



Clinical trial results:

Effects of ultra-long acting bronchodilator therapy assessed by impulse oscillometry in smoking asthmatics taking inhaled corticosteroids

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-005317-23 |
| Trial protocol | GB |
| Global end of trial date | 22 May 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 25 November 2020 |
| First version publication date | 25 November 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 2013RC06 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02682862 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | University of Dundee - NHS Tayside |
| Sponsor organisation address | Residency Block, Level 3, Ninewells Hospital, George Pirie Way, Dundee, United Kingdom, DD1 9SY |
| Public contact | General Enquiries, Scottish Centre for Respiratory Research, 44 (0)1382 383902, scrr@dundee.ac.uk |
| Scientific contact | General Enquiries, Scottish Centre for Respiratory Research, 44 (0)1382 383902, scrr@dundee.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 | 22 May 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 May 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 May 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the effects of olodaterol alone versus olodaterol plus tiotropium given once daily as add-on therapy to pre-existing inhaled corticosteroids using impulse oscillometry in smoking asthmatics

Protection of trial subjects:

The study Sponsor carried out a study risk assessment before issuing approval. The study was approved by the East of Scotland Research Ethics Service (Ref: 15/ES/0032). Informed consent was obtained from all participants. Participants were checked against all inclusion and exclusion criteria and only participants deemed clinically stable were recruited into the study. A medically-qualified person confirmed that it was safe for the participant to receive the IMP. Participants were issued a peak flow and symptom diary to assess clinical stability throughout the study. Participants were also issued an out-of-hours contact card with the mobile number carried by medical staff for advice if they encountered any adverse effects. One week after the end of each treatment period, patients were contacted by phone as a safety follow-up.

Background therapy:

After the screening visit, participants entered a 2-4 week run-in period when LABA or LAMA were stopped and participants' ICS dose was rounded to equivalent reference ICS as HFA-BDP (Clenil Modulite pMDI). This dose of Clenil was then continued unchanged throughout the study.

Evidence for comparator:

We used the LABA olodaterol (OLO), and the combination of olodaterol with the LAMA tiotropium (OLO/TIO) both delivered via the soft mist Respimat inhaler. The rationale for choosing the Respimat device was that it was possible to deliver the OLO and OLO/TIO via the same device.

| | |
|---|--------------|
| Actual start date of recruitment | 11 July 2016 |
| 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 | United Kingdom: 29 |
| Worldwide total number of subjects | 29 |
| EEA total number of subjects | 29 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|----|
| wk | |
| 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) | 29 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subject recruitment began 11 July 2016 and the study completed on 22 May 2019. Of the 29 patients screened, 17 were randomised and 16 completed per protocol and were included in the final analysis.

Pre-assignment

Screening details:

Diagnosis of persistent asthma, current smokers, age 18-65 years, taking at least 400µg per day of ICS (as HFA-BDP Clenil equivalent dose). Patients with COPD or ACO were excluded. Patients who had an asthma exacerbation requiring systemic corticosteroids within 1 month of screening or requiring hospital admission within 3 months were excluded.

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 29 |
| Number of subjects completed | 17 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|--|
| Reason: Number of subjects | Did Not Meet Inclusion Criteria: 9 |
| Reason: Number of subjects | Worsening Asthma Symptoms During Run-In: 3 |

Period 1

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

Blinding implementation details:

Not applicable as this was an open-label study.

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|------------------|------------|
| Arm title | Olodaterol |
|------------------|------------|

Arm description: -

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Olodaterol |
| Investigational medicinal product code | |
| Other name | Striverdi Respimat |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

Participants inhaled 2 puffs (2.5 micrograms/puff) of olodaterol once daily in the morning for 2 - 4 weeks.

| | |
|------------------|-----------------------|
| Arm title | Olodaterol-Tiotropium |
|------------------|-----------------------|

Arm description: -

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Olodaterol-Tiotropium |
| Investigational medicinal product code | |
| Other name | Spiolto Respimat |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

Participants inhaled 2 puffs (2.5 micrograms/2.5micrograms per puff) of olodaterol-tiotropium once daily in the morning for 2 - 4 weeks.

| Number of subjects in period 1 | Olodaterol | Olodaterol-Tiotropium |
|--|------------|-----------------------|
| Started | 16 | 17 |
| Completed | 16 | 16 |
| Not completed | 0 | 1 |
| Unable to comply with procedures of the protocol | - | 1 |

Baseline characteristics

Reporting groups^[1]

| | |
|-----------------------|---------------|
| Reporting group title | Overall Trial |
|-----------------------|---------------|

Reporting group description: -

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: The worldwide number enrolled is the number of subjects screened into the study (29).

The number of subjects in the baseline period is the number who were randomised into the study (17).

Of these 17 subjects, 16 completed the study per protocol and were able to be analysed.

| Reporting group values | Overall Trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 17 | 17 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 17 | 17 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 42.41 | | |
| standard deviation | ± 11.72 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 10 | 10 | |
| Male | 7 | 7 | |

End points

End points reporting groups

| | |
|--|-----------------------|
| Reporting group title | Olodaterol |
| Reporting group description: - | |
| Reporting group title | Olodaterol-Tiotropium |
| Reporting group description: - | |
| Subject analysis set title | Completed Subjects |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| Sixteen (16) current smokers with persistent asthma who completed both arms of the study per protocol. | |

Primary: Total Airway Resistance (R5)

| | |
|------------------------|------------------------------|
| End point title | Total Airway Resistance (R5) |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|---|---------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: kPa/l/s | | | | |
| arithmetic mean (confidence interval 95%) | | | | |
| Pooled baseline | 0.58 (0.51 to 0.65) | 0.58 (0.51 to 0.65) | | |
| Peak first dose | 0.44 (0.37 to 0.51) | 0.43 (0.37 to 0.49) | | |
| Peak last dose | 0.45 (0.37 to 0.52) | 0.44 (0.36 to 0.51) | | |
| Final trough | 0.56 (0.47 to 0.66) | 0.51 (0.42 to 0.59) | | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | Repeated measures ANOVA |
| Comparison groups | Olodaterol v Olodaterol-Tiotropium |

| | |
|---|---------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | ANOVA |

Secondary: FEV1

| | |
|------------------------|-----------|
| End point title | FEV1 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: litre(s) | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 2.40 (± 0.18) | 2.40 (± 0.18) | | |
| Peak first dose | 2.64 (± 0.19) | 2.65 (± 0.20) | | |
| Peak last dose | 2.70 (± 0.19) | 2.74 (± 0.18) | | |
| Final trough | 2.53 (± 0.18) | 2.60 (± 0.18) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: FEF 25-75

| | |
|------------------------|-----------|
| End point title | FEF 25-75 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: L/s | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 1.46 (± 0.17) | 1.46 (± 0.17) | | |
| Peak first dose | 1.79 (± 0.20) | 1.78 (± 0.23) | | |
| Peak last dose | 1.82 (± 0.21) | 1.85 (± 0.21) | | |
| Final trough | 1.58 (± 0.18) | 2.51 (± 0.17) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: FVC

| | |
|------------------------|-----------|
| End point title | FVC |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: litre(s) | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 3.49 (± 0.20) | 3.49 (± 0.20) | | |
| Peak first dose | 3.65 (± 0.21) | 3.63 (± 0.21) | | |
| Peak last dose | 3.71 (± 0.21) | 3.77 (± 0.20) | | |
| Final trough | 3.59 (± 0.21) | 3.69 (± 0.20) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: R20

| | |
|------------------------|-----------|
| End point title | R20 |
| End point description: | |
| End point type | Secondary |

End point timeframe:

2-4 weeks

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: kPa/l/s | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 0.42 (± 0.02) | 0.42 (± 0.02) | | |
| Peak first dose | 0.36 (± 0.02) | 0.35 (± 0.02) | | |
| Peak last dose | 0.36 (± 0.02) | 0.36 (± 0.02) | | |
| Final trough | 0.41 (± 0.02) | 0.39 (± 0.02) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: R5-R20

| | |
|------------------------|-----------|
| End point title | R5-R20 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: kPa/l/s | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 0.17 (± 0.03) | 0.17 (± 0.03) | | |
| Peak first dose | 0.09 (± 0.02) | 0.08 (± 0.02) | | |
| Peak final dose | 0.09 (± 0.02) | 0.08 (± 0.02) | | |
| Final trough | 0.15 (± 0.03) | 0.12 (± 0.03) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AX

| | |
|------------------------|-----------|
| End point title | AX |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: kPa/l | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 1.81 (± 0.32) | 1.81 (± 0.32) | | |
| Peak first dose | 0.84 (± 0.23) | 0.75 (± 0.21) | | |
| Peak last dose | 0.80 (± 0.23) | 0.70 (± 0.22) | | |
| Final trough | 1.54 (± 0.40) | 1.16 (± 0.34) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fres

| | |
|------------------------|-----------|
| End point title | Fres |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: hertz | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 19.75 (± 1.19) | 19.75 (± 1.19) | | |
| Peak first dose | 14.66 (± 1.17) | 14.48 (± 1.15) | | |
| Peak last dose | 14.09 (± 1.27) | 13.69 (± 1.19) | | |
| Final trough | 18.40 (± 1.54) | 16.11 (± 1.48) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: X5

End point title X5

End point description:

End point type Secondary

End point timeframe:

2-4 weeks

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|---------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: kPa/l/s | | | | |
| arithmetic mean (standard error) | | | | |
| Polled baseline | -0.24 (\pm 0.03) | -0.24 (\pm 0.03) | | |
| Peak first dose | -0.17 (\pm 0.03) | -0.15 (\pm 0.02) | | |
| Peak last dose | -0.16 (\pm 0.02) | -0.15 (\pm 0.02) | | |
| Final trough | -0.21 (\pm 0.03) | -0.19 (\pm 0.03) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Symptoms AM

End point title Symptoms AM

End point description:

End point type Secondary

End point timeframe:

2-4 weeks

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|--------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: units | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 0.71 (\pm 0.12) | 0.63 (\pm 0.10) | | |
| End of treatment | 0.51 (\pm 0.14) | 0.39 (\pm 0.10) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Symptoms PM

End point title Symptoms PM

End point description:

End point type Secondary

End point timeframe:

2-4 weeks

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: units | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 0.63 (± 0.10) | 0.63 (± 0.10) | | |
| End of treatment | 0.31 (± 0.12) | 0.27 (± 0.08) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Reliever AM

End point title Reliever AM

End point description:

End point type Secondary

End point timeframe:

2-4 weeks

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: puffs | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 1.05 (± 0.20) | 10.5 (± 0.20) | | |
| End of treatment | 0.55 (± 0.17) | 0.45 (± 0.15) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Reliever PM

| | |
|------------------------|-------------|
| End point title | Reliever PM |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: puffs | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 0.92 (± 0.20) | 0.91 (± 0.20) | | |
| End of treatment | 0.55 (± 0.15) | 0.33 (± 0.09) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PEF AM

| | |
|------------------------|-----------|
| End point title | PEF AM |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: L/min | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 369 (± 26) | 369 (± 26) | | |
| End of treatment | 408 (± 34) | 420 (± 31) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PEF PM

| | |
|------------------------|-----------|
| End point title | PEF PM |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 2-4 weeks | |

| End point values | Olodaterol | Olodaterol-Tiotropium | | |
|----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: L/min | | | | |
| arithmetic mean (standard error) | | | | |
| Pooled baseline | 388 (± 31) | 388 (± 31) | | |
| End of treatment | 408 (± 34) | 420 (± 31) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the time a participant consented to join the study until the last study visit.

Adverse event reporting additional description:

Participants received training on how to record adverse events on trial-specific diary cards. At each study visit, participants were asked about the occurrence of any adverse events.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Received IMP |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | Received IMP | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Gastrointestinal disorders | | | |
| Irritable Bowel Syndrome | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Received IMP | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 17 (88.24%) | | |
| Injury, poisoning and procedural complications | | | |
| Limb Injury | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |

| | | | |
|--|-----------------|--|--|
| Headache | | | |
| subjects affected / exposed | 5 / 17 (29.41%) | | |
| occurrences (all) | 8 | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 3 | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 3 | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | | |
| occurrences (all) | 3 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Influenza-like illness | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | | |
| occurrences (all) | 2 | | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Tongue Blistering | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspepsia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 17 (5.88%)</p> <p>1</p> <p>1 / 17 (5.88%)</p> <p>1</p> <p>1 / 17 (5.88%)</p> <p>1</p> <p>1 / 17 (5.88%)</p> <p>1</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Lower respiratory tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 17 (29.41%)</p> <p>6</p> <p>2 / 17 (11.76%)</p> <p>2</p> <p>3 / 17 (17.65%)</p> <p>3</p> <p>1 / 17 (5.88%)</p> <p>1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Back Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Musculoskeletal stiffness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthritis</p> | <p>1 / 17 (5.88%)</p> <p>1</p> <p>2 / 17 (11.76%)</p> <p>2</p> <p>1 / 17 (5.88%)</p> <p>1</p> | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | | |
| Infections and infestations | | | |
| Oral Candidiasis | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | | |
| occurrences (all) | 2 | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Genital infection | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 15 December 2015 | REC Amendment - Amendment to notify REC of changes made during application to MHRA for initial study approval. |
| 02 August 2016 | REC & MHRA Amendment - Amendment to specify that Clenil Modulite is the steroid inhaler to be used as background medication during the study. |
| 03 April 2018 | REC Amendment - Amendment for use of additional sources for patient recruitment. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported