



Clinical trial results: GRAVITAS-309: A Phase 2/3 Study of Itacitinib and Corticosteroids as Initial Treatment for Chronic Graft-Versus-Host Disease

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2018-001606-29 |
| Trial protocol | BE GB FR SE DE PL DK ES GR FI IT |
| Global end of trial date | 03 November 2023 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 |
| This version publication date | 25 October 2024 |
| First version publication date | 25 October 2024 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | INCB 39110-309 |
|-----------------------|----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Incyte Corporation |
| Sponsor organisation address | 1801 Augustine Cutoff Drive, Wilmington, United States, 19803 |
| Public contact | Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com |
| Scientific contact | Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 03 November 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 November 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Part 1 and Part 1 expansion: to identify an appropriate dose of itacitinib in combination with corticosteroids as initial treatment for moderate or severe chronic graft-versus-host disease (cGVHD).

Part 2: to compare the efficacy of itacitinib versus placebo in combination with corticosteroids as initial treatment for moderate or severe cGVHD.

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 17 January 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 24 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Austria: 2 |
| Country: Number of subjects enrolled | Belgium: 5 |
| Country: Number of subjects enrolled | Canada: 6 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | Germany: 27 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | Spain: 20 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Greece: 10 |
| Country: Number of subjects enrolled | Israel: 3 |
| Country: Number of subjects enrolled | Italy: 22 |
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | United States: 57 |
| Worldwide total number of subjects | 160 |
| EEA total number of subjects | 90 |

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) | 123 |
| From 65 to 84 years | 37 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted at 65 study centers in Austria, Belgium, Canada, Denmark, Germany, Greece, Israel, Italy, Poland, Spain, Switzerland, United Kingdom, and the United States.

Period 1

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

Arms

| | |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part 1: itacitinib 200 mg QD + CS |

Arm description:

Participants were treated with oral itacitinib 200 milligrams (mg) once daily (QD) + corticosteroids (CS) for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg (kg) QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (chronic graft-versus-host disease [cGVHD] progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | corticosteroids (methylprednisolone, prednisone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

starting dose 0.5-1.0 mg/kg per day prednisone (or methylprednisolone equivalent to prednisone dose); may have varied based on institutional practice

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

Dosage and administration details:

Two 100-mg sustained-release tablets taken orally

| | |
|------------------|-----------------------------------|
| Arm title | Part 1: itacitinib 300 mg QD + CS |
|------------------|-----------------------------------|

Arm description:

Participants were treated with oral itacitinib 300 mg QD + CS for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | corticosteroids (methylprednisolone, prednisone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

starting dose 0.5-1.0 mg/kg per day prednisone (or methylprednisolone equivalent to prednisone dose); may have varied based on institutional practice

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

Dosage and administration details:

Three 100-mg sustained-release tablets taken orally

| | |
|------------------|---|
| Arm title | Part 1 Expansion: itacitinib 300 mg QD + CS |
|------------------|---|

Arm description:

Participants were treated with oral itacitinib 300 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | corticosteroids (methylprednisolone, prednisone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

starting dose 0.5-1.0 mg/kg per day prednisone (or methylprednisolone equivalent to prednisone dose); may have varied based on institutional practice

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

Dosage and administration details:

Three 100-mg sustained-release tablets taken orally

| | |
|------------------|---|
| Arm title | Part 1 Expansion: itacitinib 400 mg QD + CS |
|------------------|---|

Arm description:

Participants were treated with oral itacitinib 400 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | corticosteroids (methylprednisolone, prednisone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

starting dose 0.5-1.0 mg/kg per day prednisone (or methylprednisolone equivalent to prednisone dose); may have varied based on institutional practice

| | |
|---|--|
| Investigational medicinal product name | itacitinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Prolonged-release tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two 100-mg sustained-release tablets taken orally | |
| Arm title | Part 1 Expansion: itacitinib 300 mg BID + CS |

Arm description:

Participants were treated with oral itacitinib 300 mg twice daily (BID) + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). The itacitinib dose could have been decreased to 200 mg BID if a boundary was reached during safety run-in. This treatment group was discontinued due to concern of a potential increase in relapse rate. Participants in this treatment group who were ongoing were allowed to reduce to 400 mg QD plus CS. Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | corticosteroids (methylprednisolone, prednisone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

starting dose 0.5-1.0 mg/kg per day prednisone (or methylprednisolone equivalent to prednisone dose); may have varied based on institutional practice

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

Dosage and administration details:

Three 100-mg sustained-release tablets taken orally

| | |
|------------------|----------------------------------|
| Arm title | Part 1 Expansion: CS monotherapy |
|------------------|----------------------------------|

Arm description:

Participants were treated with CS alone. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | corticosteroids (methylprednisolone, prednisone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

starting dose 0.5-1.0 mg/kg per day prednisone (or methylprednisolone equivalent to prednisone dose); may have varied based on institutional practice

| Number of subjects in period 1 | Part 1: itacitinib 200 mg QD + CS | Part 1: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 300 mg QD + CS |
|---|-----------------------------------|-----------------------------------|---|
| | Started | 11 | 10 |
| Completed | 6 | 5 | 3 |
| Not completed | 5 | 5 | 32 |
| Consent withdrawn by subject | 2 | - | 2 |
| Physician decision | - | - | 4 |
| Disease Progression; cGVHD Flare | - | - | - |
| Death | 2 | 3 | 9 |
| Study Terminated by Sponsor | - | 2 | 17 |
| Lost to follow-up | 1 | - | - |
| Discontinued Treatment and Terminated CS Tapering | - | - | - |

| Number of subjects in period 1 | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|---|---|--|----------------------------------|
| | Started | 39 | 29 |
| Completed | 2 | 1 | 1 |
| Not completed | 37 | 28 | 35 |
| Consent withdrawn by subject | 4 | 2 | 3 |
| Physician decision | 3 | 2 | 3 |
| Disease Progression; cGVHD Flare | - | - | 1 |
| Death | 8 | 4 | 5 |
| Study Terminated by Sponsor | 20 | 20 | 23 |
| Lost to follow-up | 1 | - | - |
| Discontinued Treatment and Terminated CS Tapering | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: itacitinib 200 mg QD + CS |
|-----------------------|-----------------------------------|

Reporting group description:

Participants were treated with oral itacitinib 200 milligrams (mg) once daily (QD) + corticosteroids (CS) for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (chronic graft-versus-host disease [cGVHD] progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: itacitinib 300 mg QD + CS |
|-----------------------|-----------------------------------|

Reporting group description:

Participants were treated with oral itacitinib 300 mg QD + CS for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|---|
| Reporting group title | Part 1 Expansion: itacitinib 300 mg QD + CS |
|-----------------------|---|

Reporting group description:

Participants were treated with oral itacitinib 300 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|---|
| Reporting group title | Part 1 Expansion: itacitinib 400 mg QD + CS |
|-----------------------|---|

Reporting group description:

Participants were treated with oral itacitinib 400 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|--|
| Reporting group title | Part 1 Expansion: itacitinib 300 mg BID + CS |
|-----------------------|--|

Reporting group description:

Participants were treated with oral itacitinib 300 mg twice daily (BID) + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). The itacitinib dose could have been decreased to 200 mg BID if a boundary was reached during safety run-in. This treatment group was discontinued due to concern of a potential increase in relapse rate. Participants in this treatment group who were ongoing were allowed to reduce to 400 mg QD plus CS. Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Part 1 Expansion: CS monotherapy |
|-----------------------|----------------------------------|

Reporting group description:

Participants were treated with CS alone. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| Reporting group values | Part 1: itacitinib 200 mg QD + CS | Part 1: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 300 mg QD + CS |
|--|-----------------------------------|-----------------------------------|---|
| Number of subjects | 11 | 10 | 35 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |

| | | | |
|--|--------|---------|---------|
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 9 | 6 | 28 |
| From 65-84 years | 2 | 4 | 7 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 57.2 | 58.4 | 53.6 |
| standard deviation | ± 7.07 | ± 15.08 | ± 14.01 |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female | 3 | 3 | 17 |
| Male | 8 | 7 | 18 |
| Race, Customized | | | |
| Units: Subjects | | | |
| White/Caucasian | 11 | 8 | 31 |
| Black/African-American | 0 | 1 | 2 |
| Asian | 0 | 1 | 1 |
| Captured as "Other" in Database | 0 | 0 | 1 |
| Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 2 | 6 |
| Not Hispanic or Latino | 6 | 8 | 25 |
| Not Reported | 1 | 0 | 2 |
| Unknown | 0 | 0 | 2 |
| Captured as "Other" in Database | 0 | 0 | 0 |

| Reporting group values | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|---|---|--|-------------------------------------|
| Number of subjects | 39 | 29 | 36 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 30 | 26 | 24 |
| From 65-84 years | 9 | 3 | 12 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 52.6 | 52.6 | 55.7 |
| standard deviation | ± 13.79 | ± 12.86 | ± 13.32 |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female | 16 | 14 | 19 |

| | | | |
|------|----|----|----|
| Male | 23 | 15 | 17 |
|------|----|----|----|

| | | | |
|--|----|----|----|
| Race, Customized Units: Subjects | | | |
| White/Caucasian | 36 | 27 | 34 |
| Black/African-American | 0 | 0 | 0 |
| Asian | 3 | 2 | 1 |
| Captured as "Other" in Database | 0 | 0 | 1 |
| Ethnicity, Customized Units: Subjects | | | |
| Hispanic or Latino | 8 | 1 | 5 |
| Not Hispanic or Latino | 26 | 19 | 29 |
| Not Reported | 2 | 4 | 2 |
| Unknown | 1 | 1 | 0 |
| Captured as "Other" in Database | 2 | 4 | 0 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 160 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 123 | | |
| From 65-84 years | 37 | | |
| 85 years and over | 0 | | |
| Age Continuous Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male Units: participants | | | |
| Female | 72 | | |
| Male | 88 | | |
| Race, Customized Units: Subjects | | | |
| White/Caucasian | 147 | | |
| Black/African-American | 3 | | |
| Asian | 8 | | |
| Captured as "Other" in Database | 2 | | |
| Ethnicity, Customized Units: Subjects | | | |
| Hispanic or Latino | 26 | | |
| Not Hispanic or Latino | 113 | | |
| Not Reported | 11 | | |
| Unknown | 4 | | |

| | | | |
|---------------------------------|---|--|--|
| Captured as "Other" in Database | 6 | | |
|---------------------------------|---|--|--|

End points

End points reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: itacitinib 200 mg QD + CS |
|-----------------------|-----------------------------------|

Reporting group description:

Participants were treated with oral itacitinib 200 milligrams (mg) once daily (QD) + corticosteroids (CS) for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (chronic graft-versus-host disease [cGVHD] progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: itacitinib 300 mg QD + CS |
|-----------------------|-----------------------------------|

Reporting group description:

Participants were treated with oral itacitinib 300 mg QD + CS for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|---|
| Reporting group title | Part 1 Expansion: itacitinib 300 mg QD + CS |
|-----------------------|---|

Reporting group description:

Participants were treated with oral itacitinib 300 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|---|
| Reporting group title | Part 1 Expansion: itacitinib 400 mg QD + CS |
|-----------------------|---|

Reporting group description:

Participants were treated with oral itacitinib 400 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|--|
| Reporting group title | Part 1 Expansion: itacitinib 300 mg BID + CS |
|-----------------------|--|

Reporting group description:

Participants were treated with oral itacitinib 300 mg twice daily (BID) + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). The itacitinib dose could have been decreased to 200 mg BID if a boundary was reached during safety run-in. This treatment group was discontinued due to concern of a potential increase in relapse rate. Participants in this treatment group who were ongoing were allowed to reduce to 400 mg QD plus CS. Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Part 1 Expansion: CS monotherapy |
|-----------------------|----------------------------------|

Reporting group description:

Participants were treated with CS alone. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|----------------------------|--|
| Subject analysis set title | Parts 1 and 1 Expansion; PK Analysis: 100 mg QD + CS |
|----------------------------|--|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

For toxicity management purposes and/or due to coadministration of strong CYP3A4 inhibitors, participants who received a starting dose of itacitinib 200 mg or 300 mg QD + CS in Part 1 and a starting dose of itacitinib 300 mg or 400 mg QD + CS in Part 1 Expansion had first or second dose reductions to itacitinib 100 mg QD + CS and/or dose interruptions.

| | |
|----------------------------|---|
| Subject analysis set title | Parts 1 and 1 Expansion; PK Analysis: itacitinib 200 mg QD+CS |
|----------------------------|---|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants were treated with a starting dose of oral itacitinib 200 mg QD + CS in Part 1 or had a dose reduction to oral itacitinib 200 mg QD + CS in Part 1 or Part 1 Expansion. CS were given at a starting

dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). For toxicity management purposes and/or due to coadministration of strong CYP3A4 inhibitors, participants who received a starting dose of itacitinib 300 mg QD + CS in Part 1 and a starting dose of itacitinib 300 mg or 400 mg QD + CS in Part 1 Expansion had first or second dose reductions to itacitinib 200 mg QD + CS and/or dose interruptions.

| | |
|----------------------------|---|
| Subject analysis set title | Parts 1 and 1 Expansion; PK Analysis: itacitinib 300 mg QD+CS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants were treated with a starting dose of oral itacitinib 300 mg QD + CS in Part 1 or Part 1 Expansion or had a dose reduction to oral itacitinib 300 mg QC + CS in Part 1 Expansion. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (chronic graft-versus-host disease [cGVHD] progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months. For toxicity management purposes and/or due to coadministration of strong CYP3A4 inhibitors, participants who received a starting dose of itacitinib 400 mg QD + CS in Part 1 Expansion had a dose reduction to itacitinib 300 mg QD + CS and/or dose interruptions.

| | |
|----------------------------|--|
| Subject analysis set title | Part 1 Expansion; PK Analysis: itacitinib 400 mg QD + CS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants were treated with oral itacitinib 400 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months. This group also included participants who originally received itacitinib 300 mg BID + CS but were ongoing at the time the 300 mg BID + CS treatment group was discontinued due to concern of a potential increase in relapse rate. At the time of discontinuation of the itacitinib 300 mg BID + CS treatment arm, participants reduced to itacitinib 400 mg QD + CS.

| | |
|----------------------------|---|
| Subject analysis set title | Part 1 Expansion; PK Analysis: itacitinib 100 mg BID + CS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

For toxicity management purposes and/or due to coadministration of strong CYP3A4 inhibitors, participants who received a starting dose of itacitinib 300 mg BID + CS in Part 1 Expansion had first or second dose reductions to itacitinib 100 mg BID + CS and/or dose interruptions.

| | |
|----------------------------|---|
| Subject analysis set title | Part 1 Expansion; PK Analysis: itacitinib 200 mg BID + CS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants were treated with a starting dose of oral itacitinib 300 mg BID + CS in Part 1 Expansion and had their dose decreased to itacitinib 200 mg BID + CS because a boundary was reached during safety run-in or for toxicity management purposes and/or due to coadministration of strong CYP3A4 inhibitors. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months. For toxicity management purposes and/or due to coadministration of strong CYP3A4 inhibitors, participants who received a starting dose of itacitinib 300 mg BID + CS in Part 1 Expansion had a dose reduction to itacitinib 200 mg BID + CS and/or dose interruptions.

| | |
|----------------------------|---|
| Subject analysis set title | Part 1 Expansion; PK Analysis: itacitinib 300 mg BID + CS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants were treated with oral itacitinib 300 mg BID + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). The itacitinib dose could have been decreased to 200 mg BID if a boundary was reached during safety run-in. This treatment group was discontinued due to concern of a potential increase in relapse rate. Participants in this treatment group who were ongoing were allowed to reduce to 400 mg QD + CS. Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

Primary: Part 1: Number of participants with dose-limiting toxicities (DLTs)

| | |
|-----------------|---|
| End point title | Part 1: Number of participants with dose-limiting toxicities (DLTs) ^{[1][2]} |
|-----------------|---|

End point description:

A DLT was defined as the occurrence of any protocol-defined toxicity with onset up to and including Day 28, except those with a clear alternative explanation. Participants who received at least 21 of 28 doses of study drug at the level assigned or had a DLT were considered evaluable for determining tolerability of the dose. Participants who did not achieve this duration of exposure and did not have a DLT were to be replaced for purposes of toxicity identification.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

up to Day 28

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1: itacitinib 200 mg QD + CS | Part 1: itacitinib 300 mg QD + CS | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 10 | | |
| Units: participants | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 Expansion: Number of participants with any treatment-emergent adverse event (TEAE)

| | |
|-----------------|---|
| End point title | Part 1 Expansion: Number of participants with any treatment-emergent adverse event (TEAE) ^{[3][4]} |
|-----------------|---|

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

until at least 30 days after the last dose of study treatment (up to 1103 days)

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 39 | 29 | 36 |
| Units: participants | 34 | 38 | 28 | 32 |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Response rate at Months 3 and 6

| | |
|-----------------|--|
| End point title | Part 1 Expansion: Response rate at Months 3 and 6 ^[5] |
|-----------------|--|

End point description:

Response rate was defined as the percentage of participants that had CR or PR, per NIH Consensus Criteria, as determined by the investigator, within 14 days of the post-Baseline visit date until new anti-GVHD therapy or overall response-progression or relapse/progression of underlying disease. CR was defined as the complete resolution of all signs and symptoms of cGvHD in all evaluable organs. PR was defined as an improvement in at least one organ without progression in other organs.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 3 and 6

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 39 | 29 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Month 3 | 60.0 (42.1 to 76.1) | 69.2 (52.4 to 83.0) | 58.6 (38.9 to 76.5) | 50.0 (32.9 to 67.1) |
| Month 6 | 42.9 (26.3 to 60.6) | 53.8 (37.2 to 69.9) | 34.5 (17.9 to 54.3) | 36.1 (20.8 to 53.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 1 Expansion: Cmax of itacitinib

| | |
|-----------------|---|
| End point title | Parts 1 and 1 Expansion: Cmax of itacitinib |
|-----------------|---|

End point description:

Cmax was defined as the maximum observed concentration of itacitinib. 9999=Mean (SD) data cannot be reported for a single participant due to privacy concerns. 8888=Analysis was not conducted at this time point. Pharmacokinetic (PK) Evaluable Population: all participants who received at least 1 dose of

study drug and/or reference therapy and provided at least 1 corresponding post-dose plasma sample (1 PK measurement). Because Part 1 and Part 1 Expansion were both randomized, open label, and had a parallel design with the same participant population criteria, as pre-specified, the PK data for identical doses/frequency of dosing were grouped for analysis (rather than conducting analysis by treatment arm).

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Days 1, 7, and 28: predose and 1, 2, and 5 hours post-dose | |

| End point values | Parts 1 and 1 Expansion; PK Analysis: 100 mg QD + CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 200 mg QD+CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 300 mg QD+CS | Part 1 Expansion; PK Analysis: itacitinib 400 mg QD + CS |
|---|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 3 ^[6] | 27 ^[7] | 35 ^[8] | 26 ^[9] |
| Units: nanomoles per Liter (nmol/L) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 9999 (± 9999) | 655 (± 82.9) | 1050 (± 87.3) | 951 (± 68.0) |
| Day 7, n=1, 27, 32, 26, 0 14, 12 | 9999 (± 9999) | 1070 (± 88.9) | 1580 (± 125) | 1190 (± 103) |
| Day 28, n=3, 26, 27, 21, 3, 8, 10 | 486 (± 140) | 1460 (± 67.3) | 1290 (± 248) | 1350 (± 72.2) |

Notes:

[6] - PK Evaluable Population

[7] - PK Evaluable Population

[8] - PK Evaluable Population

[9] - PK Evaluable Population

| End point values | Part 1 Expansion; PK Analysis: itacitinib 100 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 200 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 300 mg BID + CS | |
|---|---|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 ^[10] | 14 ^[11] | 16 ^[12] | |
| Units: nanomoles per Liter (nmol/L) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 8888 (± 8888) | 769 (± 118) | 736 (± 79.1) | |
| Day 7, n=1, 27, 32, 26, 0 14, 12 | 8888 (± 8888) | 1520 (± 73.0) | 1110 (± 66.2) | |
| Day 28, n=3, 26, 27, 21, 3, 8, 10 | 1350 (± 29.4) | 2040 (± 62.6) | 1580 (± 51.4) | |

Notes:

[10] - PK Evaluable Population

[11] - PK Evaluable Population

[12] - PK Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 1 Expansion: Ctau of itacitinib

| | |
|-----------------|---|
| End point title | Parts 1 and 1 Expansion: Ctau of itacitinib |
|-----------------|---|

End point description:

Ctau was defined as the trough concentration of itacitinib over the dose interval. 9999=Mean (SD) data cannot be reported for a single participant due to privacy concerns. 8888=Analysis was not conducted at this time point. 7777=It was not possible to calculate the data value from PK bioavailability data due to an insufficient number of terminal PK bioavailability endpoints (after Cmax). Because Part I and Part I Expansion were both randomized, open label, and had a parallel design with the same participant population criteria, as pre-specified, the PK data for identical doses/frequency of dosing were grouped for analysis (rather than conducting analysis by treatment arm).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Days 1, 7, and 28: predose and 1, 2, and 5 hours post-dose

| End point values | Parts 1 and 1 Expansion; PK Analysis: 100 mg QD + CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 200 mg QD+CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 300 mg QD+CS | Part 1 Expansion; PK Analysis: itacitinib 400 mg QD + CS |
|---|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 3 ^[13] | 27 ^[14] | 35 ^[15] | 26 ^[16] |
| Units: nmol/L | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 8888 (± 8888) | 8888 (± 8888) | 0.153 (± 7777) | 135 (± 197) |
| Day 7, n=1, 27, 31, 24, 0, 14, 12 | 9999 (± 9999) | 53.6 (± 218) | 52.2 (± 425) | 33.5 (± 118) |
| Day 28, n=3, 26, 26, 20, 3, 8, 10 | 10.4 (± 4440) | 68.0 (± 314) | 42.2 (± 182) | 29.7 (± 152) |

Notes:

[13] - PK Evaluable Population

[14] - PK Evaluable Population

[15] - PK Evaluable Population

[16] - PK Evaluable Population

| End point values | Part 1 Expansion; PK Analysis: itacitinib 100 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 200 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 300 mg BID + CS | |
|---|---|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 ^[17] | 14 ^[18] | 16 ^[19] | |
| Units: nmol/L | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 8888 (± 8888) | 7.54 (± 7777) | 8888 (± 8888) | |
| Day 7, n=1, 27, 31, 24, 0, 14, 12 | 8888 (± 8888) | 483 (± 175) | 127 (± 177) | |
| Day 28, n=3, 26, 26, 20, 3, 8, 10 | 392 (± 85.6) | 460 (± 123) | 195 (± 116) | |

Notes:

[17] - PK Evaluable Population

[18] - PK Evaluable Population

[19] - PK Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 1 Expansion: tmax of itacitinib

| | |
|------------------------|--|
| End point title | Parts 1 and 1 Expansion: tmax of itacitinib |
| End point description: | tmax was defined as the time to the maximum concentration of itacitinib. 9999=Mean (SD) data cannot be reported for a single participant due to privacy concerns. 8888=Analysis was not conducted at this time point. Because Part I and Part I Expansion were both randomized, open label, and had a parallel design with the same participant population criteria, as pre-specified, the PK data for identical doses/frequency of dosing were grouped for analysis (rather than conducting analysis by treatment arm). |
| End point type | Secondary |
| End point timeframe: | Days 1, 7, and 28: predose and 1, 2, and 5 hours post-dose |

| End point values | Parts 1 and 1 Expansion; PK Analysis: 100 mg QD + CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 200 mg QD+CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 300 mg QD+CS | Part 1 Expansion; PK Analysis: itacitinib 400 mg QD + CS |
|-----------------------------------|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 3 ^[20] | 27 ^[21] | 35 ^[22] | 26 ^[23] |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 9999 (9999 to 9999) | 2.1 (0.9 to 4.8) | 2.1 (0.8 to 5.0) | 2.0 (0.0 to 5.0) |
| Day 7, n=1, 27, 32, 26, 0, 14, 12 | 9999 (9999 to 9999) | 2.1 (0.0 to 5.0) | 2.0 (1.0 to 13.4) | 2.0 (1.0 to 5.2) |
| Day 28, n=3, 26, 27, 21, 3, 8, 10 | 4.0 (1.0 to 4.8) | 3.1 (0.8 to 12.0) | 2.0 (0.0 to 16.9) | 2.1 (0.9 to 5.0) |

Notes:

[20] - PK Evaluable Population

[21] - PK Evaluable Population

[22] - PK Evaluable Population

[23] - PK Evaluable Population

| End point values | Part 1 Expansion; PK Analysis: itacitinib 100 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 200 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 300 mg BID + CS | |
|-----------------------------------|---|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 ^[24] | 14 ^[25] | 16 ^[26] | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 8888 (8888 to 8888) | 2.0 (1.0 to 5.0) | 2.4 (1.0 to 5.0) | |
| Day 7, n=1, 27, 32, 26, 0, 14, 12 | 8888 (8888 to 8888) | 1.9 (0.0 to 10.7) | 2.0 (0.9 to 5.0) | |
| Day 28, n=3, 26, 27, 21, 3, 8, 10 | 2.0 (2.0 to 2.2) | 2.3 (2.0 to 5.6) | 2.0 (1.0 to 5.0) | |

Notes:

[24] - PK Evaluable Population

[25] - PK Evaluable Population

[26] - PK Evaluable Population

Statistical analyses

Secondary: Parts 1 and 1 Expansion: Cl/F of itacitinib

| | |
|-----------------|---|
| End point title | Parts 1 and 1 Expansion: Cl/F of itacitinib |
|-----------------|---|

End point description:

Cl/F was defined as the apparent oral dose clearance of itacitinib. 9999=Mean (SD) data cannot be reported for a single participant due to privacy concerns. 8888=Analysis was not conducted at this time point. 7777=It was not possible to calculate the data value from PK bioavailability data due to an insufficient number of terminal PK bioavailability endpoints (after C_{max}). Because Part I and Part I Expansion were both randomized, open label, and had a parallel design with the same participant population criteria, as pre-specified, the PK data for identical doses/frequency of dosing were grouped for analysis (rather than conducting analysis by treatment arm).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Days 1, 7, and 28: predose and 1, 2, and 5 hours post-dose

| End point values | Parts 1 and 1 Expansion; PK Analysis: 100 mg QD + CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 200 mg QD+CS | Parts 1 and 1 Expansion; PK Analysis: itacitinib 300 mg QD+CS | Part 1 Expansion; PK Analysis: itacitinib 400 mg QD + CS |
|---|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 3 ^[27] | 27 ^[28] | 35 ^[29] | 26 ^[30] |
| Units: Liters per hour | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 8888 (± 8888) | 8888 (± 8888) | 258 (± 7777) | 41.2 (± 130) |
| Day 7, n=1, 27, 31, 24, 0, 14, 12 | 9999 (± 9999) | 43.0 (± 105) | 48.9 (± 159) | 85.9 (± 90.7) |
| Day 28, n=3, 26, 26, 20, 3, 8, 10 | 47.7 (± 211) | 30.0 (± 96.9) | 54.8 (± 189) | 81.0 (± 65.1) |

Notes:

[27] - PK Evaluable Population

[28] - PK Evaluable Population

[29] - PK Evaluable Population

[30] - PK Evaluable Population

| End point values | Part 1 Expansion; PK Analysis: itacitinib 100 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 200 mg BID + CS | Part 1 Expansion; PK Analysis: itacitinib 300 mg BID + CS | |
|---|---|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 ^[31] | 14 ^[32] | 16 ^[33] | |
| Units: Liters per hour | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1, n=1, 23, 35, 26, 0, 12, 16 | 8888 (± 8888) | 640 (± 7777) | 8888 (± 8888) | |
| Day 7, n=1, 27, 31, 24, 0, 14, 12 | 8888 (± 8888) | 31.8 (± 82.9) | 94.4 (± 61.3) | |
| Day 28, n=3, 26, 26, 20, 3, 8, 10 | 20.2 (± 54.2) | 26.9 (± 75.5) | 67.5 (± 62.1) | |

Notes:

[31] - PK Evaluable Population

[32] - PK Evaluable Population

[33] - PK Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Response rate at Months 3, 6, and 12

End point title | Part 1: Response rate at Months 3, 6, and 12^[34]

End point description:

Response rate was defined as the percentage of participants that had CR or PR, per NIH Consensus Criteria, as determined by the investigator, within 14 days of the post-Baseline visit date until new anti-GVHD therapy or overall response-progression or relapse/progression of underlying disease. CR was defined as the complete resolution of all signs and symptoms of cGvHD in all evaluable organs. PR was defined as an improvement in at least one organ without progression in other organs.

End point type | Secondary

End point timeframe:

Months 3, 6, and 12

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1: itacitinib 200 mg QD + CS | Part 1: itacitinib 300 mg QD + CS | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 10 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Month 3 | 63.6 (30.8 to 89.1) | 50.0 (18.7 to 81.3) | | |
| Month 6 | 36.4 (10.9 to 69.2) | 50.0 (18.7 to 81.3) | | |
| Month 12 | 18.2 (2.3 to 51.8) | 20.0 (2.5 to 55.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Response rate at Month 12

End point title | Part 1 Expansion: Response rate at Month 12^[35]

End point description:

Response rate was defined as the percentage of participants that had CR or PR, per NIH Consensus Criteria, as determined by the investigator, within 14 days of the post-Baseline visit date until new anti-GVHD therapy or overall response-progression or relapse/progression of underlying disease. CR was defined as the complete resolution of all signs and symptoms of cGvHD in all evaluable organs. PR was defined as an improvement in at least one organ without progression in other organs.

End point type | Secondary

End point timeframe:

Month 12

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 39 | 29 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 22.9 (10.4 to 40.1) | 41.0 (25.6 to 57.9) | 24.1 (10.3 to 43.5) | 19.4 (8.2 to 36.0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Time to response

| | |
|------------------------|--|
| End point title | Part 1 Expansion: Time to response ^[36] |
| End point description: | Time to response was defined as the interval between randomization and the first response (CR or PR) before initiation of new therapy. CR was defined as the complete resolution of all signs and symptoms of cGvHD in all evaluable organs. PR was defined as an improvement in at least one organ without progression in other organs. |
| End point type | Secondary |
| End point timeframe: | up to Month 12 |

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 31 | 25 | 26 |
| Units: days | | | | |
| median (full range (min-max)) | 16.0 (12 to 120) | 16.0 (12 to 86) | 16.0 (13 to 145) | 16.0 (13 to 88) |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Duration of response

| | |
|-----------------|--|
| End point title | Part 1 Expansion: Duration of response ^[37] |
|-----------------|--|

End point description:

Duration to response was defined as the interval between the first response and cGVHD progression, death, or the initiation of a new systemic cGVHD therapy. 9999=the median and the upper limit of the confidence interval were not estimable because too few participants had disease progression or died or initiated new systemic cGVHD therapy.

End point type Secondary

End point timeframe:

up to 24 months

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 31 | 25 | 26 |
| Units: days | | | | |
| median (confidence interval 95%) | 581.0 (147.0 to 807.0) | 9999 (306.0 to 9999) | 512.0 (161.0 to 9999) | 197.0 (103.0 to 9999) |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Overall survival

End point title Part 1 Expansion: Overall survival^[38]

End point description:

Overall survival was defined as the interval between the date of randomization and the date of death due to any cause. -9999, 9999=the median and the upper and lower limits of the confidence interval were not estimable because too few participants died.

End point type Secondary

End point timeframe:

up to 36 months

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 39 | 29 | 36 |
| Units: days | | | | |
| median (confidence interval 95%) | 9999 (694.0 to 9999) | 9999 (-9999 to 9999) | 9999 (-9999 to 9999) | 9999 (-9999 to 9999) |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Percentage of participants with a $\geq 50\%$ reduction in daily corticosteroid dose at Day 180 from the corticosteroid dose on Day 1

| | |
|-----------------|---|
| End point title | Part 1 Expansion: Percentage of participants with a $\geq 50\%$ reduction in daily corticosteroid dose at Day 180 from the corticosteroid dose on Day 1 ^[39] |
|-----------------|---|

End point description:

The corticosteroid dose at Day 180 was compared to the corticosteroid dose on Day 1 to assess reduction.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1; Day 180

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 27 | 17 | 18 |
| Units: percentage of participants | | | | |
| number (not applicable) | 90.5 | 100.0 | 100.0 | 100.0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Percentage of participants successfully tapered off all corticosteroids at Day 180

| | |
|-----------------|--|
| End point title | Part 1 Expansion: Percentage of participants successfully tapered off all corticosteroids at Day 180 ^[40] |
|-----------------|--|

End point description:

The percentage of participants who were not taking any corticosteroids at Day 180 was assessed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 180

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 27 | 17 | 18 |
| Units: percentage of participants | | | | |
| number (not applicable) | 52.4 | 66.7 | 47.1 | 44.4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Nonrelapse mortality (NRM) rate

End point title | Part 1 Expansion: Nonrelapse mortality (NRM) rate^[41]

End point description:

NRM was defined as the percentage of participants who died due to causes other than a relapse of their primary hematologic disease.

End point type | Secondary

End point timeframe:

up to 24 months

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 37 | 28 | 35 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 25.7 (12.5 to 43.3) | 15.4 (6.2 to 32.0) | 10.3 (2.3 to 28.2) | 11.1 (3.2 to 26.7) |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Time to primary hematologic disease relapse

End point title | Part 1 Expansion: Time to primary hematologic disease

End point description:

Time to primary hematologic disease relapse was defined as the interval between the date of randomization and the date of relapse. -9999, 9999=the median and the upper and lower limits of the confidence interval were not estimable because too few participants relapsed.

End point type Secondary

End point timeframe:

up to 24 months

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 3 | 4 | 1 |
| Units: days | | | | |
| median (confidence interval 95%) | 9999 (-9999 to 9999) | 9999 (-9999 to 9999) | 9999 (-9999 to 9999) | 9999 (-9999 to 9999) |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 Expansion: Relapse rate of malignant and nonmalignant hematologic diseases

End point title Part 1 Expansion: Relapse rate of malignant and nonmalignant hematologic diseases^[43]

End point description:

The relapse rate was defined as percentage of participants whose underlying disease relapsed at any time during the course of the study.

End point type Secondary

End point timeframe:

up to 1073 days

Notes:

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

Justification: Statistical analysis was not conducted for this endpoint.

| End point values | Part 1 Expansion: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: CS monotherapy |
|-----------------------------------|---|---|--|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 39 | 29 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 5.7 (0.7 to 19.2) | 7.7 (1.6 to 20.9) | 13.8 (3.9 to 31.7) | 2.8 (0.1 to 14.5) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

until at least 30 days after the last dose of study treatment (up to 1103 days)

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs), defined as any adverse events either reported for the first time or the worsening of pre-existing events after the first dose of study drug, have been reported.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: itacitinib 200 mg QD + CS |
|-----------------------|-----------------------------------|

Reporting group description:

Participants were treated with oral itacitinib 200 milligrams (mg) once daily (QD) + corticosteroids (CS) for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kilogram (kg) QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (chronic graft-versus-host disease [cGVHD] progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: itacitinib 300 mg QD + CS |
|-----------------------|-----------------------------------|

Reporting group description:

Participants were treated with oral itacitinib 300 mg QD + CS for a maximum of 36 months. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|---|
| Reporting group title | Part 1 Expansion: itacitinib 300 mg QD + CS |
|-----------------------|---|

Reporting group description:

Participants were treated with oral itacitinib 300 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|---|
| Reporting group title | Part 1 Expansion: itacitinib 400 mg QD + CS |
|-----------------------|---|

Reporting group description:

Participants were treated with oral itacitinib 400 mg QD + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|--|
| Reporting group title | Part 1 Expansion: itacitinib 300 mg BID + CS |
|-----------------------|--|

Reporting group description:

Participants were treated with oral itacitinib 300 mg twice daily (BID) + CS. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD (prednisone or methylprednisolone equivalent to prednisone dose). The itacitinib dose could have been decreased to 200 mg BID if a boundary was reached during safety run-in. This treatment group was discontinued due to concern of a potential increase in relapse rate. Participants in this treatment group who were ongoing were allowed to reduce to 400 mg QD plus CS. Itacitinib treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| | |
|-----------------------|-------------------------|
| Reporting group title | Part 1 Expansion: Total |
|-----------------------|-------------------------|

Reporting group description:

Participants received 300 mg QD, 400 mg QD, or 300 mg BID itacitinib plus corticosteroids.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Part 1 Expansion: CS monotherapy |
|-----------------------|----------------------------------|

Reporting group description:

Participants were treated with CS alone. CS were given at a starting dose of 0.5 to 1.0 mg/kg QD

(prednisone or methylprednisolone equivalent to prednisone dose). Treatment was to continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months.

| Serious adverse events | Part 1: itacitinib 200 mg QD + CS | Part 1: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 300 mg QD + CS |
|---|-----------------------------------|-----------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 11 (54.55%) | 5 / 10 (50.00%) | 18 / 35 (51.43%) |
| number of deaths (all causes) | 2 | 3 | 9 |
| number of deaths resulting from adverse events | 1 | 1 | 3 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Small cell lung cancer | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 limb pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Venoocclusive disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Malaise | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Oedema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Physical deconditioning | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (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 |
| Bronchiolitis obliterans syndrome | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Psychiatric decompensation subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood lactic acid increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| International normalised ratio increased | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 | | | |
| Bundle branch block left | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 failure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|----------------|
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (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 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic neuritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Eye disorders | | | |
| Blindness unilateral | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Retinal vein occlusion | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (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 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Colitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Oesophagitis | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Hepatobiliary disorders | | | |
| Hepatic fibrosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver injury | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Cystitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Dysuria | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (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 | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Myositis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|----------------|-----------------|----------------|
| Bronchopulmonary aspergillosis subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Clostridial sepsis subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Clostridium difficile colitis subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Cytomegalovirus infection reactivation subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Cytomegalovirus infection subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis viral subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Cytomegalovirus oesophagitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis Escherichia coli | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Herpes zoster cutaneous disseminated | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parainfluenzae virus infection | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 fungal | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Respiratory syncytial virus infection | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonella sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (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 |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Urinary tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection viral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Food intolerance | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|-------------------------------|-------------------|-------------------|-------------------|
| Serious adverse events | Part 1 Expansion: | Part 1 Expansion: | Part 1 Expansion: |
|-------------------------------|-------------------|-------------------|-------------------|

| | itacitinib 400 mg QD + CS | itacitinib 300 mg BID + CS | Total |
|---|------------------------------|-------------------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 39 (56.41%) | 12 / 29 (41.38%) | 52 / 103 (50.49%) |
| number of deaths (all causes) | 8 | 4 | 21 |
| number of deaths resulting from adverse events | 4 | 1 | 8 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Small cell lung cancer | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic limb pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Venooclusive disease | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Catheter site inflammation | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Physical deconditioning | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 0 / 29 (0.00%) | 4 / 103 (3.88%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Bronchiolitis obliterans syndrome | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric decompensation | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |

| | | | |
|---|----------------|----------------|-----------------|
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood lactic acid increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|----------------|----------------|-----------------|
| SARS-CoV-2 test positive subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Lumbar vertebral fracture subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thoracic vertebral fracture subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Bundle branch block left subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic neuritis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 29 (3.45%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Blindness unilateral | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal vein occlusion | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------|----------------|-----------------|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 3 / 103 (2.91%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 3 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal haemorrhage | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Colitis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 29 (3.45%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 29 (3.45%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatic fibrosis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver injury | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Cystitis haemorrhagic | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Myositis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 29 (6.90%) | 6 / 103 (5.83%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 1 / 6 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |

| | | | |
|---|----------------|----------------|-----------------|
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridial sepsis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus infection reactivation | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis viral | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus oesophagitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia bacteraemia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis Escherichia coli | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster cutaneous disseminated | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 2 / 29 (6.90%) | 9 / 103 (8.74%) |
| occurrences causally related to treatment / all | 2 / 5 | 1 / 2 | 4 / 10 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Pneumonia parainfluenzae viral | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 3 / 103 (2.91%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 29 (3.45%) | 3 / 103 (2.91%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonella sepsis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic infection | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 2 / 103 (1.94%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection viral | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Food intolerance | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-------------------------------------|--|--|
| Serious adverse events | Part 1 Expansion: CS monotherapy | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 36 (25.00%) | | |
| number of deaths (all causes) | 5 | | |
| number of deaths resulting from adverse events | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Small cell lung cancer | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic limb pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venoocclusive disease | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Malaise | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Physical deconditioning | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchiolitis obliterans syndrome | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric decompensation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Aspartate aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood bilirubin increased | | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood lactic acid increased | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gamma-glutamyltransferase increased | | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| International normalised ratio increased | | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Platelet count decreased | | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| SARS-CoV-2 test positive | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Injury, poisoning and procedural complications | | | | |
| Lumbar vertebral fracture | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Bundle branch block left | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Optic neuritis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Blindness unilateral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal vein occlusion | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal haemorrhage | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatic fibrosis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Liver injury | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Night sweats | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Cystitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 36 (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 | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Myalgia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myositis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clostridial sepsis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clostridium difficile colitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytomegalovirus infection reactivation | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cystitis viral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytomegalovirus oesophagitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis Escherichia coli | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Herpes zoster cutaneous disseminated | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia cytomegaloviral | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Salmonella sepsis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal sepsis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Systemic infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection viral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Failure to thrive | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Food intolerance | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Part 1: itacitinib 200 mg QD + CS | Part 1: itacitinib 300 mg QD + CS | Part 1 Expansion: itacitinib 300 mg QD + CS |
|---|-----------------------------------|-----------------------------------|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 11 (100.00%) | 10 / 10 (100.00%) | 33 / 35 (94.29%) |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 2 / 10 (20.00%) | 6 / 35 (17.14%) |
| occurrences (all) | 2 | 3 | 6 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 0 | 3 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Microangiopathy subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 4 / 35 (11.43%) 5 |
| Chest discomfort subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Fatigue subjects affected / exposed occurrences (all) | 4 / 11 (36.36%) 4 | 2 / 10 (20.00%) 3 | 6 / 35 (17.14%) 7 |
| Influenza like illness subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Oedema subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 0 / 10 (0.00%) 0 | 6 / 35 (17.14%) 6 |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 1 / 10 (10.00%) 1 | 4 / 35 (11.43%) 6 |
| Immune system disorders | | | |
| Seasonal allergy subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Reproductive system and breast disorders | | | |
| Breast pain subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Vulvovaginal dryness subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 3 | 1 / 10 (10.00%) 1 | 5 / 35 (14.29%) 7 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 1 / 10 (10.00%) 1 | 2 / 35 (5.71%) 2 |
| Productive cough subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Pulmonary oedema subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 35 (0.00%) 0 |
| Depression | | | |

| | | | |
|---------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 10 (10.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 1 | 1 | 3 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 5 / 35 (14.29%) |
| occurrences (all) | 0 | 2 | 7 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 10 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 5 | 0 | 5 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 3 | 1 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 2 / 10 (20.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 3 | 2 | 3 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 2 / 10 (20.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 6 | 2 | 3 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium increased | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Blood sodium decreased subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Blood triglycerides increased subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Cytomegalovirus test positive subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 35 (0.00%) 0 |
| Drug level increased subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 2 / 10 (20.00%) 2 | 3 / 35 (8.57%) 3 |
| Haemoglobin increased subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Liver function test increased subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Platelet count decreased subjects affected / exposed occurrences (all) | 5 / 11 (45.45%) 5 | 3 / 10 (30.00%) 3 | 6 / 35 (17.14%) 6 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Weight increased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 2 / 35 (5.71%) 2 |
| Fall subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 3 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 3 |
| Limb injury subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Tooth fracture subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Wound subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 2 / 35 (5.71%) 2 |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 3 / 35 (8.57%) 3 |
| Bradycardia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Cardiac failure subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Tachycardia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 4 / 35 (11.43%) 5 |
| Nervous system disorders | | | |
| Balance disorder subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |

| | | | |
|--------------------------------------|-----------------|-----------------|------------------|
| Dizziness | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 1 | 3 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Headache | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 2 / 10 (20.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 2 | 2 | 2 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 1 | 2 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Presyncope | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 2 |
| Tremor | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 2 / 10 (20.00%) | 14 / 35 (40.00%) |
| occurrences (all) | 4 | 2 | 18 |
| Febrile neutropenia | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 0 | 3 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 4 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 5 / 35 (14.29%) |
| occurrences (all) | 0 | 0 | 8 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 10 (20.00%) | 8 / 35 (22.86%) |
| occurrences (all) | 2 | 2 | 9 |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cataract | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Cataract nuclear | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Dry eye | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Lacrimation increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 1 | 2 |

| | | | |
|----------------------------------|----------------|-----------------|-----------------|
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 1 | 0 | 3 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 6 / 35 (17.14%) |
| occurrences (all) | 0 | 0 | 6 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 4 / 35 (11.43%) |
| occurrences (all) | 0 | 1 | 4 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 10 (20.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 3 | 4 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 4 / 10 (40.00%) | 6 / 35 (17.14%) |
| occurrences (all) | 1 | 5 | 6 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 10 (20.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 2 | 3 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 1 | 2 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |

| | | | |
|--|---------------------|----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 10 (10.00%) 1 | 8 / 35 (22.86%) 10 |
| Paraesthesia oral subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 4 / 35 (11.43%) 6 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 10 (10.00%) 1 | 0 / 35 (0.00%) 0 |
| Dermatitis atopic subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Dermatitis contact subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 3 / 10 (30.00%) 3 | 3 / 35 (8.57%) 3 |
| Nail ridging subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Rash subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Skin exfoliation subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 1 / 35 (2.86%) 1 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 2 / 10 (20.00%) 2 | 3 / 35 (8.57%) 3 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 35 (0.00%) 0 |
| Renal failure subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 1 / 10 (10.00%) 1 | 0 / 35 (0.00%) 0 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 35 (0.00%) 0 |
| Endocrine disorders Cushingoid subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 1 / 10 (10.00%) 1 | 3 / 35 (8.57%) 3 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Muscular weakness subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 3 | 4 / 10 (40.00%) 4 | 5 / 35 (14.29%) 5 |
| Neck pain | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 1 | 2 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Osteoporosis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tendon pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 1 | 3 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 4 / 35 (11.43%) |
| occurrences (all) | 0 | 0 | 4 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Cytomegalovirus viraemia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 2 | 0 | 1 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 1 | 0 | 3 |

| | | | |
|---|-----------------|-----------------|----------------|
| Cytomegalovirus infection reactivation | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 10 (10.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 2 | 1 | 6 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Epstein-Barr virus infection reactivation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 0 | 3 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 10 (20.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Respiratory tract infection | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 0 | 3 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 3 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 1 | 1 | 2 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 4 / 35 (11.43%) |
| occurrences (all) | 0 | 0 | 4 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| Hyperglycaemia | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 10 (0.00%) | 4 / 35 (11.43%) |
| occurrences (all) | 3 | 0 | 4 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 3 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 1 | 1 | 2 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 4 / 35 (11.43%) |
| occurrences (all) | 0 | 0 | 4 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 5 / 35 (14.29%) |
| occurrences (all) | 0 | 1 | 9 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 5 / 35 (14.29%) |
| occurrences (all) | 0 | 1 | 8 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 1 | 2 |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |

| Non-serious adverse events | Part 1 Expansion: itacitinib 400 mg QD + CS | Part 1 Expansion: itacitinib 300 mg BID + CS | Part 1 Expansion: Total |
|---|---|--|----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 37 / 39 (94.87%) | 27 / 29 (93.10%) | 97 / 103 (94.17%) |
| Vascular disorders | | | |

| | | | |
|--|----------------------|-----------------------|-------------------------|
| Deep vein thrombosis subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| Hot flush subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 3 / 29 (10.34%) 3 | 4 / 103 (3.88%) 4 |
| Hypertension subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 8 | 9 / 29 (31.03%) 10 | 22 / 103 (21.36%) 24 |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 1 | 4 / 103 (3.88%) 4 |
| Microangiopathy subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 2 | 2 / 29 (6.90%) 2 | 7 / 103 (6.80%) 9 |
| Chest discomfort subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| Fatigue subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 8 | 4 / 29 (13.79%) 4 | 17 / 103 (16.50%) 19 |
| Influenza like illness subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 29 (6.90%) 5 | 2 / 103 (1.94%) 5 |
| Oedema subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 29 (6.90%) 2 | 4 / 103 (3.88%) 4 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 6 / 29 (20.69%) 7 | 17 / 103 (16.50%) 18 |
| Pyrexia | | | |

| | | | |
|--|----------------------|----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 6 | 6 / 29 (20.69%) 6 | 15 / 103 (14.56%) 18 |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Erectile dysfunction subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Vulvovaginal dryness subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 4 | 2 / 29 (6.90%) 2 | 6 / 103 (5.83%) 6 |
| Dyspnoea subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 1 / 29 (3.45%) 1 | 8 / 103 (7.77%) 10 |
| Epistaxis subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 3 / 29 (10.34%) 5 | 5 / 103 (4.85%) 7 |
| Nasal congestion subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| Productive cough | | | |

| | | | |
|---|-----------------------|-----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Pulmonary oedema subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 1 / 29 (3.45%) 1 | 4 / 103 (3.88%) 4 |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Insomnia subjects affected / exposed occurrences (all) | 8 / 39 (20.51%) 8 | 4 / 29 (13.79%) 5 | 15 / 103 (14.56%) 16 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 6 / 39 (15.38%) 14 | 6 / 29 (20.69%) 10 | 17 / 103 (16.50%) 31 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 6 | 2 / 29 (6.90%) 4 | 9 / 103 (8.74%) 15 |
| Blood phosphorus decreased subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 1 / 29 (3.45%) 1 | 3 / 103 (2.91%) 3 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 1 / 29 (3.45%) 1 | 4 / 103 (3.88%) 4 |
| Blood cholesterol increased | | | |

| | | | |
|---------------------------------------|-----------------|-----------------|-------------------|
| subjects affected / exposed | 4 / 39 (10.26%) | 4 / 29 (13.79%) | 11 / 103 (10.68%) |
| occurrences (all) | 5 | 4 | 12 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 3 / 29 (10.34%) | 10 / 103 (9.71%) |
| occurrences (all) | 7 | 5 | 15 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 29 (3.45%) | 3 / 103 (2.91%) |
| occurrences (all) | 1 | 1 | 3 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 29 (6.90%) | 2 / 103 (1.94%) |
| occurrences (all) | 0 | 2 | 2 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Cytomegalovirus test positive | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 1 | 0 | 1 |
| Drug level increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 1 / 29 (3.45%) | 6 / 103 (5.83%) |
| occurrences (all) | 6 | 2 | 9 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 3 / 103 (2.91%) |
| occurrences (all) | 0 | 0 | 3 |
| Haemoglobin increased | | | |

| | | | |
|---|----------------------|-----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Liver function test increased subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 3 | 1 / 29 (3.45%) 1 | 3 / 103 (2.91%) 4 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 5 | 0 / 29 (0.00%) 0 | 4 / 103 (3.88%) 5 |
| Platelet count decreased subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 7 | 9 / 29 (31.03%) 11 | 22 / 103 (21.36%) 24 |
| Weight increased subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 1 / 29 (3.45%) 1 | 4 / 103 (3.88%) 4 |
| Fall subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 2 | 2 / 29 (6.90%) 2 | 4 / 103 (3.88%) 7 |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Tooth fracture subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Wound subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Cardiac disorders | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 5 / 103 (4.85%) |
| occurrences (all) | 2 | 0 | 5 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 29 (3.45%) | 6 / 103 (5.83%) |
| occurrences (all) | 1 | 1 | 7 |
| Nervous system disorders | | | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 29 (6.90%) | 7 / 103 (6.80%) |
| occurrences (all) | 2 | 2 | 7 |
| Dysgeusia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 29 (0.00%) | 5 / 103 (4.85%) |
| occurrences (all) | 3 | 0 | 5 |
| Headache | | | |
| subjects affected / exposed | 6 / 39 (15.38%) | 1 / 29 (3.45%) | 9 / 103 (8.74%) |
| occurrences (all) | 6 | 1 | 9 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences (all) | 2 | 0 | 2 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences (all) | 0 | 0 | 2 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences (all) | 0 | 0 | 2 |
| Sciatica | | | |

| | | | |
|---|-----------------------|------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Presyncope subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Polyneuropathy subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 2 |
| Tremor subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 29 (6.90%) 2 | 4 / 103 (3.88%) 4 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 9 / 39 (23.08%) 13 | 10 / 29 (34.48%) 12 | 33 / 103 (32.04%) 43 |
| Febrile neutropenia subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 1 | 1 / 103 (0.97%) 1 |
| Haemolysis subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| Lymphopenia subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 5 |
| Neutropenia subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 11 | 3 / 29 (10.34%) 6 | 11 / 103 (10.68%) 25 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 8 | 5 / 29 (17.24%) 5 | 20 / 103 (19.42%) 22 |
| Eye disorders | | | |
| Blepharitis | | | |

| | | | |
|-----------------------------|-----------------|----------------|-------------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 29 (6.90%) | 2 / 103 (1.94%) |
| occurrences (all) | 0 | 2 | 2 |
| Cataract | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Cataract nuclear | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry eye | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 29 (6.90%) | 6 / 103 (5.83%) |
| occurrences (all) | 4 | 2 | 7 |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 1 | 1 |
| Vision blurred | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 29 (6.90%) | 6 / 103 (5.83%) |
| occurrences (all) | 2 | 2 | 6 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 29 (6.90%) | 5 / 103 (4.85%) |
| occurrences (all) | 1 | 2 | 5 |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 29 (3.45%) | 7 / 103 (6.80%) |
| occurrences (all) | 3 | 2 | 8 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 7 / 103 (6.80%) |
| occurrences (all) | 0 | 1 | 7 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 2 / 29 (6.90%) | 13 / 103 (12.62%) |
| occurrences (all) | 7 | 2 | 13 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 4 / 103 (3.88%) |
| occurrences (all) | 1 | 0 | 5 |

| | | | |
|--|-----------------|-----------------|-------------------|
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 6 / 29 (20.69%) | 16 / 103 (15.53%) |
| occurrences (all) | 6 | 9 | 21 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 29 (6.90%) | 6 / 103 (5.83%) |
| occurrences (all) | 2 | 2 | 7 |
| Dysphagia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 3 / 103 (2.91%) |
| occurrences (all) | 2 | 0 | 3 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 3 / 103 (2.91%) |
| occurrences (all) | 1 | 0 | 3 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 1 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 2 / 29 (6.90%) | 15 / 103 (14.56%) |
| occurrences (all) | 6 | 2 | 18 |
| Paraesthesia oral | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 29 (0.00%) | 5 / 103 (4.85%) |
| occurrences (all) | 2 | 0 | 8 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences (all) | 2 | 0 | 2 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 5 / 103 (4.85%) 5 |
| Nail ridging subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 1 / 29 (3.45%) 1 | 3 / 103 (2.91%) 3 |
| Rash subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 4 | 0 / 29 (0.00%) 0 | 4 / 103 (3.88%) 5 |
| Skin exfoliation subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Renal and urinary disorders | | | |
| Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 1 | 4 / 103 (3.88%) 4 |
| Haematuria subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 4 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 4 |
| Renal failure subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 1 / 29 (3.45%) 2 | 2 / 103 (1.94%) 3 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 1 | 1 / 103 (0.97%) 1 |
| Endocrine disorders | | | |
| Cushingoid subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| Arthralgia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 3 / 29 (10.34%) | 9 / 103 (8.74%) |
| occurrences (all) | 4 | 4 | 11 |
| Back pain | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 29 (6.90%) | 7 / 103 (6.80%) |
| occurrences (all) | 3 | 2 | 7 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 29 (0.00%) | 3 / 103 (2.91%) |
| occurrences (all) | 3 | 0 | 3 |
| Muscle spasms | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 4 / 29 (13.79%) | 6 / 103 (5.83%) |
| occurrences (all) | 2 | 4 | 6 |
| Muscular weakness | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 0 / 29 (0.00%) | 9 / 103 (8.74%) |
| occurrences (all) | 4 | 0 | 9 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences (all) | 0 | 0 | 2 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 29 (3.45%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 1 | 1 |
| Osteoporosis | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 29 (0.00%) | 2 / 103 (1.94%) |
| occurrences (all) | 2 | 0 | 2 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 29 (6.90%) | 3 / 103 (2.91%) |
| occurrences (all) | 2 | 2 | 4 |
| Tendon pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 29 (0.00%) | 1 / 103 (0.97%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bronchiolitis | | | |

| | | | |
|--|-----------------------|----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 3 |
| COVID-19 subjects affected / exposed occurrences (all) | 6 / 39 (15.38%) 6 | 4 / 29 (13.79%) 4 | 14 / 103 (13.59%) 14 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Cytomegalovirus viraemia subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 3 / 29 (10.34%) 4 | 9 / 103 (8.74%) 10 |
| Cytomegalovirus infection subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 1 | 3 / 103 (2.91%) 4 |
| Cytomegalovirus infection reactivation subjects affected / exposed occurrences (all) | 8 / 39 (20.51%) 14 | 4 / 29 (13.79%) 5 | 15 / 103 (14.56%) 25 |
| Device related infection subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Epstein-Barr virus infection reactivation subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 3 | 0 / 29 (0.00%) 0 | 4 / 103 (3.88%) 6 |
| Hordeolum subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Herpes zoster subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Oral candidiasis | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 3 | 1 / 29 (3.45%) 1 | 3 / 103 (2.91%) 4 |
| Pneumonia viral subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Pneumonia subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 1 / 29 (3.45%) 1 | 5 / 103 (4.85%) 5 |
| Parainfluenzae virus infection subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Paronychia subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Respiratory syncytial virus infection subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 2 | 4 / 103 (3.88%) 5 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 1 / 29 (3.45%) 1 | 5 / 103 (4.85%) 7 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 29 (6.90%) 2 | 2 / 103 (1.94%) 2 |
| Skin infection subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 1 / 29 (3.45%) 1 | 4 / 103 (3.88%) 4 |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 103 (0.97%) 1 |
| Urinary tract infection enterococcal | | | |

| | | | |
|---|----------------------|----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 1 / 29 (3.45%) 1 | 3 / 103 (2.91%) 3 |
| Urinary tract infection bacterial subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 2 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 4 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 5 / 103 (4.85%) 5 |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 29 (3.45%) 1 | 2 / 103 (1.94%) 2 |
| Fluid retention subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 29 (0.00%) 0 | 0 / 103 (0.00%) 0 |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 1 / 29 (3.45%) 1 | 5 / 103 (4.85%) 5 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 4 / 29 (13.79%) 5 | 13 / 103 (12.62%) 14 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 2 | 0 / 29 (0.00%) 0 | 3 / 103 (2.91%) 5 |
| Hypertriglyceridaemia subjects affected / exposed occurrences (all) | 8 / 39 (20.51%) 9 | 3 / 29 (10.34%) 3 | 13 / 103 (12.62%) 14 |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 3 | 0 / 29 (0.00%) 0 | 5 / 103 (4.85%) 7 |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 6 | 1 / 29 (3.45%) 3 | 8 / 103 (7.77%) 18 |
| Hyponatraemia subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 5 | 3 / 29 (10.34%) 4 | 11 / 103 (10.68%) 17 |

| | | | |
|--|----------------------|----------------------|-------------------------|
| Hypophosphataemia subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 3 | 2 / 29 (6.90%) 2 | 5 / 103 (4.85%) 7 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 6 | 6 / 29 (20.69%) 8 | 12 / 103 (11.65%) 16 |
| Steroid diabetes subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 29 (6.90%) 2 | 3 / 103 (2.91%) 3 |
| Vitamin D deficiency subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 29 (0.00%) 0 | 2 / 103 (1.94%) 2 |

| Non-serious adverse events | Part 1 Expansion: CS monotherapy | | |
|--|-------------------------------------|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 31 / 36 (86.11%) | | |
| Vascular disorders | | | |
| Deep vein thrombosis subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Hot flush subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Hypertension subjects affected / exposed occurrences (all) | 7 / 36 (19.44%) 7 | | |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Microangiopathy subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |

| | | | |
|---|----------------------|--|--|
| Chest discomfort subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Fatigue subjects affected / exposed occurrences (all) | 5 / 36 (13.89%) 5 | | |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Oedema subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 6 / 36 (16.67%) 6 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 4 | | |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Vulvovaginal dryness subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Cough | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Depression | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Insomnia | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Investigations | | | |

| | | | |
|---------------------------------------|----------------|--|--|
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 2 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood triglycerides increased | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Cytomegalovirus test positive subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Drug level increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Haemoglobin increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Liver function test increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Weight increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|---------------------|--|--|
| Contusion subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Fall subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | | |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Tooth fracture subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Wound subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Cardiac failure subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Tachycardia subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Nervous system disorders Balance disorder subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Dysgeusia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Headache | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Tremor | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Leukopenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cataract nuclear | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vision blurred | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Paraesthesia oral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Dermatitis atopic | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Dermatitis contact | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Dry skin | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Nail ridging | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Pruritus | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Skin exfoliation | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Haematuria | | | |
| subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Renal failure | | | |

| | | | |
|---|---|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Urinary incontinence subjects affected / exposed occurrences (all)</p> | <p>0 / 36 (0.00%) 0</p> <p>1 / 36 (2.78%) 1</p> | | |
| <p>Endocrine disorders</p> <p>Cushingoid subjects affected / exposed occurrences (all)</p> <p>Hypothyroidism subjects affected / exposed occurrences (all)</p> | <p>0 / 36 (0.00%) 0</p> <p>0 / 36 (0.00%) 0</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia subjects affected / exposed occurrences (all)</p> <p>Back pain subjects affected / exposed occurrences (all)</p> <p>Musculoskeletal chest pain subjects affected / exposed occurrences (all)</p> <p>Muscle spasms subjects affected / exposed occurrences (all)</p> <p>Muscular weakness subjects affected / exposed occurrences (all)</p> <p>Neck pain subjects affected / exposed occurrences (all)</p> <p>Musculoskeletal pain subjects affected / exposed occurrences (all)</p> <p>Osteonecrosis</p> | <p>0 / 36 (0.00%) 0</p> <p>1 / 36 (2.78%) 1</p> <p>0 / 36 (0.00%) 0</p> <p>1 / 36 (2.78%) 1</p> <p>1 / 36 (2.78%) 1</p> <p>0 / 36 (0.00%) 0</p> <p>0 / 36 (0.00%) 0</p> <p>0 / 36 (0.00%) 0</p> | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Osteoporosis subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Tendon pain subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Infections and infestations | | | |
| Bronchiolitis subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Bronchitis subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| COVID-19 subjects affected / exposed occurrences (all) | 5 / 36 (13.89%) 5 | | |
| Conjunctivitis subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | | |
| Cytomegalovirus viraemia subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Cytomegalovirus infection subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Cytomegalovirus infection reactivation subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 6 | | |
| Device related infection | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epstein-Barr virus infection reactivation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Paronychia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---------------------|--|--|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Skin infection subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Urinary tract infection enterococcal subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Urinary tract infection bacterial subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Fluid retention subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | | |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Hyperkalaemia | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Steroid diabetes | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 16 August 2018 | The primary purpose of this amendment was to respond to Regulatory Authority feedback. |
| 02 November 2018 | The primary purpose of this amendment was to respond to Voluntary Harmonisation Procedure (VHP). |
| 30 November 2018 | The primary purpose of this amendment was to respond to VHP. |
| 07 June 2019 | The primary purpose of this amendment was to update and clarify exclusion criteria, the definition for treatment failure, dose-limiting toxicity (DLT) criteria, treatment of overdose, and maximum duration of study treatment, as well as to respond to health authorities. |
| 30 August 2019 | The primary purpose of this amendment was to ensure consistency between sections of the Protocol describing the reasons for discontinuation in response to VHP request. |
| 16 December 2019 | The primary purpose of this amendment was to specify the dose for Part 2 based on the analysis of data from Part 1 of the study, to update the dose modification and interruption guidelines, and to provide clarification in several areas of the Protocol. |
| 03 April 2020 | The primary purpose of this amendment was for the addition of a Part 1 Expansion part of the study and to update inclusion criteria, dose reduction scheme for concomitant medications, and itacitinib taper. |
| 30 September 2021 | The primary purpose of this amendment was for the discontinuation of Treatment Group C in the Part 1 Expansion part of the study and to update risk/benefit information, the dose reduction scheme for concomitant medications, and the frequency of pulmonary function tests in graft-versus-host disease (GVHD) follow-up. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Based on Part 1 expansion preliminary efficacy data, Part 2 did not enroll participants. Part 1 Expansion participants who were tolerating and continuing to receive benefit from itacitinib could continue itacitinib treatment in study INCB 39110-801.

Notes: