Clinical trial results:
A Multicentre, Randomised, Double-blind, Parallel-group, Placebo-controlled, 52-Week, Phase III Study with an Open-label Extension to Evaluate the Efficacy and Safety of Benralizumab in Patients with Non-Cystic Fibrosis Bronchiectasis (MAHALE)

Summary

EudraCT number	2020-004068-24
Trial protocol	DK DE PL IT
Global end of trial date	16 April 2024

Results information

Result version number	v1 (current)
This version publication date	02 May 2025
First version publication date	02 May 2025

Trial information

Trial identification

Sponsor protocol code	D325BC00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05006573
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	151 85, Sodertalje, Sweden,
Public contact	AstraZeneca Information Center, AstraZeneca, +1 8002369933, information.center@astrazeneca.com
Scientific contact	Global Clinical Head, AstraZeneca, +1 8772409479, 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	17 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of benralizumab 30 mg Q4W on bronchiectasis exacerbations

Protection of trial subjects:

This study is conducted in accordance with the protocol and with the following: Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines; Applicable International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP) Guidelines; Applicable laws and regulations. The protocol, protocol amendments, Informed Consent Form (ICF), Investigator Brochure, and other relevant documents (e.g. advertisements) must be submitted to an Institutional Review Board/Independent Ethics Committee (IRB/IEC) by the Investigator and reviewed and approved by the IRB/IEC before the study is initiated. Any amendments to the protocol will require IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study patients. Where applicable as per relevant laws and regulations, amendments will also be submitted to, reviewed and approved by regulatory authorities/national competent authorities.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	8 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	China: 6
Country: Number of subjects enrolled	India: 5
Country: Number of subjects enrolled	Philippines: 3
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Viet Nam: 19
Country: Number of subjects enrolled	Argentina: 12
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 7

Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	139
EEA total number of subjects	42

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)	77
From 65 to 84 years	62
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

100 participants were randomized to receive treatment in study D325BC00001 (MAHALE) with benralizumab 30 mg or placebo. Of the 100 patients randomized, 99 (99%) received treatment with study drug. 54 (54%) patients received benralizumab 30 mg and 45 (45%) patients received placebo.

Pre-assignment

Screening details:

All patients completed a screening period of 2 to 6 weeks during which inclusion/exclusion criteria was assessed, disease activity, lung function and patient reported outcomes (PROs) were recorded, medical history and clinical laboratory were taken.

Period 1

Period 1 title	Double-blind treatment period
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	Benralizumab 30 mg

Arm description:

Benralizumab 30 mg injection delivered subcutaneously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	Fasenra
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30 mg administered subcutaneously every 4 weeks

Arm title	Placebo

Arm description:

Matching placebo injection delivered subcutaneously every 4 weeks

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo administrated subcutaneously every 4 weeks

Number of subjects in period 1[1]	Benralizumab 30 mg	Placebo
Started	54	45
Completed	42	42
Not completed	12	3
Physician decision	2	-
Consent withdrawn by subject	7	2
other reasons	-	1
Study terminated by sponsor	1	-
Protocol deviation	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: Not every enrolled participant got dosed. Some participants enrolled (signed consent) but failed screening so they did not start double-blind treatment period.

Period 2

Period 2 title	Open-label extension period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Benralizumab 30 mg

Arm description:

Benralizumab 30 mg injection delivered subcutaneously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	Fasenra
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30 mg administered subcutaneously every 4 weeks

Arm title	Placebo switched to Benralizumab 30 mg

Arm description:

Subjects who received placebo in the double-blind period switched to Benralizumab 30 mg injection delivered subcutaneously every 4 weeks in open-label extension period

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	Fasenra
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30 mg administrated subcutaneously every 4 weeks

Number of subjects in period 2[2]	Benralizumab 30 mg	Placebo switched to Benralizumab 30 mg
Started	38	40
Completed	38	39
Not completed	0	1
other reason	-	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: Not all participants enrolled in the open-label extension period.

Baseline characteristics

Reporting groups	
Reporting group title	Benralizumab 30 mg
Reporting group description:	
Benralizumab 30 mg injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo
Reporting group description:	
Matching placebo injection delivered subcutaneously every 4 weeks	

Reporting group values	Benralizumab 30 mg	Placebo	Total
Number of subjects	54	45	99
Age Categorical Units: participants			
>= 18 to <= 65 years	34	21	55
> 65 years	20	24	44
Age Continuous Units: years			
arithmetic mean	59.2	59.2	
standard deviation	± 13.14	± 15.49	-
Sex: Female, Male Units:			
Female	37	35	72
Male	17	10	27
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	17	14	31
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	36	31	67
More than one race	1	0	1
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	7	11
Not Hispanic or Latino	50	38	88
Unknown or Not Reported	0	0	0

Subject analysis sets	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants who were randomized and received any Investigational Product.	

Reporting group values	Full Analysis Set		
Number of subjects	99		
Age Categorical Units: participants			
>= 18 to <= 65 years	55		
> 65 years	44		
Age Continuous Units: years			
arithmetic mean	59.2		
standard deviation	± 14.18		
Sex: Female, Male Units:			
Female	72		
Male	27		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	31		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	67		
More than one race	1		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11		
Not Hispanic or Latino	88		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Benralizumab 30 mg
Reporting group description:	
Benralizumab 30 mg injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo
Reporting group description:	
Matching placebo injection delivered subcutaneously every 4 weeks	
Reporting group title	Benralizumab 30 mg
Reporting group description:	
Benralizumab 30 mg injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo switched to Benralizumab 30 mg
Reporting group description:	
Subjects who received placebo in the double-blind period switched to Benralizumab 30 mg injection delivered subcutaneously every 4 weeks in open-label extension period	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants who were randomized and received any Investigational Product.	

Primary: Annualized bronchiectasis exacerbations rate in the double-blind period

End point title	Annualized bronchiectasis exacerbations rate in the double-blind period
End point description:	
Annualized Non-Cystic Fibrosis Bronchiectasis (NCFB) exacerbations rate through end of double-blind treatment period.	
End point type	Primary
End point timeframe:	
Double-blind period	

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: exacerbations per year				
least squares mean (confidence interval 95%)	1.44 (1.05 to 1.97)	1.27 (0.89 to 1.80)		

Statistical analyses

Statistical analysis title	negative binomial model
Statistical analysis description:	
The rate ratio (Benralizumab/Placebo) and its 95% CI are estimated using a negative binomial model. The covariates include treatment arm, baseline blood eosinophil category, and number of exacerbations from previous year.	
Comparison groups	Benralizumab 30 mg v Placebo

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.5911
Method	negative binomial model
Parameter estimate	Risk ratio (RR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.82

Notes:

[1] - marginal standardization method is used.

Secondary: Time to first exacerbation in the double-blind treatment period

End point title	Time to first exacerbation in the double-blind treatment period

End point description:

Time to first NCFB exacerbation in the double-blind treatment period

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: participants	32	26		

Statistical analyses

Statistical analysis title	Cox proportional hazards model

Statistical analysis description:

The analysis is performed using cox proportional hazards model with covariates of treatment group, number of exacerbations in previous year and baseline eosinophil category.

Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6677
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.91

Secondary: Change from baseline in QoL-B-RSS over the double-blind period

End point title	Change from baseline in QoL-B-RSS over the double-blind period

End point description:

Change from baseline in Quality of Life-Bronchiectasis-Respiratory Symptoms Scale over the double-blind treatment period. QoL-B-RSS scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	6.6 (± 12.57)	3.1 (± 11.65)		
Week 4	5.8 (± 12.53)	-1.5 (± 12.49)		
Week 6	6.8 (± 14.39)	0.7 (± 10.94)		
Week 8	6.6 (± 14.17)	2.1 (± 16.29)		
Week 10	5.3 (± 13.02)	-1.0 (± 14.46)		
Week 12	7.2 (± 11.47)	0.9 (± 15.44)		
Week 14	8.0 (± 12.28)	3.7 (± 14.63)		
Week 16	6.2 (± 14.51)	1.3 (± 15.79)		
Week 18	8.6 (± 14.41)	2.6 (± 18.60)		
Week 20	8.6 (± 15.41)	1.4 (± 18.58)		
Week 22	8.4 (± 13.30)	3.9 (± 20.33)		
Week 24	9.3 (± 17.31)	4.4 (± 17.70)		
Week 26	7.4 (± 15.07)	3.8 (± 18.40)		
Week 28	6.5 (± 15.92)	2.7 (± 21.33)		
Week 30	7.5 (± 14.26)	1.2 (± 17.32)		
Week 32	12.1 (± 14.37)	2.4 (± 19.09)		
Week 34	7.6 (± 12.58)	2.8 (± 18.90)		
Week 36	9.6 (± 17.44)	3.6 (± 19.31)		
Week 38	8.1 (± 14.96)	1.3 (± 17.68)		
Week 40	9.6 (± 17.32)	-1.1 (± 18.50)		
Week 42	7.1 (± 14.93)	3.3 (± 16.25)		
Week 44	7.5 (± 15.00)	0.8 (± 20.76)		
Week 46	8.6 (± 17.76)	3.4 (± 18.89)		
Week 48	8.1 (± 16.75)	3.2 (± 20.52)		

Week 50	9.8 (± 14.63)	0.1 (± 15.42)		
Week 52	7.3 (± 17.91)	0.2 (± 18.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in pre-dose pre-BD FEV1 over the double-blind treatment period

End point title	Change from baseline in pre-dose pre-BD FEV1 over the double-blind treatment period

End point description:

Change from baseline in pre-dose pre-bronchodilator (BD) forced expiratory volume in one second (FEV1) over the double-blind treatment period

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: liter				
arithmetic mean (standard deviation)				
Week 4	0.0139 (± 0.14327)	-0.0477 (± 0.10758)		
Week 8	0.0048 (± 0.15392)	-0.0465 (± 0.15263)		
Week 16	-0.0191 (± 0.15964)	-0.0282 (± 0.11452)		
Week 24	-0.0378 (± 0.17290)	-0.0595 (± 0.16409)		
Week 32	-0.0248 (± 0.16782)	-0.0921 (± 0.17543)		
Week 40	-0.0597 (± 0.18924)	-0.1037 (± 0.16808)		
Week 48	-0.1236 (± 0.16353)	-0.0849 (± 0.13783)		
Week 52	-0.1093 (± 0.13130)	-0.1186 (± 0.14969)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in LCQ total score over the double-blind period

End point title	Change from baseline in LCQ total score over the double-blind

	period

End point description:

Change from baseline in Leicester Cough Questionnaire (LCQ) total score over the double-blind treatment period. LCQ total scores range from 3 to 21. Higher scores indicate better quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	0.5 (± 2.22)	0.5 (± 2.13)		
Week 4	0.7 (± 2.35)	0.0 (± 2.15)		
Week 6	0.8 (± 2.76)	0.6 (± 2.56)		
Week 8	0.8 (± 3.37)	0.3 (± 2.85)		
Week 10	1.0 (± 2.77)	0.1 (± 2.76)		
Week 12	1.0 (± 2.51)	0.4 (± 3.03)		
Week 14	1.4 (± 2.78)	0.8 (± 3.16)		
Week 16	0.9 (± 2.61)	0.5 (± 3.10)		
Week 18	1.0 (± 3.42)	1.1 (± 3.55)		
Week 20	1.4 (± 3.28)	0.8 (± 3.39)		
Week 22	0.9 (± 3.32)	0.8 (± 4.03)		
Week 24	1.0 (± 3.43)	1.2 (± 3.48)		
Week 26	0.9 (± 3.58)	1.0 (± 3.54)		
Week 28	0.5 (± 4.31)	0.9 (± 4.08)		
Week 30	0.7 (± 3.33)	0.8 (± 4.06)		
Week 32	1.8 (± 3.45)	0.7 (± 4.14)		
Week 34	0.8 (± 2.43)	0.8 (± 3.92)		
Week 36	1.2 (± 3.48)	0.8 (± 3.95)		
Week 38	1.0 (± 3.61)	0.6 (± 4.24)		
Week 40	1.2 (± 3.93)	0.2 (± 3.86)		
Week 42	0.6 (± 3.42)	0.3 (± 4.19)		
Week 44	0.5 (± 3.23)	0.3 (± 4.02)		
Week 46	0.7 (± 3.68)	0.6 (± 4.22)		
Week 48	0.3 (± 3.78)	0.5 (± 4.20)		
Week 50	0.7 (± 3.29)	-0.2 (± 3.41)		
Week 52	0.2 (± 3.94)	-0.1 (± 2.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Physical Functioning Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Physical Functioning Scale

End point description:

change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Physical Functioning Scale. QoL-B Physical Functioning Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	0.5 (± 12.23)	-0.0 (± 16.50)		
Week 4	1.5 (± 17.68)	0.8 (± 19.39)		
Week 6	4.1 (± 20.81)	0.2 (± 17.97)		
Week 8	3.3 (± 15.07)	0.3 (± 20.81)		
Week 10	1.5 (± 19.22)	1.0 (± 22.06)		
Week 12	3.1 (± 19.54)	0.5 (± 21.89)		
Week 14	4.4 (± 15.48)	4.2 (± 22.15)		
Week 16	3.5 (± 18.06)	3.3 (± 25.17)		
Week 18	4.8 (± 19.15)	2.2 (± 23.01)		
Week 20	4.5 (± 18.45)	4.7 (± 25.18)		
Week 22	3.1 (± 19.62)	2.2 (± 22.96)		
Week 24	5.2 (± 18.21)	4.7 (± 23.03)		
Week 26	3.6 (± 20.68)	3.6 (± 24.40)		
Week 28	3.8 (± 24.77)	4.8 (± 24.39)		
Week 30	2.5 (± 21.33)	4.8 (± 25.50)		
Week 32	6.7 (± 18.80)	5.9 (± 24.73)		
Week 34	2.7 (± 19.14)	3.5 (± 24.90)		
Week 36	0.6 (± 22.76)	4.7 (± 24.78)		
Week 38	1.9 (± 16.40)	3.5 (± 23.5)		
Week 40	2.1 (± 23.55)	4.1 (± 25.01)		
Week 42	1.3 (± 21.13)	5.5 (± 28.92)		
Week 44	0.6 (± 23.62)	4.2 (± 24.03)		
Week 46	2.0 (± 22.89)	7.9 (± 23.42)		
Week 48	0.0 (± 27.89)	7.6 (± 22.98)		
Week 50	5.3 (± 23.46)	1.3 (± 21.08)		
Week 52	5.1 (± 23.90)	2.1 (± 19.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Role Functioning Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Role Functioning Scale

End point description:

Change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Role Functioning Scale. QoL-B Role Functioning Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	1.1 (± 13.64)	-1.2 (± 11.11)		
Week 4	2.8 (± 13.00)	-0.3 (± 14.53)		
Week 6	2.7 (± 14.80)	2.5 (± 12.05)		
Week 8	0.5 (± 16.27)	0.2 (± 15.02)		
Week 10	1.2 (± 14.09)	2.7 (± 16.32)		
Week 12	1.7 (± 16.36)	2.3 (± 16.96)		
Week 14	3.0 (± 16.10)	2.1 (± 16.70)		
Week 16	0.1 (± 17.77)	-0.3 (± 16.60)		
Week 18	2.4 (± 16.93)	-0.0 (± 17.67)		
Week 20	0.9 (± 16.01)	0.5 (± 18.25)		
Week 22	2.8 (± 21.11)	4.0 (± 20.47)		
Week 24	1.9 (± 22.60)	0.6 (± 19.67)		
Week 26	-0.1 (± 21.44)	1.2 (± 18.36)		
Week 28	-1.9 (± 21.02)	2.7 (± 17.79)		
Week 30	1.1 (± 20.83)	-0.3 (± 19.04)		
Week 32	4.4 (± 15.08)	0.2 (± 18.17)		
Week 34	1.4 (± 18.01)	1.7 (± 17.97)		
Week 36	-0.6 (± 19.18)	0.5 (± 16.69)		
Week 38	1.4 (± 18.15)	-2.2 (± 19.65)		
Week 40	1.7 (± 22.20)	0.2 (± 21.80)		
Week 42	-1.3 (± 21.48)	1.8 (± 20.19)		
Week 44	0.6 (± 25.33)	-1.4 (± 17.46)		
Week 46	0.4 (± 23.89)	4.0 (± 19.00)		
Week 48	-1.2 (± 25.03)	0.2 (± 18.16)		
Week 50	0.7 (± 21.26)	-1.9 (± 12.55)		
Week 52	-0.8 (± 23.28)	1.1 (± 17.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Emotional Functioning Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Emotional Functioning Scale

End point description:

Change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Emotional Functioning Scale. QoL-B Emotional Functioning Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	0.2 (± 13.63)	2.0 (± 17.43)		
Week 4	-0.7 (± 14.07)	1.4 (± 14.42)		
Week 6	3.5 (± 17.99)	4.2 (± 14.98)		
Week 8	-1.2 (± 16.84)	1.4 (± 17.77)		
Week 10	0.2 (± 16.43)	-1.0 (± 16.58)		
Week 12	2.8 (± 17.30)	1.6 (± 21.38)		
Week 14	4.7 (± 14.31)	1.8 (± 20.79)		
Week 16	2.2 (± 16.56)	1.2 (± 22.48)		
Week 18	3.2 (± 15.57)	3.8 (± 21.68)		
Week 20	3.9 (± 15.82)	1.4 (± 22.27)		
Week 22	2.8 (± 18.46)	2.1 (± 23.09)		
Week 24	2.4 (± 17.80)	2.9 (± 19.32)		
Week 26	3.0 (± 17.15)	4.3 (± 22.00)		
Week 28	0.4 (± 25.82)	1.6 (± 24.43)		
Week 30	2.7 (± 22.55)	1.5 (± 23.79)		
Week 32	4.0 (± 15.82)	3.0 (± 22.42)		
Week 34	1.4 (± 19.64)	1.9 (± 23.23)		
Week 36	1.9 (± 17.89)	4.5 (± 22.75)		
Week 38	2.6 (± 20.79)	1.9 (± 22.64)		
Week 40	1.7 (± 23.35)	2.3 (± 22.28)		
Week 42	1.1 (± 21.97)	3.4 (± 22.67)		
Week 44	1.9 (± 25.89)	1.8 (± 18.95)		
Week 46	3.9 (± 22.02)	6.8 (± 22.77)		
Week 48	5.8 (± 22.10)	5.4 (± 22.83)		
Week 50	5.5 (± 20.69)	3.0 (± 18.14)		
Week 52	6.0 (± 26.30)	0.9 (± 24.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Social Functioning Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Social Functioning Scale

End point description:

Change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Social Functioning Scale. QoL-B Social Functioning Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	6.4 (± 17.60)	4.5 (± 17.35)		
Week 4	4.4 (± 18.62)	6.3 (± 22.69)		
Week 6	8.4 (± 21.60)	5.8 (± 20.05)		
Week 8	9.7 (± 23.10)	9.2 (± 20.53)		
Week 10	9.4 (± 19.64)	6.0 (± 20.31)		
Week 12	10.6 (± 23.32)	5.8 (± 21.42)		
Week 14	10.9 (± 23.03)	7.7 (± 20.52)		
Week 16	9.1 (± 20.73)	6.0 (± 23.53)		
Week 18	11.6 (± 21.61)	10.3 (± 22.43)		
Week 20	11.8 (± 22.59)	8.9 (± 21.43)		
Week 22	7.2 (± 20.42)	9.5 (± 24.09)		
Week 24	10.1 (± 24.90)	10.7 (± 24.14)		
Week 26	10.1 (± 22.86)	9.9 (± 22.46)		
Week 28	8.8 (± 24.67)	8.7 (± 24.83)		
Week 30	10.2 (± 26.57)	7.7 (± 24.82)		
Week 32	12.8 (± 23.84)	8.6 (± 24.48)		
Week 34	9.6 (± 27.93)	9.3 (± 24.95)		
Week 36	12.0 (± 27.06)	8.1 (± 25.53)		
Week 38	10.2 (± 27.83)	6.5 (± 25.41)		
Week 40	13.9 (± 32.35)	8.3 (± 27.77)		
Week 42	10.2 (± 29.40)	8.6 (± 28.16)		
Week 44	9.9 (± 28.68)	1.8 (± 24.50)		
Week 46	9.1 (± 27.40)	6.6 (± 29.11)		
Week 48	12.1 (± 27.11)	3.9 (± 30.74)		
Week 50	10.2 (± 23.60)	-1.7 (± 26.85)		
Week 52	11.6 (± 27.91)	2.3 (± 25.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Vitality Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Vitality Scale

End point description:

Change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Vitality Scale. QoL-B Vitality Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	3.0 (± 18.77)	-2.4 (± 13.54)		
Week 4	3.1 (± 17.82)	0.3 (± 15.21)		
Week 6	4.0 (± 18.83)	-2.0 (± 13.88)		
Week 8	4.9 (± 17.84)	-1.1 (± 16.26)		
Week 10	6.4 (± 16.32)	-3.1 (± 18.83)		
Week 12	5.8 (± 18.48)	-3.9 (± 16.24)		
Week 14	8.8 (± 20.69)	-2.7 (± 18.22)		
Week 16	5.2 (± 19.66)	-0.5 (± 19.71)		
Week 18	5.0 (± 19.78)	-1.4 (± 18.69)		
Week 20	7.1 (± 19.99)	-1.3 (± 19.28)		
Week 22	5.7 (± 21.66)	-0.6 (± 21.04)		
Week 24	4.1 (± 20.87)	1.0 (± 19.67)		
Week 26	6.2 (± 20.18)	-1.6 (± 20.66)		
Week 28	3.9 (± 21.75)	-2.1 (± 21.57)		
Week 30	4.4 (± 21.84)	-4.3 (± 22.74)		
Week 32	6.1 (± 19.97)	0.0 (± 20.49)		
Week 34	1.1 (± 18.98)	-0.8 (± 20.96)		
Week 36	1.0 (± 18.59)	-2.7 (± 18.72)		
Week 38	4.1 (± 18.88)	-0.0 (± 19.52)		
Week 40	2.6 (± 23.01)	-2.7 (± 21.97)		
Week 42	3.0 (± 21.54)	-1.0 (± 24.37)		
Week 44	2.9 (± 21.11)	-3.4 (± 21.24)		

Week 46	5.2 (± 24.65)	1.0 (± 20.10)		
Week 48	2.0 (± 23.48)	-1.3 (± 20.97)		
Week 50	7.7 (± 20.81)	0.0 (± 18.14)		
Week 52	5.3 (± 18.74)	-5.3 (± 23.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Health Perceptions Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Health Perceptions Scale

End point description:

Change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Health Perceptions Scale. QoL-B Health Perceptions Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	1.3 (± 12.95)	3.3 (± 14.12)		
Week 4	1.2 (± 14.87)	-0.2 (± 16.72)		
Week 6	3.5 (± 16.90)	3.7 (± 16.06)		
Week 8	5.3 (± 17.23)	4.3 (± 18.46)		
Week 10	5.6 (± 16.57)	2.1 (± 18.47)		
Week 12	7.5 (± 16.69)	3.3 (± 17.74)		
Week 14	7.4 (± 16.78)	1.4 (± 18.99)		
Week 16	1.9 (± 16.25)	2.4 (± 20.35)		
Week 18	5.8 (± 16.68)	1.7 (± 20.69)		
Week 20	4.6 (± 18.21)	3.9 (± 21.70)		
Week 22	5.0 (± 16.70)	6.3 (± 21.99)		
Week 24	7.2 (± 17.18)	5.0 (± 19.85)		
Week 26	2.8 (± 16.76)	5.0 (± 20.26)		
Week 28	3.4 (± 18.81)	2.4 (± 20.68)		
Week 30	4.5 (± 18.03)	4.3 (± 21.87)		
Week 32	7.0 (± 16.37)	2.4 (± 20.09)		
Week 34	4.2 (± 17.68)	2.9 (± 22.29)		
Week 36	3.5 (± 17.84)	2.0 (± 20.56)		
Week 38	4.2 (± 16.30)	3.0 (± 22.90)		
Week 40	5.1 (± 16.95)	1.4 (± 22.35)		
Week 42	4.7 (± 18.38)	4.4 (± 23.77)		

Week 44	4.8 (± 21.03)	1.5 (± 20.78)		
Week 46	6.6 (± 22.45)	1.8 (± 19.07)		
Week 48	7.3 (± 21.32)	3.9 (± 23.68)		
Week 50	6.9 (± 20.42)	4.7 (± 18.65)		
Week 52	4.0 (± 21.53)	0.4 (± 24.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Treatment Burden Scale

End point title	Change from baseline in QoL-B scales (excluding QoL-B-RSS) over the double-blind period: Treatment Burden Scale

End point description:

Change from baseline in Quality of Life-Bronchiectasis (QoL-B) scales (excluding QoL-B-RSS) over the double-blind treatment period: Treatment Burden Scale. QoL-B Treatment Burden Scale scores range from 0 to 100, with higher scores indicative of better health-related quality of life.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 2	3.6 (± 22.56)	-2.2 (± 16.75)		
Week 4	3.7 (± 18.62)	-2.1 (± 13.34)		
Week 6	6.0 (± 23.20)	-2.1 (± 15.72)		
Week 8	4.8 (± 18.35)	-1.9 (± 14.87)		
Week 10	4.0 (± 17.31)	1.1 (± 17.83)		
Week 12	0.3 (± 17.27)	-0.4 (± 12.54)		
Week 14	0.6 (± 20.74)	-4.1 (± 14.73)		
Week 16	4.4 (± 20.10)	-1.1 (± 16.34)		
Week 18	-1.9 (± 16.28)	-1.2 (± 14.92)		
Week 20	4.1 (± 16.01)	0.3 (± 15.84)		
Week 22	-1.3 (± 14.37)	-0.8 (± 16.82)		
Week 24	-1.0 (± 18.58)	-1.1 (± 14.45)		
Week 26	1.9 (± 17.32)	2.5 (± 15.37)		
Week 28	-5.1 (± 24.00)	1.4 (± 15.11)		
Week 30	-2.0 (± 19.14)	-1.1 (± 18.39)		
Week 32	-2.1 (± 16.32)	-0.8 (± 15.12)		
Week 34	-0.4 (± 16.70)	-4.0 (± 17.95)		
Week 36	-0.7 (± 16.68)	-1.5 (± 16.69)		
Week 38	-4.2 (± 25.27)	-2.9 (± 21.04)		
Week 40	-2.0 (± 24.76)	-0.4 (± 16.15)		

Week 42	-1.5 (± 23.52)	1.7 (± 18.78)		
Week 44	2.1 (± 17.22)	1.4 (± 21.00)		
Week 46	-0.0 (± 18.59)	4.6 (± 14.62)		
Week 48	-0.9 (± 17.25)	3.6 (± 19.96)		
Week 50	-2.0 (± 22.13)	-1.9 (± 18.77)		
Week 52	-1.9 (± 25.64)	1.7 (± 14.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in SGRQ total score over the double-blind treatment period

End point title	Change from baseline in SGRQ total score over the double-blind treatment period

End point description:

Change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score over the double-blind treatment period. SGRQ total scores range from 0 to 100. 100 represents the worst possible health status and 0 indicates the best possible health status.

End point type	Secondary

End point timeframe:

Double-blind period

End point values	Benralizumab 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	45		
Units: score				
arithmetic mean (standard deviation)				
Week 4	-4.7 (± 14.92)	0.6 (± 14.89)		
Week 8	-4.3 (± 15.99)	-2.4 (± 15.33)		
Week 16	-4.4 (± 15.03)	-0.1 (± 16.06)		
Week 24	-6.3 (± 16.21)	-3.9 (± 21.08)		
Week 32	-5.8 (± 15.73)	-1.6 (± 21.46)		
Week 40	-5.8 (± 17.63)	-1.6 (± 24.51)		
Week 48	-4.9 (± 18.58)	-0.0 (± 22.45)		
Week 52	-4.4 (± 20.37)	4.8 (± 23.33)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Double-blind (DB) period and Open-label Extension (OLE) period. DB Period: From first dose of study drug until end of DB period, up to 52 weeks. OLE Period: From the end of the DB period (week 25 to 53) to the end of OLE period, up to 40 weeks.

Adverse event reporting additional description:

For analysis of Adverse Events, Safety Analysis Set is used. Safety Analysis Set: All participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Matching placebo injection delivered subcutaneously every 4 weeks

Reporting group title	Benralizumab 30 mg

Reporting group description:

Benralizumab 30 mg injection delivered subcutaneously every 4 weeks

Serious adverse events	Placebo	Benralizumab 30 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 45 (15.56%)	13 / 54 (24.07%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 45 (2.22%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	6 / 45 (13.33%)	9 / 54 (16.67%)	
occurrences causally related to treatment / all	0 / 7	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			
subjects affected / exposed	0 / 45 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Benralizumab 30 mg	
Total subjects affected by non-serious adverse events subjects affected / exposed	23 / 45 (51.11%)	37 / 54 (68.52%)	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	2 / 54 (3.70%) 2	
Headache subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 9	5 / 54 (9.26%) 5	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	3 / 54 (5.56%) 3	
Pyrexia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 5	1 / 54 (1.85%) 1	
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	3 / 54 (5.56%) 4	
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	3 / 54 (5.56%) 4	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	4 / 54 (7.41%) 6	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	2 / 45 (4.44%)	4 / 54 (7.41%)	
occurrences (all)	3	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	10 / 45 (22.22%)	21 / 54 (38.89%)	
occurrences (all)	12	21	
Nasopharyngitis			
subjects affected / exposed	6 / 45 (13.33%)	6 / 54 (11.11%)	
occurrences (all)	6	10	
Sinusitis			
subjects affected / exposed	2 / 45 (4.44%)	4 / 54 (7.41%)	
occurrences (all)	3	4	
Upper respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)	4 / 54 (7.41%)	
occurrences (all)	2	5	
Urinary tract infection			
subjects affected / exposed	0 / 45 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2023	The initial protocol plan was to randomise approximately 420 eligible patients to investigational product with stratification for blood eosinophil count category. However, the coronavirus disease 2019 pandemic's impact on population characteristics that are part of the trial's inclusion criteria has resulted in recruitment challenges. These challenges, combined with other external uncertainties, have led to the sponsor's decision to stop further recruitment into the study. This decision was not due to safety or efficacy concerns for benralizumab in the non-cystic fibrosis bronchiectasis (NCFB) population. Therefore, all randomised patients are allowed to continue the treatment. The collected data will be analysed and shared with the scientific community to enhance understanding of NCFB. Due to the sponsor's decision to stop recruitment early, this clinical study protocol has been modified such that the duration of the double-blind period for each patient is 28 to 52 weeks, after which eligible patients will enter an open-label extension of approximately 32 weeks (approximately 24 weeks of benralizumab administration followed by an 8-week follow-up visit) that will focus on safety assessments. The protocol, including the study duration, sample size, primary study population, evaluated parameters, the timing of endpoint analyses, statistical analyses to be performed, and frequency and timing of activities in the schedule of assessments have been updated to reflect the significant changes in the overall study design and conduct.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the decision to stop recruitment early and small sample size in ≥ the threshold of blood eosinophil count stratum, the study is not powered to assess the hypothesis test for the primary efficacy endpoint.

Notes: