191 (5.24%)	1 / 73 (1.37%)	
occurrences (all)	17	1	
Vascular disorders			
Haematoma			
subjects affected / exposed	26 / 191 (13.61%)	3 / 73 (4.11%)	
occurrences (all)	39	4	
Hypertension			
subjects affected / exposed	21 / 191 (10.99%)	3 / 73 (4.11%)	
occurrences (all)	22	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	48 / 191 (25.13%)	9 / 73 (12.33%)	
occurrences (all)	58	10	
Chest pain			
subjects affected / exposed	4 / 191 (2.09%)	4 / 73 (5.48%)	
occurrences (all)	6	4	
Chills			

subjects affected / exposed	8 / 191 (4.19%)	0 / 73 (0.00%)	
occurrences (all)	8	0	
Fatigue			
subjects affected / exposed	44 / 191 (23.04%)	8 / 73 (10.96%)	
occurrences (all)	53	8	
General physical health deterioration			
subjects affected / exposed	10 / 191 (5.24%)	4 / 73 (5.48%)	
occurrences (all)	12	4	
Oedema peripheral			
subjects affected / exposed	63 / 191 (32.98%)	21 / 73 (28.77%)	
occurrences (all)	104	23	
Peripheral swelling			
subjects affected / exposed	10 / 191 (5.24%)	0 / 73 (0.00%)	
occurrences (all)	11	0	
Pyrexia			
subjects affected / exposed	43 / 191 (22.51%)	6 / 73 (8.22%)	
occurrences (all)	84	7	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	47 / 191 (24.61%)	12 / 73 (16.44%)	
occurrences (all)	58	14	
Dyspnoea			
subjects affected / exposed	47 / 191 (24.61%)	13 / 73 (17.81%)	
occurrences (all)	63	13	
Dyspnoea exertional			
subjects affected / exposed	14 / 191 (7.33%)	2 / 73 (2.74%)	
occurrences (all)	19	3	
Epistaxis			
subjects affected / exposed	24 / 191 (12.57%)	5 / 73 (6.85%)	
occurrences (all)	34	5	
Oropharyngeal pain			
subjects affected / exposed	10 / 191 (5.24%)	3 / 73 (4.11%)	
occurrences (all)	12	3	
Rales			

subjects affected / exposed	10 / 191 (5.24%)	1 / 73 (1.37%)	
occurrences (all)	13	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	10 / 191 (5.24%)	0 / 73 (0.00%)	
occurrences (all)	11	0	
Insomnia			
subjects affected / exposed	18 / 191 (9.42%)	7 / 73 (9.59%)	
occurrences (all)	20	8	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 191 (3.14%)	0 / 73 (0.00%)	
occurrences (all)	6	0	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 191 (3.14%)	0 / 73 (0.00%)	
occurrences (all)	7	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 191 (3.14%)	0 / 73 (0.00%)	
occurrences (all)	8	0	
Cardiac murmur			
subjects affected / exposed	11 / 191 (5.76%)	3 / 73 (4.11%)	
occurrences (all)	14	3	
Gamma-glutamyltransferase increased			
subjects affected / exposed	12 / 191 (6.28%)	1 / 73 (1.37%)	
occurrences (all)	12	1	
Haemoglobin decreased			
subjects affected / exposed	10 / 191 (5.24%)	3 / 73 (4.11%)	
occurrences (all)	16	4	
Platelet count decreased			
subjects affected / exposed	21 / 191 (10.99%)	2 / 73 (2.74%)	
occurrences (all)	36	2	
Weight decreased			
subjects affected / exposed	10 / 191 (5.24%)	6 / 73 (8.22%)	
occurrences (all)	11	6	
Weight increased			

subjects affected / exposed	34 / 191 (17.80%)	1 / 73 (1.37%)	
occurrences (all)	38	2	
White blood cell count increased			
subjects affected / exposed	8 / 191 (4.19%)	0 / 73 (0.00%)	
occurrences (all)	9	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	9 / 191 (4.71%)	1 / 73 (1.37%)	
occurrences (all)	12	1	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	10 / 191 (5.24%)	1 / 73 (1.37%)	
occurrences (all)	15	1	
Atrial fibrillation			
subjects affected / exposed	12 / 191 (6.28%)	1 / 73 (1.37%)	
occurrences (all)	14	2	
Palpitations			
subjects affected / exposed	14 / 191 (7.33%)	0 / 73 (0.00%)	
occurrences (all)	17	0	
Tachycardia			
subjects affected / exposed	9 / 191 (4.71%)	4 / 73 (5.48%)	
occurrences (all)	13	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	26 / 191 (13.61%)	5 / 73 (6.85%)	
occurrences (all)	28	5	
Headache			
subjects affected / exposed	31 / 191 (16.23%)	4 / 73 (5.48%)	
occurrences (all)	42	4	
Paraesthesia			
subjects affected / exposed	20 / 191 (10.47%)	4 / 73 (5.48%)	
occurrences (all)	21	5	
Sciatica			
subjects affected / exposed	9 / 191 (4.71%)	1 / 73 (1.37%)	
occurrences (all)	12	1	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	90 / 191 (47.12%)	8 / 73 (10.96%)	
occurrences (all)	137	8	
Leukocytosis			
subjects affected / exposed	10 / 191 (5.24%)	0 / 73 (0.00%)	
occurrences (all)	11	0	
Thrombocytopenia			
subjects affected / exposed	98 / 191 (51.31%)	10 / 73 (13.70%)	
occurrences (all)	200	13	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	10 / 191 (5.24%)	1 / 73 (1.37%)	
occurrences (all)	13	2	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	14 / 191 (7.33%)	3 / 73 (4.11%)	
occurrences (all)	17	3	
Abdominal pain			
subjects affected / exposed	24 / 191 (12.57%)	12 / 73 (16.44%)	
occurrences (all)	34	14	
Abdominal pain upper			
subjects affected / exposed	21 / 191 (10.99%)	4 / 73 (5.48%)	
occurrences (all)	28	5	
Ascites			
subjects affected / exposed	9 / 191 (4.71%)	3 / 73 (4.11%)	
occurrences (all)	9	4	
Constipation			
subjects affected / exposed	21 / 191 (10.99%)	3 / 73 (4.11%)	
occurrences (all)	23	3	
Diarrhoea			
subjects affected / exposed	67 / 191 (35.08%)	13 / 73 (17.81%)	
occurrences (all)	107	19	
Dyspepsia			
subjects affected / exposed	13 / 191 (6.81%)	4 / 73 (5.48%)	
occurrences (all)	14	4	
Gastrooesophageal reflux disease			

subjects affected / exposed	12 / 191 (6.28%)	0 / 73 (0.00%)	
occurrences (all)	12	0	
Nausea			
subjects affected / exposed	35 / 191 (18.32%)	7 / 73 (9.59%)	
occurrences (all)	42	7	
Vomiting			
subjects affected / exposed	31 / 191 (16.23%)	1 / 73 (1.37%)	
occurrences (all)	42	1	
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	12 / 191 (6.28%)	0 / 73 (0.00%)	
occurrences (all)	18	0	
Eczema			
subjects affected / exposed	7 / 191 (3.66%)	4 / 73 (5.48%)	
occurrences (all)	8	4	
Hyperhidrosis			
subjects affected / exposed	12 / 191 (6.28%)	0 / 73 (0.00%)	
occurrences (all)	12	0	
Night sweats			
subjects affected / exposed	31 / 191 (16.23%)	6 / 73 (8.22%)	
occurrences (all)	37	6	
Pruritus			
subjects affected / exposed	21 / 191 (10.99%)	13 / 73 (17.81%)	
occurrences (all)	37	16	
Rash			
subjects affected / exposed	14 / 191 (7.33%)	1 / 73 (1.37%)	
occurrences (all)	16	1	
Rosacea			
subjects affected / exposed	7 / 191 (3.66%)	1 / 73 (1.37%)	
occurrences (all)	10	1	
Skin lesion			
subjects affected / exposed	14 / 191 (7.33%)	0 / 73 (0.00%)	
occurrences (all)	19	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	37 / 191 (19.37%)	8 / 73 (10.96%)	
occurrences (all)	52	9	
Back pain			
subjects affected / exposed	27 / 191 (14.14%)	10 / 73 (13.70%)	
occurrences (all)	33	11	
Bone pain			
subjects affected / exposed	11 / 191 (5.76%)	4 / 73 (5.48%)	
occurrences (all)	12	4	
Muscle spasms			
subjects affected / exposed	32 / 191 (16.75%)	5 / 73 (6.85%)	
occurrences (all)	39	5	
Musculoskeletal chest pain			
subjects affected / exposed	11 / 191 (5.76%)	1 / 73 (1.37%)	
occurrences (all)	11	1	
Musculoskeletal pain			
subjects affected / exposed	12 / 191 (6.28%)	1 / 73 (1.37%)	
occurrences (all)	13	1	
Osteoarthritis			
subjects affected / exposed	10 / 191 (5.24%)	1 / 73 (1.37%)	
occurrences (all)	13	1	
Pain in extremity			
subjects affected / exposed	35 / 191 (18.32%)	4 / 73 (5.48%)	
occurrences (all)	50	5	
Infections and infestations			
Bronchitis			
subjects affected / exposed	40 / 191 (20.94%)	5 / 73 (6.85%)	
occurrences (all)	57	5	
Cystitis			
subjects affected / exposed	16 / 191 (8.38%)	3 / 73 (4.11%)	
occurrences (all)	24	5	
Gastroenteritis			
subjects affected / exposed	15 / 191 (7.85%)	1 / 73 (1.37%)	
occurrences (all)	19	1	
Herpes zoster			

subjects affected / exposed	21 / 191 (10.99%)	0 / 73 (0.00%)	
occurrences (all)	24	0	
Lower respiratory tract infection			
subjects affected / exposed	5 / 191 (2.62%)	0 / 73 (0.00%)	
occurrences (all)	7	0	
Nasopharyngitis			
subjects affected / exposed	44 / 191 (23.04%)	9 / 73 (12.33%)	
occurrences (all)	86	10	
Respiratory tract infection			
subjects affected / exposed	11 / 191 (5.76%)	3 / 73 (4.11%)	
occurrences (all)	13	3	
Rhinitis			
subjects affected / exposed	10 / 191 (5.24%)	0 / 73 (0.00%)	
occurrences (all)	11	0	
Upper respiratory tract infection			
subjects affected / exposed	11 / 191 (5.76%)	1 / 73 (1.37%)	
occurrences (all)	17	1	
Urinary tract infection			
subjects affected / exposed	25 / 191 (13.09%)	2 / 73 (2.74%)	
occurrences (all)	44	8	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 191 (12.57%)	4 / 73 (5.48%)	
occurrences (all)	26	4	
Gout			
subjects affected / exposed	9 / 191 (4.71%)	1 / 73 (1.37%)	
occurrences (all)	14	2	
Hyperuricaemia			
subjects affected / exposed	8 / 191 (4.19%)	1 / 73 (1.37%)	
occurrences (all)	12	1	
Iron overload			
subjects affected / exposed	8 / 191 (4.19%)	0 / 73 (0.00%)	
occurrences (all)	8	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2009	UK Only: The duration of study treatment for the Core and Extension was clarified as 144 weeks after last patient first treatment in the Core study. A final analysis will be conducted at this time. In addition, if commercial drug is not available at the conclusion of the study an open-label extension study would be available to those continuing patients who may continue to benefit from study treatment.
23 June 2009	Similar to Amendment 1 the duration of study treatment for the Core and Extension was clarified as 144 weeks after last patient first treatment in the Core study. A final analysis will be conducted at this time. In addition, if commercial drug is not available at the conclusion of the study an open-label extension study would be available to those continuing patients who may continue to benefit from study treatment. Monitoring frequency and discontinuation criteria for toxicity have been clarified with more frequent pregnancy testing and extending contraception discussions/requirements to males. At week 4 and week 12, an ECG 2 hours post INC424 dose was added. The window for baseline MRI has been extended to accommodate operational considerations to include central confirmation on acceptable MRI quality with repeat testing if needed. In addition more detail has been included for the efficacy endpoints and for Inclusion Criterion # 4, anemia is further clarified and for criterion # 6 total bilirubin has been replaced with direct bilirubin. Consideration for the use of CYP3A4 inducers has been revised to allow the use of certain inducers where no good alternative may be available.
25 February 2010	1. Deletion or replacement of all references to Incyte Corporation or its staff with that of Novartis to align with the change of sponsorship*, following the acquisition of the codevelopment rights of the Incyte compound by Novartis; 2. Change to adverse event, data management and administrative sections to align with Novartis processes and procedures; 3. Deletion of an interim analysis at the time of the planned analysis of study INCB 18424351 to assure the final statistical analysis for the study is not compromised.

15 October 2010	1. Modify the current definition of duration of response and add an additional definition to be more consistent with the usual definition that measures duration from the time of first response until clear criteria for loss of response. The current language is modified to include all responders in the calculation of duration of response. In addition, a more conventional analysis was added. 2. Classify secondary efficacy endpoints as key and other. Response rate at week 24 should be classified as a Key Secondary Endpoint. With the designation of "Key", a testing procedure can be applied that controls the overall Type I error for both the primary and key secondary endpoints. The proposal canbe implemented without any effect on the primary endpoint power. 3. Extend the current +7 day window at week 48 visit to + 21 days as +7 days is not long enough in the event that there are data quality issues with the scan. In addition, a response observed up to 21 days after the visit should be allowed since the LPLV is projected to be approximately 23 December. Patients who miss their scheduled scan during the Week of 20 December 2010 may not have an opportunity to obtain this scan until the week of either 3 January 2011 or 10 January 2011. It is not expected that their spleen size would be measurably changed in weeks 47-51 (new proposal) compared with weeks 47-49 (current language). 4. Use stratified methods for estimation and hypothesis testing of endpoints as the study design is stratified by prognostic risk group, high risk versus intermediate-2 risk, and so the statistical methods should be stratified to match the design. 5. Align population nomenclature with ICH E9 guidelines 6. Other minor modifications to the statistical section have been incorporated. (e.g. we eliminated many formal comparisons for exploratory endpoints, introduced a time to definitive deterioration in patient reported outcomes and made some minor editorial changes).
02 February 2011	The primary rationale for this amendment is to: 1. Permit all Best Available Therapy (BAT) patients to receive INC424 and move to the Extension phase of the study after demonstration of superiority for the primary or key secondary endpoints and providing INC424 continues to show an acceptable safety profile. 2. Include additional patient discontinuation rules. 3. Modify the requirement for central imaging and review of spleen volumes,using MRI/CT scans. 4. Eliminate the requirement for a maximum dose of INC424 to be 5mg BID less than the dose which caused a platelet count reduction < 100,000. Restricting the dose to no higher than 5 mg BID less than any dose that caused a platelet count < 100,000 has limited the capacity of physician-investigators to dose patients higher when their platelet counts have improved above 100,000, sometimes even to within normal range. 5. Continue with ECG monitoring using local read only, thus eliminating the current central read process. 6. Change the requirement of Bone Marrow Biopsy to be performed at the discretion of the investigator and not as a timed procedure. 7. Eliminate the blood specimen for the determination of INC424 in plasma after the week 60 visit as further sampling is not considered likely to provide additional pharmacokinetic information to the existing data base. 8. Eliminate sample collection for the pharmacodynamic (PD) markers and CD34+, as collection after week 48 is not likely to provide additional information regarding the pharmodynamic effect of INC424. 9. Change the blood sample collection for JAK mutation to eliminate the collection at week 72. 10.Continue with all central laboratory for safety with exception of pancreatic lipase and amylase as there were no safety signals detected to warrant ongoing routine monitoring. 11.Eliminate IVRS use for drug supply as ongoing drug needs can easily be managed by monitoring manually at the site level.

01 June 2011	Sweden only: The MPA requested a change in the rationale of bullet #6 of Amendment 5 to clarify why the Bone marrow Biopsy is no longer mandated as this is a secondary endpoint of the study. Bullet point #6 of Amendment 5 read as follows: 6. Change the requirement of Bone Marrow Biopsy to be performed at the discretion of the investigator and not as a timed procedure. Bone marrow examinations are performed as a tool for diagnostic purposes in myelofibrosis but are not a standard requirement for the management of the disease. Transformation to acute leukemia (a secondary endpoint of the study) is an event that can be monitored with peripheral blood counts and verified, when necessary, with an additional bone marrow examination For Sweden only bullet point #6 will read as follows: [6. Change the requirement of Bone Marrow Biopsy to be performed at the discretion of the investigator and not as a mandated procedure. Bone marrow examinations are performed as a tool for diagnostic purposes in myelofibrosis but are not a standard requirement for the management of the disease. Change in bone marrow histomorphology is one of many secondary endpointsin the core phase of the study, and since the primary endpoint has been met it is no longer imperative to follow bone marrow examination during the extension phase. Transformation to acute leukemia (a secondary endpoint of the study) is an event that can be equally monitored with peripheral blood counts and verified, when necessary, with an additional bone marrow examination. Bone marrow biopsies can be performed at any time,if deemed necessary by the treating physician therefore this change does not impose any risks to patients but rather alleviates the burden in assessments-for Sweden only]
21 May 2012	The protocol will be extended until January 2015 to allow at least 5 years of treatment follow up. Starting November 2012, the following changes will apply to the patient visit schedule: 1. Elimination of 6 weekly interim laboratory sampling with sampling frequency changed to every 12 weeks at the time of the clinical visit. This will align the laboratory sampling frequency in this population with standard clinical practice. 2. Change of imaging assessments to every 24 weeks, as revised from the previous imaging assessment schedule of either every 12 or 24 weeks based on the patient's response status. This imaging assessment schedule is not based on standard clinical practice, but will continue to provide key data on long-term efficacy as defined by the protocol while reducing patient burden through less frequent imaging assessment visits. 3. Change of bone marrow biopsy to mandatory every 48 weeks starting with the first visit on/after November 2012 and at end of study if a bone marrow biopsy has not been performed in the last 48 weeks.This assessment was previously not mandatory in the Extension Phase of the study and was performed only as per the Investigator's decision. Collecting the bone marrow biopsies will allow us to obtain further information regarding longer term changes in the bone marrow (such as fibrosis scores) from baseline that may potentially be related to treatment with INC424. 4. Change the blood sample collection frequency of JAK mutation to every 24 weeks from every 48 weeks given the emergence of data supporting the measurement of allele burden as a potential marker for a disease modifying effect by INC424 in a subset of patients 5. Inclusion of comprehensive physical examination and serum pregnancy test in the End of Study visit with the 28-Day Follow-Up Visit limited to adverse events after discontinuation of study drug.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: