



Clinical trial results:

A PHASE II RANDOMIZED AND CONTROLLED INVESTIGATION OF SIX WEEKS OF ORAL VALGANCICLOVIR THERAPY IN INFANTS AND CHILDREN WITH CONGENITAL CYTOMEGALOVIRUS INFECTION AND HEARING LOSS.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2014-001920-31 |
| Trial protocol | GB |
| Global end of trial date | 03 January 2020 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 21 December 2022 |
| First version publication date | 21 December 2022 |
| Summary attachment (see zip file) | Summary report (HHSN272201100035C Annual Report 15 Oct 2019.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | DMID11-0069 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01649869 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | The UK Sponsor is: UCL: 08-0172 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | University College London |
| Sponsor organisation address | Gower Street, London, United Kingdom, |
| Public contact | Prof Paul Griffiths, University College London, p.griffiths@ucl.ac.uk |
| Scientific contact | Prof Paul Griffiths, University College London, p.griffiths@ucl.ac.uk |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 15 August 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 January 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 January 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess whether a six week course of oral valganciclovir can stabilize the hearing of children with congenital CMV infection who present with hearing loss. This will be accomplished by evaluating changes in hearing in either ear at 6 months from baseline.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 15 September 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 24 |
| Country: Number of subjects enrolled | United States: 11 |
| Worldwide total number of subjects | 35 |
| 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) | 24 |
| Children (2-11 years) | 11 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

For this study, subjects were enrolled once they signed the informed consent form (ICF). It was not until after hearing loss was confirmed by audiology testing and confirmation of congenital CMV by dried blood spot that a subject was randomized and started on study drug. This reduced protocol enrolment from 54 to 35.

Pre-assignment

Screening details:

Hearing loss was confirmed by audiology testing and congenital CMV was confirmed by dried blood spot.

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

27 Children between 1 month and 3 years of age (up to 4th birthday) with sensorineural hearing loss and documented CMV infection will receive placebo orally twice a day for 6 weeks

Placebo: Simple Syrup as 60-90% sucrose in purified water: given orally twice a day for 6 weeks

| | |
|--|-------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Simple Syrup as 60-90% sucrose in purified water: given orally twice a day for 6 weeks.

| | |
|------------------|--------|
| Arm title | Active |
|------------------|--------|

Arm description:

27 Children between 1 month and 3 years of age (up to 4th birthday) with sensorineural hearing loss and documented CMV infection will receive valganciclovir HCl 16.0 mg/kg orally twice a day for 6 weeks

Valganciclovir: Valcyte (valganciclovir hydrochloride) 50 mg of valganciclovir free base per 1 mL, oral solution: given at 16.0 mg/kg, twice a day for 6 weeks.

| | |
|--|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Valganciclovir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Valcyte (valganciclovir hydrochloride) 50 mg of valganciclovir free base per 1 mL, oral solution: given at 16.0 mg/kg, twice a day for 6 weeks

| Number of subjects in period 1 | Placebo | Active |
|---|---------|--------|
| Started | 18 | 17 |
| Completed | 16 | 16 |
| Not completed | 2 | 1 |
| Required treatment outside protocol | 1 | - |
| Family member illness | 1 | - |
| Severe hearing loss borderline eligible | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---------|
| Reporting group title | Placebo |
| Reporting group description: 27 Children between 1 month and 3 years of age (up to 4th birthday) with sensoneural hearing loss and documented CMV infection will receive placebo orally twice a day for 6 weeks | |
| Placebo: Simple Syrup as 60-90% sucrose in purified water: given orally twice a day for 6 weeks | |
| Reporting group title | Active |
| Reporting group description: 27 Children between 1 month and 3 years of age (up to 4th birthday) with sensoneural hearing loss and documented CMV infection will receive valganciclovir HCl 16.0 mg/kg orally twice a day for 6 weeks | |
| Valganciclovir: Valcyte (valganciclovir hydrochloride) 50 mg of valganciclovir free base per 1 mL, oral solution: given at 16.0 mg/kg, twice a day for 6 weeks. | |

| Reporting group values | Placebo | Active | Total |
|--|---------|--------|-------|
| Number of subjects | 18 | 17 | 35 |
| Age categorical | | | |
| 27 Children between 1 month and 3 years of age (up to 4th birthday) with sensoneural hearing loss and documented CMV infection will receive placebo orally twice a day for 6 weeks | | | |
| Placebo: Simple Syrup as 60-90% sucrose in purified water: given orally twice a day for 6 weeks | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: months | | | |
| median | 19.5 | 17.8 | |
| standard deviation | ± 13.1 | ± 5.8 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 8 | 6 | 14 |
| Male | 10 | 11 | 21 |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Placebo |
| Reporting group description: 27 Children between 1 month and 3 years of age (up to 4th birthday) with sensorineural hearing loss and documented CMV infection will receive placebo orally twice a day for 6 weeks | |
| Placebo: Simple Syrup as 60-90% sucrose in purified water: given orally twice a day for 6 weeks | |
| Reporting group title | Active |
| Reporting group description: 27 Children between 1 month and 3 years of age (up to 4th birthday) with sensorineural hearing loss and documented CMV infection will receive valganciclovir HCl 16.0 mg/kg orally twice a day for 6 weeks | |
| Valganciclovir: Valcyte (valganciclovir hydrochloride) 50 mg of valganciclovir free base per 1 mL, oral solution: given at 16.0 mg/kg, twice a day for 6 weeks. | |
| Subject analysis set title | Randomized |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Randomized children between 1 month and 3 years of age (up to 4th birthday) with sensorineural hearing loss and documented CMV infection will receive placebo orally twice a day for 6 weeks | |

Primary: Number of Ears That Had (1) Improved Hearing or no Change in Hearing (2) Worsened Hearing.

| | |
|---|--|
| End point title | Number of Ears That Had (1) Improved Hearing or no Change in Hearing (2) Worsened Hearing. |
| End point description: A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss. Not both ears are evaluable for all subjects. In some subjects, only one ear is evaluable. | |
| End point type | Primary |
| End point timeframe: Day 1 through Day 180 | |

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Ears | | | | |
| Improve + no change | 27 | 20 | | |
| Worsened | 1 | 6 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0859 |
| Method | Generalized linear model for binary outc |

Secondary: Number of Best Ear That Had (1) Improved Hearing or no Change in Hearing (2) Worsened Hearing [ex. Improved+ no Change (Normal to Normal) Versus Other].

| | |
|-----------------|--|
| End point title | Number of Best Ear That Had (1) Improved Hearing or no Change in Hearing (2) Worsened Hearing [ex. Improved+ no Change (Normal to Normal) Versus Other]. |
|-----------------|--|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss. For this outcome, we combine the improved hearing and no change for the special case only of normal to normal. Other category include worsened and no change from (1) mild to mild hearing loss, (2) moderate to moderate hearing loss, or (3) severe to severe hearing loss.

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

End point timeframe:

Day 1 through Day 180

| End point values | Placebo | Active | | |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 12 | | |
| Units: Participants | | | | |
| Improved + normal to normal | 9 | 6 | | |
| No change abnormal or worsened | 6 | 6 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7068 |
| Method | Fisher exact |

Secondary: Adverse Event (AE) Resulting in Unanticipated Medically Attended Visit

| | |
|-----------------|--|
| End point title | Adverse Event (AE) Resulting in Unanticipated Medically Attended Visit |
|-----------------|--|

End point description:

Adverse event resulting in unanticipated medically attended visit. This outcome summarizes the number of adverse events (AEs) that resulted in the unanticipated medically attended visit.

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

End point timeframe:

Day 1 thru day 70

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 17 | | |
| Units: Participants | | | | |
| No | 15 | 17 | | |
| Yes | 3 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Event (AE) Resulting in Unresolved Outcome

| | |
|-----------------|--|
| End point title | Adverse Event (AE) Resulting in Unresolved Outcome |
|-----------------|--|

End point description:

Adverse event resulting in unresolved outcome. This outcome summarizes the number of adverse events (AEs) that resulted in unresolved outcome of that AE.

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

End point timeframe:

Day 1 thru day 70

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 17 | | |
| Units: Participants | | | | |
| No | 18 | 17 | | |
| Yes | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adverse Events in the Active Group That Resulted in Discontinuation of Valganciclovir

| | |
|-----------------|--|
| End point title | Number of Adverse Events in the Active Group That Resulted in Discontinuation of Valganciclovir ^[1] |
|-----------------|--|

End point description:

AE resulting in discontinuation of valganciclovir (active group only). This outcome summarizes the number of adverse events (AEs) that resulted in the discontinuation of valganciclovir in the active group only.

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

End point timeframe:

Day 1 thru day 70

Notes:

[1] - 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 just for the participants who had randomised to receive the IMP.

| End point values | Active | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: Participants | | | | |
| No | 17 | | | |
| Yes | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: The Quantitative Log Reduction in CMV in Saliva Detected After 6 Weeks of Therapy

| | |
|-----------------|---|
| End point title | The Quantitative Log Reduction in CMV in Saliva Detected After 6 Weeks of Therapy |
|-----------------|---|

End point description:

The quantitative log reduction in CMV in saliva (urine) detected after 6 weeks of therapy. Quantitative viral load by PCR in log 10 units measured in urine after 6 weeks of therapy; if undetectable, viral load is assigned a value of 10 (1 in log 10 units)

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

End point timeframe:

Baseline thru months 6

| End point values | Placebo | Active | | |
|--|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 17 | | |
| Units: log10 IU/ml | | | | |
| least squares mean (confidence interval 95%) | 0.0057 (-0.6395 to 0.6508) | 1.3202 (0.6894 to 1.9509) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: The Quantitative Log Reduction in Viruria Detected After 6 Weeks of Therapy

| | |
|---|---|
| End point title | The Quantitative Log Reduction in Viruria Detected After 6 Weeks of Therapy |
| End point description: | |
| The quantitative log reduction in viruria (urine) detected after 6 weeks of therapy. Quantitative viral load by PCR in log 10 units measured in urine after 6 weeks of therapy; if undetectable, viral load is assigned a value of 10 (1 in log 10 units) | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline thru months 6 | |

| End point values | Placebo | Active | | |
|--|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 15 | | |
| Units: log10 IU/ml | | | | |
| least squares mean (confidence interval 95%) | 0.8390 (-0.05057 to 1.7286) | 1.2152 (0.5274 to 1.9029) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: The Quantitative Log Change in Viremia From Baseline to Month 6.

| | |
|---|--|
| End point title | The Quantitative Log Change in Viremia From Baseline to Month 6. |
| End point description: | |
| The quantitative change (Month 6 minus baseline) in viremia (blood) Quantitative viral load by PCR in log 10 units measured in urine after 6 weeks of therapy; if undetectable, viral load is assigned a value of 10 (1 in log 10 units). | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to month 6 | |

| End point values | Placebo | Active | | |
|--|-----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 17 | | |
| Units: log10 IU/ml | | | | |
| least squares mean (confidence interval 95%) | -0.1528 (-0.5721 to 0.2664) | 0.4908 (0.08108 to 0.9005) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Detection of CMV in Saliva PCR Six Month After Trial Entry

| | |
|---|--|
| End point title | Detection of CMV in Saliva PCR Six Month After Trial Entry |
| End point description: | |
| Each subject either has positive or negative PCR results. Virus is detected if the PCR is positive. | |
| End point type | Secondary |
| End point timeframe: | |
| At 6 months | |

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: Participants | | | | |
| Positive | 8 | 7 | | |
| Negative | 8 | 9 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Fisher exact |

Secondary: Detection of CMV in Saliva by PCR Six Weeks After Trial Entry

| | |
|-----------------|---|
| End point title | Detection of CMV in Saliva by PCR Six Weeks After Trial Entry |
|-----------------|---|

End point description:

Each subject either has positive or negative PCR results. Virus is detected if the PCR is positive.

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

End point timeframe:

At 6 weeks (Day 42)

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: Participants | | | | |
| Positive | 9 | 3 | | |
| Negative | 7 | 13 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0659 |
| Method | Fisher exact |

Secondary: Detection of Viremia (Blood) by PCR Six Month After Trial Entry

| | |
|-----------------|---|
| End point title | Detection of Viremia (Blood) by PCR Six Month After Trial Entry |
|-----------------|---|

End point description:

Each subject either has positive or negative PCR results. Virus is detected if the PCR is positive.

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

End point timeframe:

At 6 months

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 15 | | |
| Units: Participants | | | | |
| Positive | 4 | 3 | | |
| Negative | 11 | 12 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 30 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Fisher exact |

Secondary: Detection of Viremia (Blood) by PCR Six Weeks After Trial Entry

| | |
|------------------------|---|
| End point title | Detection of Viremia (Blood) by PCR Six Weeks After Trial Entry |
| End point description: | Each subject either has positive or negative PCR results. Virus is detected if the PCR is positive. |
| End point type | Secondary |
| End point timeframe: | At 6 weeks (Day 42) |

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | Placebo | Active | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 14 | | |
| Units: Participants | | | | |
| Positive | 4 | 2 | | |
| Negative | 11 | 12 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 29 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6513 |
| Method | Fisher exact |

Secondary: Detection of Viruria (Urine) by PCR Six Month After Trial Entry

| | |
|-----------------|---|
| End point title | Detection of Viruria (Urine) by PCR Six Month After Trial Entry |
|-----------------|---|

End point description:

Each subject either has positive or negative PCR results. Virus is detected if the PCR is positive.

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

End point timeframe:

At 6 months

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 14 | | |
| Units: Participants | | | | |
| Positive | 10 | 11 | | |
| Negative | 1 | 3 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6043 |
| Method | Fisher exact |

Secondary: Detection of Viruria (Urine) by PCR Six Weeks After Trial Entry

| | |
|-----------------|---|
| End point title | Detection of Viruria (Urine) by PCR Six Weeks After Trial Entry |
|-----------------|---|

End point description:

Each subject either has positive or negative PCR results. Virus is detected if the PCR is positive.

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

End point timeframe:

At 6 weeks (Day 42)

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: Participants | | | | |
| Positive | 11 | 1 | | |
| Negative | 1 | 11 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 24 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | Fisher exact |

Secondary: Change in Total Ear Hearing Assessments [Worse Versus Other] Between Baseline and Study Month 6.

| | |
|-----------------|--|
| End point title | Change in Total Ear Hearing Assessments [Worse Versus Other] Between Baseline and Study Month 6. |
|-----------------|--|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss.

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

End point timeframe:

Day 1 through Day 180

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Ears | | | | |
| Worsened | 1 | 6 | | |
| Other | 27 | 20 | | |

Statistical analyses

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |

| | |
|---|--|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0859 |
| Method | Generalized linear model for binary outc |

Secondary: Change in Total Ear Hearing Assessments [Worse+ no Change (Abnormal to Abnormal) Versus Other] Between Baseline and Study Month 6.

| | |
|-----------------|--|
| End point title | Change in Total Ear Hearing Assessments [Worse+ no Change (Abnormal to Abnormal) Versus Other] Between Baseline and Study Month 6. |
|-----------------|--|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss.

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

End point timeframe:

Day 1 through Day 180

| End point values | Placebo | Active | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Ears | | | | |
| worse + no change (abnormal to abnormal) | 19 | 20 | | |
| Other | 9 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Total Ear Hearing Assessments [Improved Versus Other] Between Baseline and Study Month 6.

| | |
|-----------------|---|
| End point title | Change in Total Ear Hearing Assessments [Improved Versus Other] Between Baseline and Study Month 6. |
|-----------------|---|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss.

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

End point timeframe:
Day 1 through Day 180

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Ears | | | | |
| Improved | 0 | 0 | | |
| Other | 28 | 26 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Best Ear Hearing Assessments [Worse Versus Other] Between Baseline and Study Month 6.

| | |
|-----------------|---|
| End point title | Change in Best Ear Hearing Assessments [Worse Versus Other] Between Baseline and Study Month 6. |
|-----------------|---|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss.

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

End point timeframe:
Day 1 through Day 180

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 12 | | |
| Units: Participants | | | | |
| Worsened | 0 | 3 | | |
| Other | 15 | 9 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |

| | |
|---|---------------|
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0752 |
| Method | Fisher exact |

Secondary: Change in Best Ear Hearing Assessments [Worse + no Change (Abnormal to Abnormal) Versus Other] Between Baseline and Study Month 6.

| | |
|-----------------|--|
| End point title | Change in Best Ear Hearing Assessments [Worse + no Change (Abnormal to Abnormal) Versus Other] Between Baseline and Study Month 6. |
|-----------------|--|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss.

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

End point timeframe:

Day 1 through Day 180

| End point values | Placebo | Active | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 12 | | |
| Units: Participants | | | | |
| No change abnormal to abnormal + worsened | 6 | 6 | | |
| Improved + normal to normal | 9 | 6 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7068 |
| Method | Fisher exact |

Secondary: Change in Best Ear Hearing Assessments [Improved Versus Other] Between Baseline and Study Month 6.

| | |
|-----------------|---|
| End point title | Change in Best Ear Hearing Assessments [Improved Versus |
|-----------------|---|

End point description:

A single, independent study audiologist who is masked (blinded) to treatment assignment will assess the audiology test battery for each subject and assign the classifications of normal hearing, mild hearing loss, moderate hearing loss, or severe hearing loss based upon their hearing thresholds (in decibels). The classifications will be assigned by ear (one for the left ear and one for the right ear), giving "total ear" classifications. At the analyses stage, the "best ear" classification for the subject at that study visit will be determined; for example, if a subject had mild hearing loss in their left ear and severe hearing loss in their right ear, then the "best ear" classification will be mild hearing loss.

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

End point timeframe:

Day 1 through Day 180

| End point values | Placebo | Active | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 12 | | |
| Units: Participants | | | | |
| Improved | 0 | 0 | | |
| No change or worsened | 15 | 12 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Active |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Fisher exact |

Secondary: Association of Change in Viral Load (Blood) With Change in Total Ear Hearing at 6 Months

| | |
|-----------------|--|
| End point title | Association of Change in Viral Load (Blood) With Change in Total Ear Hearing at 6 Months |
|-----------------|--|

End point description:

Analysis of actual viral load was done using log base 10 transformation. Undetectable viral load value was replaced by a value of 10. A summary measure of the viral load over time considers all time points available by calculating the average area under the curve (AUC) (trapezoidal rule) applied to the log base 10 viral load. Average is based on the maximum period of time with viral load data for a given subject. The average or standardize AUC units is therefore the original AUC units of log 10 copies/ml*days divided by days in study which equals log 10 copies/ml.

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

End point timeframe:

At 6 months

| End point values | Randomized | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 31 | | | |
| Units: Ears | | | | |
| log mean (standard deviation) | | | | |
| Improved + normal to normal | 1.396 (\pm 0.542) | | | |
| No change abnormal + worsened | 1.326 (\pm 0.566) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Association of Change in Viral Load (Saliva) With Change in Total Ear Hearing at 6 Months

| | |
|-----------------|---|
| End point title | Association of Change in Viral Load (Saliva) With Change in Total Ear Hearing at 6 Months |
|-----------------|---|

End point description:

Analysis of actual viral load was done using log base 10 transformation. Undetectable viral load value was replaced by a value of 10. A summary measure of the viral load over time considers all time points available by calculating the average area under the curve (AUC) (trapezoidal rule) applied to the log base 10 viral load. Average is based on the maximum period of time with viral load data for a given subject. The average or standardize AUC units is therefore the original AUC units or log 10 copies/ml*days divided by days in study which equals log 10 copies/ml.

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

End point timeframe:

At 6 months

| End point values | Randomized | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 31 | | | |
| Units: log 10 copies/ml | | | | |
| log mean (standard deviation) | | | | |
| Improved + normal to normal | 2.447 (\pm 1.715) | | | |
| No change abnormal + worsened | 2.290 (\pm 1.349) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Association of Change in Viral Load (Urine) With Change in Total Ear Hearing at 6 Months

| | |
|-----------------|--|
| End point title | Association of Change in Viral Load (Urine) With Change in Total Ear Hearing at 6 Months |
|-----------------|--|

End point description:

Analysis of actual viral load was done using log base 10 transformation. Undetectable viral load value was replaced by a value of 10. A summary measure of the viral load over time considers all time points available by calculating the average area under the curve (AUC) (trapezoidal rule) applied to the log base 10 viral load. Average is based on the maximum period of time with viral load data for a given subject. The average or standardize AUC units is therefore the original AUC units of log 10 copies/ml*days divided by days in study which equals log 10 copies/ml.

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

End point timeframe:

At 6 months

| | | | | |
|-------------------------------|----------------------|--|--|--|
| End point values | Randomized | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 29 | | | |
| Units: log 10 copies/ml | | | | |
| log mean (standard deviation) | | | | |
| Improved + normal to normal | 3.562 (\pm 1.139) | | | |
| No change abnormal + worsened | 3.583 (\pm 1.370) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Association of Change in Viral Load (Blood) With Change in Best Ear Hearing at 6 Months

| | |
|-----------------|---|
| End point title | Association of Change in Viral Load (Blood) With Change in Best Ear Hearing at 6 Months |
|-----------------|---|

End point description:

Analysis of actual viral load was done using log base 10 transformation. Undetectable viral load value was replaced by a value of 10. A summary measure of the viral load over time considers all time points available by calculating the average area under the curve (AUC) (trapezoidal rule) applied to the log base 10 viral load. Average is based on the maximum period of time with viral load data for a given subject. The average or standardize AUC units is therefore the original AUC units of log 10 copies/ml*days divided by days in study which equals log 10 copies/ml.

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

End point timeframe:

At 6 months

| End point values | Randomized | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 27 | | | |
| Units: log 10 copies/ml | | | | |
| log mean (standard deviation) | | | | |
| Improved + normal to normal | 1.396 (± 0.542) | | | |
| No change abnormal + worsened | 1.359 (± 0.668) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Association of Change in Viral Load (Saliva) With Change in Best Ear Hearing at 6 Months

| | |
|-----------------|--|
| End point title | Association of Change in Viral Load (Saliva) With Change in Best Ear Hearing at 6 Months |
|-----------------|--|

End point description:

Analysis of actual viral load was done using log base 10 transformation. Undetectable viral load value was replaced by a value of 10. A summary measure of the viral load over time considers all time points available by calculating the average area under the curve (AUC) (trapezoidal rule) applied to the log base 10 viral load. Average is based on the maximum period of time with viral load data for a given subject. The average or standardize AUC units is therefore the original AUC units of log 10 copies/ml*days divided by days in study which equals log 10 copies/ml.

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

End point timeframe:

At 6 months

| End point values | Randomized | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 27 | | | |
| Units: log 10 copies/ml | | | | |
| log mean (standard deviation) | | | | |
| Improved + normal to normal | 2.447 (± 1.715) | | | |
| No change abnormal + worsened | 2.423 (± 1.484) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Association of Change in Viral Load (Urine) With Change in Best Ear Hearing at 6 Months

| | |
|-----------------|---|
| End point title | Association of Change in Viral Load (Urine) With Change in Best Ear Hearing at 6 Months |
|-----------------|---|

End point description:

Analysis of actual viral load was done using log base 10 transformation. Undetectable viral load value was replaced by a value of 10. A summary measure of the viral load over time considers all time points available by calculating the average area under the curve (AUC) (trapezoidal rule) applied to the log base 10 viral load. Average is based on the maximum period of time with viral load data for a given subject. The average or standardize AUC units is therefore the original AUC units of log 10 copies/ml*days divided by days in study which equals log 10 copies/ml.

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

End point timeframe:

At 6 months

| | | | | |
|-------------------------------|----------------------|--|--|--|
| End point values | Randomized | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 25 | | | |
| Units: log 10 copies/ml | | | | |
| log mean (standard deviation) | | | | |
| Improved + normal to normal | 3.562 (± 1.139) | | | |
| No change abnormal + worsened | 3.831 (± 1.570) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were recorded from Study Day 1 until 4 weeks after last dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Active Group |
|-----------------------|--------------|

Reporting group description:

Participants received study drug.

| | |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description:

Participants received placebo.

| Serious adverse events | Active Group | Placebo Group | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Active Group | Placebo Group | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 17 (76.47%) | 12 / 18 (66.67%) | |
| General disorders and administration site conditions | | | |
| Hypermetropia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pyrexia | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 4 / 18 (22.22%) 4 | |
| Condition aggravated subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 2 / 18 (11.11%) 6 | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Bronchiolitis subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 0 / 18 (0.00%) 0 | |
| Nasal congestion subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Rhinitis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 2 | 2 / 18 (11.11%) 3 | |
| Rhinovirus infection subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Asthma subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Psychiatric disorders | | | |

| | | | |
|--|----------------------|----------------------|--|
| Screaming subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Lethargy subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Hallucination subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Agitation subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Psychomotor hyperactivity subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Crying subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 2 / 18 (11.11%) 2 | |
| Investigations Blood urine present subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Protein urine present subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Injury, poisoning and procedural complications Injury subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 0 / 18 (0.00%) 0 | |
| Fracture subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Limb injury | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Fall subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 2 / 18 (11.11%) 4 | |
| Monocytopenia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Ear and labyrinth disorders Ear infection subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 1 / 18 (5.56%) 1 | |
| Auditory disorder subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 3 | 0 / 18 (0.00%) 0 | |
| Otitis media subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 2 / 18 (11.11%) 3 | |
| Vomiting subjects affected / exposed occurrences (all) | 5 / 17 (29.41%) 5 | 2 / 18 (11.11%) 5 | |
| Decreased appetite subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Weight decreased subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Gastroenteritis viral | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Teething | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 2 / 18 (11.11%) | |
| occurrences (all) | 2 | 2 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 18 (5.56%) | |
| occurrences (all) | 1 | 2 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Reflux gastritis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Petechiae | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Impetigo | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rash papular | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pallor | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 18 (5.56%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|--|--|--|
| Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Musculoskeletal and connective tissue disorders Osteopenia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |
| Infections and infestations Viral infection subjects affected / exposed occurrences (all) Hand-foot-and-mouth disease subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all) Postoperative wound infection subjects affected / exposed occurrences (all) Varicella subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 | 2 / 18 (11.11%) 3 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 2 / 18 (11.11%) 2 | |
| Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 18 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported