



Clinical trial results:

Phase 2, Open-label, Multiple-dose Trial to Assess the Safety, Tolerability, Pharmacokinetics, and Efficacy of Delamanid (OPC-67683) in Pediatric Multidrug-resistant Tuberculosis Patients on Therapy With an Optimized Background Regimen of Antituberculosis Drugs over a 6-Month Treatment Period

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2012-004620-38 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 13 January 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 29 July 2020 |
| First version publication date | 29 July 2020 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 242-12-233 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01859923 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Otsuka Pharmaceutical Development & Commercialization, Inc. |
| Sponsor organisation address | 2440 Research Boulevard, Rockville, United States, 20850 |
| Public contact | Global Clinical Development, Otsuka Pharmaceutical Development & Commercialization, Inc., +1 609-524-6788, clinicaltransparency@otsuka-us.com |
| Scientific contact | Global Clinical Development, Otsuka Pharmaceutical Development & Commercialization, Inc., +1 609-524-6788, clinicaltransparency@otsuka-us.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001113-PIP01-10 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 January 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 January 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to assess the safety, tolerability, pharmacokinetics, and efficacy of long-term (6-month) treatment with delamanid plus an optimized background regimen (OBR) of other anti-tuberculosis drugs in paediatric participants who completed Study 242-12-232 (NCT01856634; 2012-004473-25).

Protection of trial subjects:

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

Background therapy:

All participants were required to be on a standard-of-care, optimized background regimen (OBR) for at least 2 weeks prior to baseline assessments. Medications for the OBR for Multidrug-resistant tuberculosis (MDR-TB) treatment for each trial participant were procured through the standard mechanisms available for a given site ordinarily used for procurement of OBR medications for treating MDR-TB participants. Selection and administration of the treatment medications were based on World Health Organization's Guidelines for the programmatic management of MDR-TB, in conjunction with national TB program guidelines in each country.

Evidence for comparator:

This study did not include a comparator as it involved only a single investigational therapy (delamanid) that was administered to participants already receiving a standard-of-care OBR for MDR-TB.

| | |
|---|--------------|
| Actual start date of recruitment | 20 July 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | South Africa: 12 |
| Country: Number of subjects enrolled | Philippines: 25 |
| Worldwide total number of subjects | 37 |
| EEA total number of subjects | 0 |

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) | 7 |
| Children (2-11 years) | 23 |
| Adolescents (12-17 years) | 7 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 3 investigative sites in Philippines and South Africa from July 20, 2013 to January 13, 2020. Participants received delamanid up to Day 182 in the treatment period and were followed up to Day 365 for safety and efficacy and up to Day 730 (Month 24) for treatment outcome.

Pre-assignment

Screening details:

Pediatric participants with a diagnosis of MDR-TB who were on therapy with an optimized background regimen (OBR) of anti-tuberculosis drugs and completed study 242-12-232 (NCT01856634; 2012-004473-25) were enrolled in this extension study 242-12-233 to receive delamanid based on the participant's age and weight.

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 | Group 1: 12 to 17 Years of Age |

Arm description:

Participants 12 to 17 years old (inclusive) received adult formulation of delamanid 100 milligrams (mg) (2x50 mg tablets), orally, twice daily (BID) plus optimized background regimen (OBR) up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Delamanid |
| Investigational medicinal product code | |
| Other name | OPC-67683 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received adult formulation delamanid as per regimen specified in the arm description. Morning dose of the delamanid BID regimen was given within 30 minutes after the start of a standard breakfast meal. The evening dose of the BID dose regimen was given 10 hours post morning dose and within 30 minutes after the start of a standard dinner meal.

| | |
|------------------|-------------------------------|
| Arm title | Group 2: 6 to 11 Years of Age |
|------------------|-------------------------------|

Arm description:

Participants 6 to 11 years old (inclusive) received adult formulation delamanid 50 mg (1x50 mg tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Delamanid |
| Investigational medicinal product code | |
| Other name | OPC-67683 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received adult formulation delamanid as per regimen specified in the arm description. Morning dose of the delamanid BID regimen was given within 30 minutes after the start of a standard breakfast meal. The evening dose of the BID dose regimen was given 10 hours post morning dose and within 30 minutes after the start of a standard dinner meal.

| | |
|------------------|------------------------------|
| Arm title | Group 3: 3 to 5 Years of Age |
|------------------|------------------------------|

Arm description:

Participants 3 to 5 years old (inclusive) received 25 mg pediatric formulation of delamanid (DPF - suspension prepared using dispersible tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Delamanid |
| Investigational medicinal product code | |
| Other name | OPC-67683, Delamanid Pediatric Formulation (DPF) |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received delamanid as an extemporaneous suspension using the delamanid pediatric dispersible tablet formulation. Morning dose of the delamanid BID/once daily (QD) regimen was given within 30 minutes after the start of a standard breakfast meal. The evening dose of the BID dose regimen was given 10 hours post morning dose and within 30 minutes after the start of a standard meal.

| | |
|------------------|----------------------------------|
| Arm title | Group 4: Birth to 2 Years of Age |
|------------------|----------------------------------|

Arm description:

Participants from birth to 2 years old (inclusive) received DPF (suspension prepared using dispersible tablet) for 182 days plus OBR. Participants continued to receive OBR up to Day 365. The DPF dose was based on the participant's body weight during the baseline visit:

- Participants >10 kilograms (kg) received DPF 10 mg BID plus OBR
- Participants >8 kg and ≤10 kg received DPF 5 mg BID plus OBR
- Participants ≥5.5 kg and ≤8 kg received DPF 5 mg once per day (QD) plus OBR

Delamanid dose was adjusted as needed for Group 4 participants based on the weight measurement at specified study visits [Visits 5 (Day 28), 7 (Day 56), 9 (Day 84), 11 (Day 126) and 12 (Day 154)].

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Delamanid |
| Investigational medicinal product code | |
| Other name | OPC-67683, Delamanid Pediatric Formulation (DPF) |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received delamanid as an extemporaneous suspension using the delamanid pediatric dispersible tablet formulation. Morning dose of the delamanid BID/once daily (QD) regimen was given within 30 minutes after the start of a standard breakfast meal. The evening dose of the BID dose regimen was given 10 hours post morning dose and within 30 minutes after the start of a standard meal.

| Number of subjects in period 1 | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age |
|---------------------------------------|--------------------------------|-------------------------------|------------------------------|
| Started | 7 | 6 | 12 |
| Completed | 7 | 6 | 11 |
| Not completed | 0 | 0 | 1 |
| Adverse event, serious fatal | - | - | 1 |

| Number of subjects in period 1 | Group 4: Birth to 2 Years of Age |
|---------------------------------------|----------------------------------|
| Started | 12 |
| Completed | 11 |
| Not completed | 1 |
| Adverse event, serious fatal | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Group 1: 12 to 17 Years of Age |
|-----------------------|--------------------------------|

Reporting group description:

Participants 12 to 17 years old (inclusive) received adult formulation of delamanid 100 milligrams (mg) (2x50 mg tablets), orally, twice daily (BID) plus optimized background regimen (OBR) up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Group 2: 6 to 11 Years of Age |
|-----------------------|-------------------------------|

Reporting group description:

Participants 6 to 11 years old (inclusive) received adult formulation delamanid 50 mg (1x50 mg tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|-----------------------|------------------------------|
| Reporting group title | Group 3: 3 to 5 Years of Age |
|-----------------------|------------------------------|

Reporting group description:

Participants 3 to 5 years old (inclusive) received 25 mg pediatric formulation of delamanid (DPF - suspension prepared using dispersible tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Group 4: Birth to 2 Years of Age |
|-----------------------|----------------------------------|

Reporting group description:

Participants from birth to 2 years old (inclusive) received DPF (suspension prepared using dispersible tablet) for 182 days plus OBR. Participants continued to receive OBR up to Day 365. The DPF dose was based on the participant's body weight during the baseline visit:

- Participants >10 kilograms (kg) received DPF 10 mg BID plus OBR
- Participants >8 kg and ≤10 kg received DPF 5 mg BID plus OBR
- Participants ≥5.5 kg and ≤8 kg received DPF 5 mg once per day (QD) plus OBR

Delamanid dose was adjusted as needed for Group 4 participants based on the weight measurement at specified study visits [Visits 5 (Day 28), 7 (Day 56), 9 (Day 84), 11 (Day 126) and 12 (Day 154)].

| Reporting group values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age |
|--|--------------------------------|-------------------------------|------------------------------|
| Number of subjects | 7 | 6 | 12 |
| Age categorical | | | |
| Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 6 | 12 |
| Adolescents (12-17 years) | 7 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 15.37 | 9.51 | 4.37 |
| standard deviation | ± 1.63 | ± 1.49 | ± 0.98 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 3 | 4 | 6 |
| Male | 4 | 2 | 6 |
| Race | | | |
| Units: Subjects | | | |
| Black or African American | 0 | 0 | 2 |
| Asian | 7 | 4 | 8 |
| Other | 0 | 2 | 2 |
| Ethnicity | | | |
| Units: Subjects | | | |

| | | | |
|------------------------|---|---|----|
| Not Hispanic or Latino | 7 | 6 | 12 |
|------------------------|---|---|----|

| Reporting group values | Group 4: Birth to 2 Years of Age | Total | |
|--|----------------------------------|-------|--|
| Number of subjects | 12 | 37 | |
| Age categorical Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 7 | 7 | |
| Children (2-11 years) | 5 | 23 | |
| Adolescents (12-17 years) | 0 | 7 | |
| Age continuous Units: years | | | |
| arithmetic mean | 1.79 | | |
| standard deviation | ± 0.59 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 6 | 19 | |
| Male | 6 | 18 | |
| Race Units: Subjects | | | |
| Black or African American | 0 | 2 | |
| Asian | 6 | 25 | |
| Other | 6 | 10 | |
| Ethnicity Units: Subjects | | | |
| Not Hispanic or Latino | 12 | 37 | |

End points

End points reporting groups

| | |
|---|----------------------------------|
| Reporting group title | Group 1: 12 to 17 Years of Age |
| Reporting group description: Participants 12 to 17 years old (inclusive) received adult formulation of delamanid 100 milligrams (mg) (2x50 mg tablets), orally, twice daily (BID) plus optimized background regimen (OBR) up to Day 182. Participants continued to receive OBR up to Day 365. | |
| Reporting group title | Group 2: 6 to 11 Years of Age |
| Reporting group description: Participants 6 to 11 years old (inclusive) received adult formulation delamanid 50 mg (1x50 mg tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365. | |
| Reporting group title | Group 3: 3 to 5 Years of Age |
| Reporting group description: Participants 3 to 5 years old (inclusive) received 25 mg pediatric formulation of delamanid (DPF - suspension prepared using dispersible tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365. | |
| Reporting group title | Group 4: Birth to 2 Years of Age |
| Reporting group description: Participants from birth to 2 years old (inclusive) received DPF (suspension prepared using dispersible tablet) for 182 days plus OBR. Participants continued to receive OBR up to Day 365. The DPF dose was based on the participant's body weight during the baseline visit: <ul style="list-style-type: none">• Participants >10 kilograms (kg) received DPF 10 mg BID plus OBR• Participants >8 kg and ≤10 kg received DPF 5 mg BID plus OBR• Participants ≥5.5 kg and ≤8 kg received DPF 5 mg once per day (QD) plus OBR Delamanid dose was adjusted as needed for Group 4 participants based on the weight measurement at specified study visits [Visits 5 (Day 28), 7 (Day 56), 9 (Day 84), 11 (Day 126) and 12 (Day 154)]. | |
| Subject analysis set title | Delamanid |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants received delamanid 25, 50 or 100 mg based on age and weight plus OBR up to Day 182. Participants continued to receive OBR up to Day 365. | |

Primary: Number of Participants With At Least One Treatment Emergent Adverse Event (TEAE)

| | |
|---|---|
| End point title | Number of Participants With At Least One Treatment Emergent Adverse Event (TEAE) ^[1] |
| End point description: An adverse event (AE) is defined as any untoward medical occurrence in a clinical trial participant and that does not necessarily have a causal relationship with the treatment. A TEAE is defined as an AE that occurred after the administration of investigational medicinal product (IMP). The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation. | |
| End point type | Primary |
| End point timeframe: From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365) | |

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: Inferential statistical analyses was not performed for the safety endpoints. Descriptive statistics are included (number of participants).

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|-----------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 12 |
| Units: subjects | 7 | 6 | 12 | 12 |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Physical Examination Values

| | |
|-----------------|---|
| End point title | Number of Participants With Abnormal Physical Examination Values ^[2] |
|-----------------|---|

End point description:

Physical examination included the examination of the abdomen; extremities; head, eyes, ears, nose (HEENT); neurological; skin and mucosae; thorax; urogenital; audiometry assessment and visual assessment. Participants with abnormal values, as assessed by the investigator were reported. The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation. Number of participants analysed are the participants with data available for analyses.

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

End point timeframe:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

Notes:

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

Justification: Inferential statistical analyses was not performed for the safety endpoints. Descriptive statistics are included (number of participants).

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|-----------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 11 |
| Units: subjects | | | | |
| Abdomen | 1 | 1 | 4 | 2 |
| Extremities | 2 | 0 | 1 | 1 |
| HEENT | 7 | 6 | 12 | 10 |
| Neurological | 1 | 0 | 1 | 1 |
| Skin and Mucosae | 2 | 6 | 6 | 8 |
| Thorax | 5 | 2 | 6 | 7 |
| Urogenital | 0 | 0 | 1 | 3 |
| Audiometry Assessment | 4 | 3 | 9 | 7 |
| Visual Assessment | 0 | 1 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormal Vital Sign Values

| | |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Abnormal Vital Sign Values ^[3] |
|-----------------|--|

End point description:

Vital signs included weight (kg), height (cm), body temperature (degree Celsius), heart rate (beats/min), respiratory rate (breaths/minute), systolic and diastolic blood pressure (mm Hg), body mass index (BMI) (kg/m²). The criteria for clinically significant abnormal value for weight was decrease or increase of $\geq 5\%$ in body weight relative to Baseline. Only categories with data for potentially clinically significant abnormal vital sign parameter values are reported. The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation. Number of participants analysed are the participants with data available for analyses.

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

End point timeframe:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

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: Inferential statistical analyses was not performed for the safety endpoints. Descriptive statistics are included (number of participants).

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|---------------------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 11 |
| Units: subjects | | | | |
| Decrease of $\geq 5\%$ in Body Weight | 0 | 2 | 0 | 1 |
| Increase of $\geq 5\%$ in Body Weight | 4 | 2 | 10 | 10 |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormalities in Electrocardiogram (ECG)

| | |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Abnormalities in Electrocardiogram (ECG) ^[4] |
|-----------------|--|

End point description:

Criteria for clinically significant abnormal ECG values were ventricular rate outlier (< 50 bpm and decrease of $\geq 25\%$, > 100 bpm and increase of $\geq 25\%$), PR outlier (increase of $\geq 25\%$ when PR > 200 milliseconds (ms), QRS outlier (increase of $\geq 25\%$ when QRS > 100 ms), QT (new onset (in treatment period but not at Baseline) [> 500 ms]), QT interval corrected by Bazett's formula (QTcB) (new onset [> 450 , > 480 , > 500 ms], increase of ≥ 30 ms and ≤ 60 ms or increase of > 60 ms), QT interval corrected by Fridericia's formula (QTcF) (new onset [> 450 , > 480 , > 500 ms], increase of ≥ 30 ms and ≤ 60 ms or increase of > 60 ms), new abnormal U waves, new ST segment changes, new T wave changes, new abnormal rhythm, new conduction abnormality were reported as categories. Only categories with data are reported. Safety Sample included participants who received any amount of IMP, regardless of any protocol deviation or violation. Number of participants analysed are participants with data available for analyses.

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

End point timeframe:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

Notes:

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

Justification: Inferential statistical analyses was not performed for the safety endpoints. Descriptive statistics are included (number of participants).

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|--|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 11 |
| Units: subjects | | | | |
| Ventricular Rate Outliers, Notable Increases | 1 | 0 | 1 | 4 |
| QRS Outliers | 1 | 0 | 0 | 0 |
| QTcB, New Onset (>480 ms) | 1 | 1 | 1 | 0 |
| QTcB, New Onset (>450 ms) | 7 | 2 | 8 | 5 |
| QTcB, New Onset (Change >= 30 and <=60 ms) | 5 | 3 | 8 | 9 |
| QTcB, New Onset (Change > 60 ms) | 1 | 0 | 0 | 2 |
| QTcF, New Onset (>450 ms) | 3 | 2 | 0 | 0 |
| QTcF, New Onset (Change >= 30 and <=60 ms) | 5 | 2 | 6 | 9 |
| QTcF, New Onset (Change > 60 ms) | 1 | 0 | 0 | 1 |
| New Abnormal Rhythm | 5 | 4 | 6 | 1 |
| New Conduction Abnormality | 6 | 5 | 5 | 8 |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Laboratory Test Abnormalities

| | |
|-----------------|---|
| End point title | Number of Participants With Clinically Significant Laboratory Test Abnormalities ^[5] |
|-----------------|---|

End point description:

Laboratory assessments included parameters for serum chemistry, hematology and urinalysis along with adrenocorticotrophic hormone, serum cortisol, free thyroxine, thyroid stimulating hormone (TSH), and high sensitivity C-reactive protein cell count. The participants were categorized based on the clinically significant laboratory values as per protocol predefined criteria. The categories with at least one participant with clinically significant value outside the normal range for laboratory assessments are reported. The normal ranges for those laboratory parameters were potassium 3.4 - 5.4 milliequivalents per liter (mEq/L, uric acid 3.9 - 8.2 mg/dL, partial thromboplastin time (PTT) 9.7 - 12.3 sec, platelet count 180 - 440 thousands platelets/ μ L. The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation.

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

End point timeframe:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

Notes:

[5] - 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: Inferential statistical analyses was not performed for the safety endpoints. Descriptive statistics are included (number of participants).

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|-----------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 12 |
| Units: subjects | | | | |
| Elevated Potassium | 0 | 0 | 0 | 1 |
| Elevated Uric Acid | 1 | 0 | 1 | 0 |
| Elevated PTT | 0 | 1 | 2 | 0 |
| Low Platelet Count | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Primary: Population Pharmacokinetic (POPPK) Model Point Estimate for Central Clearance (L) and Inter-compartmental Clearance (Q) of Delamanid

| | |
|-----------------|---|
| End point title | Population Pharmacokinetic (POPPK) Model Point Estimate for Central Clearance (L) and Inter-compartmental Clearance (Q) of Delamanid ^[6] |
|-----------------|---|

End point description:

Central clearance is defined as plasma volume in the vascular compartment that is cleared of drug per unit of time. Inter-compartmental clearance is defined as a ratio of the drug's distribution rate between the central compartment and the peripheral compartments over its circulating concentration (L/hr). Population point estimates were based on POPPK analysis to find one measure each for both L and Q. The exposure data were pooled across visits and participants to identify POPPK parameter estimates and were reported for delamanid. Population Pharmacokinetic (PK)/Pharmacodynamic (PD) analysis sample included all the participants with data available for PK/PD analysis.

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

End point timeframe:

Predose on Days 1, 56, 154, and 182, 210 and at any time point on Days 14, 98, 189, 196, 203, and 238

Notes:

[6] - 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: Inferential statistical analysis (comparison between groups) was not performed for the PK/PD endpoints.

| End point values | Delamanid | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: L/hr | | | | |
| number (not applicable) | | | | |
| Central Clearance (L) | 18.1 | | | |
| Inter-compartmental Clearance (Q) | 105 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: POPPK Model Point Estimate for Central Volume of Distribution (Vc) and Peripheral Volume of Distribution (Vp) of Delamanid

| | |
|-----------------|---|
| End point title | POPPK Model Point Estimate for Central Volume of Distribution (Vc) and Peripheral Volume of Distribution (Vp) of Delamanid ^[7] |
|-----------------|---|

End point description:

Vc is defined as the theoretical volume that would be necessary to contain the total amount of an administered drug at the same concentration that it is observed in the blood plasma. Vp is defined as the apparent volume needed to account for the total amount of drug in the body if the drug was evenly distributed throughout the body and in the same concentration as the site of sample collection such as peripheral venous plasma. Population point estimates were based on POPPK analysis to find one measure each for both Vc and Vp. The exposure data were pooled across visits and participants to identify POPPK parameter estimates and were reported for delamanid. Population PK/PD analysis sample included all the participants with data available for PK/PD analysis.

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

End point timeframe:

Predose on Days 1, 56, 154, and 182, 210 and at any time point on Days 14, 98, 189, 196, 203, and 238

Notes:

[7] - 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: Inferential statistical analysis (comparison between groups) was not performed for the PK/PD endpoints.

| | | | | |
|--|----------------------|--|--|--|
| End point values | Delamanid | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: litres (L) | | | | |
| Central Volume of Distribution (Vc) | 254 | | | |
| Peripheral Volume of Distribution (Vp) | 347 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: POPPK Model Point Estimate for Absorption Rate Constant (Ka) of Delamanid

| | |
|-----------------|--|
| End point title | POPPK Model Point Estimate for Absorption Rate Constant (Ka) of Delamanid ^[8] |
|-----------------|--|

End point description:

Ka is defined as a measure of rate at which a drug enters into the circulatory system. Population point estimate for Ka was based on population PK analysis to find one measure. Population point estimates were based on POPPK analysis to find one measure for Ka. The exposure data were pooled across visits and participants to identify POPPK parameter estimates and were reported for delamanid. Population PK/PD analysis sample included all the participants with data available for PK/PD analysis.

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

End point timeframe:

Predose on Days 1, 56, 154, and 182, 210 and at any time point on Days 14, 98, 189, 196, 203, and 238

Notes:

[8] - 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: Inferential statistical analysis (comparison between groups) was not performed for the PK/PD endpoints.

| End point values | Delamanid | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: per hour (1/hr) | | | | |
| number (not applicable) | 0.254 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: POPPK Model Point Estimate for Absorption Lag Time (ALAG1) of Delamanid

| | |
|-----------------|--|
| End point title | POPPK Model Point Estimate for Absorption Lag Time (ALAG1) of Delamanid ^[9] |
|-----------------|--|

End point description:

ALAG1 is defined as the time delay prior to the commencement of drug absorption. Population point estimates were based on POPPK analysis to find one measure for ALAG1. The exposure data were pooled across visits and participants to identify POPPK parameter estimates and were reported for delamanid. Population PK/PD analysis sample included all the participants with data available for PK/PD analysis.

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

End point timeframe:

Predose on Days 1, 56, 154, and 182, 210 and at any time point on Days 14, 98, 189, 196, 203, and 238

Notes:

[9] - 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: Inferential statistical analysis (comparison between groups) was not performed for the PK/PD endpoints.

| End point values | Delamanid | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: hour (hr) | | | | |
| number (not applicable) | 1.38 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline QT Interval Corrected by Bazett's Formula (QTcB) Effect

| | |
|-----------------|--|
| End point title | Baseline QT Interval Corrected by Bazett's Formula (QTcB) Effect |
|-----------------|--|

End point description:

The 12-lead ECG was performed to obtain recordings of heart rate (QT interval) to analyze QTcB effect. Population PK/PD analysis sample included all the participants with data available for PK/PD analysis.

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

End point timeframe:

Baseline (Day -1)

| End point values | Delamanid | | | |
|---|--------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: ms | | | | |
| arithmetic mean (confidence interval 90%) | | | | |
| Delamanid | 0.0318 (-0.113 to 0.177) | | | |
| Metabolite DM-6705 | 0.0309 (-0.112 to 0.174) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK/PD Relationship: POPPK Model Point Estimate for Slope of Linear Mixed Effects Model for Change in QTcB Interval Versus Delamanid Plasma Concentrations

| | |
|------------------------|---|
| End point title | PK/PD Relationship: POPPK Model Point Estimate for Slope of Linear Mixed Effects Model for Change in QTcB Interval Versus Delamanid Plasma Concentrations |
| End point description: | The linear mixed effects model was applied to characterize the concentration-QTcB relationship of delamanid/DM-6705 to obtain population slope estimate. |
| End point type | Secondary |
| End point timeframe: | Predose on Days 1, 56, 154, and 182, 210 and at any time point on Days 14, 98, 189, 196, 203, and 238 |

| End point values | Delamanid | | | |
|---|------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: ms/[ng/mL] | | | | |
| arithmetic mean (confidence interval 90%) | | | | |
| Delamanid | 0.00792 (-0.00132 to 0.0172) | | | |
| Metabolite DM-6705 | 0.0613 (0.016 to 0.107) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Outcome as Assessed by Principal Investigator

| | |
|-----------------|---|
| End point title | Number of Participants With Treatment Outcome as Assessed by Principal Investigator |
|-----------------|---|

End point description:

Treatment outcome was defined as favorable (cured and completed treatment) and unfavorable (lost to follow-up or died). The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation.

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

End point timeframe:

Month 24

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|---|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 12 |
| Units: subjects | | | | |
| Favorable (Cured + Treatment Completed) | 6 | 6 | 10 | 11 |
| Unfavorable (Lost To Follow-up + Died) | 1 | 0 | 2 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Chest X-ray

| | |
|-----------------|--|
| End point title | Number of Participants With Abnormal Chest X-ray |
|-----------------|--|

End point description:

The data for the chest X-ray with abnormality, as assessed by investigator is reported. The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation.

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

End point timeframe:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|-----------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 12 |
| Units: subjects | 7 | 6 | 12 | 11 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Investigator-Assessed Signs and Symptoms of Tuberculosis

| | |
|-----------------|--|
| End point title | Number of Participants With Investigator-Assessed Signs and Symptoms of Tuberculosis |
|-----------------|--|

End point description:

The following signs and symptoms of tuberculosis were assessed by the investigator: cough, fever, weight loss, failure to thrive, hemoptysis, dyspnea, chest pain, night sweats and loss of appetite. The Safety Sample included participants who received any amount of IMP in this study, regardless of any protocol deviation or violation.

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

End point timeframe:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|-----------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 12 | 12 |
| Units: subjects | | | | |
| Cough | 6 | 4 | 3 | 7 |
| Fever | 1 | 2 | 2 | 5 |
| Weight Loss | 3 | 5 | 7 | 9 |
| Failure to Thrive | 0 | 1 | 0 | 3 |
| Hemoptysis | 2 | 0 | 0 | 0 |
| Dyspnea | 1 | 1 | 3 | 2 |
| Chest Pain | 1 | 1 | 0 | 0 |
| Night Sweats | 0 | 0 | 1 | 2 |
| Loss of Appetite | 1 | 2 | 2 | 6 |

Statistical analyses

No statistical analyses for this end point

Secondary: Sputum Culture Conversion (SCC)

| | |
|-----------------|---------------------------------|
| End point title | Sputum Culture Conversion (SCC) |
|-----------------|---------------------------------|

End point description:

SCC was defined as a sputum specimen from a participant negative for growth of mycobacterium tuberculosis (MTB), followed by at least one confirmatory negative sputum culture at least 27 days after

the first negative sputum test and not followed by any sputum cultures positive for growth.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365) | |

| End point values | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age |
|-----------------------------|--------------------------------|-------------------------------|------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | 0 ^[12] | 0 ^[13] |
| Units: subjects | | | | |

Notes:

[10] - Data for SCC could not be collected due to the paucity of sputum production in the participants.

[11] - Data for SCC could not be collected due to the paucity of sputum production in the participants.

[12] - Data for SCC could not be collected due to the paucity of sputum production in the participants.

[13] - Data for SCC could not be collected due to the paucity of sputum production in the participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Palatability Score as Assessed by the Investigator

| | |
|-----------------|--|
| End point title | Number of Participants With Palatability Score as Assessed by the Investigator ^[14] |
|-----------------|--|

End point description:

The palatability of the pediatric formulation was assessed using an age-appropriate visual hedonic scale and clinical assessment (Groups 3 and 4 only). The palatability result was based on 1 of 5 responses: 1="Dislike very much", 2="Dislike a little", 3="Neither liked nor disliked", 4="Like a little", 5="Like very much". Participants were categorized based on different scores. The data per the investigator score are reported. Participants were categorized based on different scores. Participants from the safety sample aged below 5 years (Groups 3 and 4) and who received any amount of IMP in this study, regardless of any protocol deviation or violation were analyzed for this outcome measure. 'n' is the number of participants with data available for analyses at the given time point.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Days 1, 28, 56 and 182 | |

Notes:

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

Justification: This endpoint was assessed only in Groups 3 and 4.

| End point values | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age | | |
|---|------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: subjects | | | | |
| Day 1: Dislike Very Much (n= 12, 12) | 0 | 0 | | |
| Day 1: Dislike a Little (n= 12, 12) | 0 | 2 | | |
| Day 1: Neither Liked Nor Disliked (n= 12, 12) | 1 | 0 | | |
| Day 1: Like a Little (n= 12, 12) | 2 | 2 | | |

| | | | | |
|---|----|----|--|--|
| Day 1: Like Very Much (n= 12, 12) | 9 | 8 | | |
| Day 28: Dislike Very Much (n= 12, 11) | 0 | 0 | | |
| Day 28: Dislike a Little (n= 12, 11) | 0 | 0 | | |
| Day 28: Neither Liked Nor Disliked (n= 12, 11) | 2 | 0 | | |
| Day 28: Like a Little (n= 12, 11) | 1 | 2 | | |
| Day 28: Like Very Much (n= 12, 11) | 9 | 9 | | |
| Day 56: Dislike Very Much (n= 12, 11) | 0 | 0 | | |
| Day 56: Dislike a Little (n= 12, 11) | 0 | 0 | | |
| Day 56: Neither Liked Nor Disliked (n= 12, 11) | 0 | 0 | | |
| Day 56: Like a Little (n= 12, 11) | 2 | 0 | | |
| Day 56: Like Very Much (n= 12, 11) | 10 | 11 | | |
| Day 182: Dislike Very Much (n= 12, 11) | 0 | 0 | | |
| Day 182: Dislike a Little (n= 12, 11) | 0 | 1 | | |
| Day 182: Neither Liked Nor Disliked (n= 12, 11) | 0 | 0 | | |
| Day 182: Like a Little (n= 12, 11) | 1 | 5 | | |
| Day 182: Like Very Much (n= 12, 11) | 11 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Palatability Score as Assessed by the Parent or Participant

| | |
|-----------------|---|
| End point title | Number of Participants With Palatability Score as Assessed by the Parent or Participant ^[15] |
|-----------------|---|

End point description:

The palatability of the pediatric formulation was assessed using an age-appropriate visual hedonic scale and clinical assessment (Groups 3 and 4 only). The palatability result was based on 1 of 5 responses: 1="Dislike very much", 2="Dislike a little", 3="Neither liked nor disliked", 4="Like a little", 5="Like very much". The data per parent/patient score are reported. Participants were categorized based on different scores. Participants from the safety sample aged below 5 years (Groups 3 and 4) and who received any amount of IMP in this study, regardless of any protocol deviation or violation were analyzed for this outcome measure. 'n' is the number of participants with data available for analyses at the given time point.

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

End point timeframe:

Days 1, 28, 56 and 182

Notes:

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

Justification: This endpoint was assessed only in Groups 3 and 4.

| End point values | Group 3: 3 to 5 Years of Age | Group 4: Birth to 2 Years of Age | | |
|--------------------------------------|------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: subjects | | | | |
| Day 1: Dislike Very Much (n= 12, 12) | 0 | 0 | | |
| Day 1: Dislike a Little (n= 12, 12) | 0 | 1 | | |

| | | | | |
|---|----|----|--|--|
| Day 1: Neither Liked Nor Disliked (n= 12, 12) | 1 | 1 | | |
| Day 1: Like a Little (n= 12, 12) | 2 | 3 | | |
| Day 1: Like Very Much (n= 12, 12) | 9 | 7 | | |
| Day 28: Dislike Very Much (n= 12, 11) | 0 | 0 | | |
| Day 28: Dislike a Little (n= 12, 11) | 1 | 0 | | |
| Day 28: Neither Liked Nor Disliked (n= 12, 11) | 0 | 0 | | |
| Day 28: Like a Little (n= 12, 11) | 1 | 3 | | |
| Day 28: Like Very Much (n= 12, 11) | 10 | 8 | | |
| Day 56: Dislike Very Much (n= 12, 11) | 0 | 0 | | |
| Day 56: Dislike a Little (n= 12, 11) | 0 | 0 | | |
| Day 56: Neither Liked Nor Disliked (n= 12, 11) | 1 | 0 | | |
| Day 56: Like a Little (n= 12, 11) | 0 | 0 | | |
| Day 56: Like Very Much (n= 12, 11) | 11 | 11 | | |
| Day 182: Dislike Very Much (n= 12, 11) | 0 | 0 | | |
| Day 182: Dislike a Little (n= 12, 11) | 0 | 0 | | |
| Day 182: Neither Liked Nor Disliked (n= 12, 11) | 0 | 1 | | |
| Day 182: Like a Little (n= 12, 11) | 1 | 4 | | |
| Day 182: Like Very Much (n= 12, 11) | 11 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug up to the end of the Post-treatment Follow-up Period (Up to Day 365)

Adverse event reporting additional description:

The Safety Sample included participants who received any amount of investigational medicinal product (IMP) in this study, regardless of any protocol deviation or violation.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Group 1: 12 to 17 Years of Age |
|-----------------------|--------------------------------|

Reporting group description:

Participants 12 to 17 years old (inclusive) received adult formulation of delamanid 100 mg (2x50 mg tablets), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Group 2: 6 to 11 Years of Age |
|-----------------------|-------------------------------|

Reporting group description:

Participants 6 to 11 years old (inclusive) received adult formulation delamanid 50 mg (1x50 mg tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|-----------------------|------------------------------|
| Reporting group title | Group 3: 3 to 5 Years of Age |
|-----------------------|------------------------------|

Reporting group description:

Participants 3 to 5 years old (inclusive) received 25 mg pediatric formulation of delamanid (DPF - suspension prepared using dispersible tablet), orally, BID plus OBR up to Day 182. Participants continued to receive OBR up to Day 365.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Group 4: Birth to 2 Years of Age |
|-----------------------|----------------------------------|

Reporting group description:

Participants from birth to 2 years old (inclusive) received DPF (suspension prepared using dispersible tablet) for 182 days plus OBR. Participants continued to receive OBR up to Day 365. The DPF dose was based on the participant's body weight during the baseline visit:

- Participants >10 kilograms (kg) received DPF 10 mg BID plus OBR
- Participants >8 kg and ≤10 kg received DPF 5 mg BID plus OBR
- Participants ≥5.5 kg and ≤8 kg received DPF 5 mg once per day (QD) plus OBR

Delamanid dose was adjusted as needed for Group 4 participants based on the weight measurement at specified study visits [Visits 5 (Day 28), 7 (Day 56), 9 (Day 84), 11 (Day 126) and 12 (Day 154)].

| Serious adverse events | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age |
|---|--------------------------------|-------------------------------|------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Non-Hodgkin's lymphoma | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (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 |
| Nervous system disorders | | | |
| Lethargy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (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 | | | |
| Immune thrombocytopenic purpura | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (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 | | | |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Vulvovaginal candidiasis | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------------------------|--|--|
| Serious adverse events | Group 4: Birth to 2 Years of Age | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Immune thrombocytopenic purpura | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oral candidiasis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vulvovaginal candidiasis | | | |
| subjects affected / exposed | 0 / 12 (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 | Group 1: 12 to 17 Years of Age | Group 2: 6 to 11 Years of Age | Group 3: 3 to 5 Years of Age |
|--|-----------------------------------|----------------------------------|---------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 7 (100.00%) | 6 / 6 (100.00%) | 12 / 12 (100.00%) |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 1 | 2 |
| General disorders and administration site conditions | | | |
| Infusion site extravasation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 6 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 2 | 0 | 2 |
| Social circumstances | | | |
| Sexual abuse | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|----------------|----------------|----------------|
| Reproductive system and breast disorders | | | |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Cough | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Abnormal behaviour | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Aggression | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Alanine aminotransferase increased | | | |

| | | | |
|--|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood corticotrophin increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Coagulation time prolonged | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Contusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye injury | | | |

| | | | |
|--------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 1 | 2 |
| Tooth injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Amnesia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 5 / 7 (71.43%) | 3 / 6 (50.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 7 | 3 | 4 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Anaemia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Eosinophilia subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Immune thrombocytopenic purpura subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Conductive deafness subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 2 | 0 / 12 (0.00%) 0 |
| Deafness neurosensory subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Middle ear effusion subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 12 (0.00%) 0 |
| Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Vernal keratoconjunctivitis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 1 / 6 (16.67%) 1 | 1 / 12 (8.33%) 1 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Abdominal pain upper | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Dental caries | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 2 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingival swelling | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip ulceration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral discomfort | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 6 (33.33%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 3 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all) | 2 | 2 | 2 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Angioedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Butterfly rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin fissures | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|----------------------|
| Urticaria papular subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 | 2 / 12 (16.67%) 2 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 3 / 7 (42.86%) 3 | 2 / 6 (33.33%) 2 | 3 / 12 (25.00%) 4 |
| Arthritis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Bone pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Bursitis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Costochondritis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Muscular weakness subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 4 | 1 / 6 (16.67%) 1 | 0 / 12 (0.00%) 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Soft tissue swelling subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Infections and infestations | | | |
| Acarodermatitis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Ascariasis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Folliculitis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 6 (16.67%) 1 | 1 / 12 (8.33%) 1 |
| Genital candidiasis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Gingivitis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 1 |
| Helminthic infection subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 12 (8.33%) 2 |
| Impetigo subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 12 (0.00%) 0 |
| Lower respiratory tract infection | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 1 | 2 |
| Mumps | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Parasitic gastroenteritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all) | 3 | 1 | 2 |
| Pustule | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyuria | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract infection | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 6 (33.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Rubella | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Systemic viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea versicolour | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 3 / 6 (50.00%) | 5 / 12 (41.67%) |
| occurrences (all) | 9 | 5 | 9 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Viral upper respiratory tract infection | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 6 (16.67%) 2 | 0 / 12 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 6 (16.67%) | 4 / 12 (33.33%) |
| occurrences (all) | 2 | 1 | 5 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| | | | |
|--|-------------------------------------|--|--|
| Non-serious adverse events | Group 4: Birth to 2 Years of Age | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 12 (91.67%) | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Infusion site extravasation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Social circumstances | | | |
| Sexual abuse | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |

| | | | |
|--|---|--|--|
| Menorrhagia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 | | |
| Psychiatric disorders Abnormal behaviour subjects affected / exposed occurrences (all) Aggression subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Hallucination subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 | | |
| Investigations Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 | | |

| | | | |
|--|----------------------|--|--|
| Blood corticotrophin increased subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Coagulation time prolonged subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Hepatic enzyme increased subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Liver function test increased subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Prothrombin time prolonged subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 3 / 12 (25.00%) 3 | | |
| Injury, poisoning and procedural complications | | | |
| Animal bite subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Concussion subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Craniocerebral injury subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Eye injury subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Muscle strain | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Skin abrasion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Skin laceration</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tooth injury</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 12 (0.00%)</p> <p>0</p> <p>1 / 12 (8.33%)</p> <p>1</p> <p>1 / 12 (8.33%)</p> <p>1</p> <p>1 / 12 (8.33%)</p> <p>1</p> | | |
| <p>Cardiac disorders</p> <p>Wolff-Parkinson-White syndrome</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 12 (0.00%)</p> <p>0</p> | | |
| <p>Nervous system disorders</p> <p>Amnesia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Paraesthesia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Psychomotor hyperactivity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> | | |
| <p>Blood and lymphatic system disorders</p> <p>Anaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Eosinophilia</p> | <p>1 / 12 (8.33%)</p> <p>1</p> | | |

| | | | |
|---------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Immune thrombocytopenic purpura | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 3 | | |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Conductive deafness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Deafness neurosensory | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Middle ear effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Vernal keratoconjunctivitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aphthous ulcer | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival swelling | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lip dry | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lip ulceration | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Butterfly rash | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash papular | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin discolouration | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin fissures | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Urticaria papular | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|--|--|--|
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Bursitis subjects affected / exposed occurrences (all) Costochondritis subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Musculoskeletal chest pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 1 / 12 (8.33%) 3 | | |

| | | | |
|---|----------------------|--|--|
| Soft tissue swelling subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Infections and infestations | | | |
| Acarodermatitis subjects affected / exposed occurrences (all) | 3 / 12 (25.00%) 3 | | |
| Ascariasis subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Folliculitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Gastroenteritis subjects affected / exposed occurrences (all) | 4 / 12 (33.33%) 4 | | |
| Genital candidiasis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Gingivitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Helminthic infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Impetigo subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Lower respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Mumps | | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | |
| occurrences (all) | 3 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Parasitic gastroenteritis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pustule | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | | |
| occurrences (all) | 9 | | |
| Respiratory tract infection viral | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rubella | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Systemic viral infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tinea infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Tinea versicolour | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|----------------------|--|--|
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 3 / 12 (25.00%) 3 | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 11 March 2013 | The following updates were made as per Amendment 01: <ul style="list-style-type: none">• Revision of introduction; modification of exclusion criteria• Revision of schedule of assessments• Addition of details regarding several procedures• Clarification of text |
| 14 October 2014 | The following updates were made as per Amendment 02: <ul style="list-style-type: none">• Modification of inclusion/exclusion criteria• Update of prohibited medications• Addition of PK blood draw at the early termination visit• Clarification of text |
| 29 June 2015 | The following updates were made as per Amendment 03: <ul style="list-style-type: none">• Addition of information for Groups 3 and 4• Clarification of safety monitoring• Clarification of text |
| 04 October 2016 | Addition of information for Group 4; clarification of text; modification of blood sampling schedule; update of sponsor representative information. |
| 28 February 2019 | The following update was made as per Amendment 04: <ul style="list-style-type: none">• Addition of an interim analysis |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported