



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) | EMA-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 | Subject, Investigator |

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 |
| Withdrawal 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 standard deviation | 57.5 ± 13.8 | 57.8 ± 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

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|----------------------------|--|
| 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 (\pm 0.39) | 24.5 (\pm 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

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|--|------------------|
| 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 |

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|---------------------|---------|
| 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)

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|-----------------|---|
| 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 home care, 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 (0.0 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 (\pm 0.313) | 3.19 (\pm 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 (\pm 0.221) | 4.37 (\pm 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 occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 750 (0.00%) 0 / 0 0 / 0 | | | |
| pneumonia viral alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 750 (0.27%) 0 / 2 0 / 1 | | | |
| pulmonary sepsis alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 750 (0.13%) 0 / 1 0 / 1 | | | |
| septic shock alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 13 / 750 (1.73%) 0 / 13 0 / 11 | | | |
| sepsis alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 750 (0.40%) 1 / 3 0 / 0 | | | |
| severe acute respiratory syndrome alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 750 (0.13%) 0 / 1 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