Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Phase 3 Study of Baricitinib in Patients with COVID-19 Infection

Summary

EudraCT number	2020-001517-21
Trial protocol	GB DE ES IT
Global end of trial date	10 June 2021

Results information

Result version number	v1
This version publication date	01 March 2022
First version publication date	01 March 2022

Trial information

Trial identification

Sponsor protocol code	I4V-MC-KHAA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04421027
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17830

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001220-PIP07-20
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	Interim
Date of interim/final analysis	12 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 February 2021
Global end of trial reached?	Yes
Global end of trial date	10 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The reason for this study is to see if the study drug baricitinib is effective in hospitalized participants with COVID-19.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Puerto Rico: 11
Country: Number of subjects enrolled	Argentina: 208
Country: Number of subjects enrolled	United States: 309
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	India: 50
Country: Number of subjects enrolled	Russian Federation: 112
Country: Number of subjects enrolled	Spain: 87
Country: Number of subjects enrolled	Korea, Republic of: 36
Country: Number of subjects enrolled	Brazil: 337
Country: Number of subjects enrolled	Mexico: 281
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Germany: 20
Worldwide total number of subjects	1525
EEA total number of subjects	132

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)	1026
From 65 to 84 years	474
85 years and over	25

Subject disposition

Recruitment

Recruitment details:

Participants reported are those that completed the primary outcome timepoint at Day 28. Ongoing participants reflect those remaining in study for 60 day extension.

Pre-assignment

Screening details:

No Text Entered

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Standard of Care (SOC)

Arm description:

Placebo tablets administered orally every day (QD) with standard of care.

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

Dosage and administration details:

Placebo given as two placebo tablets administered orally QD with standard of care.

Arm title	Baricitinib + SOC

Arm description:

4 milligrams (mg) baricitinib administered orally QD with standard of care.

Arm type	Experimental
Investigational medicinal product name	Baricitinib
Investigational medicinal product code	LY3009104
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

4 milligrams (mg) of baricitinib (given as two 2 mg tablets) administered orally QD with standard of care.

Number of subjects in period 1	Placebo + Standard of Care (SOC)	Baricitinib + SOC
Started	761	764
Received at least one dose of study drug	752	750
Completed	1	3
Not completed	760	761
Physician decision	1	-
Screen Failure	3	2
Adverse event, non-fatal	-	1
Death	100	62
Other-Unknown	10	6
Ongoing	616	646
Withdawal by subject	13	-
Lost to follow-up	17	19
Withdrawal by subject	-	25

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + Standard of Care (SOC)
Reporting group description:	
Placebo tablets administered orally every day (QD) with standard of care.	
Reporting group title	Baricitinib + SOC
Reporting group description:	
4 milligrams (mg) baricitinib administered orally QD with standard of care.	

Reporting group values	Placebo + Standard of Care (SOC)	Baricitinib + SOC	Total
Number of subjects	761	764	1525
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	57.5	57.8	
standard deviation	± 13.8	± 14.3	-
Gender categorical			
Units: Subjects			
Female	288	274	562
Male	473	490	963
Race (NIH/OMB)			
The American Indian or Alaska Native category includes Mexico and Latin America.			
Units: Subjects			
American Indian or Alaska Native	168	148	316
Asian	94	80	174
Native Hawaiian or Other Pacific Islander	2	3	5
Black or African American	36	39	75
White	440	480	920
More than one race	1	2	3
Unknown or Not Reported	20	12	32
Region of Enrollment			
Units: Subjects			
Puerto Rico	3	8	11
Argentina	101	107	208
United States	155	154	309
Japan	19	19	38
United Kingdom	7	4	11
India	31	19	50
Russia	54	58	112
Spain	42	45	87
South Korea	20	16	36
Brazil	165	172	337
Mexico	143	138	281
Italy	10	15	25
Germany	11	9	20

End points

End points reporting groups

Reporting group title	Placebo + Standard of Care (SOC)
Reporting group description:	
Placebo tablets administered orally every day (QD) with standard of care.	
Reporting group title	Baricitinib + SOC
Reporting group description:	
4 milligrams (mg) baricitinib administered orally QD with standard of care.	

Primary: Percentage of Participants who Die or Require Non-Invasive Ventilation/High-Flow Oxygen or Invasive Mechanical Ventilation (including extracorporeal membraneoxygenation [ECMO])

End point title	Percentage of Participants who Die or Require Non-Invasive Ventilation/High-Flow Oxygen or Invasive Mechanical Ventilation (including extracorporeal membraneoxygenation [ECMO])
End point description:	
Percentage of participants who die or require non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation (including ECMO). Analysis Population Description (APD): All participants randomly assigned to study intervention. Participants with missing baseline ordinal scale values were excluded.	
End point type	Primary
End point timeframe:	
Day 1 to Day 28	

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	756	762		
Units: percentage of participants				
number (confidence interval 95%)	30.5 (27.2 to 33.8)	27.8 (24.6 to 31.0)		

Statistical analyses

Statistical analysis title	Died or Required Supplemental Oxygen Population 1
Comparison groups	Placebo + Standard of Care (SOC) v Baricitinib + SOC

Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.08

Primary: Percentage of Participants who Die or Require Non-Invasive Ventilation/High-Flow Oxygen or Invasive Mechanical Ventilation (including extracorporeal membrane oxygenation [ECMO] Population 2

End point title	Percentage of Participants who Die or Require Non-Invasive Ventilation/High-Flow Oxygen or Invasive Mechanical Ventilation (including extracorporeal membrane oxygenation [ECMO] Population 2

End point description:

Percentage of participants who die or require non-invasive ventilation or invasive mechanical ventilation, including ECMO.

APD: All participants randomly assigned to study intervention who at baseline required oxygen supplementation and did not receive dexamethasone, or other systemic corticosteroids for the primary study condition.

End point type	Primary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	96		
Units: percentage of participants				
number (confidence interval 95%)	27.1 (18.7 to 35.6)	28.9 (19.6 to 38.2)		

Statistical analyses

Statistical analysis title	Died or Required Supplemental Oxygen Population 2
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)

Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.728
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	2.16

Secondary: Percentage of Participants with at Least 1-Point Improvement on National Institute of Allergy and Infectious Diseases Ordinal Scale (NIAID-OS) or Live Discharge from Hospital

End point title	Percentage of Participants with at Least 1-Point Improvement on National Institute of Allergy and Infectious Diseases Ordinal Scale (NIAID-OS) or Live Discharge from Hospital

End point description:

The National Institute of Allergy and Infectious Diseases ordinal scale (NIAID-OS) is an assessment of clinical status. The scale is as follows: 1) Not hospitalized, no limitations on activities; 2) Not hospitalized, limitation on activities and/or requiring home oxygen; 3) Hospitalized, not requiring supplemental oxygen – no longer requires ongoing medical care; 4) Hospitalized, not requiring supplemental oxygen – requiring ongoing medical care (COVID-19 related or otherwise); 5) Hospitalized, requiring supplemental oxygen; 6) Hospitalized, on non-invasive ventilation or high-flow oxygen devices; 7) Hospitalized, on invasive mechanical ventilation or ECMO; 8) Death.
APD: All participants randomly assigned to study intervention. Participants with missing baseline ordinal scale values were excluded from analysis.

End point type	Secondary

End point timeframe:

Day 10

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	756	762		
Units: percentage of participants				
number (confidence interval 95%)	63.5 (60.1 to 67.0)	65.0 (61.6 to 68.5)		

Statistical analyses

Statistical analysis title	At Least 1-Point Improvement on NIAID-OS
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)

Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5444
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.34

Secondary: Number of Ventilator-Free Days

End point title	Number of Ventilator-Free Days

End point description:

Number of days free of invasive mechanical ventilation.

All participants randomly assigned to study intervention. Participants with missing baseline ordinal scale values were excluded.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	756	762		
Units: days				
least squares mean (standard error)	23.7 (± 0.39)	24.5 (± 0.39)		

Statistical analyses

Statistical analysis title	Number of Ventilator-Free Days
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0586
Method	ANOVA
Parameter estimate	LS Mean difference (net)
Point estimate	0.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.399

Secondary: Time to Recovery

End point title	Time to Recovery

End point description:

Recovery assessed by the NIAID-OS. Time to reach NIAID-OS 1, 2, or 3 for the first time. The date reached is the first full day that OS 1, 2, or 3 is the participant's maximum OS for the day.
NIAID-OS 1. Not hospitalized, no limitations on activities 2. Not hospitalized, limitation on activities and/or requiring home oxygen 3. Hospitalized, not requiring supplemental oxygen – no longer requires ongoing medical care: (This would include those kept in hospital for quarantine/infection control, awaiting bed in rehabilitation facility or homecare, etc.)
APD: All participants randomly assigned to study intervention.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	761	764		
Units: Days				
median (confidence interval 95%)	11.0 (10.0 to 12.0)	10.0 (9.0 to 11.0)		

Statistical analyses

Statistical analysis title	Time to Recovery
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1525
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1453
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.24

Secondary: Overall Improvement on the National Institute of Allergy and Infectious Diseases Ordinal Scale (NIAID-OS)

End point title	Overall Improvement on the National Institute of Allergy and Infectious Diseases Ordinal Scale (NIAID-OS)

End point description:

Overall improvement on the National Institute of Allergy and Infectious Diseases ordinal scale:
1. Not hospitalized, no limitations on activities; 2. Not hospitalized, limitation on activities and/or requiring home oxygen; 3. Hospitalized, not requiring supplemental oxygen – no longer requires ongoing medical care: (This would include those kept in hospital for quarantine/infection control, awaiting bed in rehabilitation facility or homecare, etc.); 4. Hospitalized, not requiring supplemental oxygen – requiring ongoing medical care (COVID-19 related or otherwise); 5. Hospitalized, requiring supplemental oxygen; 6.Hospitalized, on noninvasive ventilation or high-flow oxygen devices; 7. Hospitalized, on invasive mechanical ventilation or ECMO; 8. Death.
APD: All participants randomly assigned to study intervention. Participants with missing baseline ordinal scale were excluded.

End point type	Secondary

End point timeframe:

Days 4, 7, 10, and 14

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	756	762		
Units: score on a scale				
number (confidence interval 95%)				
Day 4 NIAID-OS 1	4.6 (3.1 to 6.1)	5.2 (3.6 to 6.8)		
Day 4 NIAID-OS 2	1.5 (0.6 to 2.4)	1.5 (0.6 to 2.4)		
Day 4 NIAID-OS 3	0.8 (0.2 to 1.4)	0.3 (0.0 to 0.7)		
Day 4 NIAID-OS 4	19.4 (16.6 to 22.3)	23.6 (20.6 to 26.7)		
Day 4 NIAID-OS 5	41.0 (37.5 to 44.5)	39.0 (35.5 to 42.5)		
Day 4 NIAID-OS 6	22.4 (19.5 to 25.4)	21.8 (18.9 to 24.8)		
Day 4 NIAID-OS 7	8.9 (6.8 to 10.9)	8.1 (6.2 to 10.1)		
Day 4 NIAID-OS 8	1.4 (0.5 to 2.2)	0.4 (00.0 to 0.9)		
Day 7 NIAID-OS 1	20.2 (17.3 to 23.1)	25.2 (22.1 to 28.4)		
Day 7 NIAID-OS 2	6.6 (4.8 to 8.4)	5.8 (4.1 to 7.5)		
Day 7 NIAID-OS 3	0.5 (0.0 to 1.1)	0.2 (0.0 to 0.5)		
Day 7 NIAID-OS 4	21.2 (18.2 to 24.1)	20.6 (17.6 to 23.5)		

Day 7 NIAID-OS 5	22.5 (19.5 to 25.5)	22.5 (19.4 to 25.5)		
Day 7 NIAID-OS 6	14.5 (12.0 to 17.0)	13.8 (11.3 to 16.2)		
Day 7 NIAID-OS 7	11.2 (9.0 to 13.5)	10.8 (8.6 to 13.0)		
Day 7 NIAID-OS 8	3.3 (2.0 to 4.5)	1.2 (0.4 to 2.0)		
Day 10 NIAID-OS 1	37.7 (34.2 to 41.2)	40.4 (36.9 to 44.0)		
Day 10 NIAID-OS 2	9.4 (7.3 to 11.5)	10.9 (8.7 to 13.2)		
Day 10 NIAID-OS 3	0.10 (0.0 to 0.4)	0.1 (0.0 to 0.4)		
Day 10 NIAID-OS 4	16.2 (13.6 to 18.9)	14.1 (11.6 to 16.6)		
Day 10 NIAID-OS 5	12.8 (10.3 to 15.2)	12.4 (10.0 to 14.8)		
Day 10 NIAID-OS 6	8.1 (6.1 to 10.0)	8.9 (6.8 to 11.0)		
Day 10 NIAID-OS 7	10.6 (8.4 to 12.9)	10.4 (8.2 to 12.6)		
Day 10 NIAID-OS 8	5.1 (3.5 to 6.7)	2.6 (1.5 to 3.8)		
Day 14 NIAID-OS 1	51.6 (48.0 to 55.2)	56.3 (52.7 to 59.9)		
Day 14 NIAID-OS 2	11.2 (8.9 to 13.5)	11.1 (8.8 to 13.4)		
Day 14 NIAID-OS 3	0.3 (0.0 to 0.6)	0.1 (0.0 to 0.4)		
Day 14 NIAID-OS 4	8.0 (6.0 to 10.0)	7.6 (5.7 to 9.6)		
Day 14 NIAID-OS 5	8.4 (6.4 to 10.5)	7.3 (5.4 to 9.2)		
Day 14 NIAID-OS 6	3.6 (2.2 to 4.9)	3.7 (2.3 to 5.1)		
Day 14 NIAID-OS 7	9.4 (7.3 to 11.6)	8.9 (6.9 to 11.0)		
Day 14 NIAID-OS 8	7.5 (5.6 to 9.4)	4.9 (3.4 to 6.5)		

Statistical analyses

Statistical analysis title	Overall Improvement on the NIAID-OS Day 4
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0464
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.47

Statistical analysis title	Overall Improvement on the NIAID-OS Day 7
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0172
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.49

Statistical analysis title	Overall Improvement on the NIAID-OS Day 10
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0921
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.41

Statistical analysis title	Overall Improvement on the NIAID-OS Day 14
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0168
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.56

Secondary: Duration of Hospitalization

End point title	Duration of Hospitalization

End point description:

Duration of hospitalization.

APD: All participants randomly assigned to study intervention. Participants with missing baseline ordinal scale were excluded.

End point type	Secondary

End point timeframe:

Days 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	756	762		
Units: days				
least squares mean (standard error)	13.7 (± 0.40)	12.9 (± 0.40)		

Statistical analyses

Statistical analysis title	Duration of Hospitalization
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0626
Method	ANOVA
Parameter estimate	LS Mean difference (net)
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.408

Secondary: Percentage of Participants with a Change in Oxygen Saturation from <94% to ≥94% from Baseline

End point title	Percentage of Participants with a Change in Oxygen Saturation from <94% to ≥94% from Baseline

End point description:

Percentage of participants with a change in oxygen saturation from less than (<) 94% to greater than or equal to (≥) 94% from baseline based on National Early Warning Score (NEWS). Measure of the oxygen level of the blood is measure by pulse oximetry. The score is determined from six physiological parameters readily measured over time in hospitalized participants: Respiration rate; oxygen saturation; temperature; systolic blood pressure; heart (pulse) rate, and level of consciousness, as measured by Alert Voice Pain Unresponsive (AVPU). A score is assigned to each parameter, the magnitude of the score representing the extremity of variation from the norm. A weighting score is added for participants needing supplemental oxygen (oxygen delivery by mask or by cannula) The aggregate score is reflective of the participants status.

End point type	Secondary

End point timeframe:

Day 10
APD: All participants randomly assigned to study intervention whose oxygen saturation (based on National Early Warning Score) is <94% at baseline and have non-missing baseline and at least 1 postbaseline observation are in this population.

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	282		
Units: percentage of participants				
number (confidence interval 95%)	52.5 (46.7 to 58.2)	56.7 (50.9 to 62.4)		

Statistical analyses

Statistical analysis title	Percentage of Participants with Change in Oxygen
Comparison groups	Placebo + Standard of Care (SOC) v Baricitinib + SOC
Number of subjects included in analysis	564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.429
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.63

Secondary: Overall Mortality

End point title	Overall Mortality

End point description:

Number of deaths by Day 28.

APD: All participants randomly assigned to study intervention.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	761	764		
Units: event of death				
number (not applicable)	104	65		

Statistical analyses

Statistical analysis title	Overall Mortality
Comparison groups	Placebo + Standard of Care (SOC) v Baricitinib + SOC
Number of subjects included in analysis	1525
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0018
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.78

Secondary: Duration of Stay in the Intensive Care Unit (ICU) in Days

End point title	Duration of Stay in the Intensive Care Unit (ICU) in Days

End point description:

Duration of stay in the ICU in days.

APD: All participants randomly assigned to study intervention with non-missing baseline NIAID OS and at least 1 postbaseline NIAID OS observation.

End point type	Secondary
End point timeframe:	
Day 1 to Day 28	

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	754	758		
Units: days				
least squares mean (standard error)	3.17 (± 0.313)	3.19 (± 0.315)		

Statistical analyses

Statistical analysis title	Duration of Stay in the Intensive Care Unit (ICU)
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1512
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9526
Method	ANOVA
Parameter estimate	LS Mean difference (net)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.323

Secondary: Time to Clinical Deterioration (one-category increase on the NIAID-OS)

End point title	Time to Clinical Deterioration (one-category increase on the NIAID-OS)

End point description:

Time to Clinical Deterioration (one-category increase on the NIAID-OS). 9999 = Data not available (N/A).

APD: All participants randomly assigned to study intervention.

End point type	Secondary
End point timeframe:	
Day 1 to Day 28	

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	761[1]	764[2]		
Units: days				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Notes:

[1] - Median not evaluable due to less than half the participants meeting criteria.

[2] - Median not evaluable due to less than half the participants meeting criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Resolution of Fever, in Participants with Fever at Baseline

End point title	Time to Resolution of Fever, in Participants with Fever at Baseline

End point description:

Time to resolution of fever, in participants with fever at baseline was calculated using cox proportional hazard regression model adjusted for baseline disease severity (OS 4, OS 5, OS 6), age (<65 years, >=65 years), region (United States, Europe, rest of world), and systemic corticosteroids used at baseline for primary study condition (Yes/No).

APD: All participants randomly assigned to study intervention who had a fever at baseline.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	354	357		
Units: days				
median (confidence interval 95%)	4.00 (3.00 to 4.00)	3.00 (3.00 to 4.00)		

Statistical analyses

Statistical analysis title	Time to Resolution of Fever
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	711
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0243
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.202

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.017
upper limit	1.421

Secondary: Mean Change from Baseline on the National Early Warning Score (NEWS)

End point title	Mean Change from Baseline on the National Early Warning Score (NEWS)

End point description:

The NEWS is used to detect and report changes in illness severity in participants with acute illness. The score is determined from six physiological parameters readily measured over time in hospitalized participants: Respiration rate; oxygen saturation; temperature; systolic blood pressure; heart (pulse) rate, and level of consciousness, as measured by Alert Voice Pain Unresponsive (AVPU). A score is assigned to each parameter, the magnitude of the score representing the extremity of variation from the norm. A weighting score is added for participants needing supplemental oxygen (oxygen delivery by mask or by cannula) The aggregate score is reflective of the participants status, with higher scores representing higher level of acuity; a score of 7 or greater reflects high clinical risk for worsening acuity. APD: All participants randomly assigned to study intervention with baseline and 1 postbaseline observation.

End point type	Secondary

End point timeframe:

Baseline, Day 4; Baseline, Day 7; Baseline, Day 10; Baseline, Day 14

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	636	647		
Units: score on a scale				
least squares mean (standard error)				
Day 4: n = 636, 647	-0.59 (± 0.127)	-0.76 (± 0.125)		
Day 7: n = 488, 485	-0.86 (± 0.145)	-1.04 (± 0.143)		
Day 10: n = 388, 399	-1.33 (± 0.160)	-1.45 (± 0.158)		
Day 14: n = 300, 299	-1.41 (± 0.183)	-1.66 (± 0.182)		

Statistical analyses

Statistical analysis title	Mean Change from Baseline on the NEWS Score Day 4
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)

Number of subjects included in analysis	1283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.191
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.128

Statistical analysis title	Mean Change from Baseline on the NEWS Score Day 7
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.278
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.161

Statistical analysis title	Mean Change from Baseline on the NEWS Score Day 10
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.496
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.24

Variability estimate	Standard error of the mean
Dispersion value	0.187

Statistical analysis title	Mean Change from Baseline on the NEWS Score Day 14
Comparison groups	Placebo + Standard of Care (SOC) v Baricitinib + SOC
Number of subjects included in analysis	1283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.263
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.226

Secondary: Time to Definitive Extubation	
End point title	Time to Definitive Extubation

End point description:

Time to definitive extubation included participants who progressed to OS 7 at any time prior to Day 28. 9999=Data Not Available (N/A).

APD: All participants randomly assigned to study intervention who were intubated at some time during study.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136[3]	125[4]		
Units: days				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Notes:

[3] - Median not evaluable due to less than half the participants meeting criteria.

[4] - Median not evaluable due to less than half the participants meeting criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Independence from Non-Invasive Mechanical Ventilation

End point title	Time to Independence from Non-Invasive Mechanical Ventilation

End point description:

Time to independence from non-invasive mechanical ventilation (NMV) was measured in days among participants who required non-invasive mechanical ventilation.
APD: All participants randomly assigned to study intervention whose baseline OS was 6 and were on non-invasive mechanical ventilation.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	183		
Units: days				
median (confidence interval 95%)	11.00 (9.00 to 13.00)	12.00 (9.00 to 14.00)		

Statistical analyses

Statistical analysis title	Time to Independence from NMV
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6436
Method	Logrank

Secondary: Time to Independence from Oxygen Therapy in Days

End point title	Time to Independence from Oxygen Therapy in Days

End point description:

Time to independence from oxygen therapy in days.

APD: All randomized participants who had an ordinal scale score of 5 or 6 at baseline.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	659	673		
Units: days				
median (confidence interval 95%)	8.00 (8.00 to 9.00)	8.00 (7.00 to 8.00)		

Statistical analyses

Statistical analysis title	Time to Independence from Oxygen Therapy
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127
Method	Logrank

Secondary: Number of Days with Supplemental Oxygen Use

End point title	Number of Days with Supplemental Oxygen Use

End point description:

Number of days with supplemental oxygen use.
APD: All participants randomly assigned to study intervention who have non-missing baseline and at least one postbaseline observation.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	754	758		
Units: days				
least squares mean (standard error)	4.60 (± 0.221)	4.37 (± 0.222)		

Statistical analyses

Statistical analysis title	Number of Days with Supplemental Oxygen Use
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)
Number of subjects included in analysis	1512
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3058
Method	ANOVA
Parameter estimate	LS Mean Difference (Net)
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.228

Secondary: Number of Days of Resting Respiratory Rate <24 Breaths per Minute

End point title	Number of Days of Resting Respiratory Rate <24 Breaths per Minute

End point description:

Number of days of resting respiratory rate <24 breaths per minute.
APD: All participants randomly assigned to study intervention who had non-missing baseline and at least one postbaseline respiratory rate.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	Placebo + Standard of Care (SOC)	Baricitinib + SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	743	745		
Units: days				
least squares mean (standard error)	9.62 (± 0.300)	9.73 (± 0.304)		

Statistical analyses

Statistical analysis title	Resting Respiratory Rate <24 Breaths per Minute
Comparison groups	Baricitinib + SOC v Placebo + Standard of Care (SOC)

Number of subjects included in analysis	1488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7073
Method	ANOVA
Parameter estimate	LS Mean Difference (Net)
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.306

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Baseline up to 119 days
Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study drug including participants who entered the post-treatment follow-up (f/u) period. One participant receiving baricitinib had 2 events with fatal outcomes, 1 event in main study period and 1 event in f/u period, the participant's death was counted in the main study and f/u periods.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo tablets administered orally every day (QD) with standard of care.

Reporting group title	Baricitinib-4mg-QD Follow-up

Reporting group description:

4 milligrams (mg) baricitinib administered orally QD with standard of care.

Reporting group title	Placebo Follow-up

Reporting group description:

Placebo tablets administered orally every day (QD) with standard of care.

Reporting group title	Baricitinib-4mg-QD

Reporting group description:

4 mg baricitinib administered orally QD with standard of care.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No treatment-emergent non-serious AEs occurring in >5% of patients within arm and period were observed.

Serious adverse events	Placebo	Baricitinib-4mg-QD Follow-up	Placebo Follow-up
Total subjects affected by serious adverse events			
subjects affected / exposed	135 / 752 (17.95%)	18 / 645 (2.79%)	12 / 613 (1.96%)
number of deaths (all causes)	104	14	11
number of deaths resulting from adverse events	2	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
breast neoplasm			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

deep vein thrombosis alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 752 (0.66%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dry gangrene alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
embolism venous alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	1 / 645 (0.16%)	0 / 613 (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
hypotension alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
peripheral artery thrombosis alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
peripheral embolism alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
shock alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
shock haemorrhagic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Surgical and medical procedures			
palliative care			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General disorders and administration site conditions			
hypothermia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 752 (0.66%)	1 / 645 (0.16%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 1
Reproductive system and breast disorders			
acquired phimosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[2]	0 / 473 (0.00%)	0 / 415 (0.00%)	1 / 377 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			

acute respiratory distress syndrome alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 752 (0.40%)	1 / 645 (0.16%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 1
acute respiratory failure alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	29 / 752 (3.86%)	2 / 645 (0.31%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	2 / 29	0 / 2	0 / 1
deaths causally related to treatment / all	2 / 18	0 / 2	0 / 1
dyspnoea alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
pneumomediastinum alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
pneumothorax alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 752 (0.27%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
pulmonary embolism alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	7 / 752 (0.93%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	2 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory distress alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	4 / 752 (0.53%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	17 / 752 (2.26%)	1 / 645 (0.16%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 17	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 7	0 / 0	0 / 0
Investigations			
fibrin d dimer increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	1 / 645 (0.16%)	0 / 613 (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
hepatic enzyme increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
transaminases increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
acute myocardial infarction			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
atrial fibrillation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
bradycardia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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 arrest			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 752 (0.40%)	0 / 645 (0.00%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
cardio-respiratory arrest			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	6 / 752 (0.80%)	1 / 645 (0.16%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 6	0 / 1	0 / 1
cardiogenic shock			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cardiopulmonary failure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

coronary artery thrombosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
myocardial infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
cerebral infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cerebrovascular accident			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	1 / 645 (0.16%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
depressed level of consciousness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
guillain-barre syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhage intracranial			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
ischaemic stroke			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
neuralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
paresis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
disseminated intravascular coagulation			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
lymphopenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 752 (0.27%)	0 / 645 (0.00%)	0 / 613 (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
thrombocytopenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
Eye disorders			
diplopia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
acute abdomen			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	1 / 645 (0.16%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	10 / 752 (1.33%)	0 / 645 (0.00%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	1 / 10	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	3 / 752 (0.40%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal impairment			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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			
muscular weakness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
bacterial infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
covid-19			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	10 / 752 (1.33%)	1 / 645 (0.16%)	1 / 613 (0.16%)
occurrences causally related to treatment / all	0 / 10	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 9	0 / 1	0 / 1
covid-19 pneumonia			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	21 / 752 (2.79%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 21	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 21	0 / 0	0 / 0
device related bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
empyema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
endocarditis staphylococcal			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
enterobacter bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
klebsiella bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
klebsiella sepsis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

pneumonia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	10 / 752 (1.33%)	1 / 645 (0.16%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 0
pneumonia bacterial			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 752 (0.40%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
pneumonia staphylococcal			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia viral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 752 (0.27%)	1 / 645 (0.16%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
pulmonary sepsis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
septic shock			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	24 / 752 (3.19%)	5 / 645 (0.78%)	4 / 613 (0.65%)
occurrences causally related to treatment / all	0 / 24	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 16	0 / 4	0 / 4
sepsis			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	4 / 752 (0.53%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
severe acute respiratory syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 752 (0.40%)	1 / 645 (0.16%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
staphylococcal bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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 infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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 sepsis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (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
systemic candida			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 752 (0.27%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
hyperglycaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (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
metabolic acidosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 752 (0.13%)	0 / 645 (0.00%)	0 / 613 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Serious adverse events	Baricitinib-4mg-QD		
Total subjects affected by serious adverse events			
subjects affected / exposed	110 / 750 (14.67%)		
number of deaths (all causes)	65		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
breast neoplasm			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 750 (0.53%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
dry gangrene			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
embolism venous			

alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypotension				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	2 / 750 (0.27%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
peripheral artery thrombosis				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
peripheral embolism				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
shock				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	2 / 750 (0.27%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
shock haemorrhagic				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
palliative care				
alternative dictionary used: MedDRA 24.0				

subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
hypothermia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 750 (0.53%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Reproductive system and breast disorders			
acquired phimosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[2]	0 / 490 (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 distress syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 750 (0.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
acute respiratory failure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	17 / 750 (2.27%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 9		
dyspnoea			
alternative dictionary used:			

MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumomediastinum				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pneumothorax				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	6 / 750 (0.80%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
pulmonary embolism				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	12 / 750 (1.60%)			
occurrences causally related to treatment / all	4 / 12			
deaths causally related to treatment / all	0 / 1			
respiratory distress				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	3 / 750 (0.40%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
respiratory failure				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	10 / 750 (1.33%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 4			
Investigations				
fibrin d dimer increased				
alternative dictionary used: MedDRA 24.0				

subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatic enzyme increased				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
transaminases increased				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
acute coronary syndrome				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
acute myocardial infarction				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
atrial fibrillation				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
bradycardia				
alternative dictionary used: MedDRA 24.0				

subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cardiac arrest				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardio-respiratory arrest				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	3 / 750 (0.40%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 3			
cardiogenic shock				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiopulmonary failure				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	2 / 750 (0.27%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
coronary artery thrombosis				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
myocardial infarction				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Nervous system disorders			
cerebral infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cerebrovascular accident			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
depressed level of consciousness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
guillain-barre syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
haemorrhage intracranial			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ischaemic stroke			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 750 (0.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
neuralgia			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
paresis				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
subarachnoid haemorrhage				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
anaemia				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
disseminated intravascular coagulation				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lymphopenia				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thrombocytopenia				
alternative dictionary used: MedDRA 24.0				

subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
diplopia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
acute abdomen			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	7 / 750 (0.93%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
renal failure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
renal impairment			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
muscular weakness			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
bacterial infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
covid-19			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	8 / 750 (1.07%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 4		
covid-19 pneumonia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	21 / 750 (2.80%)		
occurrences causally related to treatment / all	0 / 21		
deaths causally related to treatment / all	0 / 21		
device related bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
empyema			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
endocarditis staphylococcal			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
enterobacter bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
klebsiella bacteraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
klebsiella sepsis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 750 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pneumonia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	8 / 750 (1.07%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 3		
pneumonia bacterial			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 750 (0.53%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		

pneumonia staphylococcal				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	0 / 750 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia viral				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	2 / 750 (0.27%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
pulmonary sepsis				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
septic shock				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	13 / 750 (1.73%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 11			
sepsis				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	3 / 750 (0.40%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
severe acute respiratory syndrome				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
staphylococcal bacteraemia				
alternative dictionary used: MedDRA 24.0				

subjects affected / exposed	2 / 750 (0.27%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
staphylococcal infection				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	2 / 750 (0.27%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
staphylococcal sepsis				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
systemic candida				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
urinary tract infection				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
hyperglycaemia				
alternative dictionary used: MedDRA 24.0				
subjects affected / exposed	1 / 750 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
metabolic acidosis				
alternative dictionary used: MedDRA 24.0				

subjects affected / exposed	0 / 750 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Non-serious adverse events	Placebo	Baricitinib-4mg-QD Follow-up	Placebo Follow-up
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 752 (0.00%)	0 / 645 (0.00%)	0 / 613 (0.00%)

Non-serious adverse events	Baricitinib-4mg-QD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 750 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2020	Protocol B: The main purpose of this protocol is to address the comments regarding primary endpoint, inclusion/exclusion criteria, and other required clarifications, added clarifications of analyses population.
12 August 2020	Protocol C (For European countries): Overall rationale for the amendment is to increase sample size to accommodate involving changes in standard-of-care therapy, especially concomitant use of dexamethasone.
20 October 2020	Protocol D: The protocol amendment is to provide the opportunity for the sample size to be increased (sample size re-estimation) during an interim analysis and to add a follow-up visit at Day 60.
25 November 2020	Protocol E (For European Countries): The main purpose of the protocol amendment is to address the sample size re-estimation and the addition of subpopulation for the primary endpoint (OS7 patients).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported