



Clinical trial results:

An Open-Label, Single-Arm, Phase 1/2 Study Evaluating the Safety and Efficacy of Itacitinib in Participants With Bronchiolitis Obliterans Syndrome Following Lung Transplantation

Summary

EudraCT number	2019-004171-39
Trial protocol	BE
Global end of trial date	13 October 2023

Results information

Result version number	v1
This version publication date	26 October 2024
First version publication date	26 October 2024

Trial information

Trial identification

Sponsor protocol code	INCB 39110-214
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 554633463, medinfo@incyte.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	13 October 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase 1: To identify an appropriate dose of itacitinib as a treatment for Grade 1 through 3 Bronchiolitis Obliterans Syndrome (BOS) following lung transplantation.

Phase 2: To evaluate the efficacy of itacitinib as a treatment for Grade 1 through 3 BOS following lung transplantation.

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, Good Clinical Practices as defined in Title 21 of the United States Code of Federal Regulations Parts 11, 50, 54, 56, and 312, as well as International Conference on Harmonisation Good Clinical Practice (ICH GCP) consolidated guidelines (E6) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 February 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	23
EEA total number of subjects	7

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)	17
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted at 7 study centers in the United States, Canada, and Belgium. The site in Canada had a screen failure but did not recruit any participants.

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	Itacitinib 300/200 mg

Arm description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 milligrams (mg) twice daily (BID). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 200 mg BID. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in forced expiratory volume in 1 second (FEV1), confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	itacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

100-milligram prolonged-release tablets

Arm title	Itacitinib 400/300 mg
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Arm description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg once daily (QD). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	itacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

100-milligram prolonged-release tablets

Arm title	Itacitinib 600/400 mg
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Arm description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 600 mg QD. Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	itacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

100-milligram prolonged-release tablets

Arm title	Other
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Arm description:

Participants received a starting dose of itacitinib 200 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	itacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

100-milligram prolonged-release tablets

Number of subjects in period 1	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg
Started	7	7	8
Completed	6	2	3
Not completed	1	5	5
Adverse event, serious fatal	-	2	2
Consent withdrawn by subject	-	-	1
Transitioned to Itacitinib Rollover Trial	1	3	2

Number of subjects in period 1	Other
Started	1
Completed	1
Not completed	0
Adverse event, serious fatal	-
Consent withdrawn by subject	-

Transitioned to Itacitinib Rollover Trial	-
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Baseline characteristics

Reporting groups

Reporting group title	Itacitinib 300/200 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 milligrams (mg) twice daily (BID). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 200 mg BID. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in forced expiratory volume in 1 second (FEV1), confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Itacitinib 400/300 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg once daily (QD). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Itacitinib 600/400 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 600 mg QD. Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Other
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Reporting group description:

Participants received a starting dose of itacitinib 200 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg
Number of subjects	7	7	8
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	5	6
From 65-84 years	2	2	2
85 years and over	0	0	0

Age Continuous			
120=Mean (SD) age cannot be reported for a single participant without risking re-identification of the participant.			
Units: years			
arithmetic mean	59.9	48.0	59.0
standard deviation	± 5.55	± 17.01	± 6.72
Sex: Female, Male			
Units: participants			
Female	2	2	1
Male	5	5	7
Cannot Be Reported Due to Privacy Concerns	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	1
White	6	6	7
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Cannot Be Reported Due to Privacy Concerns	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	6	7	7
Unknown or Not Reported	0	0	1
Cannot Be Reported Due to Privacy Concerns	0	0	0

Reporting group values	Other	Total	
Number of subjects	1	23	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	17	
From 65-84 years	0	6	
85 years and over	0	0	
Age Continuous			
120=Mean (SD) age cannot be reported for a single participant without risking re-identification of the participant.			
Units: years			
arithmetic mean	120		
standard deviation	± 120	-	

Sex: Female, Male Units: participants			
Female	0	5	
Male	0	17	
Cannot Be Reported Due to Privacy Concerns	1	1	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	3	
White	0	19	
More than one race	0	0	
Unknown or Not Reported	0	0	
Cannot Be Reported Due to Privacy Concerns	1	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	0	20	
Unknown or Not Reported	0	1	
Cannot Be Reported Due to Privacy Concerns	1	1	

End points

End points reporting groups

Reporting group title	Itacitinib 300/200 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 milligrams (mg) twice daily (BID). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 200 mg BID. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in forced expiratory volume in 1 second (FEV1), confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Itacitinib 400/300 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg once daily (QD). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Itacitinib 600/400 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 600 mg QD. Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Other
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Reporting group description:

Participants received a starting dose of itacitinib 200 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in forced expiratory volume in 1 second (FEV1), confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Subject analysis set title	Itacitinib 200 mg QD
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants in the PK-Evaluable Population received itacitinib 200 mg QD during the course of the study. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in forced expiratory volume in 1 second (FEV1), confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Subject analysis set title	Itacitinib 300 mg QD
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants in the PK-Evaluable Population received itacitinib 300 mg QD during the course of the study. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Subject analysis set title	Itacitinib 300 mg BID
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants in the PK-Evaluable Population received itacitinib 300 mg BID during the course of the study. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Subject analysis set title	Itacitinib 400 mg QD
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants in the PK-Evaluable Population received itacitinib 400 mg QD during the course of the study. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Subject analysis set title	Itacitinib 600 mg QD
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants in the PK-Evaluable Population received itacitinib 600 mg QD during the course of the study. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Primary: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Number of participants with any treatment-emergent adverse event (TEAE) ^[1]
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End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as either an AE reported for the first time or the worsening of a pre-existing condition after the first dose of itacitinib until 30 days after the last dose of itacitinib.

End point type	Primary
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End point timeframe:

up to approximately 162 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: Statistical analysis was not conducted for this endpoint.

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	1
Units: participants	7	7	8	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any Grade 3 or higher TEAE

End point title	Number of participants with any Grade 3 or higher TEAE ^[2]
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End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. A TEAE was defined as either an AE reported for the first time or the worsening of a pre-existing condition after the first dose of itacitinib until 30 days after the last dose of itacitinib. The severity of AEs was assessed using Common Terminology Criteria for Adverse Events v5.0. Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated. Grade 2: moderate; minimal, local, or noninvasive treatment indicated; limiting age appropriate activities of daily living. Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living. Grade 4: life-threatening consequences; urgent treatment indicated. Grade 5: fatal.

End point type	Primary
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End point timeframe:

up to approximately 162 weeks

Notes:

[2] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	1
Units: participants	6	7	6	1

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in forced expiratory volume in 1 second (FEV1) at Week 12

End point title	Change from Baseline in forced expiratory volume in 1 second (FEV1) at Week 12 ^[3]
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End point description:

FEV1 was defined as the volume of air exhaled in 1 second. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=Mean (SD) data cannot be reported for a single participant due to privacy concerns. 8888=No participants were analyzed at this time point.

End point type	Primary
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End point timeframe:

Baseline; Week 12

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not conducted for this endpoint.

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 ^[4]	7 ^[5]	8 ^[6]	1 ^[7]
Units: liters				
arithmetic mean (standard deviation)				
Baseline, n=7, 7, 8, 1	1.72 (± 0.962)	1.57 (± 0.672)	1.59 (± 0.511)	9999 (± 9999)

Change from Baseline, n=5, 7, 5, 0	0.09 (± 0.168)	0.04 (± 0.114)	0.22 (± 0.571)	8888 (± 8888)
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Notes:

[4] - Full Analysis Set. Only participants with available data were analyzed.

[5] - Full Analysis Set. Only participants with available data were analyzed.

[6] - Full Analysis Set. Only participants with available data were analyzed.

[7] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Duration of FEV1 response

End point title	Phase 1: Duration of FEV1 response
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End point description:

Duration of FEV1 response was defined as the interval between the onset of response and the earliest of bronchiolitis obliterans syndrome progression, loss of clinical benefit as determined by the investigator, or death. -9999, 9999=The median and the upper and lower limits of the confidence interval were not estimable because there were too few events of bronchiolitis obliterans syndrome progression or loss of clinical benefit.

End point type	Secondary
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End point timeframe:

up to 34.9 months

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1 ^[8]	2 ^[9]	1 ^[10]	0 ^[11]
Units: days				
median (confidence interval 95%)	9999 (-9999 to 9999)	491.5 (401.0 to 9999)	9999 (-9999 to 9999)	(to)

Notes:

[8] - Full Analysis Set. Only those participants with a response were analyzed.

[9] - Full Analysis Set. Only those participants with a response were analyzed.

[10] - Full Analysis Set. Only those participants with a response were analyzed.

[11] - Full Analysis Set. Only those participants with a response were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Change from Baseline in the St. George's Respiratory Questionnaire (SGRQ) total score

End point title	Phase 1: Change from Baseline in the St. George's Respiratory Questionnaire (SGRQ) total score
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End point description:

The SGRQ is a disease-specific instrument designed to measure the impact on overall health, daily life, and perceived well-being in participants with obstructive airway disease. It consists of 50 items covering 3 domains: symptoms (8 items), activity (16 items), and impacts (26 items). A component score was to be calculated for each of the 3 domains. One total score was to be calculated if none of the component scores was missing. All scales (both domain and total) have a score ranging between 0 and 100, with higher scores indicating a worse quality of life. Change from Baseline was to be calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary
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End point timeframe:
Baseline; up to 158.4 weeks

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[12]	0 ^[13]	0 ^[14]	0 ^[15]
Units: scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[12] - As specified in the SAP, SGRQ analysis was not performed due to early study termination.

[13] - As specified in the SAP, SGRQ analysis was not performed due to early study termination.

[14] - As specified in the SAP, SGRQ analysis was not performed due to early study termination.

[15] - As specified in the SAP, SGRQ analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Change from Baseline in the Quality of Life-Short Form-12 (QOL-SF-12) questionnaire scores

End point title	Phase 1: Change from Baseline in the Quality of Life-Short Form-12 (QOL-SF-12) questionnaire scores
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End point description:

The QOL-SF-12 v2 is a 12-item subset of the QOL-SF-36 v2 scale that captures changes in health status during the course of treatment. The QOL-SF-12 assesses 8 health concepts related to limitations in physical activities, social activities, bodily pain, general mental and physical health, and vitality. For this questionnaire, 1 component score was to be provided for each of 8 health concepts. Two summary scores, physical component summary and mental component summary, were also to be provided. For each item, scores range from 0 to 100; a higher score indicates a better health state. Change from Baseline was to be calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary
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End point timeframe:

Baseline; up to 158.4 weeks

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[16]	0 ^[17]	0 ^[18]	0 ^[19]
Units: scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[16] - As specified in the SAP, QOL-SF-12 analysis was not performed due to early study termination.

[17] - As specified in the SAP, QOL-SF-12 analysis was not performed due to early study termination

[18] - As specified in the SAP, QOL-SF-12 analysis was not performed due to early study termination

[19] - As specified in the SAP, QOL-SF-12 analysis was not performed due to early study termination

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to progression

End point title	Phase 1: Time to progression
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End point description:

Time to progression was defined as defined as the interval between the start of treatment and bronchiolitis obliterans syndrome progression ($\geq 10\%$ absolute decrease in FEV1 compared to baseline), or death. -9999, 9999=The median and the upper and lower limits of the confidence interval were not estimable because too few participants had disease progression or died.

End point type	Secondary
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End point timeframe:

up to 36.4 months

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 ^[20]	7 ^[21]	8 ^[22]	1 ^[23]
Units: days				
median (confidence interval 95%)	516.0 (13.0 to 9999)	485.0 (19.0 to 750.0)	9999 (56.0 to 9999)	9999 (9999 to 9999)

Notes:

[20] - Full Analysis Set

[21] - Full Analysis Set

[22] - Full Analysis Set

[23] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Change from Baseline in the EQ-5D-3L questionnaire scores

End point title	Phase 1: Change from Baseline in the EQ-5D-3L questionnaire scores
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End point description:

The EQ-5D-3L essentially consists of 2 components: the EQ-5D descriptive scale and the EQ-VAS. The EQ-5D-3L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, anxiety/depression, and pain/discomfort. Each dimension has 3 levels: no problems, some problems, and extreme problems. The EQ-VAS records the respondent's self-rated health on a vertical visual analog scale on which the endpoints are labeled as "the best health you can imagine" and "the worst health you can imagine." At each specific visit (starting on Day 1), the participant was to be asked to indicate their health state. The categorical outcomes for the 5 dimensions (mobility, self-care, usual activities, anxiety/depression, and pain/discomfort) were to be reported. The change from Baseline in the EQ-VAS score was to be reported. Change from Baseline was to be calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary
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End point timeframe:

Baseline; up to 158.4 weeks

End point values	Itacitinib 300/200 mg	Itacitinib 400/300 mg	Itacitinib 600/400 mg	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[24]	0 ^[25]	0 ^[26]	0 ^[27]
Units: scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[24] - As specified in the SAP, EQ-5D-3L analysis was not performed due to early study termination.

[25] - As specified in the SAP, EQ-5D-3L analysis was not performed due to early study termination.

[26] - As specified in the SAP, EQ-5D-3L analysis was not performed due to early study termination.

[27] - As specified in the SAP, EQ-5D-3L analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Cmax of itacitinib

End point title	Phase 1: Cmax of itacitinib
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End point description:

Cmax was defined as the maximum observed concentration of itacitinib. Participants in the Pharmacokinetic (PK)-Evaluable Population, defined as all enrolled participants who received at least 1 dose of itacitinib and provided at least 1 post-dose PK sample, have been analyzed. Data were analyzed by dose rather than by treatment arm because approximately one-third of the participants had a dose adjustment (dose reduction) during the course of the study. 9999=Data cannot be reported for a single participant due to privacy concerns.

End point type	Secondary
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End point timeframe:

pre-dose and 1, 2, and 5 hours post-dose on Day 1 (Baseline) and at Week 4

End point values	Itacitinib 200 mg QD	Itacitinib 300 mg QD	Itacitinib 300 mg BID	Itacitinib 400 mg QD
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1 ^[28]	1 ^[29]	6 ^[30]	6 ^[31]
Units: nanomoles per liter (nmol/L)				
geometric mean (geometric coefficient of variation)	9999 (± 9999)	9999 (± 9999)	1820 (± 33.9)	2050 (± 53.0)

Notes:

[28] - PK-Evaluable Population

[29] - PK-Evaluable Population

[30] - PK-Evaluable Population

[31] - PK-Evaluable Population

End point values	Itacitinib 600 mg QD			
Subject group type	Subject analysis set			
Number of subjects analysed	6 ^[32]			
Units: nanomoles per liter (nmol/L)				
geometric mean (geometric coefficient of variation)	2410 (± 61.7)			

Notes:

[32] - PK-Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Ctau of itacitanib

End point title	Phase 1: Ctau of itacitanib
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End point description:

Ctau was defined as the observed itacitanib concentration at the end of the dosing interval. Data were analyzed by dose rather than by treatment arm because approximately one-third of the participants had a dose adjustment (dose reduction) during the course of the study. 9999=Data cannot be reported for a single participant due to privacy concerns.

End point type	Secondary
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End point timeframe:

pre-dose and 1, 2, and 5 hours post-dose on Day 1 (Baseline) and at Week 4

End point values	Itacitinib 200 mg QD	Itacitinib 300 mg QD	Itacitinib 300 mg BID	Itacitinib 400 mg QD
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1 ^[33]	1 ^[34]	5 ^[35]	6 ^[36]
Units: nmol/L				
geometric mean (geometric coefficient of variation)	9999 (± 9999)	9999 (± 9999)	510 (± 130)	16.5 (± 675)

Notes:

[33] - PK-Evaluable Population

[34] - PK-Evaluable Population

[35] - PK-Evaluable Population

[36] - PK-Evaluable Population

End point values	Itacitinib 600 mg QD			
Subject group type	Subject analysis set			
Number of subjects analysed	6 ^[37]			
Units: nmol/L				
geometric mean (geometric coefficient of variation)	43.4 (± 92.7)			

Notes:

[37] - PK-Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: AUC0-24h of itacitanib

End point title	Phase 1: AUC0-24h of itacitanib
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End point description:

AUC0-24h was defined as the area under the plasma concentration-time curve over the last 24-hour dosing interval. Data were analyzed by dose rather than by treatment arm because approximately one-third of the participants had a dose adjustment (dose reduction) during the course of the study. 9999=Data cannot be reported for a single participant due to privacy concerns.

End point type	Secondary
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End point timeframe:

pre-dose and 1, 2, and 5 hours post-dose on Day 1 (Baseline) and at Week 4

End point values	Itacitinib 200 mg QD	Itacitinib 300 mg QD	Itacitinib 300 mg BID	Itacitinib 400 mg QD
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1 ^[38]	1 ^[39]	5 ^[40]	6 ^[41]
Units: hours x nmol/L				
geometric mean (geometric coefficient of variation)	9999 (± 9999)	9999 (± 9999)	26800 (± 62.0)	11900 (± 68.6)

Notes:

[38] - PK-Evaluable Population

[39] - PK-Evaluable Population

[40] - PK-Evaluable Population

[41] - PK-Evaluable Population

End point values	Itacitinib 600 mg QD			
Subject group type	Subject analysis set			
Number of subjects analysed	6 ^[42]			
Units: hours x nmol/L				
geometric mean (geometric coefficient of variation)	14300 (± 77.2)			

Notes:

[42] - PK-Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: tmax of itacitinib

End point title	Phase 1: tmax of itacitinib
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End point description:

tmax was defined as the time to the maximum observed concentration of itacitinib. Data were analyzed by dose rather than by treatment arm because approximately one-third of the participants had a dose adjustment (dose reduction) during the course of the study. -9999, 9999=Data cannot be reported for a single participant due to privacy concerns.

End point type	Secondary
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End point timeframe:

pre-dose and 1, 2, and 5 hours post-dose on Day 1 (Baseline) and at Week 4

End point values	Itacitinib 200 mg QD	Itacitinib 300 mg QD	Itacitinib 300 mg BID	Itacitinib 400 mg QD
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1 ^[43]	1 ^[44]	6 ^[45]	6 ^[46]
Units: hours				
median (full range (min-max))	9999 (-9999 to 9999)	9999 (-9999 to 9999)	3.2 (1.8 to 4.5)	2.0 (1.8 to 4.1)

Notes:

[43] - PK-Evaluable Population

[44] - PK-Evaluable Population

[45] - PK-Evaluable Population

[46] - PK-Evaluable Population

End point values	Itacitinib 600 mg QD			
Subject group type	Subject analysis set			
Number of subjects analysed	6 ^[47]			
Units: hours				
median (full range (min-max))	1.9 (1.0 to 4.0)			

Notes:

[47] - PK-Evaluable Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to approximately 162 weeks

Adverse event reporting additional description:

Treatment-emergent adverse events, defined as either adverse events reported for the first time or the worsening of pre-existing conditions after the first dose of itacitinib until 30 days after the last dose of itacitinib, have been reported.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Itacitinib 300/200 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 milligrams (mg) twice daily (BID). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 200 mg BID. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in forced expiratory volume in 1 second (FEV1), confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Itacitinib 600/400 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 600 mg QD. Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Other
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Reporting group description:

Participants received a starting dose of itacitinib 200 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Reporting group title	Itacitinib 400/300 mg
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Reporting group description:

Participants not taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 400 mg once daily (QD). Participants taking a concomitant strong CYP3A inhibitor received a starting dose of itacitinib 300 mg QD. Participants may have had dose reductions or modifications during the course of treatment based on adverse events, clinical evaluation, changes to concomitant medications, and laboratory assessments. Itacitinib treatment was continued until progression of bronchiolitis obliterans syndrome (defined as a $\geq 10\%$ absolute decrease from Baseline in FEV1, confirmed by 2 consecutive spirometric assessments ≥ 3 weeks apart), unacceptable toxicity, loss of clinical benefit, or withdrawal of consent.

Serious adverse events	Itacitinib 300/200 mg	Itacitinib 600/400 mg	Other
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	6 / 8 (75.00%)	1 / 1 (100.00%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome with single lineage dysplasia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Thrombosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
General disorders and administration site conditions			
Cardiac death			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Transplant rejection subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Epistaxis subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Organising pneumonia subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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 / 7 (0.00%)	1 / 8 (12.50%)	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
Respiratory failure subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Investigations			
Donor specific antibody present subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Cryptococcus test positive subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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

Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Cardiac failure acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Febrile neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Pancreatitis acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Chronic kidney disease			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Haematuria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Nephrolithiasis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Musculoskeletal and connective tissue disorders			
Spinal synovial cyst			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 7 (0.00%)	3 / 8 (37.50%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Cytomegalovirus viraemia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	0 / 1 (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

Large intestine infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Klebsiella bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Herpes simplex pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (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
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Parainfluenzae virus infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Pneumonia fungal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Pneumonia pseudomonal			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (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
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Q fever			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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
Viral infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Metabolism and nutrition disorders			
Acidosis hyperchloraemic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	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

Serious adverse events	Itacitinib 400/300		
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	mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome with single lineage dysplasia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Cardiac death			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			

Transplant rejection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Organising pneumonia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Donor specific antibody present			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cryptococcus test positive			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
End stage renal disease			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Spinal synovial cyst			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 1		
Bronchopulmonary aspergillosis			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Escherichia bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Large intestine infection				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella bacteraemia				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes simplex pneumonia				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parainfluenzae virus infection				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia fungal				
subjects affected / exposed	0 / 7 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	1 / 7 (14.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				

subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Q fever			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Acidosis hyperchloraemic			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Itacitinib 300/200 mg	Itacitinib 600/400 mg	Other
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	7 / 8 (87.50%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Colorectal adenoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	1 / 1 (100.00%)
occurrences (all)	2	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	2 / 7 (28.57%)	3 / 8 (37.50%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Feeling jittery			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Polyp			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Transplant rejection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			

Scrotal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Scrotal swelling			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Haemoptysis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	1	4	0
Sinus congestion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Respiratory tract congestion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Throat irritation			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vasomotor rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Blood pressure increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Immunosuppressant drug level increased			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Myelocyte count increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Prostatic specific antigen increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Immunisation reaction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Procedural pain			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Skin abrasion subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Skin laceration subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Sunburn subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Tooth fracture subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Congenital, familial and genetic disorders Congenital dyskeratosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Disseminated superficial actinic porokeratosis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 2	0 / 1 (0.00%) 0
Cardiac flutter subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Right ventricular failure			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Headache			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Anaemia macrocytic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Lymphopenia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Ocular hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Defaecation urgency			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	4 / 8 (50.00%)	0 / 1 (0.00%)
occurrences (all)	2	5	0
Enlarged uvula			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastritis erosive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Rectal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rectal ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tongue disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nail discolouration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psoriasis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Chronic kidney disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
End stage renal disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Bursitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Groin pain			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Sjogren's syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tendon disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

COVID-19			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Cytomegalovirus infection reactivation			
subjects affected / exposed	3 / 7 (42.86%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Cytomegalovirus viraemia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Genital herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Herpes simplex reactivation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Human polyomavirus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
HCoV-OC43 infection			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Morganella infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pneumonia pseudomonal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Parainfluenzae virus infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1

Respiratory syncytial virus infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Respiratory tract infection bacterial subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Respiratory tract infection viral subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Tinea infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Tinea versicolour subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 8 (25.00%) 2	0 / 1 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Urinary tract infection enterococcal subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Wound infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0
Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0
Gout			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Itacitinib 400/300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	4		
Colorectal adenoma			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Skin papilloma			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	4		
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

Chills			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Feeling jittery			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	4		
Polyp			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Transplant rejection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Scrotal pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Scrotal swelling			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	3		
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Throat irritation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vasomotor rhinitis			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Psychiatric disorders			
Delirium			
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Insomnia			
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Aspartate aminotransferase increased			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Blood cholesterol increased			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Blood creatinine increased			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Blood pressure increased			
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Immunosuppressant drug level increased			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Myelocyte count increased			
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Prostatic specific antigen increased			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Platelet count decreased			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Troponin increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Arthropod bite			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Immunisation reaction			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Skin abrasion			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Skin laceration			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Tooth fracture			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Congenital dyskeratosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Disseminated superficial actinic porokeratosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Cardiac flutter			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Right ventricular failure			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Tachycardia			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	8		
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	7		
Anaemia macrocytic			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Iron deficiency anaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	4		
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Neutropenia			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pancytopenia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Ocular hypertension			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Retinal vein occlusion			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Abdominal pain			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Abdominal pain lower			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Anal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Defaecation urgency			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Enlarged uvula			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastritis erosive			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haemorrhoids			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Oral pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Rectal ulcer			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Tongue disorder			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Nail discolouration			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Rash papular			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	3		
Chronic kidney disease			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
End stage renal disease			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Bursitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Osteonecrosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Sjogren's syndrome			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Tendon disorder			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Cytomegalovirus infection reactivation			

subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	7		
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Genital herpes			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Herpes simplex reactivation			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Herpes virus infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	4		
Human polyomavirus infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
HCoV-OC43 infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			

bacterial			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Morganella infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Onychomycosis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Oesophageal candidiasis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	6		
Pneumonia pseudomonal			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Parainfluenzae virus infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Otitis externa			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory tract infection bacterial			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

Respiratory tract infection viral subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Sinusitis subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 3		
Tinea infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Tinea versicolour subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Urinary tract infection enterococcal subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Wound infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Metabolism and nutrition disorders			
Diabetes mellitus subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2		
Gout subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2		
Fluid retention subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Hypokalaemia			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	3		
Hypophosphataemia			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	4		
Iron deficiency			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2019	The primary purpose of this amendment was to update the eligibility criteria, clarify the schedule of assessments with regards to correlative samples, and incorporate changes resulting from review by Health Canada.
04 March 2020	The primary purpose of this amendment was to update the doses evaluated in Phase 1 of the study and the guidance regarding dose modifications when itacitinib was coadministered with strong CYP3A inhibitors.
11 August 2020	The primary purpose of this amendment was to update the schedule of assessments to require monitoring of maintenance immunosuppressive agents (e.g., calcineurin inhibitors [CNIs]) and to require that participants be on stable doses of strong CYP3A inhibitors prior for 4 weeks before starting study drug.
07 April 2021	The primary purpose of this amendment was to add a requirement to perform cytomegalovirus Polymerase Chain Reaction (CMV PCR) testing during treatment for all study participants.
30 November 2021	The study sponsor decided not to proceed to Phase 2 of the study. The primary purpose of this amendment was to update the schedule of activities and schedule of assessments to simplify and minimize the required assessments for study participants who were to continue to receive itacitinib as of the date of this decision.

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.

A business decision was made to terminate the study before the initiation of Part 2. The decision to terminate the study was unrelated to safety concerns. Results from Phase 1 of the study have been reported in this summary.

Notes: