# Clinical trial results:
# A randomised, double-blind, two-way crossover study to investigate the effect of inhaled fluticasone furoate on short-term growth in paediatric subjects with asthma

## Summary

| | |
|---|---|
| EudraCT number | 2015-000841-22 |
| Trial protocol | DK |
| Global end of trial date | 21 December 2015 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 July 2016 |
| First version publication date | 03 July 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | HZA107112 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact | GSK Response Center, GlaxoSmithKline, 1-866 +4357343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1-866 +4357343, |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000431-PIP01-08 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 13 April 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 21 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effect of two weeks treatment with inhaled fluticasone furoate versus placebo once daily on short-term lower-leg growth using a knemometer.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 September 2015 |
| 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 | Denmark: 60 |
| Worldwide total number of subjects | 60 |
| EEA total number of subjects | 60 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 60 |
| 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:

Study consisted of run-in period of two-weeks followed by two treatment periods of 14 days each (+/- 4 days) separated by a 14-day washout period and a follow-up visit of approximately 7 days post last dose. The total participation time in the study was approximately 9 Weeks.

### Pre-assignment

Screening details:

A total of 60 participants were randomized to receive one of the two treatment sequences; placebo followed by inhaled fluticasone furoate or inhaled fluticasone furoate followed by placebo. All 60 participants received at least one single dose of study medication.

### Period 1

| | |
|---|---|
| Period 1 title | Double-blind treatment Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo followed by fluticasone furoate |

Arm description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 1 participants received oral inhalation of placebo OD for 14 days +/- 4 days in Treatment Period 1, followed by oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| Investigational medicinal product name | Fluticasone furoate 50 mcg Dry Powder Inhaler |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate 50 mcg was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| **Arm title** | Fluticasone furoate followed by placebo |

Arm description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 2 participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 1 followed by oral inhalation of placebo, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were

provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| Investigational medicinal product name | Fluticasone furoate 50 mcg Dry Powder Inhaler |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate 50 mcg was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| **Number of subjects in period 1** | Placebo followed by fluticasone furoate | Fluticasone furoate followed by placebo |
|---|---|---|
| Started | 30 | 30 |
| Completed | 29 | 30 |
| Not completed | 1 | 0 |
| Adverse event, non-fatal | 1 | - |

## Period 2

| | |
|---|---|
| Period 2 title | Washout Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Monitor, Subject, Investigator, Data analyst, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo followed by fluticasone furoate |

Arm description:

The two treatment periods were separated by a two-week wash-out period in which all participants did not receive study medication, but were provided a salbutamol inhaler for symptomatic relief of asthma symptoms.

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

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| Investigational medicinal product name | Fluticasone furoate 50 mcg Dry Powder Inhaler |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate 50 mcg was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| **Arm title** | Fluticasone furoate followed by placebo |

Arm description:

The two treatment periods were separated by a two-week wash-out period in which all participants did not receive study medication, but were provided a salbutamol inhaler for symptomatic relief of asthma symptoms.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| Investigational medicinal product name | Fluticasone furoate 50 mcg Dry Powder Inhaler |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate 50 mcg was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| **Number of subjects in period 2** | Placebo followed by fluticasone furoate | Fluticasone furoate followed by placebo |
|---|---|---|
| Started | 29 | 30 |
| Completed | 28 | 30 |
| Not completed | 1 | 0 |
| Adverse event, non-fatal | 1 | - |

## Period 3

| | |
|---|---|
| Period 3 title | Double-blind treatment Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo followed by fluticasone furoate |

Arm description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 1 participants received oral inhalation of placebo OD for 14 days +/- 4 days in Treatment Period 1, followed by oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| Investigational medicinal product name | Fluticasone furoate 50 mcg Dry Powder Inhaler |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate 50 mcg was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| **Arm title** | Fluticasone furoate followed by placebo |

Arm description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 2 participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 1 followed by oral inhalation of placebo, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| | |
|---|---|
| Investigational medicinal product name | Fluticasone furoate 50 mcg Dry Powder Inhaler |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|---|
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate 50 mcg was administered once daily (OD) for 14 days +/- 4 days. Each dose was administered via dry powder inhaler.

| **Number of subjects in period 3** | Placebo followed by fluticasone furoate | Fluticasone furoate followed by placebo |
|---|---|---|
| Started | 28 | 30 |
| Completed | 28 | 30 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Double-blind treatment Period 1 |

Reporting group description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 1 participants received oral inhalation of placebo OD for 14 days +/- 4 days in Period 1, followed by oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Period 2. Sequence 2 participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Period 1 followed by oral inhalation of placebo, OD for 14 days +/- 4 days in Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| **Reporting group values** | Double-blind treatment Period 1 | Total | |
|---|---|---|---|
| Number of subjects | 60 | 60 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | <br><br>8.7<br>± 1.53 | <br><br><br>- | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 24 | 24 | |
| Male | 36 | 36 | |
| Race, Customized<br>Units: Subjects | | | |
| Asian - Central/South Asian Heritage | 1 | 1 | |
| White - White/Caucasian/European Heritage | 59 | 59 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo followed by fluticasone furoate |

Reporting group description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 1 participants received oral inhalation of placebo OD for 14 days +/- 4 days in Treatment Period 1, followed by oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Reporting group title | Fluticasone furoate followed by placebo |

Reporting group description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 2 participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 1 followed by oral inhalation of placebo, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Reporting group title | Placebo followed by fluticasone furoate |

Reporting group description:

The two treatment periods were separated by a two-week wash-out period in which all participants did not receive study medication, but were provided a salbutamol inhaler for symptomatic relief of asthma symptoms.

| | |
|---|---|
| Reporting group title | Fluticasone furoate followed by placebo |

Reporting group description:

The two treatment periods were separated by a two-week wash-out period in which all participants did not receive study medication, but were provided a salbutamol inhaler for symptomatic relief of asthma symptoms.

| | |
|---|---|
| Reporting group title | Placebo followed by fluticasone furoate |

Reporting group description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 1 participants received oral inhalation of placebo OD for 14 days +/- 4 days in Treatment Period 1, followed by oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Reporting group title | Fluticasone furoate followed by placebo |

Reporting group description:

Participants received oral inhalation of 50 microgram (mcg) fluticasone furoate (FF) once daily (OD) or placebo for 14 days in either of the treatment periods in a two-way crossover design. Sequence 2 participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days in Treatment Period 1 followed by oral inhalation of placebo, OD for 14 days +/- 4 days in Treatment Period 2. The two treatment periods were separated by a two-week wash-out period. Additionally, all participants were provided a salbutamol inhaler for symptomatic relief of asthma symptoms during the 2-week run-in, washout, and treatment periods as needed.

| | |
|---|---|
| Subject analysis set title | Placebo |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants received oral inhalation of placebo OD for 14 days +/- 4 days during Period 1 or Period 2

| | |
|---|---|
| Subject analysis set title | Fluticasone furoate |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days during Period 1 or Period 2

## Primary: Mean growth rate in lower-leg growth (mm/week), as determined by knemometry

| End point title | Mean growth rate in lower-leg growth (mm/week), as determined by knemometry |
|---|---|

End point description:

Lower leg growth rate was assessed in growth population as change in the lower leg length from start to end of each 2-week treatment period, divided by time interval (number of days) between the two measurements, multiplied by 7. The Growth Population is defined as the Intent-To-Treat (ITT) population excluding participants having any of the following: did not fulfill growth-specific criteria; did not have growth assessment(s) at any defined time point; withdrawal from study due to adverse events related to major trauma to the legs, major surgery, or severe dehydration; received protocol prohibited medications that may affect short term growth, prior to randomization and during the study; protocol deviations defined in exclusion criteria for growth population. ITT Population consists of all randomized participants who received at least one dose of study drug.

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

End point timeframe:

Over a two week (14 day) treatment period for FF 50mcg OD and Placebo respectively

| **End point values** | Placebo | Fluticasone furoate | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58[1] | 58[2] | | |
| Units: millimeter per week | | | | |
| least squares mean (standard error) | 0.3638 (± 0.02793) | 0.3118 (± 0.02793) | | |

Notes:

[1] - Growth Population

[2] - Growth Population

### Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|

Statistical analysis description:

Analysis performed using ANCOVA with covariates period-level baseline and subject-level baseline lower-leg length, age, gender, treatment and period.
Please note: To clarify system limitations, the comparison groups for statistical analysis are fluticasone furoate vs. placebo. Although the system adds the subjects in each analysis group together (total 116 below), there are only 58 subjects measured in this analysis as this is a crossover study with the same 58 subjects in each arm.

| Comparison groups | Fluticasone furoate v Placebo |
|---|---|
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[3] |
| Method | ANCOVA |
| Parameter estimate | Adjusted Mean Difference |
| Point estimate | -0.052 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1217 |
| upper limit | 0.0176 |

Notes:

[3] - Non-inferiority would be demonstrated if the lower limit of the confidence interval (0.025,1-sided significance test level) for the mean difference in lower-leg growth rate of FF 50 mcg OD versus Placebo was greater than -0.20mm/week.

## Secondary: Number of participants with any adverse events (AE) and any serious adverse event (SAE).

| End point title | Number of participants with any adverse events (AE) and any serious adverse event (SAE). |
|---|---|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Serious Adverse Event (SAE) is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect. Number of participants with AEs and SAEs have been presented. Two participants randomized to Sequence 1 (Placebo/FF), were treated with placebo in Period 1; however, neither received FF in Period 2, due to premature withdrawal.

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

End point timeframe:

From the start of study treatment until follow-up (assessed up to 54 days)

| End point values | Placebo | Fluticasone furoate | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 60[4] | 58[5] | | |
| Units: Participants | 14 | 7 | | |

Notes:

[4] - ITT Population

[5] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs and non-serious AEs were collected from start of study medication through the Study Phase (7 weeks post-dose) and assessed up to 54 days. AEs reported during the wash-out and follow-up period are considered post-treatment and are not presented.

Adverse event reporting additional description:

On-treatment Serious Adverse Events (SAEs) and non-serious Adverse Events (AEs) are reported for the ITT Population, which comprises of all randomized participants who received at least one dose of study treatment.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

### Reporting groups

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

Reporting group description:

Participants received oral inhalation of placebo OD for 14 days +/- 4 days during Period 1 or Period 2

| | |
|---|---|
| Reporting group title | Fluticasone furoate |

Reporting group description:

Participants received oral inhalation of FF 50 mcg, OD for 14 days +/- 4 days during Period 1 or Period 2

| Serious adverse events | Placebo | Fluticasone furoate | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 0 / 58 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 0 / 58 (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: 3 %

| Non-serious adverse events | Placebo | Fluticasone furoate | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 60 (25.00%) | 7 / 58 (12.07%) | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 8 / 60 (13.33%) | 3 / 58 (5.17%) | |
| occurrences (all) | 9 | 4 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | 0 / 58 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | 2 / 58 (3.45%) | |
| occurrences (all) | 3 | 2 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | 2 / 58 (3.45%) | |
| occurrences (all) | 3 | 2 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 60 (8.33%) | 4 / 58 (6.90%) | |
| occurrences (all) | 5 | 4 | |

## 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