Clinical trial results:
A multi-center, double-blinded and open-label extension study to evaluate the efficacy and safety of ligelizumab as retreatment, self-administered therapy and monotherapy in Chronic Spontaneous Urticaria patients who completed studies CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301

Summary

EudraCT number	2019-001792-37
Trial protocol	HU FR CZ ES DE AT GR EE IT BE SK DK PL NL BG HR RO
Global end of trial date	01 September 2022

Results information

Result version number	v1
This version publication date	03 March 2023
First version publication date	03 March 2023

Trial information

Trial identification

Sponsor protocol code	CQGE031C2302E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04210843
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy of ligelizumab assessed as the proportion of subjects achieving weekly urticaria activity score (UAS7) ≤6 after 12 weeks of retreatment, in subjects previously treated in CQGE031C2302/CQGE031C2303 (the core studies) as well as in the subset of subjects who previously achieved UAS7 ≤ 6 in the core studies.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

This study required concurrent use of one second-generation H1-AH at local label-approved doses as background medication except for the subgroup of subjects who were offered a choice to go off background medication in the second half of the treatment period.
The investigator instructed the subject to notify the study site about any new medications he/she takes after the subject was enrolled into the study. Each concomitant drug was individually assessed against all exclusion criteria/prohibited medication and was captured in the study eCRF.

Evidence for comparator: -

Actual start date of recruitment	08 April 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	Argentina: 81
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Brazil: 39
Country: Number of subjects enrolled	Bulgaria: 17
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Chile: 19
Country: Number of subjects enrolled	Colombia: 4
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Czechia: 15
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Estonia: 5

Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 92
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Greece: 13
Country: Number of subjects enrolled	Guatemala: 5
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	India: 48
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 67
Country: Number of subjects enrolled	Korea, Republic of: 49
Country: Number of subjects enrolled	Lebanon: 13
Country: Number of subjects enrolled	Malaysia: 14
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Netherlands: 11
Country: Number of subjects enrolled	Oman: 6
Country: Number of subjects enrolled	Peru: 7
Country: Number of subjects enrolled	Philippines: 4
Country: Number of subjects enrolled	Poland: 50
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Russian Federation: 120
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	South Africa: 18
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Taiwan: 30
Country: Number of subjects enrolled	Thailand: 23
Country: Number of subjects enrolled	Tunisia: 16
Country: Number of subjects enrolled	Turkey: 19
Country: Number of subjects enrolled	United States: 95
Country: Number of subjects enrolled	Viet Nam: 8
Worldwide total number of subjects	1033
EEA total number of subjects	291

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)	40
Adults (18-64 years)	929
From 65 to 84 years	64
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1457 participants who completed preceding studies (CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301) entered the screening period. 515 participants with UAS7 <16 during screening entered the OBS1 period. A total of 1033 participants with UAS7≥ 16 during screening or OBS1 period were assigned to 1 of the 2 treatment arms.

Period 1

Period 1 title	First half treatment period (52 weeks)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Blinding implementation details:

Participants transitioning from CQGE031C2302 and CQGE031C2303 were treated in a double-blind manner for the first 12 weeks of treatment. Thereafter, they were treated in an open-label manner. No blinding was required for participants transitioning from CQGE031C1301 and CQGE031C2202

Arms

Are arms mutually exclusive?	Yes
Arm title	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS

Arm description:

Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	CQGE031
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	CQGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 72 mg liquid in vial (LIVI) subcutaneously (s.c.) every 4 weeks (Q4W)

Arm title	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS

Arm description:

Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

Arm type	Experimental

Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	CQGE031
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	CQGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg liquid in vial (LIVI) subcutaneously (s.c.) every 4 weeks (Q4W)

Number of subjects in period 1	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Started	290	743
Completed	140	369
Not completed	150	374
Adverse event, serious fatal	-	2
Physician decision	-	3
Adverse event, non-fatal	1	11
Subject decision	11	28
Protocol deviation	-	3
Pregnancy	-	1
Study terminated by sponsor	134	322
Lost to follow-up	4	2
Lack of efficacy	-	2

Period 2

Period 2 title	Second half treatment period (52 weeks)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS

Arm description:

Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

Arm title	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS

Arm description:

Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

Number of subjects in period 2[1]	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Started	77	206
Completed	1	2
Not completed	76	204
Subject decision	5	8
Study terminated by sponsor	71	195
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: Not all subjects who completed the First half treatment period (TRT1) were eligible to start the second half treatment period (TRT2): Only participants with UAS7>6 and <16 or with UAS7 ≥ 16 for whom the benefit-risk was deemed as positive by the investigator at Week 52 of TRT1 were transitioned to the TRT2 (ligelizumab 120 mg s.c. Q4W PFS) unless a decision to stop treatment was made based on a risk-benefit assessment.

Baseline characteristics

Reporting groups	
Reporting group title	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS
Reporting group description:	
Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)	
Reporting group title	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Reporting group description:	
Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)	

Reporting group values	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS	Total
Number of subjects	290	743	1033
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	11	29	40
Adults (18-64 years)	266	663	929
From 65-84 years	13	51	64
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	42.4	42.8	
standard deviation	± 13.98	± 14.40	-
Sex: Female, Male Units: Participants			
Female	190	525	715
Male	100	218	318
Race/Ethnicity, Customized Units: Subjects			
White	209	506	715
Black or African American	1	13	14
Asian	66	199	265
Native Hawaiian or Other Pacific Islander	0	1	1
American Indian or Alaska Native	11	20	31
Multiple	3	4	7

End points

End points reporting groups

Reporting group title	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS
Reporting group description:	
Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)	
Reporting group title	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Reporting group description:	
Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)	
Reporting group title	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS
Reporting group description:	
Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)	
Reporting group title	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Reporting group description:	
Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)	

Primary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in the core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12

End point title	Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in the core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12[1]
End point description:	
The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity. A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week. The percentage of subjects transitioning from CQGE031C2302 and CQGE031C2303 and receiving the same dose regimen as in the core studies with UAS7≤ 6 at Week 12 was estimated using multiple imputation method. The 95% confidence interval was derived based on the Wilson score method with continuity correction.	
End point type	Primary
End point timeframe:	
Week 12 of the extension study	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analyses were planned for this primary endpoint	

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Percentage of participants				
number (confidence interval 95%)	53.5 (48.72 to 58.54)	57.5 (52.71 to 62.57)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in core studies and who achieved UAS7≤ 6 at week 12 in core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12 of the extension study

End point title	Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in core studies and who achieved UAS7≤ 6 at week 12 in core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12 of the extension study[2]

End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals and the intensity of the pruritus over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.
A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the UAS7 was missing for that week. Missing data was considered as non-responder.
The percentage of subjects transitioning from core studies (CQGE031C2302 and CQGE031C2303) and receiving the same dose regimen as in the core studies who achieved UAS7 ≤ 6 at week 12 in the core studies with UAS7≤ 6 at Week 12 of the extension study was estimated based on observed data.

End point type	Primary

End point timeframe:

Week 12 of the extension study

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this primary endpoint

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	144		
Units: Percentage of participants				
number (confidence interval 95%)	81.9 (74.73 to 87.92)	82.6 (75.45 to 88.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with completely controlled disease (UAS7 =0) at Week 12

End point title	Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with completely controlled disease (UAS7 =0) at Week 12

End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.
A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week.
The percentage of subjects transitioning from core studies (CQGE031C2302 and CQGE031C2303) and receiving the same dose regimen as in the core studies with UAS7 = 0 at Week 12 was estimated using multiple imputation method.

End point type	Secondary

End point timeframe:

Week 12 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Percentage of participants				
number (confidence interval 95%)	37.3 (31.63 to 43.04)	41.5 (35.61 to 47.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from extension study baseline in the UAS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point title	Change from extension study baseline in the UAS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7

indicated greater urticaria disease activity. A negative change score from extension study baseline indicates improvement.
A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week.
The absolute change from extension study baseline in the UAS7 at Week 12 was estimated using multiple imputation method.

End point type	Secondary

End point timeframe:

Extension study baseline (Week 0), Week 12 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Score on a scale				
arithmetic mean (standard error)	-19.83 (± 13.12)	-20.41 (± 12.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from extension study baseline in the ISS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point title	Change from extension study baseline in the ISS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point description:

The Itch Severity Score (ISS) was recorded by the subject twice daily in their eDiary, on a scale of 0 (none) to 3 (intense/severe). A weekly score (ISS7) was derived by adding up the average daily scores of the 7 preceding days. The ISS7 ranged from 0 to 21. A higher ISS7 indicated more severe itching. A negative change score from baseline indicates improvement.
A minimum of 4 out of 7 daily scores were needed to calculate the ISS7 values. Otherwise, the weekly score was missing for that week.
The absolute change from extension study baseline in the ISS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies was estimated using multiple imputation method.

End point type	Secondary

End point timeframe:

Extension study baseline (Week 0), Week 12 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Score on a scale				
arithmetic mean (standard error)	-9.12 (± 6.35)	-9.46 (± 6.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from extension study baseline in the HSS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point title	Change from extension study baseline in the HSS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point description:

The Hive Severity Score (HSS) was recorded by the subject twice daily in their eDiary, on a scale of 0 (none) to 3 (> 12 hives/12 hours). A weekly score (HSS7) was derived by adding up the average daily scores of the 7 preceding days. The HSS7 ranged from 0 to 21 A higher HSS7 indicated a greater number of hives. A negative change score from baseline indicates improvement.
A minimum of 4 out of 7 daily scores were needed to calculate the HSS7 values. Otherwise, the weekly score was missing for that week.
The absolute change from extension study baseline in the HSS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies was estimated using multiple imputation method.

End point type	Secondary

End point timeframe:

Extension study baseline (Week 0), Week 12 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Score on a scale				
arithmetic mean (standard error)	-10.71 (± 7.50)	-10.95 (± 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of angioedema-free weeks (AAS7=0) up to Week 12

in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point title	Cumulative number of angioedema-free weeks (AAS7=0) up to Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

End point description:

The Weekly angioedema activity score (AAS) is a validated tool to assess occurrence of episodes of angioedema. If the subject reported the occurrence of angioedema ("opening question") with "no", AAS score for this day was 0. If "yes" was the answer to the opening question, the subject continued to answer questions about the duration, severity and impact on daily functioning and appearance of the angioedema. A score between 0 and 3 was assigned to every answer field. The AAS7 was the weekly sum of the daily AAS. AAS7 scores ranged from 0-105. Higher score indicated more severe disease. AAS7 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies was estimated using multiple imputation method. The imputed AAS7 = 0 was used for the cumulative number of weeks that subjects achieved AAS7 = 0 response calculation

End point type	Secondary

End point timeframe:

From extension study baseline (Week 0) up to Week 12 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Weeks				
arithmetic mean (standard error)	9.30 (± 0.25)	9.68 (± 0.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with DLQI = 0-1 at Week 12

End point title	Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with DLQI = 0-1 at Week 12

End point description:

The Dermatology Life Quality Index (DLQI) is a 10-item dermatology-specific quality of life (QoL) measure. Subjects rated their dermatology symptoms as well as the impact of their skin condition on various aspects of their lives thinking about the previous 7 days. An overall score was calculated and ranged from 0 to 30. Higher scores indicated worse disease-related QoL. A DLQI score of 0 or 1 indicated that there was no impact of a skin disease on the patient's life.
The percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with DLQI = 0-1 at Week 12 was estimated using multiple imputation method.

End point type	Secondary

End point timeframe:

Week 12 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	276		
Units: Percentage of participants				
number (confidence interval 95%)	45.6 (39.66 to 51.52)	55.8 (49.77 to 61.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with well-controlled disease (UAS7 ≤ 6) 12 weeks after starting self-administration

End point title	Percentage of subjects with well-controlled disease (UAS7 ≤ 6) 12 weeks after starting self-administration

End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.
A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week. Missing data was considered as non-responder in the analysis.
The percentage of subjects with UAS7≤ 6 at Week 24 (i.e., 12 weeks after starting self-administration) was estimated based on observed data.

End point type	Secondary

End point timeframe:

Week 24 of the extension study

End point values	Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS	Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	383		
Units: Percentage of participants				
number (confidence interval 95%)	69.4 (60.86 to 77.07)	69.5 (64.40 to 74.21)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Week 0 until the end of the study, assessed up to maximum duration of approximately 2.5 years

Adverse event reporting additional description:

Safety analyses were performed in the safety set. Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS

Reporting group description:

Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

Reporting group title	Total

Reporting group description:

Total

Reporting group title	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS

Reporting group description:

Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

Serious adverse events	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS	Total	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 288 (2.78%)	52 / 1033 (5.03%)	44 / 745 (5.91%)
number of deaths (all causes)	0	3	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral neoplasm			

subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Papillary thyroid cancer			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testis cancer			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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

Drowning			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Chest pain			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abnormal uterine bleeding			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Comminuted fracture			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Animal bite			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Vascular encephalopathy			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Vomiting			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Cholestasis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Chronic spontaneous urticaria			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nephrolithiasis			
subjects affected / exposed	0 / 288 (0.00%)	2 / 1033 (0.19%)	2 / 745 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Polyarthritis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 288 (0.00%)	2 / 1033 (0.19%)	2 / 745 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 288 (0.35%)	12 / 1033 (1.16%)	11 / 745 (1.48%)
occurrences causally related to treatment / all	0 / 1	0 / 12	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

Peritonitis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 288 (0.35%)	1 / 1033 (0.10%)	0 / 745 (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
Pharyngitis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 1033 (0.10%)	1 / 745 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	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	Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS	Total	Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 288 (22.57%)	289 / 1033 (27.98%)	224 / 745 (30.07%)
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 288 (5.90%)	81 / 1033 (7.84%)	64 / 745 (8.59%)
occurrences (all)	39	178	139
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 288 (2.43%)	46 / 1033 (4.45%)	39 / 745 (5.23%)
occurrences (all)	8	53	45
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 288 (4.17%)	68 / 1033 (6.58%)	56 / 745 (7.52%)
occurrences (all)	13	89	76
COVID-19			
subjects affected / exposed	38 / 288 (13.19%)	155 / 1033 (15.00%)	117 / 745 (15.70%)
occurrences (all)	41	160	119

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2021	The amendment primarily aimed to introduce measures to allow more flexibility to the subjects successfully completing one of the preceding studies to be able to continue receiving investigational treatment. These measures included allowance of a limited amount of missing e-diary entries prior to the first treatment visit and ensuring exclusion criteria and prohibited medications were not more stringent than the original preceding study's criteria. Further, the original compliance criteria for eDiary HSS and ISS entries in the week prior to the Week 52 visit were removed. In case subjects did not meet full compliance with eDiary entries, the subjects could be moved to the second observation period; however, it was more appropriate for the subjects to be allowed to continue treatment even in the case of some missing eDiary entries as long as the UAS7 score was calculable as per the definition.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, disposition in OBS2 and follow-up could not be added. Please use https://www.novctrd.com/

Notes: