Clinical trial results:
A Phase II, Single-Arm, Open-Label Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Idasanutlin Monotherapy in Patients With Hydroxyurea-Resistant/Intolerant Polycythemia Vera

Summary

EudraCT number	2017-000861-58
Trial protocol	GB IT
Global end of trial date	03 June 2020

Results information

Result version number	v1 (current)
This version publication date	11 March 2021
First version publication date	11 March 2021

Trial information

Trial identification

Sponsor protocol code	NP39761

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03287245
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Infor, Hoffmann-La Roche, +41 61 6878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 March 2020
Global end of trial reached?	Yes
Global end of trial date	03 June 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is an open-label, single-arm study of idasanutlin monotherapy in subjects with hydroxyurea (HU)-resistant/intolerant Polycythemia vera (PV). The study will include two phases: initial phase and expansion phase. The initial phase will assess the safety and efficacy of idasanutlin monotherapy in ruxolitinib naïve and ruxolitinib-resistant or intolerant subjects, respectively. If the initial phase shows promising results for ruxolitinib-resistant or intolerant subjects, an expansion phase will be opened to further characterize the efficacy of idasanutlin.

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) guidelines according to the regulations and procedures described in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2017
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	Australia: 3
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	27
EEA total number of subjects	6

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	23
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Total of 27 subjects were enrolled and received study treatment. All 27 subjects were discontinued from study before the planned date of follow-up. The study was pre-maturely terminated by the sponsor's decision.

Pre-assignment

Screening details:

A total of 48 subjects were screened for enrollment; 21 were failed screening.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ruxolitinib-naïve Subjects With Splenomegaly

Arm description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).

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

Dosage and administration details:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation

Arm title	Ruxolitinib-naïve Subjects Without Splenomegaly

Arm description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).

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

Dosage and administration details:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation

Arm title	Ruxolitinib-Resistant or Intolerant With Splenomegaly

Arm description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years)

Arm type	Experimental

Investigational medicinal product name	iIasanutlin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation

Arm title	Ruxolitinib-Resistant or Intolerant Without Splenomegaly

Arm description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years)

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

Dosage and administration details:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation

Number of subjects in period 1	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly
Started	15	5	6
Completed	0	0	0
Not completed	15	5	6
Consent withdrawn by subject	8	3	3
Physician decision	3	2	-
Adverse event, non-fatal	1	-	-
Study terminated by sponsor	3	-	3

Number of subjects in period 1	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Started	1
Completed	0
Not completed	1
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-
Study terminated by sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	Ruxolitinib-naïve Subjects With Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	
Reporting group title	Ruxolitinib-naïve Subjects Without Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	
Reporting group title	Ruxolitinib-Resistant or Intolerant With Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years)	
Reporting group title	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years)	

Reporting group values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly
Number of subjects	15	5	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	5	4
From 65-84 years	2	0	2
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	54.5	56.8	60.3
standard deviation	± 10.7	± 8.8	± 8.4
Sex: Female, Male Units:			
Female	2	5	4
Male	13	0	2
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	14	5	6
Race/Ethnicity, Customized Units: Subjects			
Asian	1	0	0

White	14	5	6

Reporting group values	Ruxolitinib-Resistant or Intolerant Without Splenomegaly	Total	
Number of subjects	1	27	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	23	
From 65-84 years	0	4	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	55		
standard deviation	± 0	-	
Sex: Female, Male Units:			
Female	0	11	
Male	1	16	
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	1	26	
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	
White	1	26	

Subject analysis sets

Subject analysis set title	Ruxolitinib-Naïve Subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	
Subject analysis set title	Ruxolitinib-Resistant or Intolerant Subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	

Reporting group values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects	
Number of subjects	20	7	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	5	
From 65-84 years	2	2	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	55.1	59.6	
standard deviation	± 10.1	± 7.9	
Sex: Female, Male Units:			
Female	7	4	
Male	13	3	
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	0	
Not Hispanic or Latino	19	7	
Race/Ethnicity, Customized Units: Subjects			
Asian	1	0	
White	19	7	

End points

End points reporting groups

Reporting group title	Ruxolitinib-naïve Subjects With Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	
Reporting group title	Ruxolitinib-naïve Subjects Without Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	
Reporting group title	Ruxolitinib-Resistant or Intolerant With Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years)	
Reporting group title	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Reporting group description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years)	
Subject analysis set title	Ruxolitinib-Naïve Subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	
Subject analysis set title	Ruxolitinib-Resistant or Intolerant Subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).	

Primary: Percentage of Ruxolitinib-Naïve Subjects With Splenomegaly at Baseline who Achieved Composite Response at Week 32

End point title	Percentage of Ruxolitinib-Naïve Subjects With Splenomegaly at Baseline who Achieved Composite Response at Week 32[1][2]
End point description:	
Composite response is defined as hematocrit (Hct) control without phlebotomy and ≥35% decrease in spleen size by imaging at Week 32. Hct control is defined as protocol-specified ineligibility for phlebotomy between Weeks 8 to 32 and ≤1 instance of phlebotomy eligibility between first dose and Week 8. Eligibility for phlebotomy is defined as a Hct of ≥45% that was ≥3% higher than baseline level or a Hct of >48%. One Cycle is 28 Days.	
End point type	Primary
End point timeframe:	
Week 32	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was planned to be reported in the endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects With Splenomegaly			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Percentage of Subjects				
number (not applicable)	44.4			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Ruxolitinib-Naïve Subjects Without Splenomegaly at Baseline who Achieved Hematocrit (Hct) Control Without Phlebotomy at Week 32

End point title	Percentage of Ruxolitinib-Naïve Subjects Without Splenomegaly at Baseline who Achieved Hematocrit (Hct) Control Without Phlebotomy at Week 32[3][4]

End point description:

Hct control is defined as protocol-specified ineligibility for phlebotomy between Weeks 8 to 32 and ≤1 instance of phlebotomy eligibility between first dose and Week 8. Eligibility for phlebotomy is defined as a Hct level ≥45% that was ≥3% higher than baseline level or a Hct level of >48%.

End point type	Primary

End point timeframe:

Week 32

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was planned to be reported in the endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects Without Splenomegaly			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Percentage of Subjects				
number (not applicable)	100			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of All Ruxolitinib-Naïve Subjects (Irrespective of Spleen Size) who Achieved Hct Control Without Phlebotomy at Week 32

End point title	Percentage of All Ruxolitinib-Naïve Subjects (Irrespective of Spleen Size) who Achieved Hct Control Without Phlebotomy at Week 32[5][6]

End point description:

Hct control is defined as protocol-specified ineligibility for phlebotomy between Weeks 8 to 32 and ≤1 instance of phlebotomy eligibility between first dose and Week 8. Eligibility for phlebotomy is defined as a Hct level ≥45% that was ≥3% higher than baseline level or a Hct level of >48%.

End point type	Primary

End point timeframe:

Week 32

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was planned to be reported in the endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	2		
Units: Percentage of Subjects				
number (not applicable)	44.4	100		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of All Ruxolitinib-Resistant or Intolerant Subjects who Achieved Hct Control Without Phlebotomy at Week 32

End point title	Percentage of All Ruxolitinib-Resistant or Intolerant Subjects who Achieved Hct Control Without Phlebotomy at Week 32[7][8]

End point description:

Hct control is defined as protocol-specified ineligibility for phlebotomy between Weeks 8 to 32 and ≤1 instance of phlebotomy eligibility between first dose and Week 8. Eligibility for phlebotomy is defined as a Hct level ≥45% that was ≥3% higher than baseline level or a Hct level of >48%.

End point type	Primary

End point timeframe:

From Baseline to Week 32 (Cycle 8 Day 28)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was planned to be reported in the endpoint.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	1		
Units: Percentage of Subjects				
number (not applicable)	75.0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects who Achieved Complete Hematologic Response at Week 32

End point title	Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects who Achieved Complete Hematologic Response at Week 32

End point description:

Complete hematologic response requires all of the following: Hct control without phlebotomy; White blood cell (WBC) count ≤10 × 10^9/Liter (L) at Week 32; and Platelet count ≤400 × 10^9/L at Week 32. Hct control is defined as protocol-specified ineligibility for phlebotomy between Weeks 8 to 32 and ≤1 instance of phlebotomy eligibility between first dose and Week 8. Eligibility for phlebotomy is defined as a Hct level ≥45% that was ≥3% higher than baseline level or a Hct level of >48%.

End point type	Secondary

End point timeframe:

Week 32 (Cycle 8 Day 28)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	2	4	1
Units: Percentage of Subjects				
number (not applicable)	33.3	100	75.0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects who Achieved Complete Hematologic Remission at Cycle 11 Day 28

End point title	Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects who Achieved Complete Hematologic Remission at Cycle 11 Day 28

End point description:

Complete hematologic remission requires all of the following: Hct control without phlebotomy between Weeks 32 and Cycle 11 Day 28; WBC count ≤10 × 10^9/L at Cycle 11 Day 28; and Platelet count ≤400 × 10^9/L at Week 32. Hct control is defined as protocol-specified ineligibility for phlebotomy. Eligibility for phlebotomy is defined as a Hct level ≥45% that was ≥3% higher than baseline level or a Hct level of >48%.

End point type	Secondary

End point timeframe:

Cycle 11 Day 28

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Percentage of Subjects				
number (not applicable)	40	100	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Complete Hematologic Remission, with a Durable Responder Defined as a Subject in Remission at Week 32 and Cycle 11 Day 28

End point title	Duration of Complete Hematologic Remission, with a Durable Responder Defined as a Subject in Remission at Week 32 and Cycle 11 Day 28

End point description:

Complete hematologic remission requires all of the following: Hct control without phlebotomy between Week 32 (Cycle 8 Day 28) and Cycle 11 Day 28; WBC count ≤10 × 10^9/L at Cycle 11 Day 28; and Platelet count ≤400 × 10^9/L at Week 32. Hct control is defined as protocol-specified ineligibility for phlebotomy. Eligibility for phlebotomy is defined as a Hct level ≥45% that was ≥3% higher than baseline level or a Hct level of >48%

End point type	Secondary

End point timeframe:

Week 32 (Cycle 8 Day 28), Cycle 11 Day 28

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[9]	5[10]	6[11]	1[12]
Units: Subjects				
number (not applicable)				
Cycle 11, Day 28	2	1	0	0

Week 32	3	2	3	0

Notes:

[9] - Subject number analyzed
Cycle 11, Day 28 - 5
Week 32 - 9
[10] - Subject number analyzed
Cycle 11, Day 28 - 1
Week 32 - 2
[11] - Subject number analyzed
Cycle 11, Day 28 - 1
Week 32 - 4
[12] - Subject number analyzed
Cycle 11, Day 28 - 1
Week 32 - 1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects With Splenomegaly at Baseline by Response per Modified European Leukemia Net (ELN) Criteria

End point title	Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects With Splenomegaly at Baseline by Response per Modified European Leukemia Net (ELN) Criteria[13]

End point description:

Complete response (CR) includes all of the following: Hct <45% without phlebotomy; Platelet count ≤400 × 10^9/L; WBC count ≤10 × 10^9/L; Normal spleen size on imaging; and No disease-related symptoms. Partial response (PR): in participants who do not fulfill the criteria for CR: Hct <45% without phlebotomy or response in 3 or more of the other criteria. No response (NR): any response that does not satisfy partial response. Progressive disease (PD): increased bone marrow fibrosis from baseline, and/or transformation to myelofibrosis (MF), myelodysplastic syndrome (MDS) or acute leukemia.

The study was pre-maturely terminated by the sponsor decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 3 Day 28, Cycle 5 Day 28, Cycle 8 Day 28 (Week 32), and every 3 cycles thereafter (1 cycle is 28 days) until end of study (up to 2 years)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[14]	6[15]		
Units: Percentage of Subjects				
number (not applicable)				
Baseline	0	0		
Cycle 3, Day 28	73.3	83.3		
Cycle 5, Day 28	76.9	80.0		
Cycle 8, Day 28 (Week 32)	66.7	75.0		
Cycle 11, Day 28	80	100		
Cycle 12, Day 28	80	100		

Cycle 14, Day 28	80	100		
Cycle 17, Day 28	33.3	0		
Cycle 20, Day 28	100	0		
Final Visit (28 Days post-last dose)	20	33.3		

Notes:

[14] - Only subjects for whom data were collected are included in the analysis.

[15] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects Without Splenomegaly at Baseline by Response per Modified ELN Criteria

End point title	Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects Without Splenomegaly at Baseline by Response per Modified ELN Criteria[16]

End point description:

Complete response (CR) includes all of the following: Hct <45% without phlebotomy; Platelet count ≤400 × 10^9/L; WBC count ≤10 × 10^9/L; Normal spleen size on imaging; and No disease-related symptoms. Partial response (PR): in participants who do not fulfill the criteria for CR: Hct <45% without phlebotomy or response in 3 or more of the other criteria. No response (NR): any response that does not satisfy partial response. Progressive disease (PD): increased bone marrow fibrosis from baseline, and/or transformation to myelofibrosis (MF), myelodysplastic syndrome (MDS) or acute leukemia.

The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 3 Day 28, Cycle 5 Day 28, Cycle 8 Day 28 (Week 32), and every 3 cycles thereafter until end of study (up to 2 years)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[17]	1[18]		
Units: Percentage of Subjects				
number (not applicable)				
Baseline	0	0		
Cycle 3, Day 28	100	0		
Cycle 5 Day 28	100	0		
Cycle 8, Day 28 (Week 32)	100	0		
Cycle 14, Day 28	100	0		
Cycle 17, Day 28	100	0		
Cycle 20, Day 28	0	0		
Final (28 Days post-last dose)	75.0	0		
Cycle 11, Day 28	100	0		

Notes:

[17] - Only subjects for whom data were collected are included in the analysis.

[18] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects (Irrespective of Spleen Size) by Response per Modified ELN Criteria

End point title	Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects (Irrespective of Spleen Size) by Response per Modified ELN Criteria

End point description:

Complete response (CR) includes all of the following: Hct <45% without phlebotomy; Platelet count ≤400 × 10^9/L; WBC count ≤10 × 10^9/L; Normal spleen size on imaging; and No disease-related symptoms. Partial response (PR): in participants who do not fulfill the criteria for CR: Hct <45% without phlebotomy or response in 3 or more of the other criteria. No response (NR): any response that does not satisfy partial response. Progressive disease (PD): increased bone marrow fibrosis from baseline, and/or transformation to myelofibrosis (MF), myelodysplastic syndrome (MDS) or acute leukemia.

The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 3 Day 28, Cycle 5 Day 28, Cycle 8 Day 28 (Week 32), and every 3 cycles thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[19]	7[20]		
Units: Percentage of Subjects				
number (not applicable)				
Baseline	0	0		
Cycle 3, Day 28	78.9	71.4		
Cycle 5 Day 28	81.3	66.7		
Cycle 8, Day 28 (Week 32)	72.7	60		
Cycle 11, day 28	83.3	50		
Cycle 14, Day 28	83.3	50		
Cycle 17, Day 28	50	0		
Cycle 20, Day 28	100	0		
Final (28 Days post-last dose)	35.7	25		

Notes:

[19] - Only subjects for whom data were collected are included in the analysis.

[20] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects With Splenomegaly at Baseline With Durable Response Lasting at Least 12 Weeks from Week 32

End point title	Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects With Splenomegaly at Baseline With Durable Response Lasting at Least 12 Weeks from Week 32[21]

End point description:

The percentage of Subjects with a durable response lasting at least 12 weeks from Week 32 will be analyzed by the type of response achieved: Hct control, complete hematologic response, ELN 2009 response criteria, and composite
response, if applicable.

Reported result data start from Cycle 11 Day 28 which is 12 weeks after Week 32 (Cycle 8 Day 28). There was one timepoint for which the Subjects qualify. The study was pre-maturely terminated by the sponsor decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

From Week 32 (Cycle 8 Day 28) and at least 12 Weeks after until end of study (up to 2 years)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[22]	6[23]		
Units: Percentage of Participants				
number (not applicable)				
HCT Control	42.9	100		
Composite Response	0	0		
ELN Response	50	75		
Complete Hematologic Response	28.6	66.7		

Notes:

[22] - Only subjects for whom data were collected are included in the analysis.

[23] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response, in Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects With Splenomegaly at Baseline with Durable Response Lasting at Least 12 Weeks From Week 32

End point title	Duration of Response, in Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects With Splenomegaly at Baseline with Durable Response Lasting at Least 12 Weeks From Week 32[24]

End point description:

The duration of response in Subjects with a durable response lasting at least 12 weeks from Week 32

will be analyzed by the type of response achieved: Hct control, complete hematologic response, ELN 2009 response criteria, and composite response, if applicable.

Reported result data start from Cycle 11 Day 28 which is 12 weeks after Week 32 (Cycle 8 Day 28). There was one timepoint for which the Subjects qualify. The study was pre-maturely terminated by the sponsor decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

From Week 32 (Cycle 8 Day 28) and at least 12 Weeks after until end of study (up to 2 years)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[25]	6[26]		
Units: Subjects				
number (not applicable)				
HCT Control	3	3		
Composite Response	0	0		
ELN Response	4	3		
Complete Hematologic Response	2	2		

Notes:

[25] - Only subjects for whom data were collected are included in the analysis.

[26] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects Without Splenomegaly at Baseline With Durable Response Lasting at Least 12 Weeks from Week 32

End point title	Percentage of Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects Without Splenomegaly at Baseline With Durable Response Lasting at Least 12 Weeks from Week 32[27]

End point description:

The percentage of Subjects with a durable response lasting at least 12 weeks from Week 32 will be analyzed by the type of response achieved: Hct control, complete hematologic response, ELN 2009 response criteria, and composite response, if applicable.

Reported result data start from Cycle 11 Day 28 which is 12 weeks after Week 32 (Cycle 8 Day 28). There was one timepoint for which the Subjects qualify. The study was pre-maturely terminated by the sponsor decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

From Week 32 (Cycle 8 Day 28) and at least 12 Weeks after until end of study (up to 2 years)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[28]	1[29]		
Units: Percentage of Subjects				
number (not applicable)				
HCT Control	100	0		
Composite Response	0	0		
ELN Response	100	0		
Complete Hematologic Response	100	0		

Notes:

[28] - Only subjects for whom data were collected are included in the analysis.

[29] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response, in Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects Without Splenomegaly at Baseline with Durable Response Lasting at Least 12 Weeks From Week 32

End point title	Duration of Response, in Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects Without Splenomegaly at Baseline with Durable Response Lasting at Least 12 Weeks From Week 32[30]

End point description:

The duration of response in Subjects with a durable response lasting at least 12 weeks from Week 32 will be analyzed by the type of response achieved: Hct control, complete hematologic response, ELN 2009 response criteria, and composite response, if applicable.

Reported result data start from Cycle 11 Day 28 which is 12 weeks after Week 32 (Cycle 8 Day 28). There was one timepoint for which the Subjects qualify. The study was pre-maturely terminated by the sponsor decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

From Week 32 (Cycle 8 Day 28) and at least 12 Weeks after until end of study (up to 2 years)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was provided only for those arms which were planned to be reported.

End point values	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[31]	1[32]		
Units: Subjects				
number (not applicable)				
HCT Control	2	0		
Composite Response	0	0		
ELN Response	2	0		

Complete Hematologic Response	2	0		

Notes:

[31] - Only subjects for whom data were collected are included in the analysis.

[32] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects (Irrespective of Spleen Size) With Durable Response Lasting at Least 12 Weeks from Week 32

End point title	Percentage of All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects (Irrespective of Spleen Size) With Durable Response Lasting at Least 12 Weeks from Week 32

End point description:

The percentage of Subjects with a durable response lasting at least 12 weeks from Week 32 will be analyzed by the type of response achieved: Hct control, complete hematologic response, ELN 2009 response criteria, and composite response, if applicable.

Reported result data start from Cycle 11 Day 28 which is 12 weeks after Week 32 (Cycle 8 Day 28). There was one timepoint for which the Subjects qualify. The study was pre-maturely terminated by the sponsor decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 3 Day 28, Cycle 5 Day 28, Week 32 (Cycle 8 Day 28), Cycle 11 Day 28, and every 3 cycles thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[33]	7[34]		
Units: Percentage of Subjects				
number (not applicable)				
HCT Control	55.6	75		
Composite Response	0	0		
ELN Response	60	60		
Complete Hematologic Response	44.4	50		

Notes:

[33] - Only subjects for whom data were collected are included in the analysis.

[34] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response, in All Ruxolitinib-Naïve and Ruxolitinib-Resistant or Intolerant Subjects (Irrespective of Spleen Size) with Durable Response Lasting at Least 12 Weeks From Week 32

End point title	Duration of Response, in All Ruxolitinib-Naïve and Ruxolitinib-

	Resistant or Intolerant Subjects (Irrespective of Spleen Size) with Durable Response Lasting at Least 12 Weeks From Week 32

End point description:

The duration of response in Subjects with a durable response lasting at least 12 weeks from Week 32 will be analyzed by the type of response achieved: Hct control, complete hematologic response, ELN 2009 response criteria, and composite response, if applicable.

Reported result data start from Cycle 11 Day 28 which is 12 weeks after Week 32 (Cycle 8 Day 28). There was one timepoint for which the Subjects qualify. The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

From Week 32 (Cycle 8 Day 28) and at least 12 Weeks after until end of study (up to 2 years)

End point values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[35]	7[36]		
Units: Subjects				
number (not applicable)				
HCT Control	5	3		
Composite Response	0	0		
ELN Response	6	3		
Complete Hematologic Response	4	2		

Notes:

[35] - Only subjects for whom data were collected are included in the analysis.

[36] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Subjects With Adverse Events by Severity, Graded According to NCI CTCAE v4.0

End point title	Total Number of Subjects With Adverse Events by Severity, Graded According to NCI CTCAE v4.0

End point description:

An adverse event is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not considered related to the study drug. The adverse event severity grading scale for the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4.0) will be used for assessing adverse event severity.

During the final analyses, the focus was on the Adverse Events of severity grades >/=3 as shown below. The extensive listings of all grade AEs are available at request.

The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline to end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Subjects				
number (not applicable)				
Baseline	0	0	0	0
Grade 3-5 AE	5	2	3	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Laboratory Abnormalities: Hematology Parameters.

End point title	Percentage of Subjects With Clinical Laboratory Abnormalities: Hematology Parameters.

End point description:

Hematology parameter laboratory values falling outside the standard reference range will be recorded as either high or low.

There was no clinical laboratory abnormalities identified. The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline to end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Percentage of Subjects				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Laboratory Abnormalities: Clinical Chemistry Parameters

End point title	Percentage of Subjects With Clinical Laboratory Abnormalities: Clinical Chemistry Parameters

End point description:

Clinical chemistry parameter laboratory values falling outside the standard reference range will be recorded as either high or low.

There was no clinical chemistry abnormalities identified. The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline to end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Percentage of Subjects				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Laboratory Abnormalities: Urinalysis Parameters

End point title	Percentage of Subjects With Clinical Laboratory Abnormalities: Urinalysis Parameters

End point description:

Urinalysis parameter laboratory values falling outside the standard reference range will be recorded as either high or low.

There was no clinical laboratory (urinalysis) abnormalities identified. The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline to end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Percentage of Subjects				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Electrocardiogram Parameters: PQ(PR), QRS, QT, QTcB, QTcF, and RR Durations

End point title	Change from Baseline in Electrocardiogram Parameters: PQ(PR), QRS, QT, QTcB, QTcF, and RR Durations

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value.

The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[37]	5[38]	6[39]	1[40]
Units: Millisecond (msec)				
arithmetic mean (standard deviation)				
PR Duration Baseline	158.93 (± 24.86)	153.60 (± 22.55)	152.00 (± 17.39)	196.00 (± 0)
PQ(PR) Durations Cycle 1, Day 1, 4 hour	0.60 (± 10.89)	-2.60 (± 5.37)	-2.00 (± 9.72)	4.00 (± 0)
PQ(PR) Durations Cycle 1, Day 1, 6 hour	-2.80 (± 8.10)	-4.40 (± 15.52)	6.00 (± 25.49)	0.00 (± 0)
PQ(PR) Durations Cycle 1, Day 2, pre-dose	-14.00 (± 0)	-6.00 (± 0)	0 (± 0)	0 (± 0)
PQ(PR) Durations Cycle 1, Day 2, 24 hour	1.93 (± 10.32)	1.00 (± 16.45)	0.67 (± 22.01)	-12.00 (± 0)
PQ(PR) Durations Cycle ,1 Day 5, pre-dose	-1.00 (± 11.70)	-12.00 (± 9.38)	0.40 (± 26.59)	-4.00 (± 0)
PQ(PR) Durations Cycle 1, Day 5, 4 hour	-8.00 (± 12.68)	-6.25 (± 15.59)	-1.20 (± 29.52)	0 (± 0)

PQ(PR) Durations Cycle 1, Day 5, 6 hour	-4.77 (± 14.08)	-2.75 (± 10.81)	7.60 (± 27.29)	0 (± 0)
PQ(PR) Durations Cycle 2, Day1, pre-dose	1.43 (± 14.26)	-5.75 (± 11.79)	-2.33 (± 11.89)	-8.00 (± 0)
PQ(PR) Durations Cycle 3, Day 1, pre-dose	-6.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
PQ(PR) Durations Cycle 3, Day 1, 4 hour	-8.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
PQ(PR) Durations Cycle 3, Day 1, 6 hour	-6.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
PQ(PR) Durations Cycle 4, Day 1, pre-dose	-20.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
PQ(PR) Durations Cycle 4, Day 1, 4 hour	-20.00 (± 0)	0 (± 0)	0.00 (± 0)	0 (± 0)
QRS Duration Baseline	90.87 (± 8.25)	83.80 (± 6.42)	83.33 (± 9.77)	94.00 (± 0)
QRS Cycle 1 Day 1 (4 H)	-1.47 (± 5.83)	4.60 (± 6.69)	1.33 (± 1.03)	0 (± 0)
QRS Cycle 1 Day 1 (6 H)	-1.27 (± 5.27)	4.00 (± 3.08)	0.33 (± 5.28)	-2.00 (± 0)
QRS Cycle 1 Day 2 (PREDOSE)	-4.00 (± 0)	2.00 (± 0)	0.00 (± 2.00)	2.00 (± 0)
QRS Cycle 1 Day 2 (24 H)	1.07 (± 3.77)	1.75 (± 6.55)	3.00 (± 11.64)	-2.00 (± 0)
QRS Cycle 1 Day 5 (PREDOSE)	0.13 (± 4.63)	4.00 (± 9.09)	0.00 (± 2.00)	2.00 (± 0)
QRS Cycle 1 Day 5 (4 H)	-1.08 (± 3.12)	3.75 (± 9.46)	-0.40 (± 2.61)	0 (± 0)
QRS Cycle 1 Day 5 (6 H)	-0.92 (± 4.73)	-0.25 (± 5.19)	2.00 (± 5.83)	0 (± 0)
QRS Cycle 2 Day 1 (PREDOSE)	0.64 (± 6.25)	7.75 (± 9.46)	1.00 (± 2.76)	-4.00 (± 0)
QRS Cycle 3 Day 1 (PREDOSE)	-4.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QRS Cycle 3 Day 1 (4 H)	-4.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QRS Cycle 3 Day 1 (6 H)	-4.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QRS Cycle 4 Day 1 (PREDOSE)	-2.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QRS Cycle 4 Day 1 (4 H)	-2.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QT Duration Baseline	396.67 (± 31.96)	392.60 (± 38.74)	386.00 (± 16.78)	392.00 (± 0)
QT Duration Cycle 1 Day 1 (4 H)	-7.33 (± 26.43)	16.80 (± 13.44)	5.67 (± 10.07)	36.00 (± 0)
QT Duration Cycle 1 Day 1 (6 H)	-9.40 (± 23.70)	11.00 (± 29.14)	-1.33 (± 13.49)	36.00 (± 0)
QT Duration Cycle 1 Day 2 (PREDOSE)	-6.00 (± 0)	-18.00 (± 0)	0 (± 0)	0 (± 0)
QT Duration Cycle 1 Day 2 (24 H)	-10.21 (± 25.57)	2.75 (± 29.00)	7.00 (± 16.58)	0 (± 0)
QT Duration Cycle 1 Day 5 (PREDOSE)	-6.20 (± 19.79)	-8.75 (± 21.00)	8.00 (± 19.54)	4.00 (± 0)
QT Duration Cycle 1 Day 5 (4 H)	-4.31 (± 33.31)	15.25 (± 15.65)	3.20 (± 24.23)	-12.00 (± 0)
QT Duration Cycle 1 Day 5 (6 H)	-10.31 (± 24.83)	4.75 (± 20.93)	7.60 (± 16.40)	-4.00 (± 0)
QT Duration Cycle 2 Day 1 (PREDOSE)	5.00 (± 22.68)	10.50 (± 25.96)	19.00 (± 13.67)	12.00 (± 0)
QT Durations Cycle 3 Day 1 (PREDOSE)	-2.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QT Durations Cycle 3 Day 1 (4 H)	-10.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QT Durations Cycle 3 Day 1 (6 H)	-4.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QT Durations Cycle 4 Day 1 (PREDOSE)	-16.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QT Durations Cycle 4 Day 1 (4 H)	-16.00 (± 0)	-4.75 (± 6.18)	-1.60 (± 15.44)	-12.00 (± 0)
QTcB baseline	427.67 (± 24.23)	419.60 (± 7.70)	424.50 (± 25.74)	444.00 (± 0)
QTcB - Cycle 1 Day 1 (4 H)	3.80 (± 12.82)	21.00 (± 11.14)	13.83 (± 14.05)	-30.00 (± 0)
QTcB - Cycle 1 Day 1 (6 H)	8.00 (± 10.54)	8.40 (± 22.40)	6.33 (± 5.50)	5.00 (± 0)
QTcB - Cycle 1 Day 2 (PREDOSE)	-15.00 (± 0)	-410.00 (± 0)	0 (± 0)	0 (± 0)
QTcB - Cycle 1 Day 2 (24 H)	3.71 (± 15.59)	-0.75 (± 16.40)	4.50 (± 14.47)	-14.00 (± 0)

QTcB - Cycle 1 Day 5 (PREDOSE)	-11.07 (± 15.21)	-10.00 (± 8.76)	-9.20 (± 15.25)	-7.00 (± 0)
QTcB - Cycle 4 Day 1 (4 H)	-62.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcB - Cycle 1 Day 5 (4 H)	-2.92 (± 14.20)	1.50 (± 8.81)	-4.60 (± 18.70)	0.00 (± 0)
QTcB - Cycle 1 Day 5 (6 H)	-4.54 (± 16.10)	-4.75 (± 6.18)	-1.60 (± 15.44)	-12.00 (± 0)
QTcB - Cycle 2 Day 1 (PREDOSE)	3.93 (± 14.42)	7.75 (± 20.61)	0.17 (± 14.54)	-23.00 (± 0)
QTcB - Cycle 3 Day 1 (PREDOSE)	-16.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcB - Cycle 3 Day 1 (4 H)	6.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcB - Cycle 3 Day 1 (6 H)	8.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcB - Cycle 4 Day 1 (PREDOSE)	-62.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcF Baseline	417.93 (± 22.41)	410.00 (± 17.62)	411.17 (± 17.90)	426.00 (± 0)
QTcF Cycle 1 Day 2 (PREDOSE)	-12.00 (± 0)	-20.00 (± 0)	0 (± 0)	0 (± 0)
QTcF Cycle 1 Day 2 (24 H)	-2.36 (± 13.32)	0.00 (± 20.46)	5.33 (± 14.81)	-9.00 (± 0)
QTcF Cycle 1 Day 5 (PREDOSE)	-10.47 (± 14.17)	-9.25 (± 8.96)	-3.20 (± 14.60)	-3.00 (± 0)
QTcF Cycle 1 Day 5 (4 H)	-0.08 (± 26.39)	4.00 (± 8.98)	-2.00 (± 17.36)	-4.00 (± 0)
QTcF Cycle 1 Day 5 (6 H)	-7.85 (± 13.44)	-2.25 (± 8.46)	1.60 (± 14.10)	6.00 (± 0)
QTcF Cycle 2 Day 1 (PREDOSE)	3.36 (± 10.49)	8.0 (± 20.51)	6.83 (± 12.45)	-11.00 (± 0)
QTcF Cycle 3 Day 1 (PREDOSE)	-11.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcF Cycle 3 Day 1 (4 H)	0.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcF Cycle 3 Day 1 (6 H)	4.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcF Cycle 4 Day 1 (PREDOSE)	-45.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcF Cycle 4 Day 1 (4 H)	-45.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcF Cycle 1 Day 1 (4 H)	-1.27 (± 11.86)	18.80 (± 10.08)	11.67 (± 11.09)	-8.0 (± 0)
QTcF Cycle 1 Day 1 (6 H)	1.00 (± 8.78)	10.00 (± 21.64)	3.5 (± 7.37)	16.00 (± 0)
RR Duration Baseline	861.47 (± 133.95)	881.00 (± 151.46)	835.83 (± 139.93)	779.00 (± 0)
RR Duration Cycle 1 Day 2 (PREDOSE)	28.00 (± 0)	18.00 (± 0)	0 (± 0)	0 (± 0)
RR Duration Cycle 1 Day 2 (24 H)	-51.50 (± 121.75)	17.25 (± 65.17)	8.83 (± 29.78)	54.00 (± 0)
RR Duration Cycle 1 Day 5 (PREDOSE)	25.87 (± 97.32)	-0.75 (± 104.53)	67.80 (± 78.89)	43.00 (± 0)
RR Duration Cycle 1 Day 5 (4 H)	-26.23 (± 114.00)	79.75 (± 62.99)	24.20 (± 114.05)	-47.00 (± 0)
RR Duration Cycle 1 Day 5 (6 H)	-21.46 (± 121.82)	49.50 (± 99.21)	33.00 (± 59.05)	-56.00 (± 0)
RR Duration Cycle 2 Day 1 (PREDOSE)	7.14 (± 118.26)	23.75 (± 86.53)	78.17 (± 59.85)	144.00 (± 0)
RR Duration Cycle 3 Day 1 (PREDOSE)	48.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
RR Duration Cycle 3 Day 1 (4 H)	-59.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
RR Duration Cycle 3 Day 1 (6 H)	-43.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
RR Duration Cycle 4 Day 1 (PREDOSE)	182.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
RR Duration Cycle 4 Day 1 (4 H)	182.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
QTcB Cycle 4 Day 1 (4 H)	-62.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
RR Duration Cycle 1 Day 1 4 H	-38.87 (± 130.21)	-5.60 (± 58.23)	-36.50 (± 66.76)	292.00 (± 0)
RR Duration Cycle 1 Day 1 6 H	-65.67 (± 117.44)	14.00 (± 100.82)	-31.17 (± 49.04)	130.00 (± 0)

Notes:

[37] - Only subjects for whom data were collected are included in the analysis.

[38] - Only subjects for whom data were collected are included in the analysis.

[39] - Only subjects for whom data were collected are included in the analysis.

[40] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Heart Rate, as Measured by Electrocardiogram

End point title	Change from Baseline in Heart Rate, as Measured by Electrocardiogram

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value.
The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[41]	5[42]	6[43]	1[44]
Units: Beats per Minute				
arithmetic mean (standard deviation)				
Baseline	71.47 (± 12.74)	69.80 (± 12.28)	73.17 (± 10.07)	77.00 (± 0)
Cycle 1, Day 1, 4 Hour	4.40 (± 10.58)	0.60 (± 5.32)	2.50 (± 4.23)	-21.00 (± 0)
Cycle 1, Day 1, 6 Hour	6.20 (± 10.35)	-0.60 (± 8.65)	3.00 (± 5.44)	-11.00 (± 0)
Cycle 1 Day 2, pre-dose	-3.00 (± 0)	-1.00 (± 0)	0 (± 0)	0 (± 0)
Cycle 1 Day 2, 24 Hour	4.71 (± 10.31)	-1.75 (± 5.32)	-0.67 (± 2.50)	72.43 (± 9.59)
Cycle 1 Day 5, pre-dose	-1.47 (± 6.56)	-0.75 (± 8.14)	-5.60 (± 5.27)	-4.00 (± 0)
Cycle 1 Day 5, 4 hour	2.69 (± 8.61)	-5.00 (± 2.94)	-2.20 (± 7.92)	5.00 (± 0)
Cycle 1 Day 5, 6 hour	2.23 (± 9.39)	-3.75 (± 7.76)	-2.80 (± 4.92)	6.00 (± 0)
Cycle 2, Day 1, pre-dose	-1.43 (± 9.83)	-1.50 (± 8.39)	-6.17 (± 5.19)	-12.00 (± 0)
Cycle 3 Day 1, pre-dose	-5.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 3 Day 1, 4 hour	7.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 3 Day 1, 6 hour	5.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 4 Day 1, pre-dose	-16.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 4 Day 1, 4 hour	-16.00 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Notes:

[41] - Only subjects for whom data were collected are included in the analysis.

[42] - Only subjects for whom data were collected are included in the analysis.
[43] - Only subjects for whom data were collected are included in the analysis.
[44] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Oral Temperature

End point title	Change from Baseline in Oral Temperature

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value.
The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[45]	5[46]	6[47]	1[48]
Units: Degrees Celsius (C)				
arithmetic mean (standard deviation)				
Baseline	36.50 (± 0.37)	36.40 (± 0.25)	36.47 (± 0.28)	37.10 (± 0)
Cycle 1 Day 15	0.13 (± 0.33)	0.42 (± 0.50)	0.18 (± 0.32)	-0.30 (± 0)
Cycle 1 Day 22	0.03 (± 0.18)	0.04 (± 0.29)	0.15 (± 0.21)	-0.50 (± 0)
Cycle 2 Day 1	-0.05 (± 0.28)	0.05 (± 0.30)	0.17 (± 0.34)	-0.60 (± 0)
Cycle 2 Day 15	0.04 (± 0.27)	0.18 (± 0.24)	0.23 (± 0.38)	-0.30 (± 0)
Cycle 3 Day 1	-0.09 (± 0.36)	0.13 (± 0.45)	0.17 (± 0.43)	0.10 (± 0)
Cycle 3 Day 15	-0.04 (± 0.31)	-0.03 (± 0.06)	0.10 (± 0.26)	-0.20 (± 0)
Cycle 4 Day 1	-0.05 (± 0.26)	-0.17 (± 0.15)	0.06 (± 0.37)	-0.50 (± 0)
Cycle 5 Day 1	0.05 (± 0.16)	-0.10 (± 0.36)	0.10 (± 0.32)	-0.80 (± 0)
Cycle 6 Day 1	-0.03 (± 0.16)	-0.10 (± 0.45)	0.12 (± 0.16)	-0.40 (± 0)
Cycle 7 Day 1	0.01 (± 0.30)	-0.20 (± 0.28)	0.20 (± 0.26)	-0.60 (± 0)
Cycle 8 Day 1	-0.01 (± 0.20)	-0.05 (± 0.64)	0.20 (± 0.36)	-0.30 (± 0)
Cycle 9 Day 1	0.03 (± 0.13)	0.05 (± 0.35)	-0.07 (± 0.42)	-0.40 (± 0)
Cycle 10 Day 1	-0.08 (± 0.10)	0.30 (± 0.42)	0.10 (± 0.35)	-0.60 (± 0)
Cycle 11 Day 1	-0.07 (± 0.19)	-0.20 (± 0)	-0.10 (± 0.14)	-0.40 (± 0)
Cycle 12 Day 1	-0.10 (± 0.16)	0.30 (± 0)	-0.20 (± 0.14)	-0.70 (± 0)
Cycle 13 Day 1	0.00 (± 0.19)	-0.70 (± 0)	0 (± 0)	-0.70 (± 0)
Cycle 14 Day 1	0.00 (± 0.41)	-0.10 (± 0)	-0.30 (± 0)	-0.70 (± 0)
Cycle 15 Day 1	-0.10 (± 0.14)	-0.30 (± 0)	-0.40 (± 0)	-0.50 (± 0)

Cycle 16 Day 1	0.03 (± 0.30)	-0.80 (± 0)	-0.10 (± 0)	-0.50 (± 0)
Cycle 17 Day 1	0.03 (± 0.12)	0.60 (± 0)	0.00 (± 60)	-0.80 (± 0)
Cycle 18 Day 1	0.07 (± 0.15)	0 (± 0)	-0.20 (± 0)	-0.80 (± 0)
Cycle 19 Day 1	-0.15 (± 0.21)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 20 Day 1	0.00 (± 0.14)	0 (± 0)	0 (± 0)	-0.50 (± 0)
Cycle 21 Day 1	0 (± 0)	0 (± 0)	0 (± 0)	-0.40 (± 0)
Cycle 22 Day 1	-0.50 (± 0)	0 (± 0)	0 (± 0)	-0.70 (± 0)
Cycle 23 Day 1	0 (± 0)	0 (± 0)	0 (± 0)	-0.80 (± 0)
Final Visit	-0.08 (± 0.15)	0.26 (± 0.26)	0.08 (± 0.37)	-0.50 (± 0)

Notes:

[45] - Only subjects for whom data were collected are included in the analysis.

[46] - Only subjects for whom data were collected are included in the analysis.

[47] - Only subjects for whom data were collected are included in the analysis.

[48] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate

End point title	Change from Baseline in Pulse Rate

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value. Maint. = maintenance.

The study was pre-maturely terminated, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[49]	5[50]	6[51]	1[52]
Units: Beats per Minute				
arithmetic mean (standard deviation)				
Baseline	74.7 (± 12.3)	71.6 (± 9.2)	76.7 (± 14.1)	68.0 (± 0)
Cycle 1 Day 15	4.5 (± 13.2)	5.4 (± 5.5)	-0.7 (± 4.8)	7.0 (± 0)
Cycle 1 Day 22	3.9 (± 11.3)	8.2 (± 4.9)	-5.8 (± 3.9)	8.0 (± 0)
Cycle 2 Day 1	-1.1 (± 8.6)	1.8 (± 8.7)	-9.3 (± 6.1)	12.0 (± 0)
Cycle 2 Day 15	0.1 (± 11.0)	1.8 (± 8.5)	-5.8 (± 5.5)	9.0 (± 0)
Cycle 3 Day 1	-2.8 (± 9.4)	-2.0 (± 8.6)	-4.2 (± 9.9)	9.0 (± 0)
Cycle 3 Day 15	-1.2 (± 9.7)	10.8 (± 13.6)	-2.2 (± 11.0)	21.0 (± 0)
Cycle 4 Day 1	1.0 (± 11.2)	1.7 (± 9.9)	-6.6 (± 9.8)	24.0 (± 0)
Cycle 5 Day 1	0.6 (± 8.4)	-4.0 (± 9.3)	-3.6 (± 4.2)	28.0 (± 0)

Cycle 6 Day 1	0.4 (± 9.1)	-4.3 (± 6.8)	-1.6 (± 6.8)	14.0 (± 0)
Cycle 7 Day 1	1.4 (± 14.6)	1.5 (± 16.3)	-1.0 (± 9.8)	21.0 (± 0)
Cycle 8 Day 1	-3.9 (± 13.3)	-1.0 (± 12.7)	0.5 (± 3.1)	11.0 (± 0)
Cycle 9 Day 1	-5.4 (± 6.4)	0.0 (± 5.7)	0.3 (± 2.5)	0 (± 0)
Cycle 10 Day 1	-0.3 (± 9.9)	8.5 (± 19.1)	2.3 (± 8.5)	20.0 (± 0)
Cycle 11 Day 1	-2.5 (± 11.5)	-2.0 (± 0)	2.5 (± 0.7)	37.0 (± 0)
Cycle 12, Day 1	-0.2 (± 11.6)	-6.0 (± 0)	-1.0 (± 4.2)	21.0 (± 0)
Cycle 13, Day 1	-2.8 (± 7.8)	-5.0 (± 0)	-1.0 (± 0)	16.0 (± 0)
Cycle 14, Day 1	-3.8 (± 11.1)	-2.0 (± 0)	-4.0 (± 0)	12.0 (± 0)
Cycle 15 Day 1	-0.8 (± 10.4)	10.0 (± 0)	-2.0 (± 0)	14.0 (± 0)
Cycle 16 Day 1	-1.3 (± 15.6)	-2.0 (± 0)	-2.0 (± 0)	16.0 (± 0)
Cycle 17, Day 1	-12.7 (± 9.5)	9.0 (± 0)	1.0 (± 0)	22.0 (± 0)
Cycle 18, Day 1	-4.3 (± 3.5)	0 (± 0)	-3.0 (± 0)	16.0 (± 0)
Cycle 19, Day 1	-9.0 (± 5.7)	0 (± 0)	6.0 (± 0)	15.0 (± 0)
Cycle 20, Day 1	-5.0 (± 9.9)	0 (± 0)	4.0 (± 0)	5.0 (± 0)
Cycle 21, Day 1	2.0 (± 0)	0 (± 0)	0 (± 0)	17.0 (± 0)
Cycle 22, Day 1	-8.0 (± 0)	0 (± 0)	0 (± 0)	14 (± 0)
Cycle 23, Day 1	0 (± 0)	0 (± 0)	0 (± 0)	19.0 (± 0)
Final Visit	-1.7 (± 12.2)	0.2 (± 11.6)	0.2 (± 10.1)	16.0 (± 0)

Notes:

[49] - Only subjects for whom data were collected are included in the analysis.

[50] - Only subjects for whom data were collected are included in the analysis.

[51] - Only subjects for whom data were collected are included in the analysis.

[52] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Respiratory Rate

End point title	Change from Baseline in Respiratory Rate

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value. Maint. = maintenance.

The study was pre-maturely terminated, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[53]	5[54]	6[55]	1[56]
Units: Breaths per Minute				

arithmetic mean (standard deviation)				
Baseline	17.4 (± 2.0)	17.4 (± 1.9)	18.2 (± 2.6)	16.0 (± 0)
Cycle 1 Day 15	-0.3 (± 1.0)	-0.2 (± 1.8)	-0.2 (± 1.8)	0 (± 0)
Cycle 1 Day 22	-0.5 (± 0.8)	0.2 (± 0.4)	-0.5 (± 2.2)	0 (± 0)
Cycle 2 Day 1	-0.3 (± 1.5)	-0.3 (± 1.7)	-0.4 (± 1.7)	0 (± 0)
Cycle 2 Day 15	-0.2 (± 1.0)	0.0 (± 0.8)	-1.2 (± 1.8)	2.0 (± 0)
Cycle 3 Day 1	-0.7 (± 1.3)	-1.5 (± 3.1)	-1.8 (± 1.8)	0 (± 0)
Cycle 3 Day 15	-0.7 (± 1.3)	0.0 (± 1.0)	-1.0 (± 1.0)	0 (± 0)
Cycle 4 Day 1	-0.3 (± 1.3)	-3.3 (± 4.2)	-1.0 (± 1.0)	2.0 (± 0)
Cycle 5 Day 1	-0.4 (± 1.9)	-0.3 (± 0.6)	1.0 (± 2.2)	0 (± 0)
Cycle 6 Day 1	-0.5 (± 1.3)	-0.5 (± 1.9)	-0.6 (± 1.3)	2.0 (± 0)
Cycle 7 Day 1	-0.2 (± 1.7)	0 (± 0)	-2.3 (± 1.5)	2.0 (± 0)
Cycle 8 Day 1	0.1 (± 1.5)	-0.5 (± 2.1)	-0.8 (± 3.8)	0 (± 0)
Cycle 9 Day 1	0.4 (± 1.8)	0.5 (± 0.7)	-1.7 (± 6.0)	-2.0 (± 0)
Cycle 10 Day 1	-0.2 (± 1.6)	-0.5 (± 2.1)	-0.3 (± 5.5)	0 (± 0)
Cycle 11 Day 1	-0.8 (± 1.0)	1.0 (± 0)	-0.5 (± 0.7)	2.0 (± 0)
Cycle 12 Day 1	-0.4 (± 1.5)	1.0 (± 0)	1.5 (± 0.7)	0 (± 0)
Cycle 13 Day 1	-1.4 (± 2.8)	1.0 (± 0)	-1.0 (± 0)	2.0 (± 0)
Cycle 14 Day 1	0.8 (± 2.3)	1.0 (± 0)	1.0 (± 0)	0 (± 0)
Cycle 15 Day 1	0.0 (± 1.4)	1.0 (± 0)	-1.0 (± 0)	0 (± 0)
Cycle 16 Day 1	-0.3 (± 1.3)	1.0 (± 0)	-2.0 (± 0)	0 (± 0)
Cycle 17 Day 1	1.3 (± 2.3)	1 (± 0)	-2.0 (± 0)	0 (± 0)
Cycle 18 Day 1	1.3 (± 2.3)	0 (± 0)	-1.0 (± 0)	2.0 (± 0)
Cycle 19 Day 1	1.5 (± 2.1)	0 (± 0)	0 (± 0)	2.0 (± 0)
Cycle 20 Day 1	2.0 (± 2.8)	0 (± 0)	-3.0 (± 0)	2.0 (± 0)
Cycle 21 Day 1	2.0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 22 Day 1	0.0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 23 Day 1	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Final visit	-0.3 (± 1.5)	-1.2 (± 1.5)	-1.8 (± 1.8)	0 (± 0)

Notes:

[53] - Only subjects for whom data were collected are included in the analysis.

[54] - Only subjects for whom data were collected are included in the analysis.

[55] - Only subjects for whom data were collected are included in the analysis.

[56] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Systolic Blood Pressure

End point title	Change from Baseline in Systolic Blood Pressure

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value. Maint. = maintenance.

The study was pre-maturely terminated, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[57]	5[58]	6[59]	1[60]
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Cycle 1, Day 15	4.4 (± 9.9)	3.6 (± 13.6)	3.8 (± 15.1)	5.0 (± 0)
Cycle 1, Days 22	3.3 (± 9.4)	-5.6 (± 11.8)	4.8 (± 10.1)	-5.0 (± 0)
Cycle 2, Day 1	3.0 (± 10.3)	2.8 (± 8.4)	-4.3 (± 7.9)	10.0 (± 0)
Cycle 2 , Day 15	5.2 (± 9.8)	-2.0 (± 13.6)	-7.2 (± 9.6)	30.0 (± 0)
Cycle 3, Day 1	5.5 (± 10.8)	-3.0 (± 9.8)	7.3 (± 18.3)	0 (± 0)
Cycle 3, Day 15	1.2 (± 11.2)	-3.5 (± 14.2)	-3.8 (± 16.7)	6.0 (± 0)
Cycle 4, Day 1	2.2 (± 9.1)	-7.3 (± 9.3)	9.8 (± 8.1)	13.0 (± 0)
Cycle 5, Day 1	4.2 (± 10.5)	-2.5 (± 6.8)	3.3 (± 6.9)	16.0 (± 0)
Cycle 6 Day 1	11.2 (± 13.0)	2.5 (± 9.7)	8.6 (± 10.8)	8.0 (± 0)
Cycle 7 Day 1	4.7 (± 4.2)	-4.0 (± 15.6)	10.0 (± 5.0)	29.0 (± 0)
Cycle 8 Day 1	8.8 (± 9.0)	5.0 (± 7.1)	14.0 (± 18.8)	9.0 (± 0)
Cycle 9 Day 1	12.6 (± 8.3)	3.0 (± 9.9)	-4.3 (± 4.9)	26.0 (± 0)
Cycle 10 Day 1	11.8 (± 9.9)	-3.0 (± 2.8)	11.0 (± 13.2)	30.0 (± 0)
Cycle 11 Day 1	8.5 (± 12.3)	14.0 (± 0)	11.0 (± 12.7)	34.0 (± 0)
Cycle 12 Day 1	10.8 (± 11.5)	-8.0 (± 0)	6.5 (± 3.5)	6.0 (± 0)
Cycle 13 Day 1	13.4 (± 5.1)	-8.0 (± 0)	8.0 (± 0)	14.0 (± 0)
Cycle 14 Day 1	4.4 (± 14.7)	18.0 (± 0)	3.0 (± 0)	14.0 (± 0)
Cycle 15 Day 1	13.6 (± 7.5)	14.0 (± 0)	4.0 (± 0)	5.0 (± 0)
Cycle 16 Day 1	7.5 (± 8.6)	8.0 (± 0)	9.0 (± 0)	4.0 (± 0)
Cycle 17 Day 1	9.3 (± 5.8)	24.0 (± 0)	7.0 (± 0)	6.0 (± 0)
Cycle 18 Day 1	5.7 (± 4.2)	0 (± 0)	9.0 (± 0)	13.0 (± 0)
Cycle 19 Day 1	2.5 (± 3.5)	0 (± 0)	9.0 (± 0)	13.0 (± 0)
Cycle 20 Day 1	11.5 (± 9.2)	0 (± 0)	0 (± 0)	13.0 (± 0)
Cycle 21 Day 1	-18.0 (± 0)	0 (± 0)	0 (± 0)	7.0 (± 0)
Cycle 22 Day 1	24.0 (± 0)	0 (± 0)	0 (± 0)	6.0 (± 0)
Cycle 23 Day 1	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Final visit	1.3 (± 9.7)	7.6 (± 16.2)	12.8 (± 23.9)	19.0 (± 0)
Baseline	129.3 (± 11.5)	132.0 (± 17.2)	122.3 (± 16.9)	106.0 (± 0)

Notes:

[57] - Only subjects for whom data were collected are included in the analysis.

[58] - Only subjects for whom data were collected are included in the analysis.

[59] - Only subjects for whom data were collected are included in the analysis.

[60] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Diastolic Blood Pressure

End point title	Change from Baseline in Diastolic Blood Pressure

End point description:

Vital signs were measured prior to the infusion while the subject was in a seated position. The baseline value at visit and the change from baseline value at each timepoint are reported. The change from baseline value was calculated by subtracting the post-baseline value from the baseline value. Maint. = maintenance.

The last time point was Cycle 5 Day 1 due to early termination of the study.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Days 1, 15, and 22, Days 1 and 15 of Cycles 2 and 3, and Day 1 of Cycle 4 and each cycle thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[61]	5[62]	6[63]	1[64]
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Baseline	76.3 (± 7.8)	73.2 (± 5.2)	72.3 (± 9.0)	65.0 (± 0)
Cycle1, Day 15	5.1 (± 8.7)	10.0 (± 8.7)	-1.8 (± 3.4)	0.0 (± 0)
Cycle 1, Day 22	3.6 (± 6.1)	2.4 (± 3.2)	-2.2 (± 5.8)	-1.0 (± 0)
Cycle 2, Day 1	6.1 (± 8.3)	3.0 (± 2.9)	-0.2 (± 9.3)	3.0 (± 0)
Cycle 2, Day 15	4.1 (± 6.3)	2.5 (± 9.7)	-5.5 (± 3.4)	16.0 (± 0)
Cycle 3 Day 1	6.2 (± 8.1)	5.8 (± 10.0)	-4.0 (± 12.4)	5.0 (± 0)
Cycle 3, Day 15	1.8 (± 10.5)	2.0 (± 10.1)	-7.5 (± 7.0)	8.0 (± 0)
Cycle 4, Day 1	5.5 (± 5.7)	2.7 (± 6.8)	-0.4 (± 5.0)	1.0 (± 0)
Cycle 5, Day 1	1.7 (± 6.1)	5.0 (± 5.8)	-5.0 (± 4.5)	1.0 (± 0)
Cycle 6, Day 1	5.9 (± 4.5)	3.3 (± 11.1)	-2.0 (± 9.5)	12.0 (± 0)
Cycle 7, Day 1	2.9 (± 4.8)	4.5 (± 13.4)	-5.3 (± 9.0)	30.0 (± 0)
Cycle 8, Day 1	7.8 (± 5.4)	5.0 (± 7.1)	0.5 (± 12.3)	10.0 (± 0)
Cycle 9, Day 1	4.1 (± 8.4)	4.0 (± 5.7)	-2.7 (± 1.5)	4.0 (± 0)
Cycle 10, Day 1	3.7 (± 5.9)	5.0 (± 0)	-2.3 (± 10.1)	3.0 (± 0)
Cycle 11, Day 1	9.7 (± 14.1)	10.0 (± 0)	1.0 (± 7.1)	24.0 (± 0)
Cycle 12, Day 1	9.8 (± 8.6)	6.0 (± 0)	2.0 (± 4.2)	8.0 (± 0)
Cycle 13, Day 1	9.0 (± 7.6)	4.0 (± 0)	2.0 (± 0)	10.0 (± 0)
Cycle 14, Day 1	5.6 (± 5.1)	19.0 (± 0)	-9.0 (± 0)	11.0 (± 0)
Cycle 15, Day 1	7.0 (± 8.0)	10.0 (± 0)	-2.0 (± 0)	7.0 (± 0)
Cycle 16, Day 1	9.8 (± 7.8)	11.0 (± 0)	7.0 (± 0)	6.0 (± 0)
Cycle 17, Day 1	11.3 (± 3.5)	11.0 (± 0)	3.0 (± 0)	7.0 (± 0)
Cycle 18, Day 1	5.0 (± 1.7)	0 (± 0)	-2.0 (± 0)	3.0 (± 0)
Cycle 19, Day 1	4.0 (± 5.7)	0 (± 0)	5.0 (± 0)	8.0 (± 0)
Cycle 20, Day 1	12.5 (± 3.5)	0 (± 0)	-1.0 (± 0)	2.0 (± 0)
Cycle 21, Day 1	-3.0 (± 0)	0 (± 0)	0 (± 0)	7.0 (± 0)
Cycle 22, Day 1	22.0 (± 0)	0 (± 0)	0 (± 0)	8.0 (± 0)
Cycle 23, Day 1	0 (± 0)	0 (± 0)	0 (± 0)	7.0 (± 0)
Final visit	5.8 (± 9.0)	3.8 (± 14.0)	-2.0 (± 12.6)	11.0 (± 0)

Notes:

[61] - Only subjects for whom data were collected are included in the analysis.

[62] - Only subjects for whom data were collected are included in the analysis.

[63] - Only subjects for whom data were collected are included in the analysis.

[64] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Eastern Cooperative Oncology Group (ECOG) Performance Status Over Time

End point title	Eastern Cooperative Oncology Group (ECOG) Performance Status Over Time

End point description:

The ECOG performance status is a scale used to quantify cancer subjects' general well-being and activities of daily life. The scale ranges from 0 to 5, with 0 denoting perfect health and 5 indicating death. The 6 categories are 0=Asymptomatic (Fully active, able to carry on all pre-disease activities without restriction), 1=Symptomatic but completely ambulatory, 2=Symptomatic, < 50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours), 3=Symptomatic, > 50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours), 4=Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair), 5=Death.

Only baseline data were collectable.

The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

From Baseline to end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Percentage of Participant				
number (not applicable)				
0.0	66.7	60.0	50.0	100.0
1.0	33.3	40.0	50.0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Concomitant Medications

End point title	Percentage of Subjects With Concomitant Medications

End point description:

Subjects With Concomitant Medications at the baseline were reported and did not change during the study and the follow-up period.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

From Baseline to end of study (up to 2 years)

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Percentage of Subjects				
number (not applicable)	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration Observed (Cmax) of Idasanutlin

End point title	Maximum Serum Concentration Observed (Cmax) of Idasanutlin

End point description:

Cmax is the maximum observed concentration of drug in blood.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration (Ctrough) of Idasanutlin

End point title	Trough Concentration (Ctrough) of Idasanutlin

End point description:

Ctrough is the measured concentration of a drug at the end of a dosing interval at steady state.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Concentration Observed (tmax) of Idasanutlin

End point title	Time of Maximum Concentration Observed (tmax) of Idasanutlin

End point description:

Tmax is the time elapsed from the time of drug administration to maximum plasma concentration.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				

number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) of Idasanutlin

End point title	Clearance (CL) of Idasanutlin

End point description:

CL is a measure of the body's elimination of a drug from plasma over time.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F) of Idasanutlin

End point title	Apparent Clearance (CL/F) of Idasanutlin

End point description:

CL/F is a measure of the body's elimination of a drug from plasma over time, after oral administration.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Volume or Apparent Volume of Distribution (Vdss/F) of Idasanutlin

End point title	Volume or Apparent Volume of Distribution (Vdss/F) of Idasanutlin

End point description:

Vdss/F is the theoretical volume that would be necessary to contain the total amount of an administered drug at the same concentration that it is observed in the plasma.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve (AUC) of Idasanutlin

End point title	Area Under the Concentration-Time Curve (AUC) of Idasanutlin

End point description:

AUC (from zero to infinity) represents the total drug exposure over time.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-Naïve Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life (t1/2) of Idasanutlin

End point title	Half-life (t1/2) of Idasanutlin

End point description:

t1/2 is defined as the time required for the drug plasma concentration to be reduced to half.
The result data not derived due to early termination of the study by the sponsor's decision and did not reach the end of study.

End point type	Secondary

End point timeframe:

Days 1, 2, and 5 of Cycles 1 and 4

End point values	Ruxolitinib-naïve Subjects With Splenomegaly	Ruxolitinib-naïve Subjects Without Splenomegaly	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	6	1
Units: Number				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline and Mean Change from Baseline Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) Over Time

End point title	Baseline and Mean Change from Baseline Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) Over Time

End point description:

The MPN-SAF TSS is an assessment form to measure the severity of 9 clinically important symptoms of

polycythemia vera. These include: early satiety, abdominal discomfort, inactivity, concentration issues, night sweats, itching, bone pain, fever, and weight loss. The subject provides a severity score for each additional symptom on a scale of 0 (none/absent) to 10 (worst imaginable). A tenth symptom, fatigue, is assessed using the "worst" fatigue item from the Brief Fatigue Inventory (BFI).
The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Baseline (Cycle 1 Day 1), Cycle 2 Day 1, Cycle 3 Day 28, Cycle 5 Day 28, End of Cycle 8 (Week 32), and every 3 cycles thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[65]	7[66]		
Units: Mean Change				
arithmetic mean (standard deviation)				
Baseline (Cycle 1 Day 1)	31.95 (± 19.95)	26.00 (± 11.83)		
Cycle 2 Day 1	-5.06 (± 12.91)	0.80 (± 26.37)		
Cycle 3 Day 28	-6.38 (± 12.71)	-8.00 (± 15.08)		
Cycle 5 Day 28,	-7.00 (± 12.72)	-9.50 (± 10.56)		
Week 32	-8.20 (± 12.79)	-5.00 (± 15.26)		
Cycle 11 Day 28	-4.60 (± 3.71)	-7.50 (± 3.54)		
Cycle 14 Day 28	-4.67 (± 5.54)	-10.50 (± 4.95)		
Cycle 17 Day 28	-3.25 (± 5.38)	-12.00 (± 1.41)		
Cycle 20 Day 28	-12.00 (± 0)	-8.00 (± 0)		
Final Visit	-5.92 (± 9.96)	-7.20 (± 5.63)		

Notes:

[65] - Only subjects for whom data were collected are included in the analysis.

[66] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline and Mean Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ-C30) Scores Over Time

End point title	Baseline and Mean Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ-C30) Scores Over Time

End point description:

EORTC QLQ-C30: includes functional scales (physical, role, cognitive, emotional, and social), global health status, symptom scales (fatigue, pain, nausea/vomiting) and single items (dyspnoea, appetite loss, insomnia, constipation/diarrhea and financial difficulties). Most questions use a 4-point scale (1 'Not at all' to 4 'Very much'; 2 questions used 7-point scale [1 'very poor' to 7 'Excellent']). Scores are

averaged and transformed to 0-100 scale; higher score=better level of functioning or greater degree of symptoms.

The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

Reported EORTC QLQ-C30 Scores include: Cognitive function, Diarrhea Emotional functioning, Nausea and vomiting, Social functioning, Physical functioning, Global health status/QoL, Role functioning.

End point type	Secondary

End point timeframe:

Baseline (Cycle 1 Day 1), Cycle 2 Day 1, Cycle 3 Day 28, Cycle 5 Day 28, End of Cycle 8 (Week 32), and every 3 cycles thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[67]	7[68]		
Units: Mean Change				
arithmetic mean (standard deviation)				
Cognitive function Baseline	65.83 (± 32.21)	76.19 (± 30.21)		
Cognitive function Cycle 2, Day 1	11.11 (± 11.43)	8.33 (± 13.94)		
Cognitive function Cycle 3 Day 28	7.02 (± 16.02)	6.67 (± 19.00)		
Cognitive function Cycle 5 Day 28	1.19 (± 22.13)	11.11 (± 25.09)		
Cognitive function Week 32	6.06 (± 18.67)	-3.33 (± 21.73)		
Cognitive function Cycle 11 Day 28	8.33 (± 13.94)	0 (± 0)		
Cognitive function Cycle 14 Day 28	5.56 (± 17.21)	0 (± 0)		
Cognitive function Cycle 17 Day 28	0.00 (± 13.61)	-8.33 (± 11.79)		
Cognitive function Cycle 20 Day 28	0 (± 0)	0 (± 0)		
Cognitive function Final Visit	4.44 (± 18.33)	6.67 (± 9.13)		
Diarrhea Baseline	8.33 (± 18.34)	14.29 (± 17.82)		
Diarrhea Cycle 2 Day 1	-5.56 (± 17.15)	5.56 (± 13.61)		
Diarrhea Cycle 3 Day 28	1.75 (± 17.48)	0 (± 0)		
Diarrhea Cycle 5 Day 28	7.14 (± 19.30)	5.56 (± 13.61)		
Diarrhea Week 32	9.09 (± 26.21)	20.0 (± 18.26)		
Diarrhea Cycle 11 Day 28	5.56 (± 13.61)	0 (± 0)		
Diarrhea Cycle 14 Day 28	5.56 (± 13.61)	0 (± 0)		
Diarrhea Cycle 17 Day 28	25.00 (± 31.91)	0 (± 0)		
Diarrhea Cycle 20 Day 28	0 (± 0)	0 (± 0)		
Diarrhea Final visit	13.33 (± 32.85)	6.67 (± 14.91)		
Emotional functioning Baseline	65.83 (± 28.34)	64.29 (± 21.36)		
Emotional functioning Cycle 1 Day 28	13.43 (± 20.24)	15.28 (± 13.35)		
Emotional functioning Cycle 3 Day 28	14.04 (± 21.88)	8.33 (± 10.21)		

Emotional functioning Cycle 5 Day 28	16.07 (± 20.53)	6.94 (± 16.17)		
Emotional functioning Week 32	14.39 (± 18.29)	5.00 (± 27.39)		
Emotional functioning Cycle 11 Day 28	6.94 (± 11.08)	16.67 (± 0)		
Emotional functioning Cycle 14 Day 28	5.56 (± 10.09)	-4.17 (± 5.89)		
Emotional functioning Cycle 17 Day 28	-8.33 (± 16.67)	0 (± 0)		
Emotional functioning Cycle 20 Day 28	0 (± 0)	8.33 (± 0)		
Emotional functioning Final visit	3.33 (± 18.31)	16.67 (± 18.63)		
Nausea and vomiting Baseline	10.00 (± 16.58)	2.38 (± 6.30)		
Nausea and vomiting Cycle 2 Day 1	-4.63 (± 12.53)	8.33 (± 22.97)		
Nausea and vomiting Cycle 3 Day 28	-1.75 (± 17.48)	3.33 (± 13.94)		
Nausea and vomiting Cycle 5 Day 28	-2.38 (± 11.05)	8.33 (± 17.48)		
Nausea and vomiting Week 32	7.58 (± 23.99)	16.67 (± 16.67)		
Nausea and vomiting Cycle 11 Day 28	2.78 (± 12.55)	0 (± 23.57)		
Nausea and vomiting Cycle 14 Day 28	-2.78 (± 6.80)	-8.33 (± 11.79)		
Nausea and vomiting Cycle 20 Day 28	0 (± 0)	0 (± 0)		
Nausea and vomiting Final visit	11.11 (± 33.73)	6.67 (± 19.00)		
Social functioning Baseline	67.50 (± 35.24)	76.19 (± 13.11)		
Social functioning Cycle 2 Day 1	4.63 (± 12.53)	0 (± 10.54)		
Social functioning Cycle 3 Day 28	-1.75 (± 22.15)	3.33 (± 13.94)		
Social functioning Cycle 5 Day 28	5.95 (± 24.98)	-2.78 (± 26.70)		
Social functioning Week 32	0.00 (± 18.26)	-6.67 (± 19.00)		
Social functioning Cycle 11 Day 28	0.00 (± 18.26)	0 (± 0)		
Social functioning Cycle 14 Day 28	0.00 (± 10.54)	0 (± 0)		
Social functioning Cycle 17 Day 28	-4.17 (± 8.33)	0 (± 0)		
Social functioning Cycle 20 Day 28	0 (± 0)	0 (± 0)		
Social functioning Final visit	0.00 (± 30.86)	-6.67 (± 25.28)		
Physical functioning Baseline	86.33 (± 18.92)	81.90 (± 11.36)		
Physical functioning Cycle 2 Day 1	1.48 (± 9.02)	2.22 (± 6.89)		
Physical functioning Cycle 3 Day 28	-2.81 (± 15.45)	2.67 (± 5.96)		
Physical functioning Cycle 5 Day 28	1.43 (± 16.16)	-2.22 (± 5.44)		
Physical functioning Week 32	5.45 (± 15.72)	-4.00 (± 7.60)		
Physical functioning Cycle 11 Day 28	-1.11 (± 6.55)	-10.00 (± 14.14)		
Physical functioning Cycle 14 Day 28	-1.11 (± 2.72)	0 (± 9.43)		
Physical functioning Cycle 17 Day 28	1.67 (± 3.33)	0 (± 0)		
Physical functioning Cycle 20 Day 28	0 (± 0)	0 (± 0)		
Physical functioning Final visit	-4.44 (± 9.65)	-2.67 (± 7.60)		
Global health status/QoL Baseline	61.25 (± 20.28)	60.71 (± 7.93)		
Global health status/QoL Cycle 2 Day 1	2.31 (± 18.92)	1.39 (± 8.19)		

Global health status/QoL Cycle 3 Day 28	7.89 (± 14.56)	11.67 (± 9.50)		
Global health status/QoL Cycle 5 Day 28	7.14 (± 19.84)	0 (± 17.48)		
Global health status/QoL Week 32	9.09 (± 23.41)	-8.33 (± 13.18)		
Global health status/QoL Cycle 11 Day 28	1.39 (± 23.81)	8.33 (± 11.79)		
Global health status/QoL Cycle 14 Day 28	2.78 (± 21.52)	8.33 (± 0)		
Global health status/QoL Cycle 17 Day 28	10.42 (± 20.83)	16.67 (± 0)		
Global health status/QoL Cycle 20 Day 28	25.00 (± 0)	25.00 (± 0)		
Global health status/QoL Final visit	-3.33 (± 23.32)	13.33 (± 17.28)		
Role functioning Baseline	74.17 (± 28.85)	76.19 (± 16.27)		
Role functioning Cycle 2 Day 1	7.41 (± 17.36)	-8.33 (± 17.48)		
Role functioning Cycle 3 Day 28	2.63 (± 17.80)	0 (± 11.79)		
Role functioning Cycle 5 Day 28	7.14 (± 15.63)	-2.78 (± 22.15)		
Role functioning Week 32	15.15 (± 21.67)	0 (± 20.41)		
Role functioning Cycle 11 Day 28	-2.78 (± 19.48)	-8.33 (± 11.79)		
Role functioning Cycle 14 Day 28	5.56 (± 8.61)	0 (± 0)		
Role functioning Cycle 17 Day 28	8.33 (± 9.62)	0 (± 0)		
Role functioning Cycle 20 Day 28	16.67 (± 0)	0 (± 0)		
Role functioning Final Visit	-13.33 (± 32.24)	6.67 (± 9.13)		

Notes:

[67] - Only subjects for whom data were collected are included in the analysis.

[68] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency Count of Subject Responses to the Patient Global Impression of Change (PGIC) Question Over Time

End point title	Frequency Count of Subject Responses to the Patient Global Impression of Change (PGIC) Question Over Time

End point description:

The PGIC is a one-item measure used to assess perceived treatment benefit. Subjects were be asked "Since the start of the treatment you've received in this study, your polycythemia vera (PV) symptoms are: 'very much improved', 'much improved', 'minimally improved', 'no change', 'minimally worse', 'much worse', and 'very much worse'.
The study was pre-maturely terminated by the sponsor's decision, therefore did not reach the end of study.

End point type	Secondary

End point timeframe:

Cycle 2 Day 1, Cycle 3 Day 28, Cycle 5 Day 28, End of Cycle 8 (Week 32), and every 3 cycles thereafter (1 cycle is 28 days) until end of study (up to 2 years)

End point values	Ruxolitinib-Naïve Subjects	Ruxolitinib-Resistant or Intolerant Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[69]	7[70]		
Units: Count of Subjects				
number (not applicable)				
Cycle 2, Day 1 Very Much Improved	0	0		
Cycle 2, Day 1 Much Improved	4	1		
Cycle 2, Day 1 Minimally Improved	5	3		
Cycle 2, Day 1 No Change	6	1		
Cycle 2, Day 1 Minimally Worse	1	1		
Cycle 2, Day 1 Much Worse	0	0		
Cycle 2, Day 1 Very Much Worse	0	0		
Cycle 2, Day 1 Not Assessed	0	1		
Cycle 3 Day 28 Very Much Improved	4	1		
Cycle 3 Day 28 Much Improved	4	1		
Cycle 3 Day 28 Minimally Improved	6	3		
Cycle 3 Day 28 No Change	3	0		
Cycle 3 Day 28 Minimally Worse	0	0		
Cycle 3 Day 28 Much Worse	0	0		
Cycle 3 Day 28 Very Much Worse	0	1		
Cycle 3 Day 28 Not Assessed	2	1		
Cycle 5 Day 28 Very Much Improved	6	1		
Cycle 5 Day 28 Much Improved	2	4		
Cycle 5 Day 28 Minimally Improved	1	0		
Cycle 5 Day 28 No Change	0	0		
Cycle 5 Day 28 Minimally Worse	0	0		
Cycle 5 Day 28 Much Worse	0	0		
Cycle 5 Day 28 Very Much Worse	0	0		
Cycle 5 Day 28 Not Assessed	4	0		
Week 32 Very Much Improved	3	0		
Week 32 Much Improved	3	1		
Week 32 Minimally Improved	3	3		
Week 32 No Change	1	1		
Week 32 Minimally Worse	1	0		
Week 32 Much Worse	0	0		
Week 32 Very Much Worse	0	0		
Week 32 Not Assessed	0	0		
Cycle 11 Day 28 Very Much Improved	1	0		
Cycle 11 Day 28 Much Improved	3	2		
Cycle 11 Day 28 Minimally Improved	0	0		
Cycle 11 Day 28 No Change	0	0		
Cycle 11 Day 28 Minimally Worse	1	0		
Cycle 11 Day 28 Much Worse	0	0		
Cycle 11 Day 28 Very Much Worse	0	0		
Cycle 11 Day 28 Not Assessed	0	0		
Cycle 14 Day 28 Very Much Improved	2	0		
Cycle 14 Day 28 Much Improved	2	2		
Cycle 14 Day 28 Minimally Improved	0	0		
Cycle 14 Day 28 No change	1	0		
Cycle 14 Day 28 Minimally Worse	1	0		

Cycle 14 Day 28 Much Worse	0	0		
Cycle 14 Day 28 Very Much Worse	0	2		
Cycle 14 Day 28 Not Assessed	0	0		
Cycle 17 Day 28 Very Much Improved	1	0		
Cycle 17 Day 28 Much Improved	1	2		
Cycle 17 Day 28 Minimally Improved	1	0		
Cycle 17 Day 28 No Change	1	0		
Cycle 17 Day 28 Minimally Worse	0	0		
Cycle 17 Day 28 Much Worse	0	0		
Cycle 17 Day 28 Very Much Worse	0	0		
Cycle 17 Day 28 Not Assessed	0	0		
Cycle 20 Day 28 Very Much Improved	0	0		
Cycle 20 Day 28 Much Improved	0	0		
Cycle 20 Day 28 Minimally Improved	1	0		
Cycle 20 Day 28 No Change	0	0		
Cycle 20 Day 28 Minimally Worse	0	0		
Cycle 20 Day 28 Much Worse	0	0		
Cycle 20 Day 28 Very Much Worse	0	0		
Cycle 20 Day 28 Not Assessed	3	1		
Final Visit Very Much Improved	3	3		
Final Visit Much Improved	2	1		
Final Visit Minimally Improved	2	1		
Final Visit No Change	6	0		
Final Visit Minimally Worse	1	0		
Final Visit Much Worse	0	0		
Final Visit Very Much Worse	0	0		
Final Visit Not Assessed	2	0		

Notes:

[69] - Only subjects for whom data were collected are included in the analysis.

[70] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to end of study (up to 2 years) post initial dose or until subject discontinued. Safety follow-up: Until 28 days after the last dose of study treatment or until initiating another anti-cancer therapy.

Adverse event reporting additional description:

Reported: Safety Population. During the Safety Follow-up Period, non-Serious Adverse Events occurred at the 5% frequency threshold.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Ruxolitinib-Resistant or Intolerant With Splenomegaly

Reporting group description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).

Reporting group title	Ruxolitinib-Resistant or Intolerant Without Splenomegaly

Reporting group description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).

Reporting group title	Ruxolitinib Naive-With Splenomegaly

Reporting group description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).

Reporting group title	Ruxolitinib Naive-Without Splenomegaly

Reporting group description:

Subjects received 150 milligrams (mg) idasanutlin orally, once daily for 5 days, every 28 days, until treatment discontinuation or end of study (up to 2 years).

Serious adverse events	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly	Ruxolitinib Naive-With Splenomegaly
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	2 / 15 (13.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (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

Serious adverse events	Ruxolitinib Naive-Without Splenomegaly		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ruxolitinib-Resistant or Intolerant With Splenomegaly	Ruxolitinib-Resistant or Intolerant Without Splenomegaly	Ruxolitinib Naive-With Splenomegaly
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	1 / 1 (100.00%)	15 / 15 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Solitary fibrous tumour			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Hot flush			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	2 / 15 (13.33%)
occurrences (all)	4	0	6
Chest discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Early satiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	4 / 6 (66.67%)	1 / 1 (100.00%)	5 / 15 (33.33%)
occurrences (all)	13	3	27
Feeling abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Malaise			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Breast mass			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Dyspnoea at rest			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Nasal congestion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Disorientation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 1 (100.00%)	2 / 15 (13.33%)
occurrences (all)	3	2	2
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Libido decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Mood altered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Thinking abnormal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	2	0	4
Blood urea increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	5	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Rib fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			

subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Wrist fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	9
Headache			
subjects affected / exposed	3 / 6 (50.00%)	1 / 1 (100.00%)	3 / 15 (20.00%)
occurrences (all)	4	1	4
Migraine			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	8
Paraesthesia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Parosmia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	5 / 15 (33.33%)
occurrences (all)	0	4	14
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Middle ear inflammation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Dry eye			
subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	3
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	5
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	4
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	3 / 6 (50.00%)	1 / 1 (100.00%)	5 / 15 (33.33%)
occurrences (all)	5	6	7
Diarrhoea			
subjects affected / exposed	6 / 6 (100.00%)	1 / 1 (100.00%)	11 / 15 (73.33%)
occurrences (all)	9	2	38
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Flatulence			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Gastrointestinal tract irritation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Glossitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Irritable bowel syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	6 / 6 (100.00%)	1 / 1 (100.00%)	13 / 15 (86.67%)
occurrences (all)	25	5	60
Oral pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Stomatitis			

subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	6 / 15 (40.00%)
occurrences (all)	2	1	12
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Xeroderma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	2
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	4	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			

subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Varicella zoster virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	3 / 15 (20.00%)
occurrences (all)	2	0	3
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	4
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2

Non-serious adverse events	Ruxolitinib Naive-Without Splenomegaly		
Total subjects affected by non-serious			

adverse events subjects affected / exposed	5 / 5 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Solitary fibrous tumour			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Early satiety			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Feeling abnormal			

subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Breast mass			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Dyspnoea at rest			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Hiccups			

subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Depressed mood			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Disorientation			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Hallucination			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		

Irritability			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Libido decreased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Mood altered			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Thinking abnormal			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Rib fracture			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Upper limb fracture			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Wrist fracture			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	4		
Migraine			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Parosmia			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0		
Seizure subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Somnolence subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Taste disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0		
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 3		
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Middle ear inflammation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0		
Tinnitus			

subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	11		
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Dyspepsia			

subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Gastritis				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Gastrointestinal pain				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Gastrointestinal tract irritation				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Glossitis				
subjects affected / exposed	1 / 5 (20.00%)			
occurrences (all)	1			
Hypoaesthesia oral				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Irritable bowel syndrome				
subjects affected / exposed	1 / 5 (20.00%)			
occurrences (all)	1			
Mouth ulceration				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	5 / 5 (100.00%)			
occurrences (all)	15			
Oral pain				
subjects affected / exposed	0 / 5 (0.00%)			
occurrences (all)	0			
Paraesthesia oral				

subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 3 / 5 (60.00%) 4		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Blister subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Night sweats subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all) Xeroderma subjects affected / exposed occurrences (all)	 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 1 / 5 (20.00%) 1 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0		
Renal and urinary disorders Pollakiuria			

subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Sinusitis			

subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Varicella zoster virus infection			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Hyperphosphataemia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2019	Amended to clarify and provide additional detail to allow logistical or pragmatical concerns with the implementation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported