

**Clinical trial results:**

A Randomized, Double-Blind, 12-Week (with an Extension to 52 Weeks in a subset of Participants), Multi-Center Study to Assess the Safety of Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO Compared to BGF delivered by MDI HFA in Participants with Moderate to Very Severe Chronic Obstructive Pulmonary Disease (COPD)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2022-001476-33 |
| Trial protocol | DE PL BG |
| Global end of trial date | 26 March 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 11 April 2025 |
| First version publication date | 11 April 2025 |

Trial information**Trial identification**

| | |
|-----------------------|-------------|
| Sponsor protocol code | D5985C00003 |
|-----------------------|-------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | 151, 85 Södertälje, Sweden, |
| Public contact | Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |

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 | 10 June 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 March 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 March 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA over 12 to 52 weeks in participants with moderate to very severe COPD.

Protection of trial subjects:

Immediate safety concerns should be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study intervention.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 27 September 2022 |
| 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 | Argentina: 69 |
| Country: Number of subjects enrolled | Canada: 72 |
| Country: Number of subjects enrolled | Mexico: 18 |
| Country: Number of subjects enrolled | United States: 111 |
| Country: Number of subjects enrolled | Bulgaria: 55 |
| Country: Number of subjects enrolled | Germany: 140 |
| Country: Number of subjects enrolled | Poland: 71 |
| Country: Number of subjects enrolled | Türkiye: 5 |
| Country: Number of subjects enrolled | United Kingdom: 18 |
| Worldwide total number of subjects | 559 |
| EEA total number of subjects | 266 |

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 | 0 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 177 |
| From 65 to 84 years | 382 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|--------------------|
| Number of subjects started | 874 ^[1] |
| Number of subjects completed | 559 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---|
| Reason: Number of subjects | Screen failures: 311 |
| Reason: Number of subjects | Not randomised and not screen failed: 4 |

Notes:

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

Justification: Pre-assignment is the screening period, and the number screened is not expected to equal the number enrolled/randomised.

Period 1

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

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | BGF MDI HFO 320/14.4/9.6 µg |

Arm description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Budesonide/ Glycopyrronium/ Formoterol fumarate pressurized inhalation suspension, HFO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation vapour, Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

160/7.2/4.8 µg per actuation. 2 inhalations BID.

| | |
|------------------|-----------------------------|
| Arm title | BGF MDI HFA 320/14.4/9.6 µg |
|------------------|-----------------------------|

Arm description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Budesonide/ Glycopyrronium/ Formoterol fumarate pressurized inhalation suspension, HFA |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

160/7.2/4.8 µg per actuation. 2 inhalations BID.

| Number of subjects in period 1 | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg |
|--------------------------------|--------------------------------|--------------------------------|
| Started | 280 | 279 |
| Completed | 280 | 279 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | 12-week treatment period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | BGF MDI HFO 320/14.4/9.6 µg |

Arm description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Budesonide/ Glycopyrronium/ Formoterol fumarate pressurized inhalation suspension, HFO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation vapour, Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

160/7.2/4.8 µg per actuation. 2 inhalations BID.

| | |
|------------------|-----------------------------|
| Arm title | BGF MDI HFA 320/14.4/9.6 µg |
|------------------|-----------------------------|

Arm description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Budesonide/ Glycopyrronium/ Formoterol fumarate pressurized inhalation suspension, HFA |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

160/7.2/4.8 µg per actuation. 2 inhalations BID.

| Number of subjects in period 2 | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg |
|--|--------------------------------|--------------------------------|
| Started | 280 | 279 |
| Started treatment | 280 | 278 |
| Completed | 235 | 257 |
| Not completed | 45 | 22 |
| Consent withdrawn by subject | 8 | 5 |
| Physician decision | 1 | 2 |
| Adverse event, non-fatal | 20 | 9 |
| Protocol-specified withdrawal criterion met | 1 | - |
| Lost to follow-up | 2 | - |
| Randomised, not treated | - | 1 |
| Discontinued intervention - other reason | 10 | 4 |
| Protocol deviation | 3 | 1 |

Period 3

| | |
|------------------------------|---|
| Period 3 title | 52-week treatment period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | BGF MDI HFO 320/14.4/9.6 µg |

Arm description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Budesonide/ Glycopyrronium/ Formoterol fumarate pressurized inhalation suspension, HFO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

160/7.2/4.8 µg per actuation. 2 inhalations BID.

| | |
|--|--|
| Arm title | BGF MDI HFA 320/14.4/9.6 µg |
| Arm description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA | |
| Arm type | Active comparator |
| Investigational medicinal product name | Budesonide/ Glycopyrronium/ Formoterol fumarate pressurized inhalation suspension, HFA |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

160/7.2/4.8 µg per actuation. 2 inhalations BID.

| Number of subjects in period 3^[2] | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg |
|---|--------------------------------|--------------------------------|
| Started | 120 | 120 |
| Assigned 52 weeks and started treatment | 120 | 120 |
| Completed | 86 | 94 |
| Not completed | 34 | 26 |
| Adverse event, serious fatal | 1 | 1 |
| Consent withdrawn by subject | 9 | 5 |
| Physician decision | 2 | 2 |
| Adverse event, non-fatal | 11 | 8 |
| Lost to follow-up | 1 | 1 |
| Discontinued intervention - other reason | 9 | 8 |
| Protocol deviation | 1 | 1 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: All participants randomised were enrolled in the 12-week study. Of these, 120 participants in each arm were assigned (on first-in-study basis) to continue in the extended 52-week study. This is why the number who started the 52-week treatment period is less than the number who completed the 12-week period.

Baseline characteristics

Reporting groups

| | |
|---|-----------------------------|
| Reporting group title | BGF MDI HFO 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze) | |
| Reporting group title | BGF MDI HFA 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA | |

| Reporting group values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | Total |
|---|--------------------------------|--------------------------------|-------|
| Number of subjects | 280 | 279 | 559 |
| Age Categorical Units: participants | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 86 | 91 | 177 |
| >=65 years | 194 | 188 | 382 |
| Age Continuous Units: years | | | |
| arithmetic mean | 67.1 | 67.0 | |
| standard deviation | ± 7.7 | ± 7.0 | - |
| Sex: Female, Male Units: | | | |
| Female | 112 | 131 | 243 |
| Male | 168 | 148 | 316 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 2 | 2 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 7 | 4 | 11 |
| White | 273 | 272 | 545 |
| More than one race | 0 | 1 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 43 | 50 | 93 |
| Not Hispanic or Latino | 237 | 228 | 465 |
| Unknown or Not Reported | 0 | 1 | 1 |
| Age Continuous Units: years | | | |
| median | 68.5 | 68.0 | |
| full range (min-max) | 41 to 80 | 45 to 80 | - |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | BGF MDI HFO 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze) | |
| Reporting group title | BGF MDI HFA 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA | |
| Reporting group title | BGF MDI HFO 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze) | |
| Reporting group title | BGF MDI HFA 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA | |
| Reporting group title | BGF MDI HFO 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze) | |
| Reporting group title | BGF MDI HFA 320/14.4/9.6 µg |
| Reporting group description: Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA | |

Primary: Number and percentage of participants with serious adverse events during the 12-week treatment period

| | |
|---|--|
| End point title | Number and percentage of participants with serious adverse events during the 12-week treatment period ^[1] |
| End point description: To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA in participants with moderate to very severe COPD | |
| End point type | Primary |
| End point timeframe: Over 12 weeks | |

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: It is a safety study, and no hypothesis testing was pre-specified

| End point values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | | |
|-----------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 280 | 278 | | |
| Units: Participants | | | | |
| Any serious adverse event | 15 | 12 | | |
| No serious adverse events | 265 | 266 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number and percentage of participants with serious adverse events during the 52-week treatment period

| | |
|-----------------|--|
| End point title | Number and percentage of participants with serious adverse events during the 52-week treatment period ^[2] |
|-----------------|--|

End point description:

To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA in participants with moderate to very severe COPD

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

End point timeframe:

Over 52 weeks

Notes:

[2] - 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: It is a safety study, and no hypothesis testing was pre-specified

| End point values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | | |
|-----------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 120 | | |
| Units: Participants | | | | |
| Any serious adverse event | 17 | 16 | | |
| No serious adverse events | 103 | 104 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number and percentage of participants with non-serious adverse events >5% during the 12-week treatment period

| | |
|-----------------|--|
| End point title | Number and percentage of participants with non-serious adverse events >5% during the 12-week treatment period ^[3] |
|-----------------|--|

End point description:

To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA in participants with moderate to very severe COPD

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

End point timeframe:

Over 12 weeks

Notes:

[3] - 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: It is a safety study, and no hypothesis testing was pre-specified

| End point values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | | |
|-----------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 280 | 278 | | |
| Units: Participants | | | | |

| | | | | |
|--|-----|-----|--|--|
| Any non-serious adverse event at greater than 5% | 46 | 47 | | |
| No non-serious adverse events at greater than 5% | 234 | 231 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number and percentage of participants with non-serious adverse events >5% during the 52-week treatment period

| | |
|-----------------|--|
| End point title | Number and percentage of participants with non-serious adverse events >5% during the 52-week treatment period ^[4] |
|-----------------|--|

End point description:

To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA in participants with moderate to very severe COPD

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

End point timeframe:

Over 52 weeks

Notes:

[4] - 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: It is a safety study, and no hypothesis testing was pre-specified

| End point values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | | |
|--|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 120 | | |
| Units: Participants | | | | |
| Any non-serious adverse event at greater than 5% | 46 | 67 | | |
| No non-serious adverse events at greater than 5% | 74 | 53 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number and percentage of participants with adverse events of special interest during the 12-week treatment period

| | |
|-----------------|--|
| End point title | Number and percentage of participants with adverse events of special interest during the 12-week treatment period ^[5] |
|-----------------|--|

End point description:

To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA in participants with moderate to very severe COPD. Adverse events of special interest in this study are respiratory events such as dysphonia, cough, dyspnea, wheezing, paradoxical bronchospasm, bronchospasm, and COPD exacerbations.

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

End point timeframe:

Over 12 weeks

Notes:

[5] - 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: It is a safety study, and no hypothesis testing was pre-specified

| End point values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | | |
|---------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 280 | 278 | | |
| Units: Participants | | | | |
| Any adverse event of special interest | 52 | 55 | | |
| No adverse events of special interest | 228 | 223 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number and percentage of participants with adverse events of special interest during the 52-week treatment period

| | |
|-----------------|--|
| End point title | Number and percentage of participants with adverse events of special interest during the 52-week treatment period ^[6] |
|-----------------|--|

End point description:

To assess the safety and tolerability of BGF MDI HFO as compared to BGF MDI HFA in participants with moderate to very severe COPD. Adverse events of special interest in this study are respiratory events such as dysphonia, cough, dyspnea, wheezing, paradoxical bronchospasm, bronchospasm, and COPD exacerbations.

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

End point timeframe:

Over 52 weeks

Notes:

[6] - 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: It is a safety study, and no hypothesis testing was pre-specified

| End point values | BGF MDI HFO 320/14.4/9.6 µg | BGF MDI HFA 320/14.4/9.6 µg | | |
|---------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 120 | | |
| Units: Participants | | | | |
| Any adverse event of special interest | 40 | 47 | | |
| No adverse events of special interest | 80 | 73 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 weeks

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | BGF MDI HFA 320/14.4/9.6 µg |
|-----------------------|-----------------------------|

Reporting group description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFA

| | |
|-----------------------|-----------------------------|
| Reporting group title | BGF MDI HFO 320/14.4/9.6 µg |
|-----------------------|-----------------------------|

Reporting group description:

Budesonide, Glycopyrronium, and Formoterol Fumarate (BGF) Delivered by MDI HFO (HFO-1234ze)

| Serious adverse events | BGF MDI HFA 320/14.4/9.6 µg | BGF MDI HFO 320/14.4/9.6 µg | |
|---|--------------------------------|--------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 278 (8.63%) | 25 / 280 (8.93%) | |
| number of deaths (all causes) | 1 | 1 | |
| number of deaths resulting from adverse events | 1 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tongue neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder neoplasm | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-small cell lung cancer | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 9 / 278 (3.24%) | 6 / 280 (2.14%) | |
| occurrences causally related to treatment / all | 1 / 9 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Traumatic haemothorax | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sternal fracture | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 2 / 278 (0.72%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 2 / 280 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 278 (0.00%) | 2 / 280 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Trigeminal palsy | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Ear and labyrinth disorders | | | |
| Vertigo positional | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastric varices | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Gastritis | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Fibromyalgia | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebral lateral recess stenosis | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 2 / 280 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia haemophilus | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 2 / 280 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 278 (0.00%) | 1 / 280 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 278 (0.36%) | 0 / 280 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | BGF MDI HFA 320/14.4/9.6 µg | BGF MDI HFO 320/14.4/9.6 µg | |
|---|--------------------------------|--------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 80 / 278 (28.78%) | 64 / 280 (22.86%) | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 60 / 278 (21.58%) | 52 / 280 (18.57%) | |
| occurrences (all) | 75 | 68 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 30 / 278 (10.79%) | 20 / 280 (7.14%) | |
| occurrences (all) | 39 | 24 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 14 December 2023 | The CSP was amended primarily to comply with EU CTR requirements for drug abuse and misuse handling, SAE reporting, data archiving and breach reporting, and study results submissions to trial registries. The CSP was also revised to remove the planned clinical data lock after 12 weeks of treatment. The study will now be unblinded only once at the end of the study (after the last subject completes the 52-week treatment period). Both the 12-week analysis and the 52-week analysis will be completed after unblinding occurs at the end of the 52-week treatment period. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported