

**Clinical trial results:****A study to compare the addition of umeclidinium bromide (UMEC) to fluticasone furoate (FF)/vilanterol (VI), with placebo plus FF/VI in subjects with Chronic Obstructive Pulmonary Disease (COPD) -Study 1 Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2013-002238-19 |
| Trial protocol | RO |
| Global end of trial date | 01 April 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 02 May 2016 |
| First version publication date | 21 June 2015 |

Trial information**Trial identification**

| | |
|-----------------------|--------|
| Sponsor protocol code | 200109 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01957163 |
| 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, 1 866-435-7343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |

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 | 27 May 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 April 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy and safety of the addition of UMEC 125 mcg to FF/VI 100/25 mcg once-daily and the addition of UMEC 62.5 mcg to FF/VI 100/25 mcg once-daily, compared with placebo plus FF/VI 100/25 once-daily over 12 weeks in subjects with COPD.

Protection of trial subjects:

Spirometry procedures may cause difficulty breathing, changes in pulse rate/blood pressure, coughing, wheezing, chest tightness, or fainting. Subjects (sub.) will be monitored during the procedure for these effects, and spirometry will be discontinued if this occurs. Skin irritation is rare but could occur during ECG from the electrodes. It may be necessary to shave small patches of hair to properly attach electrodes. Sub. will be monitored during the procedure for these effects and should call their study doctor if effects do not resolve. Side effects of albuterol/salbutamol include shakiness, headache, sleeplessness, high blood pressure, heart beating fast/irregular beats, cough, wheezing, shortness of breath, increased fluid in the mouth, nausea, upset stomach, tiredness, anxiety/nervousness, or low blood potassium. Sub. should call their study doctor if they experience any of these symptoms. Sub. with poorly controlled COPD/experience an exacerbation of COPD during the run-in period will not be randomized. ICS/LABA combination therapy is associated with an increased risk of pneumonia but no other significant side effects in COPD. Sub. with a lower respiratory tract infection that required the use of antibiotics within 6 weeks prior to Visit 1 are excluded from the study in order to ensure patient safety. LABAs may increase the risk of asthma-related death. Sub. with a current diagnosis of asthma will be excluded from study participation. Cardiovascular effects such as cardiac arrhythmias, e.g., supraventricular tachycardia and extrasystoles, are also class effects associated with LABAs and LABA-containing therapy. Exclusion criteria have been set for sub. with uncontrolled or severe cardiovascular disease according to the PI's opinion where the potential risk may outweigh the benefit. The Investigator should also determine the clinical significance of abnormal ECG findings at screening and exclude sub. who would be at undue risk by participating in the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 04 October 2013 |
| 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 | Romania: 117 |
| Country: Number of subjects enrolled | United States: 197 |
| Country: Number of subjects enrolled | Chile: 150 |
| Country: Number of subjects enrolled | Canada: 150 |
| Country: Number of subjects enrolled | Argentina: 113 |
| Worldwide total number of subjects | 727 |
| EEA total number of subjects | 117 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 369 |
| From 65 to 84 years | 355 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

Participants ≥ 40 years of age with history of chronic obstructive pulmonary disease (COPD) and a smoking history of ≥ 10 pack-years were enrolled in the study. Participants completed a 4-week run-in period, in which they received fluticasone furoate 100 micrograms(μg)/vilanterol 25 μg , followed by a 12-week treatment period and 1-week follow-up.

Pre-assignment

Screening details:

A total of 619 participants (pars.) were randomized to study treatment and comprised the Intent-to-Treat (ITT) Population (participants randomized to treatment who received ≥ 1 dose of randomized study medication in the treatment period).

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 | Investigator, Monitor, Data analyst, Carer, Assessor, Subject |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Fluticasone furoate/vilanterol 100/25 μg + placebo |

Arm description:

Participants received one inhalation of fluticasone furoate (FF)/vilanterol (VI) 100/25 μg once-daily (OD) via a dry powder inhaler (DPI), followed by one inhalation of umeclidinium bromide (UMEC) matching placebo, administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

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

Dosage and administration details:

Matching placebo

| | |
|--|--------------------------------|
| Investigational medicinal product name | Fluticasone furoate/vilanterol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Fluticasone furoate/vilanterol 100/25 μg once daily

| | |
|------------------|---|
| Arm title | Fluticasone furoate/vilanterol 100/25 μg + UMEC 62.5 μg |
|------------------|---|

Arm description:

Participants received one inhalation of fluticasone furoate (FF)/vilanterol (VI) 100/25 μg once-daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide (UMEC) 62.5 μg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

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

| | |
|---|--|
| Investigational medicinal product name | UMEC |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |
| Dosage and administration details: 62.5 µg once daily | |
| Investigational medicinal product name | Fluticasone furoate/vilanterol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |
| Dosage and administration details: Fluticasone furoate/vilanterol 100/25 µg once daily | |
| Arm title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |

Arm description:

Participants received one inhalation of fluticasone furoate/vilanterol 100/25 µg once- daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide 125 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| | |
|---|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | UMEC |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |
| Dosage and administration details: 125 µg once daily | |
| Investigational medicinal product name | Fluticasone furoate/vilanterol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |
| Dosage and administration details: Fluticasone furoate/vilanterol 100/25 µg once daily | |

| Number of subjects in period 1^[1] | Fluticasone furoate/vilanterol 100/25 µg + placebo | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
|---|--|---|--|
| Started | 206 | 206 | 207 |
| Completed | 191 | 195 | 189 |
| Not completed | 15 | 11 | 18 |
| Adverse event, serious fatal | 1 | - | - |
| Consent withdrawn by subject | 4 | 2 | 4 |
| Adverse event, non-fatal | 4 | 2 | 4 |
| Met Protocol-Defined Stopping Criteria | - | - | 1 |

| | | | |
|--------------------|---|---|---|
| Lost to follow-up | - | 1 | - |
| Lack of efficacy | 5 | 4 | 9 |
| Protocol deviation | 1 | 2 | - |

Notes:

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

Justification: The baseline period includes only those enrolled participants who were randomized to treatment and received ≥ 1 dose of randomized study medication in the Treatment Period (n=619).

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + placebo |
|-----------------------|--|

Reporting group description:

Participants received one inhalation of fluticasone furoate (FF)/vilanterol (VI) 100/25 µg once-daily (OD) via a dry powder inhaler (DPI), followed by one inhalation of umeclidinium bromide (UMEC) matching placebo, administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| | |
|-----------------------|---|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg |
|-----------------------|---|

Reporting group description:

Participants received one inhalation of fluticasone furoate (FF)/vilanterol (VI) 100/25 µg once- daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide (UMEC) 62.5 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| | |
|-----------------------|--|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
|-----------------------|--|

Reporting group description:

Participants received one inhalation of fluticasone furoate/vilanterol 100/25 µg once- daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide 125 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| Reporting group values | Fluticasone furoate/vilanterol 100/25 µg + placebo | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
|------------------------------------|--|---|--|
| Number of subjects | 206 | 206 | 207 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------------|----------------|----------------|
| Age continuous Units: years arithmetic mean standard deviation | 64.7 ± 7.9 | 64.9 ± 8.72 | 63.8 ± 7.65 |
| Gender categorical Units: Subjects | | | |
| Female | 65 | 67 | 80 |
| Male | 141 | 139 | 127 |
| Race, Customized Units: Subjects | | | |
| African American/African Heritage | 5 | 4 | 5 |
| American Indian or Alaska Native | 1 | 0 | 0 |
| White - Arabic/North African Heritage | 0 | 1 | 0 |
| White - White/Caucasian/European Heritage | 200 | 201 | 202 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 619 | | |

| | | | |
|---|-----|---|--|
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | | - | |
| Gender categorical Units: Subjects | | | |
| Female | 212 | | |
| Male | 407 | | |
| Race, Customized Units: Subjects | | | |
| African American/African Heritage | 14 | | |
| American Indian or Alaska Native | 1 | | |
| White - Arabic/North African Heritage | 1 | | |
| White - White/Caucasian/European Heritage | 603 | | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + placebo |
| Reporting group description: | |
| Participants received one inhalation of fluticasone furoate (FF)/vilanterol (VI) 100/25 µg once-daily (OD) via a dry powder inhaler (DPI), followed by one inhalation of umeclidinium bromide (UMEC) matching placebo, administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms. | |
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg |
| Reporting group description: | |
| Participants received one inhalation of fluticasone furoate (FF)/vilanterol (VI) 100/25 µg once-daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide (UMEC) 62.5 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms. | |
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
| Reporting group description: | |
| Participants received one inhalation of fluticasone furoate/vilanterol 100/25 µg once-daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide 125 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms. | |

Primary: Change from Baseline (BL) in trough forced expiratory volume in one second (FEV1) at Day 85

| | |
|--|---|
| End point title | Change from Baseline (BL) in trough forced expiratory volume in one second (FEV1) at Day 85 |
| End point description: | |
| FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Trough FEV1 on Day 85 is defined as the mean of the FEV1 values obtained 23 and 24 hours after dosing on Day 84. Analysis was performed using a mixed model repeated measures (MMRM) with covariates of treatment, Baseline FEV1, smoking status, Day, treatment, Day by baseline interaction and Day by treatment interaction, Day being nominal. Baseline FEV1 is the mean of the two assessments made at 30 and 5 minutes (min) pre-dose on Day 1. The change from baseline value is the difference between the on-treatment value and the baseline value. The number of participants presented represent those with data available at the time point being presented; however, all participants in the Intent-to-Treat (ITT) Population without missing covariate information and with at least one post baseline measurement are included in the analysis. | |
| End point type | Primary |
| End point timeframe: | |
| Day 85 | |

| End point values | Fluticasone furoate/vilanterol 100/25 µg + placebo | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg | |
|-------------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 190 ^[1] | 195 ^[2] | 188 ^[3] | |
| Units: Liters | | | | |
| least squares mean (standard error) | -0.02 (± 0.0111) | 0.103 (± 0.011) | 0.108 (± 0.0111) | |

Notes:

[1] - Note: 205 subjects had analyzable data for one or more timepoints.

[2] - Note: 206 subjects had analyzable data for one or more timepoints.

[3] - Note: 206 subjects had analyzable data for one or more timepoints.

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Fluticasone furoate/vilanterol 100/25 µg + placebo v Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg |
| Number of subjects included in analysis | 385 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | < 0.001 ^[5] |
| Method | Mixed Model Repeated Measure |
| Parameter estimate | Least squared mean difference |
| Point estimate | 0.124 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.093 |
| upper limit | 0.154 |

Notes:

[4] - The data presented in this table is showing the comparison of Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg v Fluticasone furoate/vilanterol 100/25 µg + placebo

[5] - Restricted maximum likelihood (REM) – based repeated measure approach (MMRM)

| Statistical analysis title | Statistical Analysis 2 |
|---|--|
| Comparison groups | Fluticasone furoate/vilanterol 100/25 µg + placebo v Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
| Number of subjects included in analysis | 378 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | < 0.001 ^[7] |
| Method | Mixed Model Repeated Measure |
| Parameter estimate | Least squared mean difference |
| Point estimate | 0.128 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.098 |
| upper limit | 0.159 |

Notes:

[6] - The data presented in this table is showing the comparison of Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg v Fluticasone furoate/vilanterol 100/25 µg + placebo

[7] - Restricted maximum likelihood (REM) – based repeated measure approach (MMRM)

Secondary: Change from Baseline in 0-6 hour weighted mean (WM) FEV1 obtained

post-dose at Day 84

| | |
|------------------------|---|
| End point title | Change from Baseline in 0-6 hour weighted mean (WM) FEV1 obtained post-dose at Day 84 |
| End point description: | FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. The 0-6 hour weighted mean was derived by calculating the area under the FEV1/time curve over the nominal time points of 0 hour (trough value), 15 and 30 min, 1, 3 and 6 hours, using the trapezoidal rule, and then dividing by the actual time between dosing and the 6 hour assessment. Analysis was performed using MMRM with covariates of treatment, Baseline FEV1 (mean of the two assessments made 30 minutes and 5 minutes pre-dose on Day 1), smoking status, Day, and Day by Baseline and Day by treatment interactions. Baseline FEV1 is the mean of the two assessments made at 30 and 5 min pre-dose on Day 1. The change from baseline value is the difference between the on-treatment value and the baseline value. All participants in the ITT Population without missing covariate information and with at least one post baseline measurement are included in the analysis. |
| End point type | Secondary |
| End point timeframe: | Day 84 |

| End point values | Fluticasone furoate/vilanterol 100/25 µg + placebo | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg | |
|-------------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 191 ^[8] | 195 ^[9] | 189 ^[10] | |
| Units: Liters | | | | |
| least squares mean (standard error) | 0.034 (± 0.0123) | 0.187 (± 0.0122) | 0.175 (± 0.0123) | |

Notes:

[8] - Note: 205 subjects had analyzable data for one or more timepoints.

[9] - Note: 206 subjects had analyzable data for one or more timepoints.

[10] - Note: 206 subjects had analyzable data for one or more timepoints.

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Fluticasone furoate/vilanterol 100/25 µg + placebo v Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg |
| Number of subjects included in analysis | 386 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[11] |
| P-value | < 0.001 ^[12] |
| Method | Mixed Model Repeated Measure |
| Parameter estimate | Least squared mean difference |
| Point estimate | 0.153 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.118 |
| upper limit | 0.187 |

Notes:

[11] - The data presented in this table is showing the comparison of Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg v Fluticasone furoate/vilanterol 100/25 µg + placebo

[12] - Restricted maximum likelihood (REM) – based repeated measure approach (MMRM)

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Fluticasone furoate/vilanterol 100/25 µg + placebo v Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
| Number of subjects included in analysis | 380 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[13] |
| P-value | < 0.001 ^[14] |
| Method | Mixed Model Repeated Measure |
| Parameter estimate | Least squared mean difference |
| Point estimate | 0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.106 |
| upper limit | 0.175 |

Notes:

[13] - The data presented in this table is showing the comparison of Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg v Fluticasone furoate/vilanterol 100/25 µg + placebo

[14] - Restricted maximum likelihood (REM) – based repeated measure approach (MMRM)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from start of study medication until follow-up visit (up to 14 weeks).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for members of the ITT Population, comprised of all participants randomized to treatment who received at least one dose of randomized study medication in the treatment period.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 16.1 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + placebo |
|-----------------------|--|

Reporting group description:

Participants received one inhalation of fluticasone furoate/vilanterol 100/25 µg once-daily (OD) via a dry powder inhaler (DPI), followed by one inhalation of umeclidinium bromide (UMEC) matching placebo, administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| | |
|-----------------------|---|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg |
|-----------------------|---|

Reporting group description:

Participants received one inhalation of fluticasone furoate/vilanterol 100/25 µg once-daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide 62.5 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| | |
|-----------------------|--|
| Reporting group title | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
|-----------------------|--|

Reporting group description:

Participants received one inhalation of fluticasone furoate/vilanterol 100/25 µg once-daily via a dry powder inhaler followed by one inhalation of umeclidinium bromide 125 µg administered via a dry powder inhaler in the morning for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study, for symptomatic relief from COPD symptoms.

| Serious adverse events | Fluticasone furoate/vilanterol 100/25 µg + placebo | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 206 (2.91%) | 2 / 206 (0.97%) | 7 / 207 (3.38%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 206 (0.49%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal cancer | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 206 (0.00%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Shunt stenosis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 206 (0.00%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 206 (0.00%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 206 (0.00%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Nervous system disorders | | | |
| Grand mal convulsion | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 206 (0.49%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatic congestion | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 206 (0.00%) | 4 / 207 (1.93%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Klebsiella sepsis | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 0 / 206 (0.00%) | 1 / 207 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 206 (0.00%) | 0 / 207 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Fluticasone furoate/vilanterol 100/25 µg + placebo | Fluticasone furoate/vilanterol 100/25 µg + UMEC 62.5 µg | Fluticasone furoate/vilanterol 100/25 µg + UMEC 125 µg |
|--|--|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 15 / 206 (7.28%) | 26 / 206 (12.62%) | 26 / 207 (12.56%) |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 6 / 206 (2.91%) 8 | 9 / 206 (4.37%) 11 | 9 / 207 (4.35%) 10 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 3 / 206 (1.46%) 3 | 7 / 207 (3.38%) 7 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 3 / 206 (1.46%) 3 | 7 / 206 (3.40%) 10 | 5 / 207 (2.42%) 5 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 7 / 206 (3.40%) 7 | 7 / 206 (3.40%) 7 | 10 / 207 (4.83%) 11 |

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