Clinical trial results:
BURAN: Effects of BenralizUmab on AiRwAy DyNamics in Severe Eosinophilic Asthma using Functional Respiratory Imaging Parameters

Summary

EudraCT number	2022-000152-11
Trial protocol	BE ES PT FR
Global end of trial date	19 July 2024

Results information

Result version number	v1
This version publication date	20 March 2025
First version publication date	20 March 2025

Trial information

Trial identification

Sponsor protocol code	D3250R00107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05552508
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Sodertalje, Sodertalje, Sweden, 15185
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	06 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to describe the change from baseline in airway dynamics after 13 weeks following treatment with benralizumab, using total mucus volume measurements from untrimmed airways.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that were
consistent with International Council of Harmonization (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements and
the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 October 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	Belgium: 6
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Portugal: 5
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	45
EEA total number of subjects	37

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)	36
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted between 11 October 2022 to 19 July 2024 at 24 study centers.

Pre-assignment

Screening details:

Participants who met the inclusion criteria and none of the exclusion criteria were enrolled to the study. Informed Consent Form (ICF) was signed prior of screening procedures. All study assessments were performed as per the Schedule of Activities.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Benralizumab

Arm description:

Participants received 3 doses of benralizumab 30 milligrams (mg) as subcutaneous injection once every 4 weeks (Week 0, Week 4, and Week 8).

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

Dosage and administration details:

Participants received 3 doses of benralizumab 30 mg as subcutaneous injection once every 4 weeks (Week 0, Week 4, and Week 8).

Number of subjects in period 1	Benralizumab
Started	45
Completed	42
Not completed	3
Adverse event, non-fatal	3

Baseline characteristics

Reporting groups	
Reporting group title	Benralizumab
Reporting group description:	
Participants received 3 doses of benralizumab 30 milligrams (mg) as subcutaneous injection once every 4 weeks (Week 0, Week 4, and Week 8).	

Reporting group values	Benralizumab	Total	
Number of subjects	45	45	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	36	36	
From 65-84 years	9	9	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	53.4		
standard deviation	± 12.4	-	
Sex: Female, Male Units: Participants			
Female	28	28	
Male	17	17	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	6	
Not Hispanic or Latino	39	39	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Benralizumab

Reporting group description:

Participants received 3 doses of benralizumab 30 milligrams (mg) as subcutaneous injection once every 4 weeks (Week 0, Week 4, and Week 8).

Primary: Change from baseline in untrimmed total mucus volume at total lung capacity (TLC)

End point title	Change from baseline in untrimmed total mucus volume at total lung capacity (TLC)[1]

End point description:

Change from baseline in airway dynamics after 13 weeks following treatment with benralizumab, using total mucus volume (specific airway volume) at TLC measurements from untrimmed airways was assessed.
Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Primary

End point timeframe:

Baseline and Week 13

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: The statistical analysis was not included due to tool constraint.

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Milliliters (mL)				
arithmetic mean (standard deviation)				
All participants (n= 39)	-0.1279 (± 0.4199)			
Participants with >=4 mucus plugs (n= 27)	-0.1822 (± 0.4977)			
Participants with <4 mucus plugs (n= 12)	-0.0056 (± 0.0111)			
OCS-dependent participants (n= 2)	-0.1619 (± 0.4627)			
Non-OCS-dependent participants (n= 37)	-0.1260 (± 0.4244)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total mucus plugs score at TLC

End point title	Change from baseline in untrimmed total mucus plugs score at

	TLC

End point description:

Change from baseline in untrimmed total mucus plugs score at TLC was assessed. Mucus plugs was scored with a scoring system similar to that by Dunican et al. with the Severe Asthma Research Program (SARP) based on bronchopulmonary segmental anatomy. Each bronchopulmonary segment had score of 1 (mucus plug present) or 0 (mucus plug absent). Participants with (mucus plug score different from 0) or without mucus plugs (mucus plug score equal to 0) identified using CT scans.
Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score				
arithmetic mean (standard deviation)	-11.0 (± 32.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total air trapping at functional residual capacity (FRC)

End point title	Change from baseline in untrimmed total air trapping at functional residual capacity (FRC)

End point description:

Change from baseline in untrimmed total air trapping at FRC was assessed.
Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: Percentage of air trapping				
arithmetic mean (standard deviation)	-0.1410 (± 12.1660)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in trimmed distal airway wall volume at TLC

End point title	Change from baseline in trimmed distal airway wall volume at TLC

End point description:

Change from baseline in trimmed distal airway wall volume at TLC was assessed. Change from baseline in airway dynamics at Week 13 following treatment with benralizumab as measured by secondary functional respiratory imaging (FRI) endpoints, irrespective of participants characteristics was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13 where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (standard deviation)	-0.9386 (± 6.1359)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed distal airway volume at TLC

End point title	Change from baseline in untrimmed distal airway volume at TLC

End point description:

Change from baseline in untrimmed distal airway volume at TLC was assessed.
Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13 where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (standard deviation)	1.1225 (± 4.5836)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed distal airway volume at FRC

End point title	Change from baseline in untrimmed distal airway volume at FRC

End point description:

Change from baseline in untrimmed distal airway volume at FRC was assessed.
Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: mL				
arithmetic mean (standard deviation)	0.5079 (± 1.9741)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total lung volume at TLC

End point title	Change from baseline in untrimmed total lung volume at TLC

End point description:

Change from baseline in untrimmed total lung volume at TLC was assessed.
Primary analysis population set consisted portion of the evaluable population that did not have any

acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Liters (L)				
arithmetic mean (standard deviation)	0.0287 (± 0.4416)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total lung volume at FRC

End point title	Change from baseline in untrimmed total lung volume at FRC

End point description:

Change from baseline in untrimmed total lung volume at FRC was assessed.
Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: Liters (L)				
arithmetic mean (standard deviation)	-0.0275 (± 0.5101)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between trimmed distal airway wall volume at TLC and pre-BD FEV1

End point title	Correlation between trimmed distal airway wall volume at TLC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Correlation coefficient				
number (confidence interval 95%)	0.5380 (0.2738 to 0.7205)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total mucus plugs score at TLC and pre-BD FEV1

End point title	Correlation between untrimmed total mucus plugs score at TLC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.2795 (-0.5326 to 0.0260)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total air trapping at FRC and pre-BD FEV1

End point title	Correlation between untrimmed total air trapping at FRC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.6892 (-0.8210 to -0.4742)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total mucus volume measured at TLC and pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV1)

End point title	Correlation between untrimmed total mucus volume measured at TLC and pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV1)

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.2710 (-0.5260 to 0.0352)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total lung volume at FRC and pre-BD FEV1

End point title	Correlation between untrimmed total lung volume at FRC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.1655 (-0.4519 to 0.1560)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total mucus volume measured at TLC and pre-bronchodilator forced vital capacity (pre-BD FVC)

End point title	Correlation between untrimmed total mucus volume measured at TLC and pre-bronchodilator forced vital capacity (pre-BD FVC)

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.0471 (-0.3421 to 0.2574)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed distal airway volume at TLC and pre-BD FEV1

End point title	Correlation between untrimmed distal airway volume at TLC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	0.6556 (0.4360 to 0.7958)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed distal airway volume at FRC and pre-BD FEV1

End point title	Correlation between untrimmed distal airway volume at FRC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	0.4357 (0.1383 to 0.6548)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total lung volume at TLC and pre-BD FEV1

End point title	Correlation between untrimmed total lung volume at TLC and pre-BD FEV1

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	0.2122 (-0.0966 to 0.4799)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed distal airway volume at TLC and pre-BD FVC

End point title	Correlation between untrimmed distal airway volume at TLC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	0.6110 (0.3742 to 0.7670)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between trimmed distal airway wall volume at TLC and pre-BD FVC

End point title	Correlation between trimmed distal airway wall volume at TLC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Correlation coefficient				
number (confidence interval 95%)	0.5476 (0.2863 to 0.7269)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total air trapping at FRC and pre-BD FVC

End point title	Correlation between untrimmed total air trapping at FRC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.3432 (-0.5886 to -0.0311)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total mucus plugs score at TLC and pre-BD FVC

End point title	Correlation between untrimmed total mucus plugs score at TLC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	-0.0273 (-0.3247 to 0.2756)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed distal airway volume at FRC and pre-BD FVC

End point title	Correlation between untrimmed distal airway volume at FRC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Correlation coefficient				
number (confidence interval 95%)	0.4706 (0.1806 to 0.6789)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total lung volume at TLC and pre-BD FVC

End point title	Correlation between untrimmed total lung volume at TLC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Baseline (Week 0)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Correlation coefficient				
number (confidence interval 95%)	0.4947 (0.2227 to 0.6891)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between untrimmed total lung volume at FRC and pre-BD FVC

End point title	Correlation between untrimmed total lung volume at FRC and pre-BD FVC

End point description:

The relationship between airway dynamics and conventional lung function measurements, cross sectionally (at Week 0) and irrespective of participants characteristics was assessed.
Here, "Number" in measure type is indicating data of Spearman's rank correlation coefficient.
Baseline endpoints analysis set included all participants who had baseline measurements and who had at least one dose of study intervention.

End point type	Secondary
End point timeframe:	
At Baseline (Week 0)	

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Correlation coefficient				
number (confidence interval 95%)	0.1451 (-0.1761 to 0.4354)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total mucus plugs score at TLC with and without adjustment for pre-BD FEV1

End point title	Change from baseline in untrimmed total mucus plugs score at TLC with and without adjustment for pre-BD FEV1

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary
End point timeframe:	
Baseline and Week 13	

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FEV1 (n=39)	4.38 (-2.87 to 11.63)			
Adjusted for pre-BD FEV1 (n=39)	5.97 (-1.75 to 13.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total mucus volume measured at TLC with and without adjustment for pre-BD FEV1

End point title	Change from baseline in untrimmed total mucus volume measured at TLC with and without adjustment for pre-BD FEV1

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FEV1 (n=39)	0.05 (0.00 to 0.11)			
Adjusted for pre-BD FEV1 (n=39)	0.06 (0.00 to 0.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total air trapping at FRC with and without adjustment for pre-BD FEV1

End point title	Change from baseline in untrimmed total air trapping at FRC with and without adjustment for pre-BD FEV1

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: Percentage of air trapping				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FEV1 (n=34)	3.18 (-3.65 to 10.01)			
Adjusted for pre-BD FEV1 (n=34)	5.24 (-1.23 to 11.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in trimmed distal airway wall volume at TLC with and without adjustment for pre-BD FEV1

End point title	Change from baseline in trimmed distal airway wall volume at TLC with and without adjustment for pre-BD FEV1

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FEV1 (n=39)	5.29 (-1.39 to 11.97)			
Adjusted for pre-BD FEV1 (n=39)	5.61 (-1.27 to 12.48)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed distal airway volume with and without adjustment for pre-BD FEV1

End point title	Change from baseline in untrimmed distal airway volume with and without adjustment for pre-BD FEV1

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13. Here, 'number analyzed in each row' signifies the participants with available data that were analyzed for specified category.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (confidence interval 95%)				
Distal airway vol. - TLC:No adjust. for pre-BDFEV1	2.20 (-1.09 to 5.49)			
Distal airway vol. at TLC:Adjusted for pre-BD FEV1	0.61 (-2.65 to 3.88)			
Distal airway vol.-FRC:No adjust. for pre-BDFEV1	-1.28 (-2.82 to 0.27)			
Distal airway vol. at FRC:Adjusted for pre-BD FEV1	-1.52 (-3.14 to 0.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total lung volume with and without adjustment for pre-BD FEV1

End point title	Change from baseline in untrimmed total lung volume with and without adjustment for pre-BD FEV1

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13. Here, 'number analyzed in each row' signifies the participants with available data that were analyzed for specified category.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Litre				
arithmetic mean (confidence interval 95%)				
Total lung vol. at TLC:No adjust. for pre-BD FEV1	0.11 (-0.62 to 0.84)			
Total lung volume at TLC: Adjusted for pre-BD FEV1	0.13 (-0.61 to 0.88)			
Total lung vol. at FRC:No adjust. for pre-BD FEV1	0.52 (-0.16 to 1.21)			
Total lung volume at FRC: Adjusted for pre-BD FEV1	0.37 (-0.25 to 0.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total mucus volume measured at TLC with and without adjustment for pre-BD FVC

End point title	Change from baseline in untrimmed total mucus volume measured at TLC with and without adjustment for pre-BD FVC

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FVC (n=39)	0.05 (0.00 to 0.11)			
Adjusted for pre-BD FVC (n=39)	0.05 (-0.01 to 0.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total mucus plugs score at TLC with and without adjustment for pre-BD FVC

End point title	Change from baseline in untrimmed total mucus plugs score at TLC with and without adjustment for pre-BD FVC

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FVC (n=39)	4.38 (-2.87 to 11.63)			
Adjusted for pre-BD FVC (n=39)	4.65 (-3.00 to 12.30)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total air trapping at FRC with and without adjustment for pre-BD FVC

End point title	Change from baseline in untrimmed total air trapping at FRC with and without adjustment for pre-BD FVC

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any

acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: Percentage of air trapping				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FVC (n=34)	3.18 (-3.65 to 10.01)			
Adjusted for pre-BD FVC (n=34)	4.36 (-2.06 to 10.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in trimmed distal airway wall volume at TLC with and without adjustment for pre-BD FVC

End point title	Change from baseline in trimmed distal airway wall volume at TLC with and without adjustment for pre-BD FVC

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (confidence interval 95%)				
No adjustment for pre-BD FVC (n=39)	5.29 (-1.39 to 11.97)			

Adjusted for pre-BD FVC (n=39)	6.08 (-0.60 to 12.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed distal airway volume with and without adjustment for pre-BD FVC

End point title	Change from baseline in untrimmed distal airway volume with and without adjustment for pre-BD FVC

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13. Here, 'number analyzed in each row' signifies the participants with available data that were analyzed for specified category.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: mL				
arithmetic mean (confidence interval 95%)				
Distal airway vol. at TLC:No adjust. for pre-BDFVC	2.20 (-1.09 to 5.49)			
Distal airway vol. at TLC: Adjusted for pre-BD FVC	1.22 (-2.30 to 4.73)			
Distal airway vol. at FRC:No adjust. for pre-BDFVC	-1.28 (-2.82 to 0.27)			
Distal airway vol. at FRC: Adjusted for pre-BD FVC	-1.28 (-2.93 to 0.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in untrimmed total lung volume with and without adjustment for pre-BD FVC

End point title	Change from baseline in untrimmed total lung volume with and without adjustment for pre-BD FVC

End point description:

The relationship between estimated average change from baseline (Week 0) in airway dynamics at Week 13, with and without accounting for baseline measurements of conventional lung function was assessed. Primary analysis population set consisted portion of the evaluable population that did not have any acute asthma exacerbation nor lower respiratory tract infection during the study period where evaluable population was defined as those who completed the three doses of study intervention and had measurements of the outcome at both baseline and Week 13. Here, 'number analyzed in each row' signifies the participants with available data that were analyzed for specified category.

End point type	Secondary

End point timeframe:

Baseline and Week 13

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Litre				
arithmetic mean (confidence interval 95%)				
Total lung volume at TLC:No adjust. for pre-BD FVC	0.11 (-0.62 to 0.84)			
Total lung volume at TLC: Adjusted for pre-BD FVC	0.11 (-0.63 to 0.85)			
Total lung volume at FRC:No adjust. for pre-BD FVC	0.52 (-0.16 to 1.21)			
Total lung volume at FRC: Adjusted for pre-BD FVC	0.40 (-0.22 to 1.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs)

End point title	Number of participants with adverse events (AEs)

End point description:

The safety and tolerability of benralizumab was assessed. The Safety analysis set consisted of all participants who had received at least one dose of investigational product.

End point type	Secondary

End point timeframe:

From screening (Day -21) to follow-up (up to 1.9 years)

End point values	Benralizumab			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Participants				
Any AE	17			
Any serious adverse event (SAE)	2			
Any SAE with outcome death	0			
Any AE- discontinuation of study intervention	1			
Any possibly related AE	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From screening (Day -21) to follow-up (up to 1.9 years)	
Adverse event reporting additional description:	
The Safety analysis set consisted of all participants who had received at least one dose of investigational product.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Benralizumab
Reporting group description:	
Participants received 3 doses of benralizumab 30 mg as subcutaneous injection once every 4 weeks (Week 0, Week 4, and Week 8).	

Serious adverse events	Benralizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 45 (4.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Benralizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 45 (6.67%)		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported