Clinical trial results:
A Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Investigate the Use of Benralizumab for Eosinophilic Esophagitis (MESSINA)

Summary

EudraCT number	2019-002871-32
Trial protocol	ES NL PL DE GB FR IT
Global end of trial date	06 February 2023

Results information

Result version number	v1 (current)
This version publication date	20 July 2023
First version publication date	20 July 2023

Trial information

Trial identification

Sponsor protocol code	D3255C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04543409
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 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001214-PIP05-19
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the effect of a 30 mg dosing regimen of benralizumab every four weeks on histologic signs and symptoms of Eosinophilic Esophagitis in patients with symptomatic and histologically active Eosinophilic Esophagitis

Protection of trial subjects:

The independent data monitoring committee (IDMC), consisting of 2 clinicians (including at least 1 EoE expert) and a statistician, was used for this study. They had the responsibility of evaluating cumulative safety and other clinical trial data at regular intervals and made appropriate recommendations based on the available data. The IDMC functioned independently of all other individuals associated with the conduct of the studies, including the study sponsor, AstraZeneca. The committee operated in accordance with a IDMC charter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 70
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	210
EEA total number of subjects	76

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)	28
Adults (18-64 years)	179
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

404 patients were screened from 22SEP2020-22FEB2022. 211 were randomized to the treatment (104) or placebo (107) arms of the double-blind period. 1 patient, who did not meet inclusion/exclusion criteria, was incorrectly randomized but not dosed. Therefore, 103 patients started in the treatment arm and 107 in the placebo arm, for a total of 210.

Pre-assignment

Screening details:

All patients completed a run-in period of 2 to 8 weeks during which inclusion/exclusion criteria was assessed, medical history taken, endoscopy with biopsies performed, and patient reported outcomes (PROs), clinical laboratories, and diet questionnaires were administered.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Benralizumab

Arm description:

30mg Benralizumab injection delivered subcutaneously every 4 weeks through week 24

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg/mL solution for injection in accessorized prefilled syringe, 1 mL fill volume

Arm title	Placebo

Arm description:

Matching Placebo injection delivered subcutaneously every 4 weeks through week 24

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo solution for injection in accessorized prefilled syringe, 1 mL fill volume

Number of subjects in period 1	Benralizumab	Placebo
Started	103	107
Completed	101	106
Not completed	2	1
Consent withdrawn by subject	1	1
Subject perceives the IP to be ineffective.	1	-

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Benralizumab

Arm description:

30mg Benralizumab injection delivered subcutaneously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg/mL solution for injection in accessorized prefilled syringe, 1 mL fill volume

Arm title	Placebo

Arm description:

Matching Placebo injection delivered subcutaneously every 4 weeks through week 24, then 30mg Benralizumab injection delivered subcutaneously every 4 weeks after week 24

Arm type	Placebo
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe, Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg/mL solution for injection in accessorized prefilled syringe, 1 mL fill volume

Number of subjects in period 2[1]	Benralizumab	Placebo
Started	100	105
Completed	79	82
Not completed	21	23
Consent withdrawn by subject	4	3
Study terminated by sponsor	17	19
Lost to follow-up	-	1

Notes:

[1] - 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: One participant enrolled in OL treatment period off study drug (not included in this count) for the treatment group. One participant chose not to enroll in the OL treatment period for the placebo group.

Period 3

Period 3 title	Open-Label Extension Treatment Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Benralizumab

Arm description:

30mg Benralizumab injection delivered subcutaneously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg/mL solution for injection in accessorized prefilled syringe, 1 mL fill volume

Arm title	Placebo

Arm description:

Matching Placebo injection delivered subcutaneously every 4 weeks through week 24, then 30mg Benralizumab injection delivered subcutaneously every 4 weeks after week 24

Arm type	Placebo
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg/mL solution for injection in accessorized prefilled syringe, 1 mL fill volume

Number of subjects in period 3[2]	Benralizumab	Placebo
Started	45	48
Completed	0	0
Not completed	45	48
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	1
Study terminated by sponsor	44	44
No study/treatment discontinuation information	-	1
Lost to follow-up	1	-
Unable to schedule gastroscopy	-	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: 34 participants in each treatment arm from previous period chose not to enroll in optional OLE period.

Baseline characteristics

Reporting groups	
Reporting group title	Benralizumab
Reporting group description:	
30mg Benralizumab injection delivered subcutaneously every 4 weeks through week 24	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo injection delivered subcutaneously every 4 weeks through week 24	

Reporting group values	Benralizumab	Placebo	Total
Number of subjects	103	107	210
Age Categorical			
Age Group 1			
Units: Participants			
< 18 years old	14	14	28
18-21 years old	11	11	22
22-35 years old	32	35	67
>= 36 years old	46	47	93
Age Continuous			
Units: years			
arithmetic mean	33.9	33.6	
standard deviation	± 13.49	± 12.73	-
Sex: Female, Male			
Units: Participants			
Female	31	22	53
Male	72	85	157
Age, Customized			
Age Group 3			
Units: Subjects			
<= 21 years old	25	25	50
> 21 years old	78	82	160

End points

End points reporting groups

Reporting group title	Benralizumab
Reporting group description:	
30mg Benralizumab injection delivered subcutaneously every 4 weeks through week 24	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo injection delivered subcutaneously every 4 weeks through week 24	
Reporting group title	Benralizumab
Reporting group description:	
30mg Benralizumab injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo injection delivered subcutaneously every 4 weeks through week 24, then 30mg Benralizumab injection delivered subcutaneously every 4 weeks after week 24	
Reporting group title	Benralizumab
Reporting group description:	
30mg Benralizumab injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo injection delivered subcutaneously every 4 weeks through week 24, then 30mg Benralizumab injection delivered subcutaneously every 4 weeks after week 24	

Primary: Proportion of patients with a histologic response, defined as a peak esophageal intraepithelial eosinophil count ≤ 6 eos/hpf at Week 24.

End point title	Proportion of patients with a histologic response, defined as a peak esophageal intraepithelial eosinophil count ≤ 6 eos/hpf at Week 24.
End point description:	
Proportion of patients with a histologic response at Week 24. A histologic response is defined as a peak esophageal intraepithelial eosinophil count <= 6 eos/hpf across all available esophageal levels. The number analyzed represents the number of participants in the treatment group that could have made it to the timepoint by the data cut off.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 24	87.4 (80.97 to 93.79)	6.5 (1.86 to 11.23)		

Statistical analyses

Statistical analysis title	Cochran-Mantel Haenszel (CMH) Test
Statistical analysis description: Analysis completed at Week 24.	
Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	117.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.17
upper limit	361.64

Notes:

[1] - Subjects with no biopsy data at Week 24 or with intercurrent events prior to Week 24 such as changes to background medications or additional new therapies for EoE are considered non-responders.
[2] - P value was <0.0001

Primary: Changes from baseline in Dysphagia Symptom Questionnaire (DSQ) at Week 24

End point title	Changes from baseline in Dysphagia Symptom Questionnaire (DSQ) at Week 24

End point description:

The Dysphagia Symptom Questionnaire (DSQ) captures the presence and severity of dysphagia symptoms in the past day in a 4-item questionnaire. The DSQ score is calculated over 14-day periods and ranges from 0 to 84, with a lower score indicating less severe dysphagia. At least 8 days with evaluable daily score in 14-day period are required; otherwise the DSQ score for the period is set to missing.

The number analyzed represents the number of participants with data at that visit (including patients with imputed values post intercurrent events).

End point type	Primary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	100		
Units: Score				
least squares mean (confidence interval 95%)				
Week 24	-12.102 (-16.05 to -8.15)	-15.101 (-19.02 to -11.19)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis

Statistical analysis description:

Model: Change from baseline in DSQ = Treatment + baseline DSQ + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.177
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	2.999
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	7.35

Notes:

[3] - For any patients with intercurrent events, the DSQ scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

Secondary: Percent change from baseline in tissue eosinophils at Week 24

End point title	Percent change from baseline in tissue eosinophils at Week 24

End point description:

Percent change from baseline in tissue eosinophils (eos) at Week 24.

The number analyzed represents the number of participants with data at that visit (including imputed values).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	100		
Units: Percent				
least squares mean (confidence interval 95%)				
Week 24	-94.8 (-100.00 to -82.45)	1.4 (-11.75 to 14.60)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis

Statistical analysis description:

Model: Percent change from baseline in Peak Esophageal intraepithelial eosinophil counts = Treatment + baseline Peak Esophageal intraepithelial eosinophil counts.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0001 [5]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-96.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-114.53
upper limit	-77.85

Notes:

[4] - For any patients with intercurrent events, the Peak Esophageal intraepithelial eosinophil (eos) counts after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).
[5] - P-value was <0.0001

Secondary: Change from baseline in Eosinophilic Esophagitis-Histology Scoring System (EoE-HSS) total grade score at Week 24

End point title	Change from baseline in Eosinophilic Esophagitis-Histology Scoring System (EoE-HSS) total grade score at Week 24

End point description:

EoE-HSS Grade and Stage Scores evaluate eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells, and lamina propria fibrosis. Severity (grade) and extent (stage) of abnormalities will be scored using a 4-point scale (0 normal; 3 maximum change). Total grade score (TGS): mean of the grade score ratios per region. Grade score ratio per region is the sum of all available feature grade scores divided by the maximum possible score. The maximum possible total grade score is 1.

The number analyzed represents the number of participants with data at that visit (including imputed values).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	100		
Units: Score				
least squares mean (confidence interval 95%)	-0.264 (-0.297 to -0.232)	-0.089 (-0.122 to -0.056)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis

Statistical analysis description:

Model: Change from baseline in EoE-HSS total grade score = Treatment + baseline EoE-HSS grade score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.0001 [7]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.175
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	-0.14

Notes:

[6] - For any patients with intercurrent events, the EoE-HSS total grade score after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).
[7] - P-value was <0.0001

Secondary: Change from baseline in Eosinophilic Esophagitis-Histology Scoring System (EoE-HSS) total stage score at Week 24

End point title	Change from baseline in Eosinophilic Esophagitis-Histology Scoring System (EoE-HSS) total stage score at Week 24

End point description:

EoE-HSS Grade and Stage Scores evaluate eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells, and lamina propria fibrosis. Severity (grade) and extent (stage) of abnormalities will be scored using a 4-point scale (0 normal; 3 maximum change). Total stage score (TSS): mean of the stage score ratios per region. Stage score ratio per region is the sum of all available feature stage scores divided by the maximum possible score. The maximum possible total stage score is 1.

The number analyzed represents the number of participants with data at that visit (including imputed values).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	100		
Units: Score				
least squares mean (confidence interval 95%)	-0.199 (-0.228 to -0.169)	-0.077 (-0.107 to -0.046)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis

Statistical analysis description:

Model: Change from baseline in EoE-HSS total stage score = Treatment + baseline EoE-HSS stage score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.0001 [9]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.122
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	-0.09

Notes:

[8] - For any patients with intercurrent events, the EoE-HSS total stage score after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).
[9] - P-value was <0.0001

Secondary: Changes from baseline in centrally-read Endoscopic Reference Score (EREFS) at Week 24

End point title	Changes from baseline in centrally-read Endoscopic Reference Score (EREFS) at Week 24

End point description:

EREFS is a scoring system for assessing the presence and severity of the major endoscopic signs of EoE. The score ranges from 0 (normal) to 9 (severe disease). EREFS total score (TS): The worst score for each individual component from the proximal and distal scores were summed to form the EREFS total score (TS).

The number analyzed represents the number of participants with data at that visit (including patients with imputed values post intercurrent events).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	84		
Units: Score				
least squares mean (confidence interval 95%)	-0.5 (-0.91 to -0.10)	-0.4 (-0.85 to -0.01)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis

Statistical analysis description:

Model: Change from baseline in EREFS total score = Treatment + baseline EREFS total score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.7322
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	0.32

Notes:

[10] - For any patients with intercurrent events, the centrally-read EREFS total score after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Secondary: Treatment responder rate, defined as a composite of histological response (≤6eos/hpf) and clinically meaningful improvement from baseline in Dysphagia Symptom Questionnaire (DSQ) (30% improvement) at Week 24

End point title	Treatment responder rate, defined as a composite of histological response (≤6eos/hpf) and clinically meaningful improvement from baseline in Dysphagia Symptom Questionnaire (DSQ) (30% improvement) at Week 24

End point description:

Percentage of participants with a treatment response at Week 24. A treatment response is defined as composite of histologic response and clinically meaningful improvement (30% reduction) from baseline in DSQ score. Participants with missing data at Week 24 or with intercurrent events prior to Week 24 are considered non-responders.

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Percentage of Participants				
number (confidence interval 95%)	43.7 (34.11 to 53.27)	4.7 (0.67 to 8.67)		

Statistical analyses

Statistical analysis title	Cochran-Mantel Haenszel (CMH) test
Statistical analysis description:	
Controlling for region (North America and Rest of the world), baseline steroid use, and presence of strictures at baseline.	
Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	15.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.79
upper limit	43.47

Notes:

[11] - P-value was <0.0001

Secondary: Centrally-read biopsies for additional histopathology including tissue eosinophil counts at Week 24

End point title	Centrally-read biopsies for additional histopathology including tissue eosinophil counts at Week 24
End point description:	
Centrally-read biopsies for additional histopathology including tissue eosinophil counts at Week 24	
End point type	Secondary
End point timeframe:	
Week 24	

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Participants				
<1 eos/hpf	84	0		
1 to <=6 eos/hpf	6	7		
7 to <15 eos/hpf	2	3		
15 to <60 eos/hpf	0	33		
>=60 eos/hpf	2	56		

Statistical analyses

No statistical analyses for this end point

Secondary: Dysphagia-free days as captured by the Dysphagia Symptom Questionnaire (DSQ) at Week 24

End point title	Dysphagia-free days as captured by the Dysphagia Symptom Questionnaire (DSQ) at Week 24

End point description:

Dysphagia free days is a count ranging from 0-28. Higher counts indicate better outcomes.

The number analyzed represents the number of participants with data at that visit.

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	93		
Units: Days				
arithmetic mean (standard deviation)				
Week 24	12.65 (± 10.589)	16.32 (± 11.286)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of dysphagia episodes as captured by the Eosinophilic Esophagitis Daily Dysphagia Diary (EoE-3D) at Week 24

End point title	Frequency of dysphagia episodes as captured by the Eosinophilic Esophagitis Daily Dysphagia Diary (EoE-3D) at Week 24

End point description:

EoE-3D is a daily diary focused on the patient experience of EoE. Dysphagia episode frequency is summarized as the total number of dysphagia episodes occurring over each 28-day period following

randomization, scaled up to 28 days based on missing days. Requires at least 8 days of evaluable data in each 14-day period within each 28-day period; otherwise the period is set to missing.

The number analyzed represents the number of participants with data at that visit.

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	94		
Units: Days				
arithmetic mean (standard deviation)				
Week 24	20.3 (± 28.05)	13.8 (± 19.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in dysphagia associated pain, discomfort, and overall severity as captured by the EoE-3D at Week 24

End point title	Changes from baseline in dysphagia associated pain, discomfort, and overall severity as captured by the EoE-3D at Week 24

End point description:

EoE-3D is a daily diary focused on the patient experience of EoE. The dysphagia-related pain, discomfort and overall episode severity are calculated as the sum of daily average values in the 14-day period divided by the number of days with available episodes of difficulty swallowing episodes during the same 14-day period. Requires at least 8 days of evaluable data during the period; otherwise the mean scores are set to missing.
Days with 0 episode of difficulty swallowing count as evaluable even there is no severity collected. In case all 14 days with 0 episode of difficulty swallowing, the score would be set as missing.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	73		
Units: Score				
least squares mean (confidence interval 95%)				
Dysphagia-related pain	-0.452 (-0.86 to -0.05)	-0.412 (-0.84 to 0.02)		

Dysphagia-related discomfort	-0.370 (-0.73 to -0.01)	-0.189 (-0.57 to 0.19)		
Overall episode severity	-0.481 (-0.83 to -0.13)	-0.137 (-0.51 to 0.24)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis for dysphagia-related pain

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.8656
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.42

Notes:

[12] - For any patients with intercurrent events, the EoE-3D scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA model analysis for overall episode severity

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.0867
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.344
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	0.05

Notes:

[13] - For any patients with intercurrent events, the EoE-3D scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA analysis for dysphagia-related discomfort

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.3926
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.181
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.23

Notes:

[14] - For any patients with intercurrent events, the EoE-3D scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Secondary: Changes from baseline in abdominal pain and nausea as captured by the daily diary at Week 24

End point title	Changes from baseline in abdominal pain and nausea as captured by the daily diary at Week 24

End point description:

Abdominal pain severity and nausea severity were summarized individually as 14-day means scores. Requires at least 8 days of evaluable data. Otherwise the mean score is set to missing.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	101		
Units: Score				
least squares mean (confidence interval 95%)				
Abdominal pain severity	-0.549 (-0.94 to -0.16)	-0.815 (-1.20 to -0.53)		
Nausea severity	-0.524 (-0.90 to -0.15)	-0.820 (-1.19 to -0.45)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis for nausea severity

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.1575
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.296
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.71

Notes:

[15] - For any patients with intercurrent events, the EoE-3D scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA analysis for abdominal pain severity

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.2248
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.267
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.7

Notes:

[16] - For any patients with intercurrent events, the EoE-3D scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Secondary: Changes from baseline in PEESS at Week 24

End point title	Changes from baseline in PEESS at Week 24

End point description:

The Pediatric Eosinophilic Esophagitis Symptom Severity Module, Version 2, Children and Teens Report (PEESS) is a questionnaire of EoE symptom severity and frequency in patients age 8 to 18 years.

The number analyzed represents the number of participants with data at that visit.

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: Score				
arithmetic mean (standard deviation)				
Week 24	-0.8 (± 11.69)	-5.9 (± 14.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EOE-QoL-A) at Week 24

End point title	Changes from baseline in Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EOE-QoL-A) at Week 24

End point description:

The Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EoE-QoL-A) is a 30-item assessment developed specifically to measure health-related quality of life in patients with EoE. The overall score ranges from 0 to 96, with higher scores meaning better quality of life. Total Score: sum of Eating/Diet, Social Impact, Emotional Impact, Disease Anxiety and Swallow Anxiety domain scores.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	96		
Units: Score				
least squares mean (confidence interval 95%)				
Eating/Diet Impact	1.370 (-0.27 to 3.01)	1.169 (-0.46 to 2.79)		
Social Impact	1.095 (0.21 to 1.98)	0.948 (0.07 to 1.83)		
Emotional Impact	0.912 (-0.46 to 2.29)	0.902 (-0.46 to 2.27)		
Disease Anxiety	0.185 (-0.77 to 1.14)	-0.201 (-1.15 to 0.75)		
Swallowing Anxiety	0.443 (-0.23 to 1.12)	0.605 (-0.06 to 1.27)		
Total Score	4.380 (-0.36 to 9.12)	3.362 (-1.33 to 8.06)		

Statistical analyses

Statistical analysis title	ANCOVA model analysis on Eating/Diet Impact

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.8239
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.202
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	1.98

Notes:

[17] - For any patients with intercurrent events, the EoE-QoL-A scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA model analysis on Social Impact

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.7623
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.147
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.1

Notes:

[18] - For any patients with intercurrent events, the EoE-QoL-A scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA model analysis on Emotional Impact

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.9898
Method	ANCOVA
Parameter estimate	Difference of Least Squares Means
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	1.49

Notes:

[19] - For any patients with intercurrent events, the EoE-QoL-A scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA model analysis on Disease Anxiety

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	= 0.4603
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.386
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	1.41

Notes:

[20] - For any patients with intercurrent events, the EoE-QoL-A scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA model analysis on Swallowing Anxiety

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo

Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.6613
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.162
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.56

Notes:

[21] - For any patients with intercurrent events, the EoE-QoL-A scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	ANCOVA model analysis on Total Score

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.6965
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	1.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	6.13

Notes:

[22] - For any patients with intercurrent events, the EoE-QoL-A scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Secondary: Change from baseline in Short Form 36-item health survey (version 2, acute recall) (SF-36v2) at Week 24

End point title	Change from baseline in Short Form 36-item health survey (version 2, acute recall) (SF-36v2) at Week 24

End point description:

The Short Form 36-item Health Survey, version 2, acute recall (SF-36v2) is a 36-item, self-report survey of functional health and well-being, with a 1-week recall period. There are 8 domain scores: Physical Functioning (PF), Role Limitations due to Physical Health (RP), Bodily Pain (BP), General Health Perceptions (GH), Vitality (VT), Social Functioning (SF), Role Limitations due to Emotional Problems (RE), and Mental Health (MH). Psychometrically-based physical and mental health component summary scores (PCS and MCS, respectively) were computed from subscale scores to give a broader metric of physical and mental health-related quality of life. All scores range from 0-100, with higher scores meaning better outcomes.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	81		
Units: Score				
least squares mean (confidence interval 95%)				
Physical functioning	0.2 (-1.36 to 1.70)	0.5 (-0.98 to 1.97)		
Role limitations due to physical health	0.5 (-1.03 to 2.10)	1.5 (-0.06 to 2.99)		
Bodily pain	-0.6 (-2.92 to 1.82)	0.2 (-2.07 to 2.53)		
General health perceptions	-0.9 (-2.62 to 0.78)	-0.9 (-2.54 to 0.76)		
Vitality	-0.5 (-2.47 to 1.54)	-0.5 (-2.50 to 1.48)		
Social functioning	-1.5 (-3.84 to 0.92)	0.1 (-2.26 to 2.39)		
Role limitations due to emotional problems	-1.1 (-3.68 to 1.51)	-0.4 (-2.95 to 2.15)		
Mental health	-1.7 (-3.83 to 0.51)	-0.8 (-2.91 to 1.31)		
Psychometrically-based physical summary score	0.4 (-1.21 to 2.01)	0.8 (-0.75 to 2.34)		
Mental health component summary scores	-1.8 (-4.10 to 0.53)	-1.2 (-3.44 to 1.11)		

Statistical analyses

Statistical analysis title	Physical functioning
Statistical analysis description: Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.	
Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.6852
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	1.27

Notes:

[23] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Role limitations due to physical health

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	= 0.2685
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.57
upper limit	0.72

Notes:

[24] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Bodily pain

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.538
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.27
upper limit	1.71

Notes:

[25] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	General health perceptions

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo

Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	= 0.9734
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	1.75

Notes:

[26] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Vitality

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.9653
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	2.19

Notes:

[27] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Role limitations due to emotional problems

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[28]
P-value	= 0.6274
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.44
upper limit	2.08

Notes:

[28] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Social functioning

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.2326
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.04
upper limit	0.98

Notes:

[29] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Psychometrically-based physical summary score

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.6456
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.07
upper limit	1.28

Notes:

[30] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Mental health

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.4599
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.14
upper limit	1.42

Notes:

[31] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Statistical analysis title	Mental health component summary scores

Statistical analysis description:

Model: Change from baseline item score = Treatment + baseline item score + Region + Baseline steroid use + Presence of strictures at baseline.

Comparison groups	Benralizumab v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.6206
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.08
upper limit	1.84

Notes:

[32] - For any patients with intercurrent events, the SF-36 domain scores after the occurrence of those events were imputed using return-to-baseline MI. Missing data not due to intercurrent events were imputed using MI (MAR).

Secondary: Percent of patients with relevant concomitant procedures and healthcare resource utilization at Week 24 and Week 52.

End point title	Percent of patients with relevant concomitant procedures and healthcare resource utilization at Week 24 and Week 52.

End point description:

Percent of patients with any relevant concomitant procedures and healthcare resource utilization at Week 24 and Week 52.

End point type	Secondary

End point timeframe:

Week 24, Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Participants				
Week 24	3	5		
Week 52	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient reported overall severity of disease as measured by Patient Global Impression of Severity (PGI-S) at Week 24

End point title	Patient reported overall severity of disease as measured by Patient Global Impression of Severity (PGI-S) at Week 24

End point description:

Patient Global Impression of Severity (PGI-S) is an assessment of the patient's perceived disease severity. The answer options are "no symptoms," "very mild," "mild," "moderate," "severe," and "very severe."

The number analyzed represents the participants with evaluable PGI-S results at that timepoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	95		
Units: Participants				
No symptoms	4	11		
Very mild	23	27		
Mild	34	32		
Moderate	29	17		
Severe	3	6		
Very Severe	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient reported change in health status since baseline as measured by

Patient Global Impression of Change (PGI-C) at Week 24

End point title	Patient reported change in health status since baseline as measured by Patient Global Impression of Change (PGI-C) at Week 24

End point description:

Patient Global Impression of Change (PGI-C) measures the patient's overall impression of response to treatment since the initial dose. The answer options are "much better," "moderately better," "a little better," "about the same/no change," "a little worse," "moderately worse," and "much worse."

The number analyzed represents the participants with evaluable PGI-C results at that timepoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	96		
Units: Participants				
Much better	13	13		
Moderately better	13	17		
A little better	21	20		
About the same	37	36		
A little worse	7	6		
Moderately worse	3	3		
Much worse	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Benralizumab Pharmacokinetics for Double Blind Period

End point title	Benralizumab Pharmacokinetics for Double Blind Period

End point description:

Serum concentrations of benralizumab through Week 24. Geometric mean calculated using log transformed data.

End point type	Secondary

End point timeframe:

Up to week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	0[33]		
Units: ng/mL				
geometric mean (confidence interval 95%)				
Week 8 (n = 95)	1555.70 (1425.31 to 1698.02)	(to)		
Week 16 (n = 91)	1582.46 (1322.66 to 1893.30)	(to)		
Week 24 (n = 85)	1338.65 (1027.05 to 1744.78)	(to)		

Notes:

[33] - Placebo treatment, so no PK data till after week 24 (where values were mean = BLQ, CI = NA to NA)

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity of benralizumab in Double Blind period

End point title	Immunogenicity of benralizumab in Double Blind period

End point description:

Immunogenicity of benralizumab assessed by ADA and nAb in the Double Blind period.

Note: TE = Treatment Emergent. *Condition = maximum titre >median of maximum titres. Last two categories for placebo group recorded as 0, but no data calculated (due to placebo treatment).

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Participants				
ADA positive/ADA prevalence (n = 103, 107)	18	8		
ADA negative (n = 103, 107)	85	99		
TE ADA positive/ADA incidence (n = 102, 106)	18	4		
ADA persistently positive (n = 102, 106)	18	3		
ADA positive with condition* (n = 103, 107)	6	4		
nAb positive/nAb prevalence (n = 103)	10	0		
ADA persistently positive + nAb positive (n = 102)	10	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Benralizumab Pharmacokinetics for Open Label Period

End point title	Benralizumab Pharmacokinetics for Open Label Period

End point description:

Serum concentrations of benralizumab in Weeks 36 and 52. Geometric mean calculated using log transformed data.

End point type	Secondary

End point timeframe:

Week 36, Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	96		
Units: ng/mL				
geometric mean (confidence interval 95%)				
Week 36 (n = 67, 63)	1405.94 (985.94 to 2004.86)	1362.27 (1051.69 to 1764.58)		
Week 52 (n = 30, 36)	1278.13 (749.19 to 2180.52)	1495.61 (975.73 to 2292.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity of benralizumab in Double Blind + Open Label periods

End point title	Immunogenicity of benralizumab in Double Blind + Open Label periods

End point description:

Immunogenicity of benralizumab assessed by ADA and nAb in the Double Blind and Open Label periods.

Note: TE = Treatment Emergent. *Condition = maximum titre >median of maximum titres. Pos = positive.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Participants				
ADA positive/ADA prevalence (n = 103, 105)	19	17		
ADA negative (n = 103, 105)	84	88		
TE ADA positive/ADA incidence (n = 102, 105)	19	11		
ADA persistently positive (n = 102, 105)	16	10		
ADA positive with condition* (n = 103, 105)	7	7		
nAb positive/nAb prevalence (n = 103, 105)	10	5		
ADA persistently pos. & nAb pos. (n = 102, 105)	10	5		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Proportion of patients with a histologic response, defined as a peak esophageal intraepithelial eosinophil count ≤ 6 eos/hpf at Week 52

End point title	Proportion of patients with a histologic response, defined as a peak esophageal intraepithelial eosinophil count ≤ 6 eos/hpf at Week 52

End point description:

Proportion of patients with a histologic response at Week 52. A histologic response is defined as a peak esophageal intraepithelial eosinophil count <= 6 eos/hpf across all available esophageal levels.

The number analyzed represents the number of participants in the treatment group that could have made it to the timepoint by the data cut off.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	47		
Units: Percentage of Participants				
number (confidence interval 95%)	82.6 (71.66 to 93.56)	89.4 (80.55 to 98.18)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Changes from baseline in Dysphagia Symptom Questionnaire (DSQ) at Week 52

End point title	Changes from baseline in Dysphagia Symptom Questionnaire (DSQ) at Week 52

End point description:

The Dysphagia Symptom Questionnaire (DSQ) captures the presence and severity of dysphagia symptoms in the past day in a 4-item questionnaire. The DSQ score is calculated over 14-day periods and ranges from 0 to 84, with a lower score indicating less severe dysphagia. At least 8 days with evaluable daily score in 14-day period are required; otherwise the DSQ score for the period is set to missing.

The number analyzed represents the number of participants with data at that visit (including patients with imputed values post intercurrent events).

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	45		
Units: Score				
least squares mean (confidence interval 95%)	-19.409 (-25.65 to -13.17)	-19.806 (-25.70 to -13.91)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in centrally-read Endoscopic Reference Score (EREFS) at Week 52

End point title	Change from baseline in centrally-read Endoscopic Reference Score (EREFS) at Week 52

End point description:

EREFS is a scoring system for assessing the presence and severity of the major endoscopic signs of EoE. The score ranges from 0 (normal) to 9 (severe disease). EREFS total score (TS): The worst score for each individual component from the proximal and distal scores were summed to form the EREFS total score (TS).

The number analyzed represents the number of participants with data at that visit (including patients with imputed values post intercurrent events).

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Score				
least squares mean (confidence interval 95%)	-0.3 (-0.90 to 0.32)	-0.7 (-1.35 to -0.09)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Dysphagia-free days as captured by the Dysphagia Symptom Questionnaire (DSQ) at Week 52

End point title	Dysphagia-free days as captured by the Dysphagia Symptom Questionnaire (DSQ) at Week 52

End point description:

Dysphagia free days is a count ranging from 0-28. Higher counts indicate better outcomes.

The number analyzed represents the number of participants with data at that visit.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	41		
Units: Days				
arithmetic mean (standard deviation)	19.33 (± 10.950)	20.8 (± 10.472)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Frequency of dysphagia episodes as captured by the Eosinophilic Esophagitis Daily Dysphagia Diary (EoE-3D) at Week 52

End point title	Frequency of dysphagia episodes as captured by the Eosinophilic Esophagitis Daily Dysphagia Diary (EoE-3D) at Week 52

End point description:

EoE-3D is a daily diary focused on the patient experience of EoE. Dysphagia episode frequency is summarized as the total number of dysphagia episodes occurring over each 28-day period following randomization, scaled up to 28 days based on missing days. Requires at least 8 days of evaluable data in each 14-day period within each 28-day period; otherwise the period is set to missing.

The number analyzed represents the number of participants with data at that visit.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	41		
Units: Days				
arithmetic mean (standard deviation)	6.8 (± 11.59)	6.2 (± 9.83)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Changes from baseline in dysphagia associated pain, discomfort, and overall severity as captured by the EoE-3D at Week 52

End point title	Changes from baseline in dysphagia associated pain, discomfort, and overall severity as captured by the EoE-3D at Week 52

End point description:

EoE-3D is a daily diary focused on the patient experience of EoE. The dysphagia-related pain, discomfort and overall episode severity are calculated as the sum of daily average values in the 14-day period divided by the number of days with available episodes of difficulty swallowing episodes during the same 14-day period. Requires at least 8 days of evaluable data during the period; otherwise the mean scores are set to missing.
Days with 0 episode of difficulty swallowing count as evaluable even there is no severity collected. In case all 14 days with 0 episode of difficulty swallowing, the score would be set as missing.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	49		
Units: Score				
least squares mean (confidence interval 95%)				
Dysphagia-related pain	-0.511 (-1.40 to 0.38)	-0.776 (-1.65 to 0.10)		
Dysphagia-related discomfort	-0.456 (-1.14 to 0.22)	-0.625 (-1.30 to 0.05)		
Overall episode severity	-0.522 (-1.26 to 0.22)	-0.732 (-1.48 to 0.02)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Changes from baseline in abdominal pain and nausea as captured by the daily diary at Week 52

End point title	Changes from baseline in abdominal pain and nausea as captured by the daily diary at Week 52

End point description:

Abdominal pain severity and nausea severity were summarized individually as 14-day means scores. Requires at least 8 days of evaluable data. Otherwise the mean score is set to missing.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	45		
Units: Score				
least squares mean (confidence interval 95%)				
Abdominal pain severity	-0.826 (-1.44 to -0.22)	-1.039 (-1.62 to -0.46)		
Nausea severity	-0.855 (-1.43 to -0.28)	-0.960 (-1.50 to -0.42)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in PEES at Week 52

End point title	Change from baseline in PEES at Week 52

End point description:

The Pediatric Eosinophilic Esophagitis Symptom Severity Module, Version 2, Children and Teens Report (PEESS) is a questionnaire of EoE symptom severity and frequency in patients age 8 to 18 years.

The number analyzed represents the number of participants with data at that visit.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Score				
arithmetic mean (standard deviation)	-6.5 (± 18.04)	-12.5 (± 15.67)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Changes from baseline in Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EOE-QoL-A) at Week 52

End point title	Changes from baseline in Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EOE-QoL-A) at Week 52

End point description:

The Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EoE-QoL-A) is a 30-item assessment developed specifically to measure health-related quality of life in patients with EoE. The overall score ranges from 0 to 96, with higher scores meaning better quality of life. Total Score: sum of Eating/Diet, Social Impact, Emotional Impact, Disease Anxiety and Swallow Anxiety domain scores.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	47		
Units: Score				
least squares mean (confidence interval 95%)				
Eating/Diet Impact	1.408 (-1.01 to 3.83)	1.949 (-0.32 to 4.21)		
Social Impact	1.462 (0.09 to 2.83)	1.984 (0.70 to 3.27)		
Emotional Impact	1.768 (-0.21 to 3.75)	2.451 (0.58 to 4.33)		
Disease Anxiety	1.063 (-0.43 to 2.56)	1.152 (-0.27 to 2.57)		
Swallowing Anxiety	0.677 (-0.37 to 1.72)	1.085 (0.10 to 2.07)		
Total Score	6.749 (-0.35 to 13.84)	8.714 (2.03 to 15.40)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in Short Form 36-item health survey (version 2, acute recall) (SF-36v2) at Week 52

End point title	Change from baseline in Short Form 36-item health survey (version 2, acute recall) (SF-36v2) at Week 52

End point description:

The Short Form 36-item Health Survey, version 2, acute recall (SF-36v2) is a 36-item, self-report survey of functional health and well-being, with a 1-week recall period. There are 8 domain scores: Physical Functioning (PF), Role Limitations due to Physical Health (RP), Bodily Pain (BP), General Health Perceptions (GH), Vitality (VT), Social Functioning (SF), Role Limitations due to Emotional Problems (RE), and Mental Health (MH). Psychometrically-based physical and mental health component summary scores (PCS and MCS, respectively) were computed from subscale scores to give a broader metric of physical and mental health-related quality of life. All scores range from 0-100, with higher scores meaning better outcomes.

The number analyzed represents the number of participants with data at that visit (including participants with imputed values post intercurrent events).

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	38		
Units: Score				
least squares mean (confidence interval 95%)				
Physical functioning	0.3 (-1.86 to 2.51)	0.4 (-1.60 to 2.46)		
Role limitations due to physical health	-0.5 (-3.27 to 2.20)	0.9 (-1.63 to 3.51)		
Bodily pain	0.6 (-2.69 to 3.97)	1.8 (-1.34 to 5.00)		
General health perceptions	2.3 (-0.71 to 5.39)	0.7 (-2.17 to 3.59)		
Vitality	-0.2 (-2.69 to 2.31)	-2.0 (-4.42 to 0.44)		
Social functioning	0.2 (-3.73 to 4.17)	-0.5 (-4.26 to 3.34)		
Role limitations due to emotional problems	-0.1 (-3.30 to 3.19)	-0.3 (-3.39 to 2.76)		
Mental health	1.2 (-1.37 to 3.69)	-1.1 (-3.46 to 1.30)		
Psychometrically-based physical summary score	0.5 (-2.15 to 3.18)	1.4 (-1.15 to 3.85)		

Mental health component summary scores	0.5 (-2.44 to 3.50)	-1.9 (-4.78 to 0.89)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Patient reported overall severity of disease as measured by Patient Global Impression of Severity (PGI-S) at Week 52

End point title	Patient reported overall severity of disease as measured by Patient Global Impression of Severity (PGI-S) at Week 52

End point description:

Patient Global Impression of Severity (PGI-S) is an assessment of the patient's perceived disease severity. The answer options are "no symptoms," "very mild," "mild," "moderate," "severe," and "very severe."

The number analyzed represents the participants with evaluable PGI-S results at that timepoint.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	42		
Units: Participants				
No symptoms	6	10		
Very mild	12	14		
Mild	9	13		
Moderate	8	5		
Severe	0	0		
Very Severe	1	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Patient reported change in health status since baseline as measured by Patient Global Impression of Change (PGI-C) at Week 52

End point title	Patient reported change in health status since baseline as measured by Patient Global Impression of Change (PGI-C) at Week 52

End point description:

Patient Global Impression of Change (PGI-C) measures the patient's overall impression of response to treatment since the initial dose. The answer options are "much better," "moderately better," "a little better," "about the same/no change," "a little worse," "moderately worse," and "much worse."

The number analyzed represents the participants with evaluable PGI-C results at that timepoint.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	43		
Units: Participants				
Much better	12	13		
Moderately better	3	12		
A little better	8	12		
About the same	9	6		
A little worse	4	0		
Moderately worse	0	0		
Much worse	0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety and tolerability in the Open Label period

End point title	Safety and tolerability in the Open Label period

End point description:

Percentage of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) in the Open Label treatment period (past week 24).

End point type	Other pre-specified

End point timeframe:

From Week 24 up to Week 52

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	105		
Units: Participants				
Any AE	53	60		
Any SAE	2	4		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety and tolerability in Double Blind Period

End point title	Safety and tolerability in Double Blind Period

End point description:

Percentage of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) in the Double Blind treatment period (up to Week 24).

End point type	Other pre-specified

End point timeframe:

Up to Week 24

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	107		
Units: Participants				
Any AE	66	66		
Any SAE	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
On study AEs were collected from the first dose to the last date in study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo injection delivered subcutaneously every 4 weeks through week 24, then 30mg Benralizumab injection delivered subcutaneously every 4 weeks after week 24	
Reporting group title	Benra 30 mg
Reporting group description:	
30mg Benralizumab injection delivered subcutaneously every 4 weeks	

Serious adverse events	Placebo	Benra 30 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 107 (5.61%)	4 / 103 (3.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal food impaction			
subjects affected / exposed	2 / 107 (1.87%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal perforation			

subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (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			
Asthma			
subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumomediastinum			
subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Oppositional defiant disorder			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disruptive mood dysregulation disorder			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 107 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 107 (0.93%)	0 / 103 (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: 3 %

Non-serious adverse events	Placebo	Benra 30 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 107 (64.49%)	61 / 103 (59.22%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 107 (0.93%)	4 / 103 (3.88%)	
occurrences (all)	1	4	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 107 (11.21%)	12 / 103 (11.65%)	
occurrences (all)	19	15	

General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	6 / 107 (5.61%)	3 / 103 (2.91%)	
occurrences (all)	6	5	
Injection site erythema			
subjects affected / exposed	3 / 107 (2.80%)	5 / 103 (4.85%)	
occurrences (all)	4	13	
Pyrexia			
subjects affected / exposed	5 / 107 (4.67%)	3 / 103 (2.91%)	
occurrences (all)	6	3	
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	1 / 107 (0.93%)	4 / 103 (3.88%)	
occurrences (all)	1	4	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 107 (5.61%)	2 / 103 (1.94%)	
occurrences (all)	6	2	
Diarrhoea			
subjects affected / exposed	7 / 107 (6.54%)	7 / 103 (6.80%)	
occurrences (all)	11	7	
Dyspepsia			
subjects affected / exposed	4 / 107 (3.74%)	0 / 103 (0.00%)	
occurrences (all)	4	0	
Nausea			
subjects affected / exposed	4 / 107 (3.74%)	4 / 103 (3.88%)	
occurrences (all)	4	4	
Vomiting			
subjects affected / exposed	4 / 107 (3.74%)	1 / 103 (0.97%)	
occurrences (all)	4	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 107 (1.87%)	6 / 103 (5.83%)	
occurrences (all)	2	6	
Asthma			

subjects affected / exposed	7 / 107 (6.54%)	5 / 103 (4.85%)	
occurrences (all)	9	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 107 (4.67%)	1 / 103 (0.97%)	
occurrences (all)	5	1	
Back pain			
subjects affected / exposed	1 / 107 (0.93%)	4 / 103 (3.88%)	
occurrences (all)	2	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 107 (10.28%)	12 / 103 (11.65%)	
occurrences (all)	15	20	
Influenza			
subjects affected / exposed	4 / 107 (3.74%)	0 / 103 (0.00%)	
occurrences (all)	4	0	
Pharyngitis			
subjects affected / exposed	0 / 107 (0.00%)	5 / 103 (4.85%)	
occurrences (all)	0	5	
Upper respiratory tract infection			
subjects affected / exposed	7 / 107 (6.54%)	4 / 103 (3.88%)	
occurrences (all)	11	4	
COVID-19			
subjects affected / exposed	27 / 107 (25.23%)	34 / 103 (33.01%)	
occurrences (all)	28	38	
Gastroenteritis			
subjects affected / exposed	4 / 107 (3.74%)	1 / 103 (0.97%)	
occurrences (all)	6	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2020	The primary rationale for this amendment is to add study mitigation language which will provide sites with measures that may be implemented if a patient is not able to visit a study site to ensure that the clinical trial can continue whilst minimizing risk to the patient, maintaining compliance with GCP, and minimizing risks to the study integrity. The Qualitative Patient Interview Sub-study (Section 8.11.1) was also added. In addition, inclusion/exclusion criteria were clarified, and Table 9 of Restrictions (Section 6.5.4) was updated with clarifications regarding medications allowed, restricted and prohibited prior to screening. Finally, some minor clarifications were made to ensure correct interpretation of the protocol.
26 August 2020	The primary rationale for this amendment is to add study mitigation language which will provide sites with measures that may be implemented if a patient is not able to visit a study site to ensure that the clinical trial can continue whilst minimizing risk to the patient, maintaining compliance with GCP, and minimizing risks to the study integrity. The Qualitative Patient Interview Sub-study (Section 8.11.1) was also added. In addition, inclusion/exclusion criteria were clarified, and Table 9 of Restrictions (Section 6.5.4) was updated with clarifications regarding medications allowed, restricted and prohibited prior to screening. Finally, some minor clarifications were made to ensure correct interpretation of the protocol.
11 February 2021	The primary rationale for this amendment is to update the duration of the OLE-period to at least 1 year (variable duration) and to include the option of at-home or remote location self-IP administration after week 52. Inclusion/exclusion criteria were clarified, the primary estimand approach for the analyses of study data was updated to a composite strategy to more accurately account for the occurrence of the described intercurrent events which are considered to reflect a treatment failure outcome. In addition, some minor clarifications were made to ensure correct interpretation of the protocol.
30 April 2021	The primary rationale for this amendment is to add the early time point sub-study. The substudy aims to generate early time point evidence of eosinophil depletion in tissue and to understand its relationship with endoscopic findings and symptom response. In addition, some minor clarifications were made to ensure correct interpretation of the protocol.
01 April 2022	The rationale for this amendment is to adjust the ordering of endpoints within the multiple testing procedure and update the analysis method for treatment failure intercurrent events for continuous endpoints. In addition, some minor clarifications were made to ensure correct interpretation of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported