



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Active (Oseltamivir)-Controlled Study to Assess the Safety, Pharmacokinetics, and Efficacy of Baloxavir Marboxil in Otherwise Healthy Pediatric Patients 1 to <12 Years of Age With Influenza-Like Symptoms

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-002169-21 |
| Trial protocol | ES PL |
| Global end of trial date | 03 April 2019 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 |
| This version publication date | 12 October 2019 |
| First version publication date | 12 October 2019 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | CP40563 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03629184 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-002440-PIP01-18 |
| 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 | 09 July 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 April 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 April 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the safety of a single dose of baloxavir marboxil with 5 days of oseltamivir administered twice daily.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 November 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Costa Rica: 2 |
| Country: Number of subjects enrolled | Spain: 3 |
| Country: Number of subjects enrolled | Mexico: 1 |
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Russian Federation: 1 |
| Country: Number of subjects enrolled | United States: 161 |
| Worldwide total number of subjects | 173 |
| EEA total number of subjects | 8 |

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) | 16 |
| Children (2-11 years) | 157 |
| 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: -

Pre-assignment

Screening details:

173 participants were enrolled and dosed in this study.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--------------------|
| Arm title | Baloxavir Marboxil |
|------------------|--------------------|

Arm description:

Participants will receive a single oral dose of baloxavir marboxil on Day 1 (based on body weight). Oseltamivir matching placebo will also be administered orally twice daily (BID) for 5 days.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Baloxavir Marboxil |
| Investigational medicinal product code | |
| Other name | Xofluza |
| Pharmaceutical forms | Granules for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received a single oral dose of baloxavir marboxil on Day 1 (based on body weight)

| | |
|--|------------------------------|
| Investigational medicinal product name | Oseltamivir matching placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Oseltamivir matching placebo was administered orally twice daily (BID) for 5 days

| | |
|------------------|-------------|
| Arm title | Oseltamivir |
|------------------|-------------|

Arm description:

Participants will receive oseltamivir orally BID for 5 days (based on body weight). Baloxavir marboxil matching placebo will also be administered orally on Day 1

| | |
|--|----------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Oseltamivir |
| Investigational medicinal product code | |
| Other name | Tamiflu |
| Pharmaceutical forms | Powder for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received oseltamivir orally BID for 5 days (based on body weight)

| | |
|--|-------------------------------------|
| Investigational medicinal product name | Baloxavir marboxil matching placebo |
| Investigational medicinal product code | |
| Other name | |

| | |
|--------------------------|------------------------------|
| Pharmaceutical forms | Granules for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Baloxavir marboxil matching placebo was administered orally on Day 1

| Number of subjects in period 1 | Baloxavir Marboxil | Oseltamivir |
|---------------------------------------|--------------------|-------------|
| Started | 115 | 58 |
| Completed | 112 | 57 |
| Not completed | 3 | 1 |
| Consent withdrawn by subject | 2 | 1 |
| Physician decision | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|--------------------|
| Reporting group title | Baloxavir Marboxil |
| Reporting group description: | |
| Participants will receive a single oral dose of baloxavir marboxil on Day 1 (based on body weight). Oseltamivir matching placebo will also be administered orally twice daily (BID) for 5 days. | |
| Reporting group title | Oseltamivir |
| Reporting group description: | |
| Participants will receive oseltamivir orally BID for 5 days (based on body weight). Baloxavir marboxil matching placebo will also be administered orally on Day 1 | |

| Reporting group values | Baloxavir Marboxil | Oseltamivir | Total |
|--|--------------------|-------------|-------|
| Number of subjects | 115 | 58 | 173 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 9 | 7 | 16 |
| Children (2-11 years) | 106 | 51 | 157 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 6.10 | 6.02 | |
| standard deviation | ± 2.90 | ± 3.20 | - |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 60 | 32 | 92 |
| Male | 55 | 26 | 81 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Asian | 1 | 0 | 1 |
| Black or African American | 6 | 5 | 11 |
| Native Hawaiian or other Pacific Islander | 0 | 1 | 1 |
| White | 98 | 51 | 149 |
| Multiple | 4 | 0 | 4 |
| Unknown | 5 | 1 | 6 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 52 | 27 | 79 |
| Not Hispanic or Latino | 63 | 31 | 94 |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Baloxavir Marboxil |
| Reporting group description: Participants will receive a single oral dose of baloxavir marboxil on Day 1 (based on body weight). Oseltamivir matching placebo will also be administered orally twice daily (BID) for 5 days. | |
| Reporting group title | Oseltamivir |
| Reporting group description: Participants will receive oseltamivir orally BID for 5 days (based on body weight). Baloxavir marboxil matching placebo will also be administered orally on Day 1 | |

Primary: Percentage of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|--|---|
| End point title | Percentage of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) ^[1] |
| End point description: An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. A serious adverse event (SAE) is any significant hazard, contraindication, side effect that is fatal or life-threatening, requires hospitalization or prolongation of an existing hospitalization, results in persistent or significant disability/ incapacity, is a congenital anomaly/ birth defect, is medically significant or requires intervention to prevent one or other of the outcomes listed above. | |
| End point type | Primary |
| End point timeframe: Up to Day 29 | |
| 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: Descriptive stats only. No statistical analyses were pre-defined. | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|-----------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 115 | 58 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Adverse Events (AEs) | 46.1 | 53.4 | | |
| Serious Adverse Events (SAEs) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Baloxavir Marboxil - Sparce PK Population

| | |
|-----------------|---|
| End point title | Plasma Concentrations of Baloxavir Marboxil - Sparce PK Population ^[2] |
|-----------------|---|

End point description:

Concentration data are provided by body-weight groups for participants receiving Baloxavir Marboxil only. Values below lower limit of quantification (0.5 ng/mL) are set to zero. Here 99999 represents results data which was not estimable due to low number of events.

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

End point timeframe:

Days 1 (Post-Dose), 2, 4, 6 and 10

Notes:

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

Justification: Concentration data are provided for participants receiving Baloxavir Marboxil only.

| End point values | Baloxavir Marboxil | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 107 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| 5 - <10 kg (Day 1) (n=1) | 0.000 (± 99999) | | | |
| 5 - <10 kg (Day 2) (n=1) | 0.000 (± 99999) | | | |
| 5 - <10 kg (Day 4) (n=0) | 99999 (± 99999) | | | |
| 5 - <10 kg (Day 6) (n=1) | 0.000 (± 99999) | | | |
| 5 - <10 kg (Day 10) (n=0) | 99999 (± 99999) | | | |
| 10 - <15 kg (Day 1) (n=16) | 0.073 (± 0.2001) | | | |
| 10 - <15 kg (Day 2) (n=7) | 0.000 (± 0.0000) | | | |
| 10 - <15 kg (Day 4) (n=9) | 0.000 (± 0.0000) | | | |
| 10 - <15 kg (Day 6) (n=13) | 0.000 (± 0.0000) | | | |
| 10 - <15 kg (Day 10)(n=3) | 0.000 (± 0.0000) | | | |
| 15 - <20 kg (Day 1) (n=22) | 0.090 (± 0.2386) | | | |
| 15 - <20 kg (Day 2) (n=13) | 0.000 (± 0.0000) | | | |
| 15 - <20 kg (Day 4) (n=7) | 0.000 (± 0.0000) | | | |
| 15 - <20 kg (Day 6) (n=17) | 0.000 (± 0.0000) | | | |
| 15 - <20 kg (Day 10) (n=3) | 0.000 (± 0.0000) | | | |
| >=20 kg (Day 1) (n=58) | 0.048 (± 0.1936) | | | |
| >=20 kg (Day 2) (n=34) | 0.000 (± 0.0000) | | | |
| >=20 kg (Day 4) (n=25) | 0.000 (± 0.0000) | | | |
| >=20 kg (Day 6) (n=56) | 0.000 (± 0.0000) | | | |
| >=20 kg (Day 10) (n=6) | 0.000 (± 0.0000) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of S-033447 - Sparce PK Population

| | |
|-----------------|---|
| End point title | Plasma Concentrations of S-033447 - Sparce PK Population ^[3] |
|-----------------|---|

End point description:

Concentration data are provided by body-weight groups for participants receiving Baloxavir Marboxil only. Here 99999 represents results data which was not estimable due to low number of events.

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

End point timeframe:

Days 1 (Post-Dose), 2, 4, 6 and 10

Notes:

[3] - 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: Concentration data are provided for participants receiving Baloxavir Marboxil only.

| End point values | Baloxavir Marboxil | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 107 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| 5 - <10 kg (Day 1) (n=1) | 45.700 (± 99999) | | | |
| 5 - <10 kg (Day 2) (n=1) | 45.800 (± 99999) | | | |
| 5 - <10 kg (Day 4) (n=0) | 99999 (± 99999) | | | |
| 5 - <10 kg (Day 6) (n=1) | 3.110 (± 99999) | | | |
| 5 - <10 kg (Day 10) (n=0) | 99999 (± 99999) | | | |
| 10 - <15 kg (Day 1) (n=16) | 49.084 (± 53.6689) | | | |
| 10 - <15 kg (Day 2) (n=7) | 42.900 (± 16.5227) | | | |
| 10 - <15 kg (Day 4) (n=9) | 9.233 (± 5.3879) | | | |
| 10 - <15 kg (Day 6) (n=13) | 2.965 (± 1.6480) | | | |
| 10 - <15 kg (Day 10) (n=3) | 0.367 (± 0.6351) | | | |
| 15 - <20 kg (Day 1) (n=22) | 64.160 (± 73.6320) | | | |
| 15 - <20 kg (Day 2) (n=13) | 67.729 (± 46.7346) | | | |
| 15 - <20 kg (Day 4) (n=7) | 15.840 (± 10.8285) | | | |
| 15 - <20 kg (Day 6) (n=17) | 4.829 (± 3.6562) | | | |

| | | | | |
|----------------------------|--------------------|--|--|--|
| 15 - <20 kg (Day 10) (n=3) | 1.110 (± 1.9226) | | | |
| >=20 kg (Day 1) (n=58) | 29.899 (± 26.1558) | | | |
| >=20 kg (Day 2) (n=34) | 56.287 (± 40.4073) | | | |
| >=20 kg (Day 4) (n=25) | 18.674 (± 11.2179) | | | |
| >=20 kg (Day 6) (n=56) | 7.397 (± 5.0530) | | | |
| >=20 kg (Day 10) (n=6) | 3.953 (± 2.2536) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Baloxavir Marboxil - Extensive PK Population

| | |
|-----------------|--|
| End point title | Plasma Concentrations of Baloxavir Marboxil - Extensive PK Population ^[4] |
|-----------------|--|

End point description:

Concentration data are provided by body-weight groups for participants receiving Baloxavir Marboxil only. Values below lower limit of quantification (0.5 ng/mL) are set to zero. Here 99999 represents results data which was not estimable due to low number of events.

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

End point timeframe:

Days 1 (Post-Dose), 2, 4, 6 and 10

Notes:

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

Justification: Concentration data are provided for participants receiving Baloxavir Marboxil only.

| End point values | Baloxavir Marboxil | | | |
|--|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, 0.5 - 2 hrs (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 4 hrs (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 6 hrs (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 2 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 4 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 6 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 10 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 0.5 - 2 hrs (10 - <15 kg) (n=4) | 0.000 (± 0.0000) | | | |
| Day 1, 4 hrs (10 - <15 kg) (n=2) | 0.000 (± 0.0000) | | | |

| | | | | |
|--|------------------|--|--|--|
| Day 1, 6 hrs (10 - <15 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 2 (10 - <15 kg) (n=3) | 0.000 (± 0.0000) | | | |
| Day 4 (10 - <15 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 6 (10 - <15 kg) (n=3) | 0.000 (± 0.0000) | | | |
| Day 10 (10 - <15 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 1, 0.5 - 2 hrs (15 - <20 kg) (n=4) | 0.000 (± 0.0000) | | | |
| Day 1, 4 hrs (15 - <20 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 1, 6 hrs (15 - <20 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 2 (15 - <20 kg) (n=2) | 0.000 (± 0.0000) | | | |
| Day 4 (15 - <20 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 6 (15 - <20 kg) (n=3) | 0.000 (± 0.0000) | | | |
| Day 10 (15 - <20 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 0.5 - 2 hrs (≥20 kg) (n=10) | 0.051 (± 0.1600) | | | |
| Day 1, 4 hrs (≥20 kg) (n=9) | 0.062 (± 0.1863) | | | |
| Day 1, 6 hrs (≥20 kg) (n=6) | 0.000 (± 0.0000) | | | |
| Day 2 (≥20 kg) (n=5) | 0.000 (± 0.0000) | | | |
| Day 4 (≥20 kg) (n=4) | 0.000 (± 0.0000) | | | |
| Day 6 (≥20 kg) (n=9) | 0.000 (± 0.0000) | | | |
| Day 10 (≥20 kg) (n=0) | 99999 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of S-033447 - Extensive PK Population

| | |
|-----------------|--|
| End point title | Plasma Concentrations of S-033447 - Extensive PK |
|-----------------|--|

End point description:

Concentration data are provided by body-weight groups for participants receiving Baloxavir Marboxil only. Values below lower limit of quantification (0.5 ng/mL) are set to zero. Here 99999 represents results data which was not estimable due to low number of events.

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

End point timeframe:

Days 1 (Post-Dose), 2, 4, 6 and 10

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Concentration data are provided for participants receiving Baloxavir Marboxil only.

| End point values | Baloxavir Marboxil | | | |
|--|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, 0.5 - 2 hrs (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 4 hrs (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 6 hrs (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 2 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 4 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 6 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 10 (5 - <10 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 0.5 - 2 hrs (10 - <15 kg) (n=4) | 10.768 (± 14.7987) | | | |
| Day 1, 4 hrs (10 - <15 kg) (n=2) | 49.500 (± 13.0108) | | | |
| Day 1, 6 hrs (10 - <15 kg) (n=1) | 41.000 (± 99999) | | | |
| Day 2 (10 - <15 kg) (n=3) | 28.933 (± 14.7514) | | | |
| Day 4 (10 - <15 kg) (n=1) | 2.230 (± 99999) | | | |
| Day 6 (10 - <15 kg) (n=3) | 3.131 (± 2.2828) | | | |
| Day 10 (10 - <15 kg) (n=1) | 0.000 (± 99999) | | | |
| Day 1, 0.5 - 2 hrs (15 - <20 kg) (n=4) | 93.883 (± 152.5431) | | | |
| Day 1, 4 hrs (15 - <20 kg) (n=1) | 72.900 (± 99999) | | | |
| Day 1, 6 hrs (15 - <20 kg) (n=1) | 80.300 (± 99999) | | | |
| Day 2 (15 - <20 kg) (n=2) | 42.640 (± 47.6024) | | | |
| Day 4 (15 - <20 kg) (n=1) | 12.200 (± 99999) | | | |
| Day 6 (15 - <20 kg) (n=3) | 2.663 (± 1.5387) | | | |
| Day 10 (15 - <20 kg) (n=0) | 99999 (± 99999) | | | |
| Day 1, 0.5 - 2 hrs (≥20 kg) (n=10) | 19.923 (± 27.0980) | | | |
| Day 1, 4 hrs (≥20 kg) (n=9) | 69.198 (± 55.7220) | | | |
| Day 1, 6 hrs (≥20 kg) (n=6) | 65.527 (± 43.0799) | | | |
| Day 2 (≥20 kg) (n=5) | 57.980 (± 37.8922) | | | |
| Day 4 (≥20 kg) (n=4) | 21.775 (± 3.7968) | | | |
| Day 6 (≥20 kg) (n=9) | 6.240 (± 3.3702) | | | |

| | | | | |
|------------------------------|----------------------|--|--|--|
| Day 10 (≥ 20 kg) (n=0) | 99999 (\pm 99999) | | | |
|------------------------------|----------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration to Time Curve from Time 0 to Infinity (AUC0-inf) of baloxavir marboxil and S-033447

| | |
|-----------------|--|
| End point title | Area Under the Concentration to Time Curve from Time 0 to Infinity (AUC0-inf) of baloxavir marboxil and S-033447 |
|-----------------|--|

End point description:

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

End point timeframe:

Up to Day 10

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|---|--------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | | |
| Units: Pending | | | | |
| arithmetic mean (confidence interval 95%) | (to) | (to) | | |

Notes:

[6] - Results will be provided from the pop-PK report before 03-Apr-2019.

[7] - Results will be provided from the pop-PK report before 03-Apr-2019.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of baloxavir marboxil and S-033447

| | |
|-----------------|--|
| End point title | Maximum Plasma Concentration (Cmax) of baloxavir marboxil and S-033447 |
|-----------------|--|

End point description:

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

End point timeframe:

Up to Day 10

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|---|--------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | | |
| Units: Pending | | | | |
| arithmetic mean (confidence interval 95%) | (to) | (to) | | |

Notes:

[8] - Results will be provided from the pop-PK report before 03-Apr-2019.

[9] - Results will be provided from the pop-PK report before 03-Apr-2019.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of baloxavir marboxil and S-033447

| | |
|-----------------|--|
| End point title | Time to Maximum Plasma Concentration (Tmax) of baloxavir marboxil and S-033447 |
|-----------------|--|

End point description:

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

End point timeframe:

Up to Day 10

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|---|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | | |
| Units: Pending | | | | |
| arithmetic mean (confidence interval 95%) | (to) | (to) | | |

Notes:

[10] - Results will be provided from the pop-PK report before 03-Apr-2019.

[11] - Results will be provided from the pop-PK report before 03-Apr-2019.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Half-Life (T1/2) of baloxavir marboxil and S-033447

| | |
|-----------------|--|
| End point title | Apparent Half-Life (T1/2) of baloxavir marboxil and S-033447 |
|-----------------|--|

End point description:

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

End point timeframe:

Up to Day 10

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|---|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[12] | 0 ^[13] | | |
| Units: Pending | | | | |
| arithmetic mean (confidence interval 95%) | (to) | (to) | | |

Notes:

[12] - Results will be provided from the pop-PK report before 03-Apr-2019.

[13] - Results will be provided from the pop-PK report before 03-Apr-2019.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation of Influenza Signs and Symptoms

| | |
|-----------------|---|
| End point title | Time to Alleviation of Influenza Signs and Symptoms |
|-----------------|---|

End point description:

Time to alleviation of influenza signs and symptoms is defined as the length of time taken from the start of treatment to the point at which all of the following criteria are met and remain so for at least 21.5 hours: - A score of 0 (no problem) or 1 (minor problem) for cough and nasal symptoms (items 14 and 15 of the Canadian Acute Respiratory Illness and Flu Scale [CARIFS]) - A "yes" response to the following question on the CARIFS: "Since the last assessment has the subject been able to return to day care/school, or resume his or her normal daily activity in the same way as performed prior to developing the flu?" - First return to afebrile state (tympanic temperature ≤ 37.2 degree Celsius [$^{\circ}\text{C}$])

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

End point timeframe:

Up to Day 15

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|----------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 80 | 43 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 138.1 (116.6 to 163.2) | 150.0 (115.0 to 165.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Fever

| | |
|-----------------|-------------------|
| End point title | Duration of Fever |
|-----------------|-------------------|

End point description:

Length of time taken by participants to return to afebrile state [tympanic temperature $\leq 37.2^{\circ}\text{C}$] and remaining so for at least 21.5 hours.

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

End point timeframe:

Up to Day 15

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 80 | 43 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 41.2 (24.5 to 45.7) | 46.8 (30.0 to 53.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Symptoms

| | |
|---|----------------------|
| End point title | Duration of Symptoms |
| End point description: The clinical efficacy of baloxavir marboxil is evaluated by duration of symptoms i.e., alleviation of all symptoms as defined by a score of 0 [no problem] or 1 [minor problem] and remaining so for at least 21.5 hours, for all 18 symptoms specified in the CARIFS questionnaire). | |
| End point type | Secondary |
| End point timeframe: Up to Day 15 | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 80 | 43 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 66.4 (43.7 to 76.4) | 67.9 (45.8 to 88.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Return to Normal Health and Activity

| | |
|---|--|
| End point title | Time to Return to Normal Health and Activity |
| End point description: Time to Return to Normal health and activity' is identified by a 'Yes' response to the following question on the CARIFS: "Since the last assessment has the patient been able to return to day care/school, or resume his or her normal daily activity in the same way as performed prior to developing the flu?" | |
| End point type | Secondary |

End point timeframe:

Up to Day 15

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 80 | 43 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 116.5 (94.9 to 138.0) | 111.6 (80.8 to 138.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Influenza-Related Complications

| | |
|---|--|
| End point title | Frequency of Influenza-Related Complications |
| End point description: Influenza related complications include death, hospitalization, radiologically confirmed pneumonia, bronchitis, sinusitis, otitis media, encephalitis/encephalopathy, febrile seizures, myositis. | |
| End point type | Secondary |
| End point timeframe: Up to Day 29 | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 43 | | |
| Units: count of events | | | | |
| Total | 6 | 4 | | |
| Death | 0 | 0 | | |
| Hospitalization | 0 | 0 | | |
| Sinusitis | 1 | 0 | | |
| Otitis Media | 3 | 3 | | |
| Pneumonia | 1 | 0 | | |
| Bronchitis | 1 | 0 | | |
| Encephalitis/Encephalopathy | 0 | 0 | | |
| Febrile Seizures | 0 | 1 | | |
| Myositis | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Influenza-Related Complications

| | |
|-----------------|---|
| End point title | Percentage of Participants with Influenza-Related Complications |
|-----------------|---|

End point description:

Influenza related complications include death, hospitalization, radiologically confirmed pneumonia, bronchitis, sinusitis, otitis media, encephalitis/encephalopathy, febrile seizures, myositis.

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

End point timeframe:

Up to Day 29

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|-----------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 43 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Total | 7.4 | 7.0 | | |
| Death | 0 | 0 | | |
| Hospitalization | 0 | 0 | | |
| Sinusitis | 1.2 | 0 | | |
| Otitis Media | 3.7 | 4.7 | | |
| Pneumonia | 1.2 | 0 | | |
| Bronchitis | 1.2 | 0 | | |
| Encephalitis/Encephalopathy | 0 | 0 | | |
| Febrile Seizures | 0 | 2.3 | | |
| Myositis | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Requiring Antibiotics

| | |
|-----------------|--|
| End point title | Percentage of Participants Requiring Antibiotics |
|-----------------|--|

End point description:

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

End point timeframe:

Up to Day 29

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|-----------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 43 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Total | 4.9 | 4.7 | | |
| Bronchitis | 0 | 0 | | |
| Otitis Media | 2.5 | 4.7 | | |
| Pneumonia | 1.2 | 0 | | |
| Sinusitis | 1.2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cessation of Viral Shedding by Virus Titer

| | |
|---|--|
| End point title | Time to Cessation of Viral Shedding by Virus Titer |
| End point description: | |
| Time to cessation of viral shedding by virus titer is defined as the time, in hours, between the initiation of any study treatment and first time when the influenza virus titer is below the limit of detection. Number of patients with post-baseline Virology assessment and a positive virus titer on Day 1 were included in this analysis. Here 99999 represents results data which was not estimable due to low number of events. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1 - Day 29 | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 67 | 37 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | | | | |
| Virus Titer | 24.2 (23.5 to 24.6) | 75.8 (68.9 to 97.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cessation of Viral Shedding by RT-PCR

| | |
|--|---|
| End point title | Time to Cessation of Viral Shedding by RT-PCR |
| End point description: | |
| Time to cessation of viral shedding by RT-PCR, in hours, is defined as the time between the initiation of any study treatment and first time when the virus RNA by RT-PCR is below the limit of detection. | |

Number of patients with post-baseline Virology assessment and a positive RNA at Day 1 were included in this analysis. Here 99999 represents results data which was not estimable due to low number of events.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 - Day 29 | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|----------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 76 | 39 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 242.5 (235.8 to 262.8) | 238.9 (214.0 to 286.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Influenza Virus Titer at Day 2, 4, 6, 10, 15, 29

| | |
|-----------------|--|
| End point title | Change from Baseline in Influenza Virus Titer at Day 2, 4, 6, 10, 15, 29 |
|-----------------|--|

End point description:

Influenza virus titer (log₁₀TCID₅₀/ML) is the quantity of influenza virus in a given volume within the samples obtained from nasal swabs. If influenza virus titer was less than the lower limit of quantification, the virus titer was imputed as 0.749 (log₁₀TCID₅₀/mL). A lower value indicates lower viral titer.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Day 2, 3 (optional), 4, 6, 10, 15 (optional), 29 | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|---|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 67 | 38 | | |
| Units: log ₁₀ TCID ₅₀ /ML | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Baloxvir Marboxil n=67/Osetamivir n=38) | 4.43 (± 1.36) | 4.27 (± 1.48) | | |
| Day 2 (Baloxvir Marboxil n=64/Osetamivir n=37) | -3.59 (± 1.34) | -1.79 (± 1.54) | | |
| Day 3 (Baloxvir Marboxil n=3 / Osetamivir n=2) | -2.83 (± 0.58) | -2.63 (± 0.88) | | |
| Day 4 (Baloxvir Marboxil n=61 / Osetamivir n=31) | -3.53 (± 1.38) | -3.27 (± 1.54) | | |
| Day 6 (Baloxvir Marboxil n=63 / Osetamivir n=35) | -3.55 (± 1.32) | -3.52 (± 1.50) | | |
| Day 10 (Baloxvir Marboxil n=4 / Osetamivir n=4) | -3.66 (± 1.40) | -3.50 (± 1.42) | | |

| | | | | |
|---|----------------|----------------|--|--|
| Day 15 (Baloxvir Marboxil n=4 / Osetamivir n=4) | -3.75 (± 0.54) | -3.63 (± 1.45) | | |
| Day 29 (Baloxvir Marboxil n=4 / Osetamivir n=4) | -3.50 (± 1.43) | -3.75 (± 1.19) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Amount of Virus RNA (RT-PCR) at Day 2, 4, 6, 10, 15, 29

| | |
|-----------------|---|
| End point title | Change from Baseline in the Amount of Virus RNA (RT-PCR) at Day 2, 4, 6, 10, 15, 29 |
|-----------------|---|

End point description:

If the amount of virus RNA was less than the lower limit of quantification, the amount of virus RNA was imputed as 2.18 for flu A and 2.93 for flu B (log10 virus particles/mL). Here 99999 represents results data which was not estimable due to low number of events.

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

End point timeframe:

Baseline, Day 2, 3 (optional), 4, 6, 10, 15 (optional), 29

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|---|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 76 | 40 | | |
| Units: log10 virus particles/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Baloxvir Marboxil n=76/Osetamivir n=40) | 6.46 (± 1.50) | 6.86 (± 1.02) | | |
| Day 2 (Baloxvir Marboxil n=70 / Osetamivir n=39) | -1.74 (± 1.13) | -1.12 (± 1.12) | | |
| Day 3 (Baloxvir Marboxil n=4 / Osetamivir n=2) | -1.78 (± 1.50) | -2.21 (± 0.94) | | |
| Day 4 (Baloxvir Marboxil n=61 / Osetamivir n=30) | -2.40 (± 1.50) | -2.47 (± 1.35) | | |
| Day 6 (Baloxvir Marboxil n=60 / Osetamivir n=30) | -2.73 (± 1.78) | -3.32 (± 1.27) | | |
| Day 10 (Baloxvir Marboxil n=35 / Osetamivir n=15) | -3.55 (± 1.62) | -3.81 (± 1.19) | | |
| Day 15 (Baloxvir Marboxil n=2 / Osetamivir n=1) | -1.24 (± 3.06) | -4.44 (± 99999) | | |
| Day 29 (Baloxvir Marboxil n=1 / Osetamivir n=0) | 2.18 (± 99999) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Influenza Virus Titer at Day 2, 4, 6, 10

| | |
|-----------------|---|
| End point title | Percentage of Participants with Positive Influenza Virus Titer at Day 2, 4, 6, 10 |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline, Day 2, 3 (optional), 4, 6, 10

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|-----------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 43 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline | 82.7 | 88.4 | | |
| Day 2 | 12.3 | 65.1 | | |
| Day 3 (optional) | 1.2 | 2.3 | | |
| Day 4 | 19.8 | 20.9 | | |
| Day 6 | 9.9 | 4.7 | | |
| Day 10 | 1.2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Positive by RT-PCR at Day 2, 4, 6, 10, 15, 29

| | |
|-----------------|--|
| End point title | Percentage of Participants Positive by RT-PCR at Day 2, 4, 6, 10, 15, 29 |
|-----------------|--|

End point description:

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

End point timeframe:

Day 2, 3 (optional), 4, 6, 10, 15 (optional), 29

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|-----------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 43 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline | 93.8 | 93.0 | | |
| Day 2 | 86.4 | 90.7 | | |
| Day 3 (optional) | 4.9 | 4.7 | | |

| | | | | |
|-------------------|------|------|--|--|
| Day 4 | 76.5 | 74.4 | | |
| Day 6 | 72.8 | 65.1 | | |
| Day 10 | 40.7 | 34.9 | | |
| Day 15 (optional) | 2.5 | 2.3 | | |
| Day 29 | 1.2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve in Virus Titer

| | |
|--|-------------------------------------|
| End point title | Area Under the Curve in Virus Titer |
| End point description: Area under the curve (AUC) in virus titer was calculated using the trapezoidal method. | |
| End point type | Secondary |
| End point timeframe: Day 1 - Day 29 | |

| End point values | Baloxavir Marboxil | Oseltamivir | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 67 | 37 | | |
| Units: log[TCID/mL]*hours | | | | |
| arithmetic mean (standard deviation) | -863.81 (± 543.37) | -849.29 (± 684.43) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve in the Amount of Virus RNA (RT-PCR)

| | |
|---|--|
| End point title | Area Under the Curve in the Amount of Virus RNA (RT-PCR) |
| End point description: AUC in virus RNA (RT-PCR) is defined as AUC of change from baseline in the amount of virus RNA (RT-PCR) from Day 1 to Day 10. AUC is calculated using the trapezoidal method similar to AUC in virus titer. | |
| End point type | Secondary |
| End point timeframe: Day 1 - Day 10 | |

| | | | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| End point values | Baloxavir Marboxil | Oseltamivir | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 39 | | |
| Units: log VPs/mL*hours | | | | |
| arithmetic mean (standard deviation) | -381.53 (± 338.53) | -353.31 (± 304.01) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline (Day 1) until 28 days after the last dose of study drug (29 days)

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Oseltamivir |
|-----------------------|-------------|

Reporting group description:

Participants will receive oseltamivir orally BID for 5 days (based on body weight). Baloxavir marboxil matching placebo will also be administered orally on Day 1

| | |
|-----------------------|--------------------|
| Reporting group title | Baloxavir Marboxil |
|-----------------------|--------------------|

Reporting group description:

Participants will receive a single oral dose of baloxavir marboxil on Day 1 (based on body weight). Oseltamivir matching placebo will also be administered orally twice daily (BID) for 5 days.

| Serious adverse events | Oseltamivir | Baloxavir Marboxil | |
|---|----------------|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 115 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Oseltamivir | Baloxavir Marboxil | |
|---|------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 58 (22.41%) | 15 / 115 (13.04%) | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 6 / 115 (5.22%) | |
| occurrences (all) | 1 | 6 | |
| Vomiting | | | |
| subjects affected / exposed | 9 / 58 (15.52%) | 7 / 115 (6.09%) | |
| occurrences (all) | 10 | 7 | |
| Infections and infestations | | | |

| | | | |
|-----------------------------|----------------|-----------------|--|
| Otitis Media | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | 3 / 115 (2.61%) | |
| occurrences (all) | 5 | 3 | |

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