Clinical trial results:
A Phase 2b Multinational, Randomised, Double-blind, Parallel-group, 24-week Placebo-controlled Study with 28-week Extension to Investigate the Use of Benralizumab in Patients with Chronic Spontaneous Urticaria Who are Symptomatic Despite the Use of Antihistamines (ARROYO)

Summary

EudraCT number	2020-000169-17
Trial protocol	BG DE
Global end of trial date	28 March 2023

Results information

Result version number	v1 (current)
This version publication date	09 November 2023
First version publication date	09 November 2023

Trial information

Trial identification

Sponsor protocol code	D3259C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04612725
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, SE-151 85
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	28 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 March 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the clinical efficacy of benralizumab compared to placebo in participants with chronic spontaneous urticaria (CSU) who are symptomatic despite the use of H1 antihistamine treatment.

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 are consistent with International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy:

Participants were maintained on a stable and locally-approved second generation H1 antihistamine treatment for CSU throughout the run-in period.

Evidence for comparator: -

Actual start date of recruitment	27 October 2020
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	Bulgaria: 46
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Poland: 24
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	155
EEA total number of subjects	90

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	133
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 2b, randomized, double-blind study was conducted in participants with CSU who were symptomatic despite the use of antihistamines at 46 study centers. The study was terminated early by the sponsor as primary results did not support the continued development of benralizumab for the indication of CSU.

Pre-assignment

Screening details:

The study had a run-in period (10 days to 4 weeks), followed by a double-blind treatment period (24 weeks) and extension period (28 weeks). A total of 155 participants were randomized and treated in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Benralizumab 30 mg

Arm description:

Participants were randomized to receive benralizumab 30 milligram (mg) subcutaneous (SC) injection every 4 weeks (Q4W) until Week 24 in the double-blind treatment period and then 30 mg Q4W or every 8 weeks (Q8W) during the extension period until Week 52.

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	MEDI-563
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30 mg SC injection was administered Q4W until Week 24 in the double-blind treatment period and then 30 mg Q4W or Q8W during the extension period until Week 52.

Arm title	Benralizumab 60 mg

Arm description:

Participants were randomized to receive benralizumab 60 mg SC injection Q4W until Week 12 and then 30 mg Q4W until Week 24 in the double-blind treatment period followed by 30 mg Q4W or Q8W during the extension period until Week 52.

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	MEDI-563
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 60 mg SC injection was administered Q4W until Week 12 and then 30 mg Q4W until Week 24 in the double-blind treatment period followed by 30 mg Q4W or Q8W during the extension period until Week 52.

Arm title	Placebo

Arm description:

Participants were randomized to receive placebo matching with benralizumab Q4W until Week 24 in the double-blind treatment period followed by benralizumab 30 mg SC injection Q4W until Week 36 and then 30 mg Q8W until Week 52.

Arm type	Placebo
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	MEDI-563
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30 mg SC injection was administered Q4W until Week 36 and then 30 mg Q8W until Week 52 in the extension period.

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:

Placebo SC injection was administered Q4W until Week 24 in the double-blind treatment period.

Number of subjects in period 1	Benralizumab 30 mg	Benralizumab 60 mg	Placebo
Started	59	56	40
Completed the treatment period	53	53	37
Entered extension period	50	53	37
Completed	37	43	24
Not completed	22	13	16
Physician decision	2	-	-
Consent withdrawn by subject	11	6	9
Adverse event, non-fatal	4	1	1
Study terminated by sponsor	4	6	5
Unspecified	-	-	1
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Benralizumab 30 mg
Reporting group description:	
Participants were randomized to receive benralizumab 30 milligram (mg) subcutaneous (SC) injection every 4 weeks (Q4W) until Week 24 in the double-blind treatment period and then 30 mg Q4W or every 8 weeks (Q8W) during the extension period until Week 52.	
Reporting group title	Benralizumab 60 mg
Reporting group description:	
Participants were randomized to receive benralizumab 60 mg SC injection Q4W until Week 12 and then 30 mg Q4W until Week 24 in the double-blind treatment period followed by 30 mg Q4W or Q8W during the extension period until Week 52.	
Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive placebo matching with benralizumab Q4W until Week 24 in the double-blind treatment period followed by benralizumab 30 mg SC injection Q4W until Week 36 and then 30 mg Q8W until Week 52.	

Reporting group values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo
Number of subjects	59	56	40
Age Categorical Units: Subjects			
<35 years	11	15	8
>=35 to <=55 years	32	25	22
>55 years	16	16	10
Gender Categorical Units: Subjects			
Female	44	45	25
Male	15	11	15
Race Units: Subjects			
White	46	42	30
Asian	12	12	8
Black or African American	1	2	0
Not reported	0	0	2
Ethnicity Units: Subjects			
Hispanic or Latino	2	4	4
Not Hispanic or Latino	57	52	36

Reporting group values	Total		
Number of subjects	155		
Age Categorical Units: Subjects			
<35 years	34		
>=35 to <=55 years	79		
>55 years	42		

Gender Categorical Units: Subjects			
Female	114		
Male	41		
Race Units: Subjects			
White	118		
Asian	32		
Black or African American	3		
Not reported	2		
Ethnicity Units: Subjects			
Hispanic or Latino	10		
Not Hispanic or Latino	145		

End points reporting groups

Reporting group title	Benralizumab 30 mg
Reporting group description:	
Participants were randomized to receive benralizumab 30 milligram (mg) subcutaneous (SC) injection every 4 weeks (Q4W) until Week 24 in the double-blind treatment period and then 30 mg Q4W or every 8 weeks (Q8W) during the extension period until Week 52.	
Reporting group title	Benralizumab 60 mg
Reporting group description:	
Participants were randomized to receive benralizumab 60 mg SC injection Q4W until Week 12 and then 30 mg Q4W until Week 24 in the double-blind treatment period followed by 30 mg Q4W or Q8W during the extension period until Week 52.	
Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive placebo matching with benralizumab Q4W until Week 24 in the double-blind treatment period followed by benralizumab 30 mg SC injection Q4W until Week 36 and then 30 mg Q8W until Week 52.	
Subject analysis set title	Benralizumab Q4W Total
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received benralizumab 30 mg or 60 mg SC injection Q4W during the study.	
Subject analysis set title	Benralizumab Q8W Total
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received benralizumab 30 mg or 60 mg SC injection Q8W during the study.	
Subject analysis set title	Benralizumab 30 mg Q4W
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received benralizumab 30 mg SC injection Q4W during the study.	
Subject analysis set title	Benralizumab 30 mg Q8W
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received benralizumab 30 mg SC injection Q8W during the study.	
Subject analysis set title	Benralizumab 60 mg Q4W
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received benralizumab 60 mg SC injection Q4W during the study.	
Subject analysis set title	Benralizumab 60 mg Q8W
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received benralizumab 60 mg SC injection Q8W during the study.	

Primary: Least Square (LS) Mean Change From Baseline in Itch Severity Score Over 7 Days (ISS7) at Week 12

End point title	Least Square (LS) Mean Change From Baseline in Itch Severity Score Over 7 Days (ISS7) at Week 12

End point description:

The urticaria participant daily diary (UPDD) was completed twice daily (morning and evening) to capture key measures of urticaria disease activity including the itch severity score (ISS). The ISS represents severity on a scale ranging from 0 to 3 (where 0= none, 1= mild, 2= moderate and 3= severe). The ISS7 is the sum of ISS for the previous 7 days. The ISS7 represents itch severity on a scale ranging from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of itch. Baseline was defined as the sum of the daily scores for the 7 days prior to the day of randomization. The full analysis

set (FAS) included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study.

End point type	Primary

End point timeframe:

Baseline (Day -1) and Week 12

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	52	37	
Units: units on a scale				
least squares mean (confidence interval 95%)	-7.50 (-8.94 to -6.05)	-8.28 (-9.76 to -6.80)	-6.49 (-8.24 to -4.74)	

Statistical analyses

Statistical analysis title	Treatment difference in ISS7 at Week 12

Statistical analysis description:

Change from baseline in ISS7 at Week 12= Treatment + baseline ISS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3824
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.28
upper limit	1.26

Statistical analysis title	Treatment difference in ISS7 at Week 12

Statistical analysis description:

Change from baseline in ISS7 at Week 12= Treatment + baseline ISS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Comparison groups	Benralizumab 60 mg v Placebo

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1244
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	0.5

Secondary: LS Mean Change From Baseline in Urticaria Activity Score Over 7 Days (UAS7) at Weeks 12 and 24

End point title	LS Mean Change From Baseline in Urticaria Activity Score Over 7 Days (UAS7) at Weeks 12 and 24

End point description:

The UPDD was completed twice daily (morning and evening) to capture key measures of urticaria disease activity including the UAS7. Participants were asked to document the number of hives they experienced on a scale ranging from 0 to 3 (where 0= none, 1= mild [1 – 6 hives/12 hour], 2= moderate [7 – 12 hives/12 hour] and 3= intense [(> 12 hives/12 hour]). The UAS7 is the sum of UAS for the previous 7 days, that is, the sum of ISS7 and HSS7. The UAS7 represents urticaria severity on a scale from 0 (minimum) to 42 (maximum). Higher scores indicate greater severity of urticaria symptoms. Baseline was defined as the sum of the daily scores for the 7 days prior to the day of randomization. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Here, 'n' is number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	53	37	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12 (n= 55, 52, 37)	-14.48 (-17.58 to -11.38)	-16.77 (-19.94 to -13.59)	-12.41 (-16.17 to -8.65)	
Week 24 (n= 52, 53, 36)	-17.99 (-21.29 to -14.68)	-19.17 (-22.51 to -15.83)	-15.43 (-19.43 to -11.44)	

Statistical analyses

Statistical analysis title	Treatment difference in UAS7 at Week 12
Comparison groups	Benralizumab 30 mg v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4016 [1]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-2.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.95
upper limit	2.8

Notes:

[1] - Change from baseline in UAS7 at Week 12= Treatment + baseline UAS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in UAS7 at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0819 [2]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-4.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.28
upper limit	0.56

Notes:

[2] - Change from baseline in UAS7 at Week 12= Treatment + baseline UAS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in UAS7 at Week 24
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3314 [3]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.74
upper limit	2.63

Notes:

[3] - Change from baseline in UAS7 at Week 24= Treatment + baseline UAS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in UAS7 at Week 24

Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1582 [4]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-3.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.95
upper limit	1.47

Notes:

[4] - Change from baseline in UAS7 at Week 24= Treatment + baseline UAS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Secondary: LS Mean Change From Baseline in ISS7 at Week 24

End point title	LS Mean Change From Baseline in ISS7 at Week 24

End point description:

The UPDD was completed twice daily (morning and evening) to capture key measures of urticaria disease activity including the ISS. The ISS represents severity on a scale ranging from 0 to 3 (where 0= none, 1= mild, 2= moderate and 3= severe). The ISS7 is the sum of ISS for the previous 7 days. The ISS7 represents itch severity on a scale ranging from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of itch. Baseline was defined as the sum of the daily scores for the 7 days prior to the day of randomization. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Week 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	53	36	
Units: units on a scale				
least squares mean (confidence interval 95%)	-9.19 (-10.77 to -7.61)	-9.33 (-10.93 to -7.73)	-7.57 (-9.48 to -5.66)	

Statistical analyses

Statistical analysis title	Treatment difference in ISS7 at Week 24
Comparison groups	Benralizumab 30 mg v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1995 [5]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	0.86

Notes:

[5] - Change from baseline in ISS7 at Week 24= Treatment + baseline ISS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in ISS7 at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1654 [6]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.25
upper limit	0.73

Notes:

[6] - Change from baseline in ISS7 at Week 24= Treatment + baseline ISS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Secondary: Percentage of Responders at Weeks 12 and 24

End point title	Percentage of Responders at Weeks 12 and 24

End point description:

Responder was defined as a participant whose condition was considered clinically well controlled with UAS7 <=6 at specific time points. The UAS7 is the sum of UAS for the previous 7 days, that is, the sum of ISS7 and HSS7. The UAS7 represents urticaria severity on a scale from 0 (minimum) to 42 (maximum). Higher scores indicate greater severity of urticaria symptoms. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Here, 'n' is number of participants analyzed at specific time point and 99999 is no participants were analyzed.

End point type	Secondary

End point timeframe:

Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	56	40	
Units: percentage of participants				
number (not applicable)				
Week 12 (n= 59, 56, 40)	22.0	21.4	10.0	
Week 24 (n= 59, 56, 40)	28.8	37.5	27.5	

Statistical analyses

Statistical analysis title	Treatment difference in Responders at Week 12
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1373 [7]
Method	Regression, Logistic
Parameter estimate	percentage difference
Point estimate	11.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.37
upper limit	25.82

Notes:

[7] - Week 12: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Statistical analysis title	Treatment difference in Responders at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1697 [8]
Method	Regression, Logistic
Parameter estimate	percentage difference
Point estimate	10.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.42
upper limit	24.88

Notes:

[8] - Week 12: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Statistical analysis title	Treatment difference in Responders at Week 24
Comparison groups	Benralizumab 30 mg v Placebo

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9105 [9]
Method	Regression, Logistic
Parameter estimate	percentage difference
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.9
upper limit	18.96

Notes:

[9] - Week 24: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Statistical analysis title	Treatment difference in Responders at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3389 [10]
Method	Regression, Logistic
Parameter estimate	percentage difference
Point estimate	9.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.37
upper limit	27.9

Notes:

[10] - Week 24: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Secondary: LS Mean Change From Baseline in Hives Severity Score Over 7 Days (HSS7) at Weeks 12 and 24

End point title	LS Mean Change From Baseline in Hives Severity Score Over 7 Days (HSS7) at Weeks 12 and 24

End point description:

The UPDD was completed twice daily (morning and evening) to capture key measures of urticaria disease activity including the HSS7. Participants were asked to document the number of hives they experienced on a scale ranging from 0 to 3 (where 0= none, 1= mild [1 – 6 hives/12 hour], 2= moderate [7 – 12 hives/12 hour] and 3= intense [(> 12 hives/12 hour]). The HSS7 is the sum of hives severity score for the previous 7 days. The HSS7 represents hives severity on a scale from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of hives. Baseline was defined as the sum of the daily scores for the 7 days prior to the day of randomization. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Here, 'n' is number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	53	37	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12 (n= 55, 52, 37)	-7.03 (-8.84 to -5.22)	-8.47 (-10.32 to -6.62)	-5.87 (-8.06 to -3.68)	
Week 24 (n= 52, 53, 36)	-8.88 (-10.76 to -7.00)	-9.81 (-11.71 to -7.91)	-7.82 (-10.09 to -5.54)	

Statistical analyses

Statistical analysis title	Treatment difference in HSS7 at Week 12
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4203 [11]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	1.68

Notes:

[11] - Change from baseline in HSS7 at Week 12= Treatment + baseline HSS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in HSS7 at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0754 [12]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.46
upper limit	0.27

Notes:

[12] - Change from baseline in HSS7 at Week 12= Treatment + baseline HSS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in HSS7 at Week 24

Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4772 [13]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	1.89

Notes:

[13] - Change from baseline in HSS7 at Week 24= Treatment + baseline HSS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in HSS7 at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1851 [14]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.96
upper limit	0.97

Notes:

[14] - Change from baseline in HSS7 at Week 24= Treatment + baseline HSS7 + region (Europe, North America, Asia) + visit + treatment by visit.

Secondary: Time to >=5-Point Decrease in ISS7

End point title	Time to >=5-Point Decrease in ISS7

End point description:

The time to >=5-point decrease (clinically relevant decrease) in ISS7 was reported. The ISS7 is the sum of ISS for the previous 7 days. The ISS7 represents itch severity on a scale ranging from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of itch. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Only participants with at least 1 >=5-point decrease in ISS7 are analyzed.

End point type	Secondary

End point timeframe:

From Baseline (Day -1) up to Week 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	50	33	
Units: weeks				
median (confidence interval 95%)	3.0 (2.0 to 5.0)	2.0 (2.0 to 3.0)	8.0 (3.0 to 11.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Complete UAS7 Response at Weeks 12 and 24

End point title	Percentage of Participants With Complete UAS7 Response at Weeks 12 and 24

End point description:

Complete response was defined as participants with UAS7= 0 at specific time points. The UAS7 is the sum of UAS for the previous 7 days, that is, the sum of ISS7 and HSS7. The UAS7 represents urticaria severity on a scale from 0 (minimum) to 42 (maximum). Higher scores indicate greater severity of urticaria symptoms. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Here, 'n' is number of participants analyzed at specific time point and 99999 is no participants were analyzed.

End point type	Secondary

End point timeframe:

Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	56	40	
Units: percentage of participants				
number (not applicable)				
Week 12 (n= 59, 56, 40)	11.9	7.1	10.0	
Week 24 (n= 59, 56, 40)	16.9	21.4	20.0	

Statistical analyses

Statistical analysis title	Treatment difference in UAS7 Response at Week 12
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9678 [15]
Method	Regression, Logistic

Notes:

[15] - Week 12: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Statistical analysis title	Treatment difference in UAS7 Response at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3689 [16]
Method	Regression, Logistic

Notes:

[16] - Week 12: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Statistical analysis title	Treatment difference in UAS7 Response at Week 24
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6624 [17]
Method	Regression, Logistic
Parameter estimate	percentage difference
Point estimate	-3.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.96
upper limit	12.11

Notes:

[17] - Week 24: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Statistical analysis title	Treatment difference in UAS7 Response at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9726 [18]
Method	Regression, Logistic
Parameter estimate	percentage difference
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.84
upper limit	16.4

Notes:

[18] - Week 24: Estimates included treatment group, region (Europe, North America, Asia) and baseline UAS7.

Secondary: Mean Percentage of Angioedema-Free Days Over the Past 7 Days at Weeks 12 and 24

End point title	Mean Percentage of Angioedema-Free Days Over the Past 7 Days at Weeks 12 and 24

End point description:

The UPDD included a daily yes/no question asking whether the participant experienced angioedema during the past 24 hours. If yes, the participant was asked a follow-up question about how they treated the swelling. The percentage of angioedema-free days was calculated over the past 7 days by (number of angioedema-free days/number of non-missing responses) x 100. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Only participants with angioedema at baseline or history of angioedema are analyzed. Here, 'n' is number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	28	22	
Units: percentage of days				
arithmetic mean (standard deviation)				
Week 12 (n= 36, 27, 22)	77.50 (± 35.990)	85.63 (± 32.435)	81.93 (± 34.548)	
Week 24 (n= 32, 28, 20)	78.50 (± 36.992)	91.33 (± 27.032)	86.79 (± 31.798)	

Statistical analyses

No statistical analyses for this end point

Secondary: LS Mean Change From Baseline in Urticaria Control Test (UCT) at Weeks 12 and 24

End point title	LS Mean Change From Baseline in Urticaria Control Test (UCT) at Weeks 12 and 24

End point description:

Urticaria disease control was assessed by the UCT using the electronic participant-reported outcome device. The UCT has a retrospective approach using a recall period of 4 weeks and responses on 5-point Likert scales with score ranging from 0 to 4 for each question. Subsequently, the scores for all 4 questions were summed up. The UCT scale range from 0 (minimum) to 16 (maximum). Higher scores indicate better disease control. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Here, 'n' is number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	52	38	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12 (n= 55, 51, 38)	4.74 (3.71 to 5.76)	6.11 (5.05 to 7.17)	5.02 (3.78 to 6.26)	
Week 24 (n= 51, 52, 37)	5.24 (4.04 to 6.45)	6.87 (5.65 to 8.09)	5.88 (4.44 to 7.32)	

Statistical analyses

Statistical analysis title	Treatment difference in UCT at Week 12
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7256 [19]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.32

Notes:

[19] - Change from baseline in UCT at Week 12= Treatment + baseline UCT + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in UCT at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.189 [20]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	2.72

Notes:

[20] - Change from baseline in UCT at Week 12= Treatment + baseline UCT + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in UCT at Week 24

Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5048 [21]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	1.24

Notes:

[21] - Change from baseline in UCT at Week 24= Treatment + baseline UCT + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in UCT at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2991 [22]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	2.88

Notes:

[22] - Change from baseline in UCT at Week 24= Treatment + baseline UCT + region (Europe, North America, Asia) + visit + treatment by visit.

Secondary: LS Mean Change From Baseline in Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) at Weeks 12 and 24

End point title	LS Mean Change From Baseline in Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) at Weeks 12 and 24

End point description:

The CU-Q2oL is a 23-item assessment of CSU-specific health-related quality of life. Participants were asked to rate their CSU symptoms and the impact of their symptoms over the last 2 weeks on several domains: pruritus, swelling, impact on life activities, sleep problems, limits, and looks. The questions were scored as 1= not at all, 2= a little, 3= moderately, 4= very much, 5= extremely. The CU-Q2oL scale range from 0 (minimum) to 100 (maximum). Higher scores indicate greater impact of urticaria on health-related quality of life. The FAS included all randomized participants who received at least 1 dose of study drug, irrespective of their protocol adherence and continued participation in the study. Here, 'n' is number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	52	38	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12 (n= 55, 51, 38)	-16.47 (-20.10 to -12.84)	-20.34 (-24.09 to -16.60)	-18.10 (-22.46 to -13.74)	
Week 24 (n= 51, 52, 37)	-17.60 (-21.81 to -13.40)	-22.11 (-26.38 to -17.84)	-19.07 (-24.09 to -14.05)	

Statistical analyses

Statistical analysis title	Treatment difference in CU-Q2oL at Week 12
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5704 [23]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.05
upper limit	7.32

Notes:

[23] - Change from baseline in CU-Q2oL at Week 12= Treatment + baseline CU-Q2oL + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in CU-Q2oL at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4416 [24]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-2.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.98
upper limit	3.5

Notes:

[24] - Change from baseline in CU-Q2oL at Week 12= Treatment + baseline CU-Q2oL + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in CU-Q2oL at Week 24

Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6591 [25]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.09
upper limit	8.02

Notes:

[25] - Change from baseline in CU-Q2oL at Week 24= Treatment + baseline CU-Q2oL + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in CU-Q2oL at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3624 [26]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-3.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.62
upper limit	3.54

Notes:

[26] - Change from baseline in CU-Q2oL at Week 24= Treatment + baseline CU-Q2oL + region (Europe, North America, Asia) + visit + treatment by visit.

Secondary: LS Mean Change From Baseline in Dermatology Life Quality Index (DLQI) at Weeks 12 and 24

End point title	LS Mean Change From Baseline in Dermatology Life Quality Index (DLQI) at Weeks 12 and 24

End point description:

The DLQI is a 10-item assessment of dermatology-specific health-related quality of life. Participants were asked to rate their symptoms and impact of their symptoms over last week on several domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Questions (except question 7) were scored on a 4-point Likert scale: 0= not at all, 1= a little, 2= a lot, 3= very much. Scoring question 7, first part asked: 'Over the last week, has your skin prevented you from working or studying?' Scoring was for response of 0= not relevant and 3= yes. If no, a further question was asked: 'How much has your skin been a problem at work or studying', and scored as: 0= not at all, 1= a little, 2= a lot. The DLQI was calculated by summing score of each question. The DLQI scale range from 0 (minimum) to 30 (maximum). Higher scores indicate greater impact on participant's life. FAS population. n= number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	52	38	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12 (n= 55, 51, 38)	-7.58 (-9.18 to -5.98)	-9.31 (-10.96 to -7.66)	-8.06 (-9.98 to -6.14)	
Week 24 (n= 51, 52, 37)	-8.13 (-9.84 to -6.42)	-10.25 (-11.98 to -8.51)	-9.37 (-11.41 to -7.33)	

Statistical analyses

Statistical analysis title	Treatment difference in DLQI at Week 12
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7037 [27]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.02
upper limit	2.98

Notes:

[27] - Change from baseline in DLQI at Week 12= Treatment + baseline DLQI + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in DLQI at Week 12
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.332 [28]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.78
upper limit	1.29

Notes:

[28] - Change from baseline in DLQI at Week 12= Treatment + baseline DLQI + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in DLQI at Week 24
Comparison groups	Benralizumab 30 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.359 [29]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.42
upper limit	3.9

Notes:

[29] - Change from baseline in DLQI at Week 24= Treatment + baseline DLQI + region (Europe, North America, Asia) + visit + treatment by visit.

Statistical analysis title	Treatment difference in DLQI at Week 24
Comparison groups	Benralizumab 60 mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5175 [30]
Method	Mixed-effect model for repeated measures
Parameter estimate	LS mean difference
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.56
upper limit	1.8

Notes:

[30] - Change from baseline in DLQI at Week 24= Treatment + baseline DLQI + region (Europe, North America, Asia) + visit + treatment by visit.

Secondary: Serum Concentration of Benralizumab

End point title	Serum Concentration of Benralizumab

End point description:

Blood samples were collected to determine the serum concentration of benralizumab. The Pharmacokinetic (PK) analysis set included all participants who received study drug and from whom PK blood samples were assumed not to be affected by factors such as protocol violations and who had at least 1 quantifiable serum PK observation post first dose. Here, 'n' is number of participants analyzed at specific time point; 9999= below the lower limit of quantification (LLOQ). The LLOQ is 3.86 nanogram per milliliter (ng/mL) and 99999= no participants were analyzed.

End point type	Secondary

End point timeframe:

Pre-dose on Weeks 4, 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	54	34	
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 4 (n=55,54,0)	990.515 (± 448.6799)	2167.606 (± 991.7509)	99999 (± 99999)	
Week 12 (n=53,52,0)	1321.373 (± 740.5070)	3145.352 (± 1577.6726)	99999 (± 99999)	
Week 24 (n=47,49,34)	1372.806 (± 883.5830)	1638.810 (± 946.9466)	9999 (± 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibody (ADA) Response to Benralizumab

End point title	Number of Participants With Anti-Drug Antibody (ADA) Response to Benralizumab

End point description:

Blood samples were measured for presence of ADAs for benralizumab using validated assays. The ADA incidence was defined as ADA negative at baseline and post-baseline ADA positive or ADA positive at baseline and boosted pre-existing titre by > 4-fold during study period. Persistently positive was defined as ADA negative at baseline and positive at >=2 post-baseline assessments (with >=16 weeks between first and last positive) or positive at last post-baseline assessment. Transiently positive was defined as ADA negative at baseline, having at least 1 post-baseline ADA positive assessment and not fulfilling conditions of persistently positive. The median of maximum titres was calculated based on maximum titre for each ADA positive participant within each treatment group (including both baseline and post-baseline measurements). The Safety analysis set included all participants who received at least 1 dose of study drug. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Pre-dose on Weeks 12 and 24

End point values	Benralizumab 30 mg	Benralizumab 60 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[31]	56[32]	40[33]	
Units: participants				
ADA prevalence	18	13	4	
ADA negative	37	41	33	
Only baseline positive	1	1	0	
Baseline and at least 1 post-baseline positive	3	4	0	
ADA incidence	15	10	4	

ADA persistently positive	10	4	4	
ADA transiently positive	5	5	0	
ADA positive:Maximum titre>median maximum titres	8	5	1	
ADA positive:Maximum titre<=median maximum titres	10	8	3	

Notes:

[31] - n= 59, 54, 55, 59, 54, 54, 54, 59, 59.

[32] - n= 56, 54, 55, 56, 54, 54, 54, 56, 56.

[33] - n= 40, 37, 39, 40, 37, 37, 37, 40, 40.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are reported from the first dose administration up to 30 days after the last dose of study drug, a maximum of approximately 57 weeks.

Adverse event reporting additional description:

The Safety analysis set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Benralizumab 30 mg Total

Reporting group description:

Participants were randomized to receive benralizumab 30 mg SC injection Q4W until Week 24 in the double-blind treatment period and then 30 mg Q4W or Q8W during the extension period until Week 52.

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive placebo matching with benralizumab Q4W until Week 24 in the double-blind treatment period followed by benralizumab 30 mg SC injection Q4W until Week 36 and then 30 mg Q8W until Week 52.

Reporting group title	Benralizumab Q4W Total

Reporting group description:

Participants who received benralizumab 30 mg or 60 mg SC injection Q4W during the study.

Reporting group title	Benralizumab 60 mg Total

Reporting group description:

Participants were randomized to receive benralizumab 60 mg SC injection Q4W until Week 12 and then 30 mg Q4W until Week 24 in the double-blind treatment period followed by 30 mg Q4W or Q8W during the extension period until Week 52.

Reporting group title	Benralizumab Q8W Total

Reporting group description:

Participants who received benralizumab 30 mg or 60 mg SC injection Q8W during the study.

Reporting group title	Benralizumab 30 mg Q8W

Reporting group description:

Participants who received benralizumab 30 mg SC injection Q8W during the study.

Reporting group title	Benralizumab 30 mg Q4W

Reporting group description:

Participants who received benralizumab 30 mg SC injection Q4W during the study.

Reporting group title	Benralizumab 60 mg Q4W

Reporting group description:

Participants who received benralizumab 60 mg SC injection Q4W during the study.

Reporting group title	Benralizumab 60 mg Q8W

Reporting group description:

Participants who received benralizumab 60 mg SC injection Q8W during the study.

Serious adverse events	Benralizumab 30 mg Total	Placebo	Benralizumab Q4W Total
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 59 (10.17%)	2 / 40 (5.00%)	4 / 58 (6.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 59 (1.69%)	0 / 40 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 59 (0.00%)	1 / 40 (2.50%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 59 (1.69%)	0 / 40 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 59 (1.69%)	0 / 40 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 40 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 59 (1.69%)	0 / 40 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 59 (0.00%)	1 / 40 (2.50%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 59 (1.69%)	0 / 40 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 59 (0.00%)	0 / 40 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 40 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Benralizumab 60 mg Total	Benralizumab Q8W Total	Benralizumab 30 mg Q8W
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 56 (3.57%)	4 / 57 (7.02%)	3 / 29 (10.34%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 56 (0.00%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Meniscus injury			
subjects affected / exposed	0 / 56 (0.00%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 56 (1.79%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			

subjects affected / exposed	1 / 56 (1.79%)	1 / 57 (1.75%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Benralizumab 30 mg Q4W	Benralizumab 60 mg Q4W	Benralizumab 60 mg Q8W
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)	1 / 28 (3.57%)	1 / 28 (3.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Benralizumab 30 mg Total	Placebo	Benralizumab Q4W Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 59 (54.24%)	22 / 40 (55.00%)	35 / 58 (60.34%)
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	3 / 59 (5.08%)	1 / 40 (2.50%)	3 / 58 (5.17%)
occurrences (all)	3	1	3
Thermal burn			

subjects affected / exposed	2 / 59 (3.39%)	0 / 40 (0.00%)	2 / 58 (3.45%)
occurrences (all)	2	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 59 (1.69%)	1 / 40 (2.50%)	1 / 58 (1.72%)
occurrences (all)	1	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 59 (0.00%)	1 / 40 (2.50%)	2 / 58 (3.45%)
occurrences (all)	0	2	2
Headache			
subjects affected / exposed	4 / 59 (6.78%)	3 / 40 (7.50%)	5 / 58 (8.62%)
occurrences (all)	4	3	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 59 (5.08%)	2 / 40 (5.00%)	4 / 58 (6.90%)
occurrences (all)	5	2	6
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	1 / 59 (1.69%)	2 / 40 (5.00%)	4 / 58 (6.90%)
occurrences (all)	2	2	6
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	2 / 59 (3.39%)	1 / 40 (2.50%)	0 / 58 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	2 / 59 (3.39%)	0 / 40 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	3
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 59 (0.00%)	0 / 40 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 59 (3.39%)	1 / 40 (2.50%)	3 / 58 (5.17%)
occurrences (all)	2	1	3
Psychiatric disorders			

Bipolar disorder			
subjects affected / exposed	2 / 59 (3.39%)	0 / 40 (0.00%)	2 / 58 (3.45%)
occurrences (all)	2	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 59 (3.39%)	4 / 40 (10.00%)	1 / 58 (1.72%)
occurrences (all)	2	9	1
Back pain			
subjects affected / exposed	3 / 59 (5.08%)	1 / 40 (2.50%)	2 / 58 (3.45%)
occurrences (all)	3	1	3
Myalgia			
subjects affected / exposed	3 / 59 (5.08%)	1 / 40 (2.50%)	2 / 58 (3.45%)
occurrences (all)	5	1	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 59 (5.08%)	1 / 40 (2.50%)	3 / 58 (5.17%)
occurrences (all)	3	1	4
COVID-19			
subjects affected / exposed	8 / 59 (13.56%)	6 / 40 (15.00%)	9 / 58 (15.52%)
occurrences (all)	8	6	10
Nasopharyngitis			
subjects affected / exposed	5 / 59 (8.47%)	4 / 40 (10.00%)	7 / 58 (12.07%)
occurrences (all)	8	5	10
Onychomycosis			
subjects affected / exposed	2 / 59 (3.39%)	0 / 40 (0.00%)	2 / 58 (3.45%)
occurrences (all)	2	0	2
Periodontitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 40 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	2
Sinusitis			
subjects affected / exposed	3 / 59 (5.08%)	4 / 40 (10.00%)	2 / 58 (3.45%)
occurrences (all)	3	5	2

Non-serious adverse events	Benralizumab 60 mg Total	Benralizumab Q8W Total	Benralizumab 30 mg Q8W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 56 (57.14%)	29 / 57 (50.88%)	15 / 29 (51.72%)

Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 56 (1.79%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Thermal burn			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 56 (7.14%)	4 / 57 (7.02%)	1 / 29 (3.45%)
occurrences (all)	4	4	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 56 (3.57%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	5 / 56 (8.93%)	4 / 57 (7.02%)	2 / 29 (6.90%)
occurrences (all)	5	4	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 56 (5.36%)	2 / 57 (3.51%)	2 / 29 (6.90%)
occurrences (all)	4	3	3
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	3 / 56 (5.36%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	4	0	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 56 (1.79%)	3 / 57 (5.26%)	2 / 29 (6.90%)
occurrences (all)	1	3	2
Nausea			
subjects affected / exposed	3 / 56 (5.36%)	2 / 57 (3.51%)	1 / 29 (3.45%)
occurrences (all)	3	2	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			

subjects affected / exposed	2 / 56 (3.57%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 56 (3.57%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences (all)	2	1	1
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 56 (3.57%)	3 / 57 (5.26%)	1 / 29 (3.45%)
occurrences (all)	2	3	1
Back pain			
subjects affected / exposed	3 / 56 (5.36%)	4 / 57 (7.02%)	2 / 29 (6.90%)
occurrences (all)	4	4	2
Myalgia			
subjects affected / exposed	1 / 56 (1.79%)	2 / 57 (3.51%)	1 / 29 (3.45%)
occurrences (all)	2	3	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences (all)	2	1	1
COVID-19			
subjects affected / exposed	10 / 56 (17.86%)	9 / 57 (15.79%)	5 / 29 (17.24%)
occurrences (all)	11	9	5
Nasopharyngitis			
subjects affected / exposed	6 / 56 (10.71%)	4 / 57 (7.02%)	2 / 29 (6.90%)
occurrences (all)	7	5	3
Onychomycosis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	2 / 56 (3.57%)	0 / 57 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0

Sinusitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 57 (1.75%)	1 / 29 (3.45%)
occurrences (all)	0	1	1

Non-serious adverse events	Benralizumab 30 mg Q4W	Benralizumab 60 mg Q4W	Benralizumab 60 mg Q8W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 30 (56.67%)	18 / 28 (64.29%)	14 / 28 (50.00%)
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	2	1	0
Thermal burn			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	3 / 28 (10.71%)
occurrences (all)	0	1	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	2 / 30 (6.67%)	3 / 28 (10.71%)	2 / 28 (7.14%)
occurrences (all)	2	3	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 30 (3.33%)	3 / 28 (10.71%)	0 / 28 (0.00%)
occurrences (all)	2	4	0
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	1 / 30 (3.33%)	3 / 28 (10.71%)	0 / 28 (0.00%)
occurrences (all)	2	4	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1

Nausea			
subjects affected / exposed	1 / 30 (3.33%)	2 / 28 (7.14%)	1 / 28 (3.57%)
occurrences (all)	1	2	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 30 (3.33%)	2 / 28 (7.14%)	0 / 28 (0.00%)
occurrences (all)	1	2	0
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Back pain			
subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	2 / 28 (7.14%)
occurrences (all)	1	2	2
Myalgia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	4	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	2	2	0
COVID-19			
subjects affected / exposed	3 / 30 (10.00%)	6 / 28 (21.43%)	4 / 28 (14.29%)
occurrences (all)	3	7	4
Nasopharyngitis			
subjects affected / exposed	3 / 30 (10.00%)	4 / 28 (14.29%)	2 / 28 (7.14%)
occurrences (all)	5	5	2
Onychomycosis			

subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Periodontitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2020	The description of the participants to be enrolled into the study was updated to remove moderate to severe CSU and replace with participants with symptoms not well controlled by standard of care with antihistamines. The primary endpoints have been amended to replace UAS7 with the Itch Severity Score 7 (ISS7) and the secondary endpoints have been amended to replace the ISS7 with the UAS7 and details of the power calculation have been updated to reflect this change. In addition, the reference for the sample size calculation has been updated. New wording was added which would give guidance on how the study could continue in the event of a serious disruption with details of mitigation that could be employed to ensure study continuity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated early by the sponsor as the primary analysis results did not support the continued development of benralizumab for the indication of CSU.

Notes: