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, Carer, Data analyst, 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, Carer, Data analyst, 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, Carer, Data analyst, 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