Clinical trial results:
An open label, multicenter, extension study to evaluate the long-term safety of QGE031 240 mg s.c. given every 4 weeks for 52 weeks in Chronic Spontaneous Urticaria patients who completed study CQGE031C2201

Summary

EudraCT number	2015-003636-13
Trial protocol	DE ES GR GB
Global end of trial date	02 May 2019

Results information

Result version number	v3
This version publication date	04 February 2021
First version publication date	15 May 2020
Version creation reason	• Correction of full data set AEs are corrected to show both arms; and add in AE description

Trial information

Trial identification

Sponsor protocol code	CQGE031C2201E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02649218
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 6132411111, novartis.email@novartis.com
Scientific contact	Study Lead, Novartis Pharmaceuticals, 1 8627788300, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 May 2019
Global end of trial reached?	Yes
Global end of trial date	02 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the long-term safety of ligelizumab in adult CSU subjects who completed the core Study C2201 using the following evaluations:

Incidence and severity of non-serious and serious adverse events including any events of special interest

Changes in vital signs, laboratory assessments, and electrocardiograms (ECGs)

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: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2016
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	Australia: 26
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Taiwan: 24
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	226
EEA total number of subjects	70

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	211
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Of the subjects who completed core study (NCT02477332) that were eligible for extension study, 237 were screened; 226 were enrolled to open-label treatment epoch; 201 (88.9%) completed treatment epoch; 209 (92.5%) entered the post-treatment follow-up epoch and 152 (67.3%) completed the post-treatment follow-up epoch

Pre-assignment

Screening details:

226 who completed core study (NCT02477332) enrolled in this extension https://clinicaltrials.gov/ct2/show/NCT02477332?term=cqge031c2201&draw=2&rank=2

Period 1

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

Blinding implementation details:

Study was not blinded. Randomization/treatment assignment data from the core Study C2201 was not unblinded to the extension study sites until the core Study C2201 was fully completed.

Arms

Arm title	Ligelizumab

Arm description:

QGE031 240 mg s.c. q4w x 13 treatments

Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

QGE031 240 mg s.c. q4w x 13 treatments

Number of subjects in period 1	Ligelizumab
Started	226
Completed	201
Not completed	25
Physician decision	1
Consent withdrawn by subject	2
Adverse event, non-fatal	8
Pregnancy	3
Lack of efficacy	8
Protocol deviation	3

Baseline characteristics

Reporting groups	
Reporting group title	Ligelizumab
Reporting group description:	
QGE031 240 mg s.c. q4w x 13 treatments	

Reporting group values	Ligelizumab	Total	
Number of subjects	226	226	
Age Categorical Units: participants			
<65 years	211	211	
>= 65 years	15	15	
Age Continuous			
age			
Units: years			
arithmetic mean	44.5		
standard deviation	± 12.69	-	
Sex/Gender, Customized			
75.2% of participants were female, 24.8% were male			
Units: Percentage of Participants			
Female	170	170	
Male	56	56	
Race/Ethnicity, Customized			
22.6% Asian, 1.3% Black, 72.1% White, 0.4% Native American, 0.9% Unknown, 2.7% Other			
Units: Subjects			
Asian	51	51	
Black or African American	3	3	
White	163	163	
American Indian or Alaska Native	1	1	
Unknown	2	2	
Other	6	6	

Subject analysis sets	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Set: All 226 subjects who received at least one dose of study drug during this open-label study were included.	

Reporting group values	Safety Set		
Number of subjects	226		
Age Categorical Units: participants			
<65 years	211		
>= 65 years	15		

Age Continuous			
age			
Units: years			
arithmetic mean	44.5		
standard deviation	± 12.69		
Sex/Gender, Customized			
75.2% of participants were female, 24.8% were male			
Units: Percentage of Participants			
Female	170		
Male	56		
Race/Ethnicity, Customized			
22.6% Asian, 1.3% Black, 72.1% White, 0.4% Native American, 0.9% Unknown, 2.7% Other			
Units: Subjects			
Asian	51		
Black or African American	3		
White	163		
American Indian or Alaska Native	1		
Unknown	2		
Other	6		

End points

End points reporting groups

Reporting group title	Ligelizumab

Reporting group description:

QGE031 240 mg s.c. q4w x 13 treatments

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety Set: All 226 subjects who received at least one dose of study drug during this open-label study were included.

Primary: Number of participants with at least one treatment emergent adverse event (AE)

End point title	Number of participants with at least one treatment emergent adverse event (AE)[1]

End point description:

The primary objective of this study was to assess the long-term safety of one-year treatment of QGE031 in adult Chronic Spontaneous Urticaria (CSU) patients who completed the core study CQGE031C2201 using the following evaluations: number of participants with treatment emergent AEs of non-serious and serious nature including any events of special interest.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Within 16 weeks after Week 48

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 have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Either resolve this issue or provide a justification.

End point values	Ligelizumab			
Subject group type	Reporting group			
Number of subjects analysed	226			
Units: Participants	190			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to UAS7 > 6 for subjects having achieved UAS7 ≤ 6 at the end of the treatment period

End point title	Time to UAS7 > 6 for subjects having achieved UAS7 ≤ 6 at the end of the treatment period

End point description:

The secondary objective of this study was to assess the long-term efficacy of QGE031 in adult CSU patients who completed the CQGE031C2201 study using the following evaluations:
Sustained remission defined as maintaining (Urticaria Activity Score) UAS7 ≤ 6 over 48 weeks post-treatment follow up epoch among the participants achieving remission at the end of treatment epoch.

End point type	Secondary

End point timeframe:

Up to 48 weeks after Week 52

End point values	Ligelizumab			
Subject group type	Reporting group			
Number of subjects analysed	226			
Units: Median number of weeks to event	21			

Statistical analyses

No statistical analyses for this end point

Secondary: Number and proportion of participants who achieved UAS7≤ 6

End point title	Number and proportion of participants who achieved UAS7≤ 6

End point description:

Summary of subjects with UAS7 ≤ 6. The long term efficacy of one-year treatment of ligelizumab 240 mg s.c. q4w is assessed by number and proportion of participants who achieved well controlled disease (UAS7≤ 6) at end of the treatment period (Week 52) and end of follow up period (Week 100).

Proportion of participants who achieved UAS7≤ 6: Baseline 0.44%, Week 52 61.06%, 28.32%

End point type	Secondary

End point timeframe:

Baseline, Week 52, Week 100

End point values	Ligelizumab	Safety Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	226			
Units: Participants				
Baseline	1	1		
Week 52	138	138		
Week 100	64	64		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Within 16 weeks after Week 48	
Adverse event reporting additional description:	
Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	QGE031 240 mg q4w (TEAE)
Reporting group description:	
QGE031 240 mg q4w (TEAE)	
Reporting group title	QGE031 240 mg q4w (non-TEAE)
Reporting group description:	
QGE031 240 mg q4w (non-TEAE)	

Serious adverse events	QGE031 240 mg q4w (TEAE)	QGE031 240 mg q4w (non-TEAE)	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 226 (6.64%)	6 / 226 (2.65%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma stage 0			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Ligament rupture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Syncope			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth cyst			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Complicated appendicitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			

subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	QGE031 240 mg q4w (TEAE)	QGE031 240 mg q4w (non-TEAE)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	133 / 226 (58.85%)	38 / 226 (16.81%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	12 / 226 (5.31%)	1 / 226 (0.44%)	
occurrences (all)	14	1	

Nervous system disorders			
Headache			
subjects affected / exposed	29 / 226 (12.83%)	2 / 226 (0.88%)	
occurrences (all)	47	3	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	13 / 226 (5.75%)	0 / 226 (0.00%)	
occurrences (all)	33	0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	23 / 226 (10.18%)	18 / 226 (7.96%)	
occurrences (all)	37	24	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 226 (5.31%)	1 / 226 (0.44%)	
occurrences (all)	13	1	
Back pain			
subjects affected / exposed	16 / 226 (7.08%)	2 / 226 (0.88%)	
occurrences (all)	16	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	57 / 226 (25.22%)	10 / 226 (4.42%)	
occurrences (all)	94	13	
Sinusitis			
subjects affected / exposed	13 / 226 (5.75%)	2 / 226 (0.88%)	
occurrences (all)	13	2	
Upper respiratory tract infection			
subjects affected / exposed	23 / 226 (10.18%)	3 / 226 (1.33%)	
occurrences (all)	38	3	
Urinary tract infection			
subjects affected / exposed	12 / 226 (5.31%)	3 / 226 (1.33%)	
occurrences (all)	13	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported