



Clinical trial results:

A randomized, open-label, phase I/II open platform study evaluating safety and efficacy of novel ruxolitinib combinations in myelofibrosis patients

Summary

EudraCT number	2019-000373-23
Trial protocol	DK DE BE NL IT ES HU AT RO
Global end of trial date	28 August 2024

Results information

Result version number	v1 (current)
This version publication date	06 August 2025
First version publication date	06 August 2025

Trial information

Trial identification

Sponsor protocol code	CINC424H12201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04097821
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	28 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 August 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to characterize the safety, tolerability, and recommended Phase 2 dose (RP2D) of each combination partner used with ruxolitinib (Part 1 core). Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 September 2019
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: 9
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Türkiye: 1
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	45
EEA total number of subjects	28

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)	18
From 65 to 84 years	26
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All inclusion and exclusion criteria were checked at screening.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Ruxolitinib + Siremadlin 20 mg

Arm description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Arm type	Experimental
Investigational medicinal product name	Siremadlin
Investigational medicinal product code	
Other name	HDM201
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg, 20 mg, or 40 mg capsules for oral use

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg tablets for oral use

Arm title	Part 1: Ruxolitinib + Siremadlin 30 mg
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Arm description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Arm type	Experimental
Investigational medicinal product name	Siremadlin
Investigational medicinal product code	
Other name	HDM201
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg, 20 mg, or 40 mg capsules for oral use

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg tablets for oral use

Arm title	Part 1: Ruxolitinib + Siremadlin 40 mg
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Arm description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Arm type	Experimental
Investigational medicinal product name	Siremadlin
Investigational medicinal product code	
Other name	HDM201
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg, 20 mg, or 40 mg capsules for oral use

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg tablets for oral use

Arm title	Part 1: Ruxolitinib + Rineterkib 200 mg
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Arm description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

Arm type	Experimental
Investigational medicinal product name	Rineterkib
Investigational medicinal product code	
Other name	LTT462
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsule for oral use

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg tablets for oral use

Arm title	Part 1: Ruxolitinib + Crizanlizumab
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Arm description:

Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib

Arm type	Experimental
Investigational medicinal product name	Crizanlizumab
Investigational medicinal product code	
Other name	SEG101
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 100 mg/10 mL concentrate for infusion for intravenous use	
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 5 mg tablets for oral use	
Arm title	Part 1: Ruxolitinib + Sabatolimab
Arm description: Safety run-in of sabatolimab added to existing stable dose of ruxolitinib	
Arm type	Experimental
Investigational medicinal product name	Sabatolimab
Investigational medicinal product code	
Other name	MBG453
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg/mL or 400 mg/4 mL concentrate for infusion for intravenous use	
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 5 mg tablets for oral use	
Arm title	Part 1: Ruxolitinib + NIS793
Arm description: Safety run-in of NIS793 added to existing stable dose of ruxolitinib	
Arm type	Experimental
Investigational medicinal product name	NIS793
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 700 mg/7 mL concentrate for infusion for intravenous use	
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 5 mg tablets for oral use	
Arm title	Part 2: Ruxolitinib
Arm description: Existing stable dose of ruxolitinib as control for Part 2	
Arm type	Active comparator

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	INC424, Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg tablets for oral use

Number of subjects in period 1	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg
Started	7	10	6
Completed	5	8	2
Not completed	2	2	4
Adverse event, serious fatal	-	-	3
Physician decision	1	1	-
Subject Decision	-	-	-
Adverse event, non-fatal	-	-	-
Treated in Extension Phase	1	1	1
New Therapy For Study Indication	-	-	-

Number of subjects in period 1	Part 1: Ruxolitinib + Rineterkib 200 mg	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab
Started	9	6	2
Completed	5	4	0
Not completed	4	2	2
Adverse event, serious fatal	1	-	-
Physician decision	-	-	-
Subject Decision	1	2	2
Adverse event, non-fatal	1	-	-
Treated in Extension Phase	1	-	-
New Therapy For Study Indication	-	-	-

Number of subjects in period 1	Part 1: Ruxolitinib + NIS793	Part 2: Ruxolitinib
Started	4	1
Completed	3	0
Not completed	1	1
Adverse event, serious fatal	-	-
Physician decision	-	-
Subject Decision	-	1
Adverse event, non-fatal	-	-
Treated in Extension Phase	-	-
New Therapy For Study Indication	1	-

Baseline characteristics

Reporting groups

Reporting group title	Part 1: Ruxolitinib + Siremadlin 20 mg
Reporting group description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Siremadlin 30 mg
Reporting group description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Siremadlin 40 mg
Reporting group description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Rineterkib 200 mg
Reporting group description:	
Dose escalation of rineterkib added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Crizanlizumab
Reporting group description:	
Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Sabatolimab
Reporting group description:	
Safety run-in of sabatolimab added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + NIS793
Reporting group description:	
Safety run-in of NIS793 added to existing stable dose of ruxolitinib	
Reporting group title	Part 2: Ruxolitinib
Reporting group description:	
Existing stable dose of ruxolitinib as control for Part 2	

Reporting group values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg
Number of subjects	7	10	6
Age Categorical Units: participants			
<65	1	5	1
>=65	6	5	5
Age Continuous Units: years			
arithmetic mean	70.6	62.3	74.3
standard deviation	± 6.5	± 10.7	± 9.9
Sex: Female, Male Units: participants			
Female	2	6	0
Male	5	4	6
Race/Ethnicity, Customized Units: Subjects			
White	7	10	6
Unknown	0	0	0

Reporting group values	Part 1: Ruxolitinib + Rineterkib 200 mg	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab
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Number of subjects	9	6	2
Age Categorical Units: participants			
<65	4	4	1
>=65	5	2	1
Age Continuous Units: years			
arithmetic mean	67.3	65.0	62.5
standard deviation	± 7.8	± 8.1	± 12.0
Sex: Female, Male Units: participants			
Female	2	1	0
Male	7	5	2
Race/Ethnicity, Customized Units: Subjects			
White	8	5	2
Unknown	1	1	0

Reporting group values	Part 1: Ruxolitinib + NIS793	Part 2: Ruxolitinib	Total
Number of subjects	4	1	45
Age Categorical Units: participants			
<65	1	1	18
>=65	3	0	27
Age Continuous Units: years			
arithmetic mean	70.8	58.0	
standard deviation	± 7.3	± 0	-
Sex: Female, Male Units: participants			
Female	1	1	13
Male	3	0	32
Race/Ethnicity, Customized Units: Subjects			
White	4	1	43
Unknown	0	0	2

End points

End points reporting groups

Reporting group title	Part 1: Ruxolitinib + Siremadlin 20 mg
Reporting group description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Siremadlin 30 mg
Reporting group description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Siremadlin 40 mg
Reporting group description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Rineterkib 200 mg
Reporting group description:	
Dose escalation of rineterkib added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Crizanlizumab
Reporting group description:	
Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + Sabatolimab
Reporting group description:	
Safety run-in of sabatolimab added to existing stable dose of ruxolitinib	
Reporting group title	Part 1: Ruxolitinib + NIS793
Reporting group description:	
Safety run-in of NIS793 added to existing stable dose of ruxolitinib	
Reporting group title	Part 2: Ruxolitinib
Reporting group description:	
Existing stable dose of ruxolitinib as control for Part 2	
Subject analysis set title	Part 1:Ruxolitinib + Siremadlin 20 mg (AUClast for Siremadlin)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Subject analysis set title	Part 1:Ruxolitinib + Siremadlin 30 mg (AUClast for Siremadlin)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Subject analysis set title	Part 1:Ruxolitinib + Siremadlin 40 mg (AUClast for Siremadlin)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Dose escalation of siremadlin added to existing stable dose of ruxolitinib	
Subject analysis set title	Part 1:Ruxolitinib+ Rineterkib 200 mg (AUClast for Rineterkib)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Dose escalation of rineterkib added to existing stable dose of ruxolitinib	
Subject analysis set title	Part 1:Ruxolitinib + Crizanlizumab (AUClast for Crizanlizumab)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib	
Subject analysis set title	Part 1: Ruxolitinib + Sabatolimab (AUClast for Sabatolimab)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + NIS793 (AUClast for NIS793)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Siremadlin 20 mg (Cmax for Siremadlin)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Siremadlin 30 mg (Cmax for Siremadlin)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Siremadlin 40 mg (Cmax for Siremadlin)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Rineterkib 200 mg (Cmax for Rineterkib)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Crizanlizumab (Cmax for Crizanlizumab)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Sabatolimab (Cmax for Sabatolimab)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + NIS793 (Cmax for NIS793)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Siremadlin 20 mg (Tmax for Siremadlin)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Siremadlin 30 mg (Tmax for Siremadlin)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Siremadlin 40 mg (Tmax for Siremadlin)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Rineterkib 200 mg (Tmax for Rineterkib)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Crizanlizumab (Tmax for Crizanlizumab)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of crizanolizumab added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + Sabatolimab (Tmax for Sabatolimab)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

Subject analysis set title	Part 1: Ruxolitinib + NIS793 (Tmax for NIS793)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

Primary: Incidence and Severity of Dose Limiting Toxicities Within the First 2 Cycles in Part 1

End point title	Incidence and Severity of Dose Limiting Toxicities Within the First 2 Cycles in Part 1 ^{[1][2]}
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End point description:

Incidence and severity of dose limiting toxicities within the first 2 cycles (6 or 8 weeks) in Part 1 of the study. DLTs were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) criteria Version 5.0. Grade 0 was assigned for all non-missing values not graded as 1 or higher. Higher grade indicated more severity. Grade 5 was not used.

End point type	Primary
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End point timeframe:

Baseline to the end of Cycle 2 (6 or 8 weeks)

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: No statistical analysis was planned for this primary outcome.

[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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	7	5	9
Units: participants				
Grade 3	0	0	1	1
Grade 4	0	1	1	0

End point values	Part 1: Ruxolitinib + Crizanolizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	2	0 ^[3]	
Units: participants				
Grade 3	0	0		
Grade 4	0	0		

Notes:

[3] - Number analyzed is the number of participants with available data.

Statistical analyses

No statistical analyses for this end point

Primary: Response Rate at the End of Cycle 6 or Cycle 8 in Part 1

End point title	Response Rate at the End of Cycle 6 or Cycle 8 in Part 1 ^{[4][5]}
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End point description:

Composite of anemia improvement (hemoglobin level) and no spleen volume progression and no symptom worsening in Part 2 and Part 3 of the study. For a subject to be considered a responder, all three components of the composite had to be fulfilled.

End point type	Primary
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End point timeframe:

Baseline to the end of Cycle 6 or 8 (24 weeks)

Notes:

[4] - 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: No statistical analysis was planned for this primary outcome.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[6]	0 ^[7]	0 ^[8]	0 ^[9]
Units: percentage of participants				

Notes:

[6] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[7] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[8] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[9] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[10]	0 ^[11]	0 ^[12]	
Units: percentage of participants				

Notes:

[10] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[11] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[12] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving an Improvement in Hemoglobin Level of ≥ 1.5 g/dL From Baseline in Part 1

End point title	Percentage of Subjects Achieving an Improvement in Hemoglobin Level of ≥ 1.5 g/dL From Baseline in Part 1 ^[13]
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End point description:

End point type	Secondary
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End point timeframe:

Week 24, Week 48

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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	6	9
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	11.1
Week 48	0	0	0	11.1

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	4	
Units: percentage of participants				
number (not applicable)				
Week 24	16.7	0	0	
Week 48	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving an Improvement in Hemoglobin Level of at Least ≥ 2.0 g/dL From Baseline in Part 1

End point title	Percentage of Subjects Achieving an Improvement in Hemoglobin Level of at Least ≥ 2.0 g/dL From Baseline in Part 1 ^[14]
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End point description:

End point type	Secondary
End point timeframe:	
Week 24, Week 48	
Notes:	
[14] - 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: Applicable to Part 1 only.	

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	6	9
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	11.1
Week 48	0	0	0	11.1

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	4	
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	
Week 48	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Spleen Length From Baseline in Part 1

End point title	Change in Spleen Length From Baseline in Part 1 ^[15]
End point description:	
Change in spleen length measured in centimeters by manual palpation.	
End point type	Secondary
End point timeframe:	
Baseline, Week 24, Week 48	
Notes:	
[15] - 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: Applicable to Part 1 only.	

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	8	4	4
Units: centimeters				
arithmetic mean (standard deviation)				
Week 24 n=6,8,4,4,4,0,0	-3.3 (± 2.6)	-5.5 (± 3.9)	-6.3 (± 4.6)	-1.8 (± 3.9)
Week 48 n=2,1,2,1,1,0,0	-5.0 (± 0.0)	-9.0 (± 999)	-6.0 (± 7.1)	-8.0 (± 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	0 ^[16]	0 ^[17]	
Units: centimeters				
arithmetic mean (standard deviation)				
Week 24 n=6,8,4,4,4,0,0	-1.5 (± 1.9)	()	()	
Week 48 n=2,1,2,1,1,0,0	-5.0 (± 999)	()	()	

Notes:

[16] - Number analyzed is the number of participants with available data.

[17] - Number analyzed is the number of participants with available data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With ≥35% Reduction in Spleen Volume From Baseline in Part 1

End point title	Percentage of Subjects With ≥35% Reduction in Spleen Volume From Baseline in Part 1 ^[18]
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End point description:

Change in spleen volume measured by magnetic resonance imaging (MRI) or computed tomography (CT) from baseline.

End point type	Secondary
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End point timeframe:

Week 24, Week 48

Notes:

[18] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	6	9
Units: percentage of participants				
number (not applicable)				
Week 24	14.3	60.0	0	0

Week 48	14.3	10.0	16.7	0
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End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	4	
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	
Week 48	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With $\geq 25\%$ Reduction in Spleen Volume From Baseline in Part 1

End point title	Percentage of Subjects With $\geq 25\%$ Reduction in Spleen Volume From Baseline in Part 1 ^[19]
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End point description:

Change in spleen volume measured by magnetic resonance imaging (MRI) or computed tomography (CT) from baseline.

End point type	Secondary
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End point timeframe:

Week 24, Week 48

Notes:

[19] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	6	9
Units: percentage of participants				
number (not applicable)				
Week 24	28.6	60.0	0	11.1
Week 48	28.6	10.0	16.7	11.1

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
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Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	4	
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	
Week 48	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects in Part 1 With $\geq 50\%$ Reduction From Baseline in Myelofibrosis Symptom Assessment Form, Version 4.0 (MFSAF v4.0)

End point title	Percentage of Subjects in Part 1 With $\geq 50\%$ Reduction From Baseline in Myelofibrosis Symptom Assessment Form, Version 4.0 (MFSAF v4.0) ^[20]
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End point description:

The MFSAF v4.0 questionnaire focuses on the 7 core symptoms of MF: fatigue, night sweats, pruritus, abdominal discomfort, pain under the ribs on the left side, early satiety and bone pain. Subjects record symptom severity at it worst for each of the 7 symptoms on an 11-point numeric rating scale, from 0 (absent) to 10 (worst imaginable). The Total Symptom Score (TSS) is the sum of all the scores for all 7 symptoms.

End point type	Secondary
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End point timeframe:

Week 12, Week 24, Week 48

Notes:

[20] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	6	9
Units: percentage of participants				
number (not applicable)				
Week 12	42.9	30.0	16.7	11.1
Week 24	14.3	20.0	33.3	11.1
Week 48	14.3	10.0	16.7	0

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	4	
Units: percentage of participants				
number (not applicable)				

Week 12	16.7	0	0	
Week 24	16.7	0	0	
Week 48	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1

End point title	Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1
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End point description:

End point type	Secondary
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End point timeframe:

Days 1 and 5 of Cycles 1 and 2 for siremadlin and Cycles 1 and 3 for crizanlizumab, sabatolimab, and NIS793; Days 1 and 15 of Cycle 1 for rineterkib

End point values	Part 1:Ruxolitinib + Siremadlin 20 mg (AUClast for Siremadlin)	Part 1:Ruxolitinib + Siremadlin 30 mg (AUClast for Siremadlin)	Part 1:Ruxolitinib + Siremadlin 40 mg (AUClast for Siremadlin)	Part 1:Ruxolitinib+ Rineterkib 200 mg (AUClast for Rineterkib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	5	9
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 n=6,9,5,9,5,2,4	1520 (± 619)	2560 (± 1530)	3780 (± 1840)	6000 (± 5120)
Cycle 1 Day 5 n=6,7,5,0,0,0,0	2230 (± 1110)	3340 (± 2120)	4390 (± 2270)	999 (± 999)
Cycle 2 Day 1 n=5,6,3,0,0,0,0	1720 (± 1020)	2400 (± 1150)	2870 (± 326)	999 (± 999)
Cycle 2 Day 5 n=3,5,3,0,0,0,0	1590 (± 577)	2860 (± 1680)	3030 (± 786)	999 (± 999)
Cycle 1 Day 15 n=0,0,0,9,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	15800 (± 11000)
Cycle 3 Day 1 n=0,0,0,0,5,2,3	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)

End point values	Part 1:Ruxolitinib + Crizanlizumab (AUClast for Crizanlizumab)	Part 1: Ruxolitinib + Sabatolimab (AUClast for Sabatolimab)	Part 1: Ruxolitinib + NIS793 (AUClast for NIS793)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	2	4	
Units: ng*hr/mL				
arithmetic mean (standard deviation)				

Cycle 1 Day 1 n=6,9,5,9,5,2,4	14100000 (± 4990000)	34900 (± 7860)	103000000 (± 18700000)	
Cycle 1 Day 5 n=6,7,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 2 Day 1 n=5,6,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 2 Day 5 n=3,5,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 15 n=0,0,0,9,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 3 Day 1 n=0,0,0,0,5,2,3	20900000 (± 13000000)	43500 (± 9110)	166000000 (± 63600000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Ruxolitinib in Part 1

End point title	Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Ruxolitinib in Part 1 ^[21]
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End point description:

End point type	Secondary
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End point timeframe:

Days 1 and 5 of Cycles 1 and 2; Day 15 of Cycle 1

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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	2	3
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Ruxolitinib 5 mg Cycle 1 Day 1 n=0,0,2,1,0,0,0	999 (± 999)	999 (± 999)	344 (± 225)	199 (± 999)
Ruxolitinib 10 mg Cycle 1 Day 1 n=3,4,1,2,1,2,1	546 (± 412)	673 (± 290)	498 (± 999)	633 (± 393)
Ruxolitinib 15 mg Cycle 1 Day 1 n=1,0,2,1,2,0,2	1090 (± 999)	999 (± 999)	481 (± 243)	729 (± 999)
Ruxolitinib 20 mg Cycle 1 Day 1 n=3,2,1,3,1,0,0	991 (± 183)	616 (± 107)	623 (± 999)	913 (± 451)
Ruxolitinib 25 mg Cycle 1 Day 1 n=0,0,0,1,0,0,1	999 (± 999)	999 (± 999)	999 (± 999)	188 (± 999)
Ruxolitinib 5 mg Cycle 1 Day 5 n=0,0,2,0,0,0,0	999 (± 999)	999 (± 999)	245 (± 173)	999 (± 999)
Ruxolitinib 10 mg Cycle 1 Day 5 n=3,3,1,0,0,0,0,	465 (± 228)	550 (± 307)	441 (± 999)	999 (± 999)
Ruxolitinib 15 mg Cycle 1 Day 5 n=1,1,2,0,0,0,0	849 (± 999)	901 (± 999)	454 (± 212)	999 (± 999)

Ruxolitinib 20 mg Cycle 1 Day 5 n=2,4,1,0,0,0	872 (± 218)	652 (± 218)	482 (± 999)	999 (± 999)
Ruxolitinib 5 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	289 (± 999)
Ruxolitinib 10 mg Cycle 1 Day 15 n=0,0,0,2,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	592 (± 403)
Ruxolitinib 15 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0,	999 (± 999)	999 (± 999)	999 (± 999)	518 (± 999)
Ruxolitinib 20 mg Cycle 1 Day 15 n=0,0,0,3,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	957 (± 479)
Ruxolitinib 25 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	718 (± 999)
Ruxolitinib 5 mg Cycle 2 Day 1 n=0,0,1,0,0,0,0	999 (± 999)	999 (± 999)	172 (± 999)	999 (± 999)
Ruxolitinib 10 mg Cycle 2 Day 1 n=2,2,1,0,0,0,0	354 (± 101)	507 (± 225)	553 (± 999)	999 (± 999)
Ruxolitinib 15 mg Cycle 2 Day 1 n=1,2,2,0,0,0,0	1040 (± 999)	1190 (± 214)	334 (± 98.7)	999 (± 999)
Ruxolitinib 20 mg Cycle 2 Day 1 n=3,3,1,0,0,0,0	823 (± 206)	727 (± 200)	521 (± 999)	999 (± 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	2	2	
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Ruxolitinib 5 mg Cycle 1 Day 1 n=0,0,2,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 1 Day 1 n=3,4,1,2,1,2,1	440 (± 999)	336 (± 30.6)	452 (± 999)	
Ruxolitinib 15 mg Cycle 1 Day 1 n=1,0,2,1,2,0,2	662 (± 420)	999 (± 999)	1220 (± 637)	
Ruxolitinib 20 mg Cycle 1 Day 1 n=3,2,1,3,1,0,0	887 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 25 mg Cycle 1 Day 1 n=0,0,0,1,0,0,1	999 (± 999)	999 (± 999)	859 (± 999)	
Ruxolitinib 5 mg Cycle 1 Day 5 n=0,0,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 1 Day 5 n=3,3,1,0,0,0,0,	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 15 mg Cycle 1 Day 5 n=1,1,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 20 mg Cycle 1 Day 5 n=2,4,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 5 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 1 Day 15 n=0,0,0,2,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 15 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0,	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 20 mg Cycle 1 Day 15 n=0,0,0,3,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 25 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 5 mg Cycle 2 Day 1 n=0,0,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	

Ruxolitinib 10 mg Cycle 2 Day 1 n=2,2,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 15 mg Cycle 2 Day 1 n=1,2,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 20 mg Cycle 2 Day 1 n=3,3,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum (Peak) Observed Plasma Drug Concentration (Cmax) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1

End point title	Maximum (Peak) Observed Plasma Drug Concentration (Cmax) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1
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End point description:

End point type	Secondary
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End point timeframe:

Days 1 and 5 of Cycles 1 and 2 for siremadlin and Cycles 1 and 3 for crizanlizumab, sabatolimab, and NIS793; Days 1 and 15 of Cycle 1 for rineterkib

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg (Cmax for Siremadlin)	Part 1: Ruxolitinib + Siremadlin 30 mg (Cmax for Siremadlin)	Part 1: Ruxolitinib + Siremadlin 40 mg (Cmax for Siremadlin)	Part 1: Ruxolitinib + Rineterkib 200 mg (Cmax for Rineterkib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	5	9
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 n=6,9,5,9,5,2,4	118 (± 32.8)	207 (± 122)	290 (± 56.1)	469 (± 358)
Cycle 1 Day 5 n=6,7,5,0,0,0,0	161 (± 78.0)	284 (± 138)	336 (± 109)	999 (± 999)
Cycle 2 Day 1 n=5,6,3,0,0,0,0	131 (± 57.9)	142 (± 102)	268 (± 15.0)	999 (± 999)
Cycle 2 Day 5 n=3,5,3,0,0,0,0	103 (± 34.1)	193 (± 95.0)	228 (± 58.3)	999 (± 999)
Cycle 1 Day 15 n=0,0,0,9,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	987 (± 621)
Cycle 3 Day 1 n=0,0,0,0,5,2,3	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab (Cmax for Crizanlizumab)	Part 1: Ruxolitinib + Sabatolimab (Cmax for Sabatolimab)	Part 1: Ruxolitinib + NIS793 (Cmax for NIS793)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	2	4	
Units: ng/mL				
arithmetic mean (standard deviation)				

Cycle 1 Day 1 n=6,9,5,9,5,2,4	114000 (± 36400)	131 (± 17.7)	439000 (± 56100)	
Cycle 1 Day 5 n=6,7,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 2 Day 1 n=5,6,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 2 Day 5 n=3,5,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 15 n=0,0,0,9,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 3 Day 1 n=0,0,0,0,5,2,3	114000 (± 56600)	150 (± 33.2)	743000 (± 314000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum (Peak) Observed Plasma Drug Concentration (Cmax) for Ruxolitinib in Part 1

End point title	Maximum (Peak) Observed Plasma Drug Concentration (Cmax) for Ruxolitinib in Part 1 ^[22]
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End point description:

End point type	Secondary
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End point timeframe:

Days 1 and 5 of Cycles 1 and 2; Day 15 of Cycle 1

Notes:

[22] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	2	3
Units: ng/mL				
arithmetic mean (standard deviation)				
Ruxolitinib 5 mg Cycle 1 Day 1 n=0,0,2,1,0,0,0	999 (± 999)	999 (± 999)	93.3 (± 26.5)	67.4 (± 999)
Ruxolitinib 10 mg Cycle 1 Day 1 n=3,4,1,2,1,2,1	184 (± 159)	209 (± 20.8)	108 (± 999)	195 (± 41.0)
Ruxolitinib 15 mg Cycle 1 Day 1 n=1,0,2,1,2,0,2	334 (± 999)	999 (± 999)	119 (± 76.2)	193 (± 999)
Ruxolitinib 20 mg Cycle 1 Day 1 n=3,2,1,3,1,0,0	310 (± 131)	184 (± 14.8)	232 (± 999)	332 (± 33.5)
Ruxolitinib 25 mg Cycle 1 Day 1 n=0,0,0,1,0,0,1	999 (± 999)	999 (± 999)	999 (± 999)	46.0 (± 999)
Ruxolitinib 5 mg Cycle 1 Day 5 n=0,0,2,0,0,0,0	999 (± 999)	999 (± 999)	74.8 (± 13.5)	999 (± 999)
Ruxolitinib 10 mg Cycle 1 Day 5 n=3,3,1,0,0,0,0	152 (± 55.3)	149 (± 67.6)	107 (± 999)	999 (± 999)
Ruxolitinib 15 mg Cycle 1 Day 5 n=1,1,2,0,0,0,0	252 (± 999)	264 (± 999)	172 (± 96.9)	999 (± 999)
Ruxolitinib 20 mg Cycle 1 Day 5 n=2,4,1,0,0,0,0	211 (± 48.8)	232 (± 104)	180 (± 999)	999 (± 999)

Ruxolitinib 5 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	95.4 (± 999)
Ruxolitinib 10 mg Cycle 1 Day 15 n=0,0,0,2,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	158 (± 68.6)
Ruxolitinib 15 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	126 (± 999)
Ruxolitinib 20 mg Cycle 1 Day 15 n=0,0,0,3,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	369 (± 83.7)
Ruxolitinib 25 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	323 (± 999)
Ruxolitinib 5 mg Cycle 2 Day 1 n=0,0,1,0,0,0,0	999 (± 999)	999 (± 999)	82.1 (± 999)	999 (± 999)
Ruxolitinib 10 mg Cycle 2 Day 1 n=2,2,1,0,0,0,0	119 (± 66.7)	165 (± 29.7)	90.5 (± 999)	999 (± 999)
Ruxolitinib 15 mg Cycle 2 Day 1 n=1,2,2,0,0,0,0	260 (± 999)	337 (± 70.7)	100 (± 68.9)	999 (± 999)
Ruxolitinib 20 mg Cycle 2 Day 1 n=3,3,1,0,0,0,0	257 (± 71.0)	176 (± 66.0)	241 (± 999)	999 (± 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)				
Ruxolitinib 5 mg Cycle 1 Day 1 n=0,0,2,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 1 Day 1 n=3,4,1,2,1,2,1	191 (± 999)	118 (± 33.0)	132 (± 999)	
Ruxolitinib 15 mg Cycle 1 Day 1 n=1,0,2,1,2,0,2	185 (± 120)	999 (± 999)	254 (± 73.5)	
Ruxolitinib 20 mg Cycle 1 Day 1 n=3,2,1,3,1,0,0	221 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 25 mg Cycle 1 Day 1 n=0,0,0,1,0,0,1	999 (± 999)	999 (± 999)	224 (± 999)	
Ruxolitinib 5 mg Cycle 1 Day 5 n=0,0,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 1 Day 5 n=3,3,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 15 mg Cycle 1 Day 5 n=1,1,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 20 mg Cycle 1 Day 5 n=2,4,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 5 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 1 Day 15 n=0,0,0,2,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 15 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 20 mg Cycle 1 Day 15 n=0,0,0,3,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 25 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 5 mg Cycle 2 Day 1 n=0,0,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 10 mg Cycle 2 Day 1 n=2,2,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	

Ruxolitinib 15 mg Cycle 2 Day 1 n=1,2,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Ruxolitinib 20 mg Cycle 2 Day 1 n=3,3,1,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1

End point title	Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1
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End point description:

End point type	Secondary
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End point timeframe:

Days 1 and 5 of Cycles 1 and 2 for siremadlin and Cycles 1 and 3 for crizanlizumab, sabatolimab, and NIS793; Days 1 and 15 of Cycle 1 for rineterkib

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg (Tmax for Siremadlin)	Part 1: Ruxolitinib + Siremadlin 30 mg (Tmax for Siremadlin)	Part 1: Ruxolitinib + Siremadlin 40 mg (Tmax for Siremadlin)	Part 1: Ruxolitinib + Rineterkib 200 mg (Tmax for Rineterkib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	5	9
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 n=6,9,5,9,5,2,4	2.52 (1.83 to 23.5)	3.00 (1.92 to 7.45)	3.93 (2.00 to 8.00)	3.92 (1.98 to 24.0)
Cycle 1 Day 5 n=6,7,5,0,0,0,0	3.44 (1.83 to 4.07)	2.90 (2.00 to 3.97)	2.87 (1.88 to 3.03)	999 (999 to 999)
Cycle 2 Day 1 n=5,6,3,0,0,0,0	1.95 (0.980 to 4.10)	3.92 (2.83 to 23.9)	2.88 (2.08 to 7.07)	999 (999 to 999)
Cycle 2 Day 5 n=3,5,3,0,0,0,0	3.00 (2.95 to 3.17)	2.93 (2.75 to 3.17)	3.02 (2.92 to 3.08)	999 (999 to 999)
Cycle 1 Day 15 n=0,0,0,9,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	2.50 (0.500 to 4.00)
Cycle 3 Day 1 n=0,0,0,0,5,2,3	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab (Tmax for Crizanlizumab)	Part 1: Ruxolitinib + Sabatolimab (Tmax for Sabatolimab)	Part 1: Ruxolitinib + NIS793 (Tmax for NIS793)	
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	2	4	
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 n=6,9,5,9,5,2,4	1.82 (1.50 to 2.27)	1.84 (1.67 to 2.00)	2.00 (1.95 to 2.98)	
Cycle 1 Day 5 n=6,7,5,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Cycle 2 Day 1 n=5,6,3,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Cycle 2 Day 5 n=3,5,3,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Cycle 1 Day 15 n=0,0,0,9,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Cycle 3 Day 1 n=0,0,0,0,5,2,3	1.65 (0.750 to 2.13)	2.01 (1.85 to 2.17)	1.97 (1.92 to 2.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Ruxolitinib in Part 1

End point title	Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Ruxolitinib in Part 1 ^[23]
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End point description:

End point type	Secondary
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End point timeframe:

Days 1 and 5 of Cycles 1 and 2; Day 15 of Cycle 1

Notes:

[23] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	2	3
Units: hours				
median (full range (min-max))				
Ruxolitinib 5 mg Cycle 1 Day 1 n=0,0,2,1,0,0,0	999 (999 to 999)	999 (999 to 999)	0.960 (0.920 to 1.00)	0.500 (0.500 to 0.500)
Ruxolitinib 10 mg Cycle 1 Day 1 n=3,4,1,2,1,2,1	0.550 (0.330 to 6.18)	0.775 (0.500 to 1.08)	0.500 (0.500 to 0.500)	0.485 (0.470 to 0.500)
Ruxolitinib 15 mg Cycle 1 Day 1 n=1,0,2,1,2,0,2	0.650 (0.650 to 0.650)	999 (999 to 999)	1.96 (1.92 to 2.00)	0.420 (0.420 to 0.420)
Ruxolitinib 20 mg Cycle 1 Day 1 n=3,2,1,3,1,0,0	0.530 (0.500 to 1.00)	1.54 (1.08 to 2.00)	1.00 (1.00 to 1.00)	0.450 (0.420 to 1.03)

Ruxolitinib 25 mg Cycle 1 Day 1 n=0,0,0,1,0,0,1	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	0.00 (0.00 to 0.00)
Ruxolitinib 5 mg Cycle 1 Day 5 n=0,0,2,0,0,0,0	999 (999 to 999)	999 (999 to 999)	0.960 (0.920 to 1.00)	999 (999 to 999)
Ruxolitinib 10 mg Cycle 1 Day 5 n=3,3,1,0,0,0,0	1.00 (0.830 to 2.02)	0.980 (0.920 to 2.03)	1.00 (1.00 to 1.00)	999 (999 to 999)
Ruxolitinib 15 mg Cycle 1 Day 5 n=1,1,2,0,0,0,0	0.970 (0.970 to 0.970)	0.830 (0.830 to 0.830)	0.955 (0.830 to 1.08)	999 (999 to 999)
Ruxolitinib 20 mg Cycle 1 Day 5 n=2,4,1,0,0,0,0	0.925 (0.850 to 1.00)	1.00 (0.920 to 1.08)	0.830 (0.830 to 0.830)	999 (999 to 999)
Ruxolitinib 5 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	0.500 (0.500 to 0.500)
Ruxolitinib 10 mg Cycle 1 Day 15 n=0,0,0,2,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	1.98 (1.95 to 2.00)
Ruxolitinib 15 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	0.500 (0.500 to 0.500)
Ruxolitinib 20 mg Cycle 1 Day 15 n=0,0,0,3,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	0.650 (0.500 to 1.00)
Ruxolitinib 25 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	0.500 (0.500 to 0.500)
Ruxolitinib 5 mg Cycle 2 Day 1 n=0,0,1,0,0,0,0	999 (999 to 999)	999 (999 to 999)	0.900 (0.900 to 0.900)	999 (999 to 999)
Ruxolitinib 10 mg Cycle 2 Day 1 n=2,2,1,0,0,0,0	0.895 (0.870 to 0.920)	1.00 (0.920 to 1.08)	2.00 (2.00 to 2.00)	999 (999 to 999)
Ruxolitinib 15 mg Cycle 2 Day 1 n=1,2,2,0,0,0,0	1.05 (1.05 to 1.05)	1.46 (1.00 to 1.92)	4.00 (0.920 to 7.07)	999 (999 to 999)
Ruxolitinib 20 mg Cycle 2 Day 1 n=3,3,1,0,0,0,0	0.980 (0.880 to 1.02)	1.02 (1.00 to 4.00)	0.930 (0.930 to 0.930)	999 (999 to 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	2	2	
Units: hours				
median (full range (min-max))				
Ruxolitinib 5 mg Cycle 1 Day 1 n=0,0,2,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 10 mg Cycle 1 Day 1 n=3,4,1,2,1,2,1	0.580 (0.580 to 0.580)	0.460 (0.00 to 0.920)	1.67 (1.67 to 1.67)	
Ruxolitinib 15 mg Cycle 1 Day 1 n=1,0,2,1,2,0,2	1.80 (1.75 to 1.85)	999 (999 to 999)	2.42 (1.08 to 3.75)	
Ruxolitinib 20 mg Cycle 1 Day 1 n=3,2,1,3,1,0,0	1.17 (1.17 to 1.17)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 25 mg Cycle 1 Day 1 n=0,0,0,1,0,0,1	999 (999 to 999)	999 (999 to 999)	2.00 (2.00 to 2.00)	
Ruxolitinib 5 mg Cycle 1 Day 5 n=0,0,2,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 10 mg Cycle 1 Day 5 n=3,3,1,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 15 mg Cycle 1 Day 5 n=1,1,2,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 20 mg Cycle 1 Day 5 n=2,4,1,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 5 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 10 mg Cycle 1 Day 15 n=0,0,0,2,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	

Ruxolitinib 15 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 20 mg Cycle 1 Day 15 n=0,0,0,3,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 25 mg Cycle 1 Day 15 n=0,0,0,1,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 5 mg Cycle 2 Day 1 n=0,0,1,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 10 mg Cycle 2 Day 1 n=2,2,1,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 15 mg Cycle 2 Day 1 n=1,2,2,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	
Ruxolitinib 20 mg Cycle 2 Day 1 n=3,3,1,0,0,0,0	999 (999 to 999)	999 (999 to 999)	999 (999 to 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration Versus Time Profile for Siremadlin in Part 1

End point title	Concentration Versus Time Profile for Siremadlin in Part 1 ^[24]
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 of Cycles 1 and 2; Day 6 of Cycle 1; Days 2 and 5 of Cycles 1, 2, 3, 4, 5, and 6. Each cycle was 28 days.

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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	10	5	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 hr (pre-dose) n=6,7,5	0 (± 0)	0 (± 0)	0 (± 0)	
Cycle 1 Day 1, 0.5 hr n=6,8,5	7.46 (± 6.23)	4.76 (± 8.02)	12.8 (± 21.0)	
Cycle 1 Day 1, 1 hr n=6,9,5	52.7 (± 27.0)	38.8 (± 40.9)	87.0 (± 73.6)	
Cycle 1 Day 1, 2 hr n=6,9,5	104 (± 53.3)	146 (± 95.1)	199 (± 139)	
Cycle 1 Day 1, 3 hr n=6,9,4	102 (± 51.8)	178 (± 96.3)	192 (± 137)	
Cycle 1 Day 1, 4 hr n=6,9,5	92.9 (± 44.0)	181 (± 116)	201 (± 109)	
Cycle 1 Day 1, 8 hr n=6,9,5	75.7 (± 36.9)	146 (± 77.0)	212 (± 55.5)	
Cycle 1 Day 2, 24 hr n=6,10,4	42.0 (± 23.7)	59.7 (± 49.4)	95.3 (± 41.2)	
Cycle 1 Day 5, 0 hr (pre-dose) n=6,7,5	43.5 (± 42.2)	88.4 (± 73.6)	77.6 (± 84.2)	
Cycle 1 Day 5, 1 hr n=6,6,5	72.9 (± 28.3)	171 (± 89.8)	155 (± 123)	
Cycle 1 Day 5, 2 hr n=6,7,5	127 (± 63.7)	260 (± 128)	324 (± 112)	
Cycle 1 Day 5, 3 hr n=6,7,5	144 (± 74.6)	260 (± 130)	333 (± 108)	

Cycle 1 Day 5, 4 hr n=5,7,5	133 (± 67.4)	226 (± 111)	295 (± 97.9)
Cycle 1 Day 5, 8 hr n=7,8,3	110 (± 54.3)	160 (± 83.1)	247 (± 126)
Cycle 1 Day 6, 24 hr n=7,8,5	45.4 (± 35.9)	75.1 (± 66.5)	72.2 (± 90.5)
Cycle 2 Day 1, 0 hr (pre-dose) n=4,5,3	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 2 Day 1, 1 hr n=5,5,3	71.8 (± 92.9)	25.5 (± 28.4)	32.2 (± 28.7)
Cycle 2 Day 1, 2 hr n=5,5,2	116 (± 64.7)	100 (± 64.8)	144 (± 200)
Cycle 2 Day 1, 3 hr n=5,5,3	111 (± 58.2)	146 (± 99.5)	178 (± 147)
Cycle 2 Day 1, 4 hr n=5,5,3	114 (± 52.8)	158 (± 78.4)	164 (± 102)
Cycle 2 Day 1, 8 hr n=4,5,3	90.9 (± 39.1)	122 (± 54.5)	189 (± 63.2)
Cycle 2 Day 2, 24 hr n=4,5,3	67.3 (± 49.3)	48.5 (± 44.2)	31.7 (± 5.42)
Cycle 2 Day 5, 0 hr (pre-dose) n=4,7,3	24.3 (± 23.8)	42.5 (± 50.8)	29.2 (± 6.67)
Cycle 2 Day 5, 3 hr n=3,6,3	103 (± 34.1)	181 (± 89.7)	228 (± 58.3)
Cycle 2 Day 6, 24 hr n=4,5,3	34.7 (± 13.2)	51.5 (± 58.3)	27.5 (± 6.45)
Cycle 3 Day 2, 0 hr (pre-dose) n=3,4,4	43.5 (± 16.5)	79.1 (± 96.9)	39.2 (± 20.5)
Cycle 3 Day 5, 0 hr (pre-dose) n=5,6,3	56.8 (± 47.9)	81.0 (± 73.9)	29.7 (± 23.3)
Cycle 4 Day 2, 0 hr (pre-dose) n=5,5,1	36.3 (± 21.7)	63.0 (± 52.4)	10.9 (± 999)
Cycle 4 Day 5, 0 hr (pre-dose) n=5,6,1	40.4 (± 29.7)	50.1 (± 48.1)	10.5 (± 999)
Cycle 5 Day 2, 0 hr (pre-dose) n=6,4,4	40.0 (± 29.3)	146 (± 180)	49.2 (± 25.1)
Cycle 5 Day 5, 0 hr (pre-dose) n=6,4,3	78.3 (± 90.2)	124 (± 129)	32.5 (± 13.5)
Cycle 6 Day 2, 0 hr (pre-dose) n=5,2,1	48.0 (± 28.2)	60.2 (± 37.0)	16.4 (± 999)
Cycle 6 Day 5, 0 hr (pre-dose) n=4,2,1	79.0 (± 52.2)	68.9 (± 68.1)	9.02 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration Versus Time Profile for Rineterkib in Part 1

End point title	Concentration Versus Time Profile for Rineterkib in Part 1 ^[25]
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End point description:

End point type	Secondary
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End point timeframe:

Days 1, 2, 15, and 16 of Cycle 1; Day 1 of Cycles 2, 3, 4, 5, and 6. Each cycle was 28 days.

Notes:

[25] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Rineterkib 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 hr (pre-dose) n=9	0 (± 0)			
Cycle 1 Day 1, 0.5 hr n=9	68.3 (± 68.8)			
Cycle 1 Day 1, 1 hr n=8	235 (± 343)			

Cycle 1 Day 1, 2 hr n=8	340 (± 229)			
Cycle 1 Day 1, 3 hr n=9	352 (± 244)			
Cycle 1 Day 1, 4 hr n=9	325 (± 173)			
Cycle 1 Day 1, 8 hr n=7	244 (± 128)			
Cycle 1 Day 2, 24 hr n=9	261 (± 419)			
Cycle 1 Day 2, 0 hr (pre-dose) n=8	234 (± 440)			
Cycle 1 Day 15, 0 hr (pre-dose) n=8	330 (± 222)			
Cycle 1 Day 15 0.5 hr n=8	581 (± 464)			
Cycle 1 Day 15, 1 hr n=n=9	735 (± 620)			
Cycle 1 Day 15, 2 hr n=8	749 (± 512)			
Cycle 1 Day 15, 3 hr n=8	789 (± 616)			
Cycle 1 Day 15, 4 hr n=8	771 (± 484)			
Cycle 1 Day 15, 8 hr n=9	633 (± 403)			
Cycle 1 Day 16, 24 hr n=8	528 (± 618)			
Cycle 1 Day 16, 0 hr (pre-dose) n=8	305 (± 222)			
Cycle 2 Day 1, 0 hr (pre-dose) n=9	314 (± 171)			
Cycle 3 Day 1, 0 hr (pre-dose) n=6	406 (± 341)			
Cycle 4 Day 1, 0 hr (pre-dose) n=5	402 (± 364)			
Cycle 5 Day 1, 0 hr (pre-dose) n=3	232 (± 165)			
Cycle 6 Day 1, 0 hr (pre-dose) n=3	340 (± 125)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration Versus Time Profile for Crizanlizumab in Part 1

End point title	Concentration Versus Time Profile for Crizanlizumab in Part
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End point description:

EOI = end of infusion

End point type	Secondary
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End point timeframe:

Days 1, 2, 8, and 15 of Cycles 1, 2, and 3; Day 1 of Cycles 4, 5, 6, and 9. Each cycle was 28 days.

Notes:

[26] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Crizanlizumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 H / PRE-INFUSION n=4	0 (± 0)			
Cycle 1 Day 1, 1H POST EOI n=5	114000 (± 36400)			
Cycle 1 Day 2, 24H POST START OF INFUSION n=4	78700 (± 10500)			

Cycle 1 Day 8, 168H POST START OF INFUSION n=5	28700 (\pm 12200)			
Cycle 1 Day 15, 336H POST START OF INFUSION n=5	9280 (\pm 4540)			
Cycle 1 Day 15, 0 H / PRE-INFUSION n=1	7710 (\pm 999)			
Cycle 2 Day 1, 0 H / PRE-INFUSION n=5	20700 (\pm 8980)			
Cycle 2 Day 1, 1H POST EOI n=5	135000 (\pm 43100)			
Cycle 2 Day 1, 336H POST START OF INFUSION n=1,	15500 (\pm 999)			
Cycle 3 Day 1, 672H POST START OF INFUSION n=5	8710 (\pm 8350)			
Cycle 3 Day 1, 0 H / PRE-INFUSION n=5	8710 (\pm 8350)			
Cycle 3 Day 1, 1H POST EOI n=4	103000 (\pm 59200)			
Cycle 3 Day 2, 24H POST START OF INFUSION n=5	95500 (\pm 42300)			
Cycle 3 Day 8, 168H POST START OF INFUSION n=5	37100 (\pm 19400)			
Cycle 3 Day 15, 336H POST START OF INFUSION n=5	21000 (\pm 17700)			
Cycle 4 Day 1, 672H POST START OF INFUSION n=5	5900 (\pm 6710)			
Cycle 4 Day 1, 0 H / PRE-INFUSION n=5	5900 (\pm 6710)			
Cycle 4 Day 1, 1H POST EOI n=5	128000 (\pm 33200)			
Cycle 5 Day 1, 672H POST START OF INFUSION n=4	6780 (\pm 7830)			
Cycle 5 Day 1, 0 H / PRE-INFUSION n=4	6780 (\pm 7830)			
Cycle 5 Day 1, 1H POST EOI n=3	122000 (\pm 29400)			
Cycle 6 Day 1, 672H POST START OF INFUSION n=4	6930 (\pm 8000)			
Cycle 6 Day 1, 0 H / PRE-INFUSION n=4	6930 (\pm 8000)			
Cycle 6 Day 1, 1H POST EOI n=4	128000 (\pm 39600)			
Cycle 9 Day 1, 0 H / PRE-INFUSION n=3	5500 (\pm 9530)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration Versus Time Profile for Sabatolimab in Part 1

End point title	Concentration Versus Time Profile for Sabatolimab in Part 1 ^[27]
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End point description:

EOI = end of infusion

End point type	Secondary
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End point timeframe:

Days 1, 2, 8, and 15 of Cycles 1, 2, and 3; Day 1 of Cycles 4 and 5. Each cycle was 28 days.

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.

End point values	Part 1: Ruxolitinib + Sabatolimab			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 H / PRE-INFUSION n=2	0 (± 0)			
Cycle 1 Day 1, 1H POST EOI n=1	143 (± 999)			
Cycle 1 Day 2, 24H POST START OF INFUSION n=2	109 (± 13.2)			
Cycle 1 Day 8, 168H POST START OF INFUSION n=1	57.0 (± 999)			
Cycle 1 Day 15, 336H POST START OF INFUSION n=2	41.8 (± 7.28)			
Cycle 2 Day 1, 672H POST START OF INFUSION n=2	16.1 (± 9.16)			
Cycle 2 Day 1, 0 H / PRE-INFUSION n=2	16.1 (± 9.16)			
Cycle 2 Day 1, 1H POST EOI n=1	126 (± 999)			
Cycle 3 Day 1, 672H POST START OF INFUSION n=2	26.0 (± 5.09)			
Cycle 3 Day 1, 0 H / PRE-INFUSION n=2	26.0 (± 5.09)			
Cycle 3 Day 1, 1H POST EOI n=2	150 (± 33.2)			
Cycle 3 Day 2, 24H POST START OF INFUSION n=2	125 (± 10.6)			
Cycle 3 Day 8, 168H POST START OF INFUSION n=2	80.5 (± 19.1)			
Cycle 3 Day 15, 336H POST START OF INFUSION n=2	58.0 (± 12.3)			
Cycle 4 Day 1, 672H POST START OF INFUSION n=1	31.1 (± 999)			
Cycle 4 Day 1, 0 H / PRE-INFUSION n=2	30.0 (± 1.56)			
Cycle 4 Day 1, 1H POST EOI n=2	141 (± 11.3)			
Cycle 5 Day 1, 0 H / PRE-INFUSION n=2	32.9 (± 3.82)			
Cycle 5 Day 1, 1H POST EOI n=2	152 (± 9.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration Versus Time Profile for NIS793 in Part 1

End point title	Concentration Versus Time Profile for NIS793 in Part 1 ^[28]
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End point description:

EOI = end of infusion

End point type	Secondary
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End point timeframe:

Days 1, 2, 4, 8, 11, and 15 of Cycles 1, 2, and 3; Day 1 of Cycles 4 and 5. Each cycle was 28 days.

Notes:

[28] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + NIS793			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 H / PRE-INFUSION n=4	0 (± 0)			
Cycle 1 Day 1, 1H POST EOI n=4	439000 (± 56100)			
Cycle 1 Day 2, 24H POST START OF INFUSION n=4	349000 (± 52800)			
Cycle 1 Day 4, 72H POST START OF INFUSION n=4	279000 (± 48400)			
Cycle 1 Day 8, 168H POST START OF INFUSION n=3	196000 (± 31000)			
Cycle 1 Day 11, 240H POST START OF INFUSION n=4	183000 (± 45400)			
Cycle 1 Day 15, 336H POST START OF INFUSION n=4	161000 (± 37500)			
Cycle 2 Day 1, 504H POST START OF INFUSION n=4	132000 (± 33300)			
Cycle 2 Day 1, 0 H / PRE-INFUSION n=4	132000 (± 33300)			
Cycle 3 Day 1, 0 H / PRE-INFUSION n=3	187000 (± 61000)			
Cycle 3 Day 1, 1H POST EOI n=3	743000 (± 314000)			
Cycle 3 Day 2, 24H POST START OF INFUSION n=2	632000 (± 17000)			
Cycle 3 Day 4, 72H POST START OF INFUSION n=3	448000 (± 114000)			
Cycle 3 Day 8, 168H POST START OF INFUSION n=3	383000 (± 103000)			
Cycle 3 Day 11, 240H POST START OF INFUSION n=2	262000 (± 93300)			
Cycle 3 Day 15, 336H POST START OF INFUSION n=3	265000 (± 51500)			
Cycle 4 Day 1, 504H POST START OF INFUSION n=1	281000 (± 999)			
Cycle 4 Day 1, 0 H / PRE-INFUSION n=2	232000 (± 70000)			
Cycle 5 Day 1, 0 H / PRE-INFUSION n=1	280000 (± 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration Versus Time Profile for Ruxolitinib in Part 1

End point title	Concentration Versus Time Profile for Ruxolitinib in Part 1 ^[29]
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End point description:

End point type	Secondary
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End point timeframe:

Days 1, 2, 5, 6, and 15 of Cycles 1 and 2; Day 16 of Cycle 1; Days 1, 2, and 15 of Cycle 3; Days 1 and 5 of Cycles 4, 5, and 6. Each cycle was 28 days.

Notes:

[29] - 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: Applicable to Part 1 only.

End point values	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Rineterkib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8	6	8
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 hr (pre-dose) n=6,6,5,7,3,2,4	34.7 (± 17.8)	21.3 (± 14.5)	11.8 (± 13.4)	20.1 (± 16.1)
Cycle 1 Day 1, 0.5 hr n=6,5,6,8,2,2,3	284 (± 128)	152 (± 91.1)	95.7 (± 63.2)	185 (± 100)
Cycle 1 Day 1, 1 hr n=6,6,6,7,2,2,3	240 (± 78.9)	167 (± 51.7)	124 (± 64.5)	192 (± 106)
Cycle 1 Day 1, 2 hr n=6,6,6,7,2,2,3	174 (± 55.3)	143 (± 48.6)	98.9 (± 46.2)	140 (± 112)
Cycle 1 Day 1, 3 hr n=6,6,5,8,2,2,3	125 (± 36.6)	114 (± 42.1)	62.4 (± 31.1)	97.4 (± 75.7)
Cycle 1 Day 1, 4 hr n=6,6,6,8,2,2,3	93.2 (± 26.5)	77.8 (± 40.0)	50.2 (± 23.4)	59.2 (± 46.1)
Cycle 1 Day 1, 8 hr n=6,6,6,8,4,2,3	51.6 (± 18.7)	32.2 (± 19.1)	24.0 (± 15.0)	29.9 (± 19.8)
Cycle 1 Day 2, 0 hr (pre-dose) n=7,6,4,8,1,1,0	18.2 (± 13.0)	13.4 (± 11.1)	11.2 (± 16.2)	17.6 (± 19.9)
Cycle 1 Day 5, 0 hr (pre-dose) n=6,8,6,0,0,0,0	15.5 (± 13.9)	14.7 (± 14.0)	9.33 (± 10.6)	999 (± 999)
Cycle 1 Day 5, 1 hr n=6,7,6,0,0,0,0	160 (± 79.5)	221 (± 83.7)	130 (± 66.6)	999 (± 999)
Cycle 1 Day 5, 2 hr n=6,8,6,0,0,0,0	149 (± 64.0)	140 (± 45.6)	90.0 (± 41.4)	999 (± 999)
Cycle 1 Day 5, 3 hr n=6,8,6,0,0,0,0	104 (± 45.2)	100 (± 39.1)	61.8 (± 31.7)	999 (± 999)
Cycle 1 Day 5, 4 hr n=6,8,6,0,0,0,0	81.4 (± 38.4)	71.2 (± 30.1)	34.1 (± 16.1)	999 (± 999)
Cycle 1 Day 5, 8 hr n=6,8,4,0,0,0,0	37.6 (± 22.6)	22.9 (± 13.7)	16.2 (± 13.4)	999 (± 999)
Cycle 1 Day 6, 0 hr (pre-dose) n=6,7,5,0,0,0,0	11.5 (± 12.1)	37.8 (± 63.4)	6.28 (± 9.31)	999 (± 999)
Cycle 1 Day 15, 0 hr (pre-dose) n=7,8,4,7,3,2,0	23.2 (± 34.0)	23.6 (± 19.8)	11.2 (± 17.4)	11.9 (± 14.2)
Cycle 1 Day 15, 0.5 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	231 (± 115)
Cycle 1 Day 15, 1 hr n=0,0,0,8,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	194 (± 139)
Cycle 1 Day 15, 2 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	126 (± 58.7)
Cycle 1 Day 15, 3 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	103 (± 59.6)
Cycle 1 Day 15, 4 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	76.3 (± 53.5)
Cycle 1 Day 15, 8 hr n=0,0,0,8,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	27.9 (± 21.7)
Cycle 1 Day 16, 0 hr (pre-dose) n=0,0,0,6,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	14.4 (± 15.2)
Cycle 2 Day 1, 0 hr (pre-dose) n=6,7,5,8,4,2,3	25.9 (± 23.4)	19.3 (± 18.8)	11.4 (± 20.7)	45.7 (± 108)
Cycle 2 Day 1, 1 hr n=6,7,5,0,0,0,0	212 (± 89.8)	186 (± 113)	114 (± 82.4)	999 (± 999)
Cycle 2 Day 1, 2 hr n=6,7,4,0,0,0,0	144 (± 76.0)	165 (± 82.2)	56.2 (± 30.9)	999 (± 999)
Cycle 2 Day 1, 3 hr n=6,7,5,0,0,0,0	108 (± 50.8)	127 (± 61.7)	50.3 (± 26.4)	999 (± 999)

Cycle 2 Day 1, 4 hr n=5,7,5,0,0,0,0	89.9 (± 39.8)	106 (± 39.5)	45.6 (± 25.8)	999 (± 999)
Cycle 2 Day 1, 8 hr n=4,6,5,0,0,0,0	47.3 (± 31.5)	45.8 (± 19.4)	30.9 (± 28.1)	999 (± 999)
Cycle 2 Day 2, 0 hr (pre-dose) n=3,6,5,0,0,0,0	74.0 (± 62.3)	19.2 (± 19.7)	13.9 (± 20.5)	999 (± 999)
Cycle 2 Day 5, 0 hr (pre-dose) n=3,8,4,0,0,0,0	15.4 (± 6.29)	15.2 (± 11.3)	4.45 (± 4.57)	999 (± 999)
Cycle 2 Day 6, 0 hr (pre-dose) n=4,5,4,0,0,0,0	7.36 (± 7.32)	46.8 (± 80.0)	2.40 (± 2.74)	999 (± 999)
Cycle 2 Day 15, 0 hr (pre-dose) n=6,8,3,0,1,2,0	22.4 (± 17.2)	22.1 (± 22.7)	1.93 (± 1.65)	999 (± 999)
Cycle 3 Day 1, 0 hr (pre-dose) n=7,7,4,6,4,2,2	24.2 (± 15.5)	23.2 (± 21.8)	4.50 (± 4.03)	11.1 (± 10.9)
Cycle 3 Day 2, 0 hr (pre-dose) n=5,6,3,0,0,0,0	12.6 (± 13.9)	31.9 (± 38.9)	2.33 (± 1.57)	999 (± 999)
Cycle 3 Day 15, 0 hr (pre-dose) n=5,5,2,0,4,2,0	18.7 (± 18.4)	45.2 (± 41.5)	3.95 (± 4.10)	999 (± 999)
Cycle 4 Day 1, 0 hr (pre-dose) n=7,5,3,5,4,1,1	17.5 (± 18.2)	20.9 (± 22.2)	4.53 (± 6.44)	18.2 (± 33.8)
Cycle 4 Day 5, 0 hr (pre-dose) n=5,6,3,0,0,0,0	13.6 (± 13.7)	9.12 (± 13.5)	7.99 (± 11.4)	999 (± 999)
Cycle 5 Day 1, 0 hr (pre-dose) n=7,6,4,3,3,0,0	16.4 (± 16.1)	12.7 (± 12.0)	5.30 (± 5.94)	10.3 (± 13.6)
Cycle 5 Day 5, 0 hr (pre-dose) n=5,3,3,0,0,0,0	26.6 (± 16.4)	9.54 (± 13.2)	2.79 (± 2.46)	999 (± 999)
Cycle 6 Day 1, 0 hr (pre-dose) n=4,4,2,3,3,0,0	15.8 (± 19.5)	17.0 (± 19.7)	0.608 (± 0.0672)	21.9 (± 23.2)
Cycle 6 Day 5, 0 hr (pre-dose) n=3,4,2,0,0,0,0	24.8 (± 19.9)	11.5 (± 8.34)	0.957 (± 0.528)	999 (± 999)

End point values	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 1: Ruxolitinib + NIS793	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	2	4	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0 hr (pre-dose) n=6,6,5,7,3,2,4	12.9 (± 6.31)	51.2 (± 61.0)	37.9 (± 48.4)	
Cycle 1 Day 1, 0.5 hr n=6,5,6,8,2,2,3	107 (± 119)	57.1 (± 44.0)	108 (± 128)	
Cycle 1 Day 1, 1 hr n=6,6,6,7,2,2,3	65.7 (± 59.9)	110 (± 44.1)	164 (± 140)	
Cycle 1 Day 1, 2 hr n=6,6,6,7,2,2,3	170 (± 140)	72.7 (± 4.10)	187 (± 105)	
Cycle 1 Day 1, 3 hr n=6,6,5,8,2,2,3	124 (± 91.0)	54.4 (± 10.4)	184 (± 77.9)	
Cycle 1 Day 1, 4 hr n=6,6,6,8,2,2,3	101 (± 81.2)	28.3 (± 7.28)	190 (± 58.4)	
Cycle 1 Day 1, 8 hr n=6,6,6,8,4,2,3	39.5 (± 29.2)	7.75 (± 1.52)	44.4 (± 35.3)	
Cycle 1 Day 2, 0 hr (pre-dose) n=7,6,4,8,1,1,0	30.3 (± 999)	0 (± 999)	999 (± 999)	
Cycle 1 Day 5, 0 hr (pre-dose) n=6,8,6,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 5, 1 hr n=6,7,6,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 5, 2 hr n=6,8,6,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 5, 3 hr n=6,8,6,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 5, 4 hr n=6,8,6,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 5, 8 hr n=6,8,4,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 1 Day 6, 0 hr (pre-dose) n=6,7,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)	

Cycle 1 Day 15, 0 hr (pre-dose) n=7,8,4,7,3,2,0	12.6 (± 10.1)	4.06 (± 2.28)	999 (± 999)
Cycle 1 Day 15, 0.5 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 1 Day 15, 1 hr n=0,0,0,8,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 1 Day 15, 2 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 1 Day 15, 3 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 1 Day 15, 4 hr n=0,0,0,7,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 1 Day 15, 8 hr n=0,0,0,8,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 1 Day 16, 0 hr (pre-dose) n=0,0,0,6,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 1, 0 hr (pre-dose) n=6,7,5,8,4,2,3	13.7 (± 4.84)	28.4 (± 39.1)	65.1 (± 88.9)
Cycle 2 Day 1, 1 hr n=6,7,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 1, 2 hr n=6,7,4,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 1, 3 hr n=6,7,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 1, 4 hr n=5,7,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 1, 8 hr n=4,6,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 2, 0 hr (pre-dose) n=3,6,5,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 5, 0 hr (pre-dose) n=3,8,4,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 6, 0 hr (pre-dose) n=4,5,4,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 2 Day 15, 0 hr (pre-dose) n=6,8,3,0,1,2,0	63.6 (± 999)	7.95 (± 8.14)	999 (± 999)
Cycle 3 Day 1, 0 hr (pre-dose) n=7,7,4,6,4,2,2	12.0 (± 6.36)	2.44 (± 1.46)	84.6 (± 96.8)
Cycle 3 Day 2, 0 hr (pre-dose) n=5,6,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 3 Day 15, 0 hr (pre-dose) n=5,5,2,0,4,2,0	10.9 (± 6.89)	12.5 (± 9.14)	999 (± 999)
Cycle 4 Day 1, 0 hr (pre-dose) n=7,5,3,5,4,1,1	14.0 (± 7.81)	2.94 (± 999)	24.4 (± 999)
Cycle 4 Day 5, 0 hr (pre-dose) n=5,6,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 5 Day 1, 0 hr (pre-dose) n=7,6,4,3,3,0,0	20.1 (± 23.0)	999 (± 999)	999 (± 999)
Cycle 5 Day 5, 0 hr (pre-dose) n=5,3,3,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 6 Day 1, 0 hr (pre-dose) n=4,4,2,3,3,0,0	27.3 (± 32.8)	999 (± 999)	999 (± 999)
Cycle 6 Day 5, 0 hr (pre-dose) n=3,4,2,0,0,0,0	999 (± 999)	999 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus post-treatment safety follow-up, up to a maximum duration of approximately 44 months.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Part 1: Ruxolitinib + Siremadlin 20 mg
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Reporting group description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Reporting group title	Part 1: Ruxolitinib + Siremadlin 40 mg
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Reporting group description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Reporting group title	Part 1: Ruxolitinib + Siremadlin
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Reporting group description:

Total

Reporting group title	Part 1: Ruxolitinib + Siremadlin 30 mg
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Reporting group description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

Reporting group title	Part 1: Ruxolitinib + Rineterkib 200 mg
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Reporting group description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

Reporting group title	Part 1: Ruxolitinib + NIS793
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Reporting group description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

Reporting group title	Part 1: Ruxolitinib + Crizanlizumab
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Reporting group description:

Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib

Reporting group title	Part 1: Ruxolitinib + Sabatolimab
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Reporting group description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

Reporting group title	Part 2: Ruxolitinib
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Reporting group description:

Existing stable dose of ruxolitinib as control for Part 2

Reporting group title	All Subjects
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Reporting group description:

All Subjects

Serious adverse events	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Siremadlin
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	4 / 6 (66.67%)	9 / 23 (39.13%)
number of deaths (all causes)	0	3	3
number of deaths resulting from	0	1	1

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (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
Haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (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
Injury, poisoning and procedural complications			
Product administration error			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (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
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (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
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Neutrophilic dermatosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (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

Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Epididymitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (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
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Rineterkib 200 mg	Part 1: Ruxolitinib + NIS793
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	3 / 9 (33.33%)	1 / 4 (25.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Vascular disorders			
Aortic aneurysm rupture			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Investigations			
Body temperature increased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Product administration error			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Neutrophilic dermatosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
Epididymitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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
COVID-19			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (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	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 2: Ruxolitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 2 (50.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Injury, poisoning and procedural complications			
Product administration error			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Humerus fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Blood loss anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Gastritis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Neutrophilic dermatosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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
Epididymitis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (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	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 45 (33.33%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Product administration error			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood loss anaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Neutrophilic dermatosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Epididymitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1: Ruxolitinib + Siremadlin 20 mg	Part 1: Ruxolitinib + Siremadlin 40 mg	Part 1: Ruxolitinib + Siremadlin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	6 / 6 (100.00%)	23 / 23 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	2	2
Squamous cell carcinoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	2
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Angiopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	4 / 7 (57.14%)	0 / 6 (0.00%)	4 / 23 (17.39%)
occurrences (all)	4	0	4
Hypotension			

subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Venous thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 6 (33.33%)	5 / 23 (21.74%)
occurrences (all)	0	2	6
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	3 / 23 (13.04%)
occurrences (all)	1	1	3
Mucosal inflammation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed occurrences (all)	5 / 7 (71.43%) 10	2 / 6 (33.33%) 2	8 / 23 (34.78%) 15
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	1 / 23 (4.35%) 2
Dyspnoea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	1 / 6 (16.67%) 1	2 / 23 (8.70%) 3
Cough subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 6 (0.00%) 0	2 / 23 (8.70%) 2
Epistaxis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Hypoxia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Nasal cavity mass subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Confusional state subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Sleep disorder subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Insomnia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 6 (33.33%) 2	2 / 23 (8.70%) 2
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 23 (8.70%)
occurrences (all)	0	3	4
Amylase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	1	0	6
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	6
Blood folate decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Blood potassium increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	2
Lipase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	1	0	7
Heart sounds abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Heart rate decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Cardiac murmur			

subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 23 (8.70%)
occurrences (all)	0	1	2
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Tendon rupture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Transfusion reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	2
Skin abrasion			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Skin wound subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Cardiac failure subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Sinus bradycardia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 6 (16.67%) 1	2 / 23 (8.70%) 2
Dysaesthesia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Dysgeusia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 6 (33.33%) 4	2 / 23 (8.70%) 4
Headache			

subjects affected / exposed	3 / 7 (42.86%)	0 / 6 (0.00%)	4 / 23 (17.39%)
occurrences (all)	3	0	4
Migraine			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Sciatica			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Polyneuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 7 (42.86%)	5 / 6 (83.33%)	15 / 23 (65.22%)
occurrences (all)	3	19	31
Lymphopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	1	0	2
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 6 (50.00%)	11 / 23 (47.83%)
occurrences (all)	0	4	18
Splenomegaly			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)	6 / 6 (100.00%)	14 / 23 (60.87%)
occurrences (all)	1	16	29
Eye disorders			
Dry eye			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Retinal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	2	2
Retinal detachment			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Visual impairment			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Visual acuity reduced			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Serous retinopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	2	0	3
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	4 / 23 (17.39%)
occurrences (all)	3	3	8
Diarrhoea			
subjects affected / exposed	3 / 7 (42.86%)	0 / 6 (0.00%)	5 / 23 (21.74%)
occurrences (all)	6	0	9
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	1	0	2
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	3 / 23 (13.04%)
occurrences (all)	1	0	3
Oral dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	6 / 7 (85.71%)	3 / 6 (50.00%)	13 / 23 (56.52%)
occurrences (all)	16	11	34

Mouth haemorrhage subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dry skin subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Blister subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Alopecia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Actinic keratosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Night sweats subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	1 / 6 (16.67%) 3	2 / 23 (8.70%) 5
Rash subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Pain of skin subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Skin discolouration			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Skin disorder subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Skin lesion subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Skin ulcer subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Trichodysplasia spinulosa subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Dysuria subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1	1 / 23 (4.35%) 1
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Musculoskeletal and connective tissue disorders Gouty arthritis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0	0 / 23 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	0 / 6 (0.00%) 0	1 / 23 (4.35%) 2
Back pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0	1 / 23 (4.35%) 1
Arthropathy			

subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	2	2
Muscle spasms			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Muscle tightness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Sacroiliac joint dysfunction			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	3 / 23 (13.04%)
occurrences (all)	0	1	3
Erysipelas			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1

Eye infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 7 (28.57%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	2	0	2
Tooth infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Mucosal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	3
Wound infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	0 / 6 (0.00%)	3 / 23 (13.04%)
occurrences (all)	5	0	5
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Gout			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			

subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 23 (8.70%)
occurrences (all)	1	0	2
Hyperuricaemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	4 / 23 (17.39%)
occurrences (all)	1	1	4
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Iron overload			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	1	1

Non-serious adverse events	Part 1: Ruxolitinib + Siremadlin 30 mg	Part 1: Ruxolitinib + Rineterkib 200 mg	Part 1: Ruxolitinib + NIS793
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	9 / 9 (100.00%)	3 / 4 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Squamous cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Angiopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertension			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	3 / 9 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Chest discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	3 / 10 (30.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	4	2	1
Oedema peripheral			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Malaise			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	2 / 4 (50.00%)
occurrences (all)	0	1	4
Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal cavity mass			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Insomnia			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	1 / 4 (25.00%) 1
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 9 (11.11%) 1	0 / 4 (0.00%) 0
Amylase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 5	0 / 9 (0.00%) 0	0 / 4 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 4 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 9 (22.22%) 2	0 / 4 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 6	1 / 9 (11.11%) 1	0 / 4 (0.00%) 0
Blood folate decreased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 9 (11.11%) 1	0 / 4 (0.00%) 0
Blood potassium increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 4 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 4 (0.00%) 0
Lipase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 6	0 / 9 (0.00%) 0	0 / 4 (0.00%) 0
Heart sounds abnormal subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 4 (0.00%) 0
Heart rate decreased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Fall			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Incorrect dose administered			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Transfusion reaction			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Skin abrasion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin wound			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cardiac failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Migraine			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 10 (70.00%)	1 / 9 (11.11%)	2 / 4 (50.00%)
occurrences (all)	9	1	2
Lymphopenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	8 / 10 (80.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	14	0	0
Splenomegaly			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	7 / 10 (70.00%)	2 / 9 (22.22%)	0 / 4 (0.00%)
occurrences (all)	12	3	0

Eye disorders			
Dry eye			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Erythema of eyelid			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Macular oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Photopsia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Presbyopia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Serous retinopathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Retinopathy			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 9 (22.22%) 2	0 / 4 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)	6 / 9 (66.67%)	0 / 4 (0.00%)
occurrences (all)	3	6	0
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	2	4	0
Oral dysaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Nausea			
subjects affected / exposed	4 / 10 (40.00%)	3 / 9 (33.33%)	0 / 4 (0.00%)
occurrences (all)	7	3	0
Mouth haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blister			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Actinic keratosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Pain of skin			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Trichodysplasia spinulosa			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Back pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	2
Muscle tightness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sacroiliac joint dysfunction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Erysipelas			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Furuncle			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Mucosal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Wound infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gout			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Iron overload			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1: Ruxolitinib + Crizanlizumab	Part 1: Ruxolitinib + Sabatolimab	Part 2: Ruxolitinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	2 / 2 (100.00%)	0 / 1 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Angiopathy			

subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Chest discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Mucosal inflammation			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Hypoxia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Nasal cavity mass subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Sleep disorder			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood folate decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Heart sounds abnormal			

subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Heart rate decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Transfusion reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Dysaesthesia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2	2 / 2 (100.00%) 2	0 / 1 (0.00%) 0
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Erythema of eyelid subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Eye pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Macular oedema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Photopsia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Retinal haemorrhage subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Retinal detachment subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Presbyopia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Visual impairment subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Visual acuity reduced subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Serous retinopathy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0

Oral dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Actinic keratosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pain of skin			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Trichodysplasia spinulosa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Bone pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Arthropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Muscle spasms			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Muscle tightness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sacroiliac joint dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Erysipelas			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Iron overload			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 45 (95.56%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	4		
Squamous cell carcinoma			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Vascular disorders			

Capillary leak syndrome subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Angiopathy subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Hypertension subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 5		
Hypotension subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Venous thrombosis subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
General disorders and administration site conditions			
Discomfort subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Chills subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Chest pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Asthenia subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 5		
Chest discomfort subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Pyrexia subjects affected / exposed occurrences (all)	8 / 45 (17.78%) 10		
Oedema peripheral			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mucosal inflammation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Malaise</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 45 (8.89%)</p> <p>5</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>8 / 45 (17.78%)</p> <p>15</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Dyspnoea exertional</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypoxia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal cavity mass</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 45 (4.44%)</p> <p>3</p> <p>4 / 45 (8.89%)</p> <p>5</p> <p>3 / 45 (6.67%)</p> <p>3</p> <p>4 / 45 (8.89%)</p> <p>6</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>1 / 45 (2.22%)</p> <p>1</p>		
<p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Confusional state</p>	<p>1 / 45 (2.22%)</p> <p>1</p>		

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	6 / 45 (13.33%)		
occurrences (all)	6		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	5		
Amylase increased			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	7		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Blood creatinine increased			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	7		
Blood folate decreased			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Blood potassium increased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Lipase increased			

subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	8		
Heart sounds abnormal			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Heart rate decreased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Cardiac murmur			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	3		
White blood cell count decreased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	3		
Fall			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Incorrect dose administered			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Ligament sprain			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Tendon rupture			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Transfusion reaction			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Skin abrasion			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin wound			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Cardiac failure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pericardial effusion			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Sinus bradycardia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Supraventricular tachycardia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			

subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	4		
Dysaesthesia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	6		
Headache			
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	8		
Migraine			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Polyneuropathy			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 45 (42.22%)		
occurrences (all)	35		
Lymphopenia			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Neutropenia			
subjects affected / exposed	11 / 45 (24.44%)		
occurrences (all)	18		

Splenomegaly			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	19 / 45 (42.22%)		
occurrences (all)	36		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Erythema of eyelid			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Macular oedema			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Photopsia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Retinal haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Retinal detachment			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Presbyopia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Visual acuity reduced			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Serous retinopathy			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Retinopathy			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	9		
Diarrhoea			
subjects affected / exposed	13 / 45 (28.89%)		
occurrences (all)	20		
Abdominal pain			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Abdominal distension			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Gingival bleeding			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		

Vomiting			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	9		
Oral dysaesthesia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	18 / 45 (40.00%)		
occurrences (all)	39		
Mouth haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Dermatitis acneiform			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Blister			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Actinic keratosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	6		
Rash			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Pruritus			

subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Pain of skin			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin discolouration			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin disorder			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Trichodysplasia spinulosa			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Gouty arthritis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	6		
Back pain			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Arthropathy			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	5		
Muscle tightness			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Sacroiliac joint dysfunction			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Candida infection			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Erysipelas			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Eye infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Tooth infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Mucosal infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	3		
Wound infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 6		
Dehydration subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Gout subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Hyperkalaemia subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Hyperuricaemia subjects affected / exposed occurrences (all)	6 / 45 (13.33%) 6		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Iron overload subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2019	This amendment: excluded subjects eligible for allogeneic hematopoietic stem cell treatment (ASCT); clarified that any subjects scheduled for ASCT during the study were to be discontinued; aligned updated information available from the sabatolimab (MBG453) Investigator's Brochure to use highly effective forms of contraception for women of child-bearing potential (WOCBP) for up to 150 days for subjects on study treatment that included sabatolimab; clarified that the safety follow-up for subjects on study treatment that included sabatolimab was up to 150 days; safety follow-ups were to be conducted at 30, 90, and 150 days; excluded all forms of hormonal contraception for WOCBP (for consistency, hormonal contraception was excluded from all arms of the study); excluded subjects who could not discontinue drugs that strongly induce or inhibit CYP2C9; added strong inducers or inhibitors of CYP2C9 as prohibited medications, advised caution on the use of moderate inducers or inhibitors; clarified for the safety run-in of crizanlizumab and sabatolimab arms of the study in Part 1 that if 2 subjects experienced a dose-limiting toxicity (DLT) in either arm, then further enrolment into that arm would stop, and the treatment combination would not open in Part 2; clarified that intra-subject dose escalation was not allowed; added additional electrocardiogram (ECG) safety monitoring for any QTc interval prolongation > 60 msec from baseline; added a recommendation to protect skin from solar UV radiation if subjects were on study treatment that contained siremadlin; clarified that the Patient Global Impression of Change (PGIC) patient-reported outcome (PRO) was not required at screening; clarified that urine pregnancy tests would be performed monthly for all pre-menopausal women who were not surgically sterile; added further hypothetical on-study data scenarios to the Bayesian model used to guide dose escalation in Part 1 for siremadlin in combination with ruxolitinib.
17 February 2020	This amendment: clarified definition of accelerated phase for progression free survival; clarified that subjects who had participated in the CINC424H12201 study could participate in a subsequent part of the study; removed exclusion of subjects treated with hematopoietic colony-stimulating growth factors; excluded subjects who used live vaccines within 30 days of starting any study treatment; added live vaccines as prohibited medication for study treatment arms containing crizanlizumab or sabatolimab; excluded subjects who used systemic steroid therapy and other immunosuppressive drugs (> 10 mg/day prednisone or equivalent) within 14 days prior to first dose of study treatment; added use of systemic steroid therapy as prohibited medication, except for treatment of infusion reaction, treatment of immune-related adverse events, prophylaxis against imaging contrast dye allergy, replacement-dose steroids in the setting of adrenal insufficiency (providing this was ≤ 10 mg/day prednisone or equivalent), or treatment of transient exacerbation of other underlying diseases such as chronic obstructive pulmonary disease requiring treatment for ≤ 3 weeks; excluded subjects who used anticoagulation or antiplatelet therapy within 10 days of prior to first dose of study treatment and subjects who had bleeding events within 6 months prior to first dose of study treatment; updated the prohibition of anticoagulation therapy to allow the use of low molecular weight heparin or direct oral anti-coagulants if used at sub-therapeutic doses; added erythropoietin stimulating agents (ESAs) as prohibited medication; updated the dose modification tables specific to the novel agents to remove any reference to ruxolitinib; allowed subjects in Part 1 to continue on study treatment after the planned 6 cycles if the subject was still deriving clinical benefit; defined "overall safety period."

28 April 2020	This amendment: updated Exclusion Criterion #8 to exclude patients with known history of human immunodeficiency virus (HIV) as an overall positive benefit risk ratio to include HIV patients with the various novel combination treatments could not be determined at that stage. In addition, antiretroviral therapy (ART) regimen including strong CYP3A4 inhibitors could lead to the potential drug-drug interaction of one or more study medications; extended the restrictions on the use of live vaccines until the end of the follow-up period after the last dose of crizanlizumab and sabatolimab, which was within 5 half-lives of the study treatment; guidance was added on the criteria for sabatolimab dose management for dermatological adverse drug reactions (ADRs) and non-immune related toxicities; added guidance that subjects should be monitored carefully for any skin toxicity or mucositis, and that study treatment should be discontinued for any suspected case of Stevens-Johnson syndrome (SJS), or Lyell syndrome/toxic epidermal necrolysis (TEN).
25 August 2020	This amendment: added two novel compounds to Part 1 of the protocol: LTT462, which is a potent, selective, inhibitor of extracellular signal-regulated kinase 1 (ERK1) and extracellular signal regulated kinase 2 (ERK2), and NIS793, which is an anti-transforming growth factor beta (anti-TGFβ) monoclonal antibody (mAb); added additional cycles throughout the protocol, where applicable; increased the number of subjects required for Part 2 from 15 subjects per arm to 25 subjects per arm to ensure the acceptable futility probability for applying the futility rule in multiple arms.
23 February 2021	This amendment: updated the study design to allow 1) Part 2 (Selection) to be conducted for each combination treatment once the combination treatment was determined to be safe and tolerable in Part 1, and 2) to allow more than one combination treatment selected in Part 2 to enter Part 3 (Expansion); added an interim analysis per combination treatment after at least 10 subjects completed 24 weeks of study treatment in Part 2 to allow for a seamless transition into Part 3 if an efficacy threshold was reached; reduced the number of pharmacokinetic and pharmacodynamic samples collected, including removal of a few assessment visits in Part 2 and Part 3 of the study; included specific requirements for conducting the study in China, Japan, and USA.
20 July 2021	This amendment: updated the eligibility criteria to reduce the time required for patients to be treated with ruxolitinib from "at least 24 weeks" to "at least 12 weeks" prior to first dose of study treatment, and also to reduce the time required for patients to be on a stable prescribed dose of ruxolitinib (no dose adjustments) prior to first dose of study treatment from "≥ 8 weeks" to "≥ 4 weeks"; provided more detailed guidance regarding dose modifications of siremadlin, rineterkib and NIS793 in case of toxicity including to allow patients to continue on study treatment at a reduced dose level for siremadlin or rineterkib or, at a reduced frequency for NIS793 if patients derived clinical benefits as per investigator's judgement; additional precautionary measures have been implemented based on emerging new NIS793-related preclinical safety findings including update of exclusion criteria for impaired cardiac function and addition of cardiac imaging and cardiac enzymes safety assessments during treatment to enhance cardio-vascular mitigation; additional guidance on dose discontinuation for NIS793 in case of Drug-induced liver injury (DILI); removed the collection of bone marrow aspirate for megakaryocyte characterization in all parts of the study; updated the withdrawal of consent language as per the latest Novartis protocol template.
11 January 2022	This amendment: allowed patients requiring packed red blood cell (PRBC) transfusions at any timepoint prior to first dose of study treatment to participate in all parts of the study; added details on the endpoints definitions to assess the following secondary objectives (i) changes in symptoms of myelofibrosis using the Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 scale and (ii) changes in spleen volume to include pre-defined threshold of improvement; added a new strength of rineterkib to allow additional doses of rineterkib to be tested if ever required; updated exclusion criteria to provide a more comprehensive guidance on the time gap between administration of monoclonal antibody or immunoglobulin-based agent for NIS793, crizanlizumab or sabatolimab arms (within 1 year) and rineterkib or siremadlin arms (within ≤4 weeks of screening or ≤5 half-lives, whichever was shorter); added new biomarkers specific for NIS793 and sabatolimab to assess the impact of TGFβ and TIM-3 inhibition with NIS793 and MBG453 on various immune cells.

05 October 2022	This amendment reflected the changes in study conduct that were a result of the permanent enrollment halt decision by Novartis. These changes included adding an extension treatment phase and reduction of study assessments to decrease subjects' burden in Part 1.
05 December 2023	This amendment increased the duration of the extension treatment phase for the remaining patients to a maximum of 21 cycles.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results.
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Notes: