Clinical trial results:
A multi-center, randomized, double-blind, active and placebo-controlled study to investigate the efficacy and safety of ligelizumab (QGE031) in the treatment of Chronic Spontaneous Urticaria (CSU) in adolescents and adults inadequately controlled with H1-antihistamines

Summary

EudraCT number	2018-000840-24
Trial protocol	FR DE BE EE ES NL PT SK FI PL GB IT RO
Global end of trial date	14 June 2022

Results information

Result version number	v1 (current)
This version publication date	29 December 2022
First version publication date	29 December 2022

Trial information

Trial identification

Sponsor protocol code	CQGE031C2303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03580356
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, 41 613 324 11 11, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma AG, 1 (862) 778-8300, 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	14 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that ligelizumab (72 mg q4w and/or 120 mg q4w) is superior to placebo and superior to omalizumab 300 mg q4w in change from baseline in UAS7 at Week 12

Protection of trial subjects:

This 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	20 October 2018
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: 66
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 47
Country: Number of subjects enrolled	Chile: 27
Country: Number of subjects enrolled	Estonia: 12
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Germany: 92
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	India: 47
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Japan: 86
Country: Number of subjects enrolled	Lebanon: 23
Country: Number of subjects enrolled	Mexico: 26
Country: Number of subjects enrolled	Netherlands: 24
Country: Number of subjects enrolled	Philippines: 17
Country: Number of subjects enrolled	Poland: 61

Country: Number of subjects enrolled	Romania: 27
Country: Number of subjects enrolled	Russian Federation: 107
Country: Number of subjects enrolled	Slovakia: 43
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	Taiwan: 49
Country: Number of subjects enrolled	Tunisia: 24
Country: Number of subjects enrolled	United States: 153
Country: Number of subjects enrolled	Viet Nam: 15
Worldwide total number of subjects	1078
EEA total number of subjects	349

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)	55
Adults (18-64 years)	948
From 65 to 84 years	75
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

1,078 participants enrolled in 27 countries at 185 sites.

Pre-assignment

Screening details:

There were 1,023 adult subjects and 55 adolescent subjects. Out of these 3 adults were mis-randomized and hence did not enter treatment period.

901 adults and 51 adolescent subjects entered the post treatment follow-up period (this also included subjects who entered the follow up period after early treatment discontinuation).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ligelizumab 72 mg - Adults

Arm description:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

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

Dosage and administration details:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Ligelizumab 72 mg - Adolescents

Arm description:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

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

Dosage and administration details:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Ligelizumab 120 mg - Adults

Arm description:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm type	Experimental

Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Ligelizumab 120 mg - Adolescents

Arm description:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm type	Experimental
Investigational medicinal product name	Legilizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Omalizumab 300 mg - Adults

Arm description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for dispersion for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm title	Omalizumab 300 mg - Adolescents

Arm description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm title	Placebo - Ligelizumab 120mg - Adults

Arm description:

2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48

Arm type	Experimental

Investigational medicinal product name	Placebo plus study drug
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48 q4w

Arm title	Placebo - Ligelizumab 120mg - Adolescents

Arm description:

2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48

Arm type	Experimental
Investigational medicinal product name	Placebo plus study drug
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48 q4w

Number of subjects in period 1	Ligelizumab 72 mg - Adults	Ligelizumab 72 mg - Adolescents	Ligelizumab 120 mg - Adults
Started	307	16	304
Completed	269	15	259
Not completed	38	1	45
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	13	-	13
Physician decision	2	-	1
Adverse event, non-fatal	10	-	13
Technical problems	-	-	-
Misrandomized, no treatment	-	-	1
Pregnancy	1	-	7
Lost to follow-up	1	1	1
Protocol deviation	5	-	6
Lack of efficacy	6	-	2

Number of subjects in period 1	Ligelizumab 120 mg - Adolescents	Omalizumab 300 mg - Adults	Omalizumab 300 mg - Adolescents
Started	19	309	14
Completed	17	263	13
Not completed	2	46	1
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	17	-

Physician decision	-	4	-
Adverse event, non-fatal	-	5	-
Technical problems	-	1	-
Misrandomized, no treatment	-	2	-
Pregnancy	-	2	-
Lost to follow-up	-	3	-
Protocol deviation	1	9	1
Lack of efficacy	-	3	-

Number of subjects in period 1	Placebo - Ligelizumab 120mg - Adults	Placebo - Ligelizumab 120mg - Adolescents
Started	103	6
Completed	90	6
Not completed	13	0
Adverse event, serious fatal	-	-
Consent withdrawn by subject	3	-
Physician decision	1	-
Adverse event, non-fatal	6	-
Technical problems	-	-
Misrandomized, no treatment	-	-
Pregnancy	1	-
Lost to follow-up	-	-
Protocol deviation	1	-
Lack of efficacy	1	-

Period 2

Period 2 title	Post-treatment follow up period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Ligelizumab 72 mg - Adults

Arm description:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm type	Experimental

Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Ligelizumab 72 mg - Adolescents

Arm description:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

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

Dosage and administration details:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Ligelizumab 120 mg - Adults

Arm description:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

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

Dosage and administration details:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Ligelizumab 120 mg - Adolescents

Arm description:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm type	Experimental
Investigational medicinal product name	Legilizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Arm title	Omalizumab 300 mg - Adults

Arm description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm type	Experimental

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

Dosage and administration details:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm title	Omalizumab 300 mg - Adolescents

Arm description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Arm title	Placebo - Ligelizumab 120mg - Adults

Arm description:

This is when patients switched to Ligelizumab: 2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48

Arm type	Experimental
Investigational medicinal product name	Placebo plus study drug
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48 q4w

Arm title	Placebo - Ligelizumab 120mg - Adolescents

Arm description:

2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48

Arm type	Experimental
Investigational medicinal product name	Placebo plus study drug
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48 q4w

Number of subjects in period 2	Ligelizumab 72 mg - Adults	Ligelizumab 72 mg - Adolescents	Ligelizumab 120 mg - Adults
Started	272	15	275
Completed	260	15	256
Not completed	12	0	19
Consent withdrawn by subject	6	-	12
Physician decision	-	-	-
Adverse event, non-fatal	1	-	3
Pregnancy	1	-	-
Lost to follow-up	3	-	2
Protocol deviation	1	-	1
Lack of efficacy	-	-	1

Number of subjects in period 2	Ligelizumab 120 mg - Adolescents	Omalizumab 300 mg - Adults	Omalizumab 300 mg - Adolescents
Started	18	265	13
Completed	17	259	13
Not completed	1	6	0
Consent withdrawn by subject	1	4	-
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Pregnancy	-	-	-
Lost to follow-up	-	1	-
Protocol deviation	-	-	-
Lack of efficacy	-	1	-

Number of subjects in period 2	Placebo - Ligelizumab 120mg - Adults	Placebo - Ligelizumab 120mg - Adolescents
Started	89	6
Completed	82	5
Not completed	7	1
Consent withdrawn by subject	6	1
Physician decision	1	-
Adverse event, non-fatal	-	-
Pregnancy	-	-
Lost to follow-up	-	-
Protocol deviation	-	-
Lack of efficacy	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Ligelizumab 72 mg - Adults
Reporting group description:	
Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 72 mg - Adolescents
Reporting group description:	
Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 120 mg - Adults
Reporting group description:	
Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 120 mg - Adolescents
Reporting group description:	
Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Omalizumab 300 mg - Adults
Reporting group description:	
Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Reporting group title	Omalizumab 300 mg - Adolescents
Reporting group description:	
Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Reporting group title	Placebo - Ligelizumab 120mg - Adults
Reporting group description:	
2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48	
Reporting group title	Placebo - Ligelizumab 120mg - Adolescents
Reporting group description:	
2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48	

Reporting group values	Ligelizumab 72 mg - Adults	Ligelizumab 72 mg - Adolescents	Ligelizumab 120 mg - Adults
Number of subjects	307	16	304
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adults|<=18 years	0	0	0
Adolescents|<=18 years	0	16	0
Adults|Between 18 and 65 years	288	0	278
Adolescents|Between 18 and 65 years	0	0	0
Adults|>=65 years	19	0	26
Adolescents|>=65 years	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	41.7	14.3	43.0
standard deviation	± 13.42	± 1.39	± 14.11

Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	227	0	211
Adolescent|Female	0	10	0
Adult|Male	80	0	93
Adolescent|Male	0	6	0
Race/Ethnicity, Customized Units: Subjects			
Adult White	227	0	218
Adolescent White	0	9	0
Adult Black or African American	5	0	12
Adolescent Black or African American	0	1	0
Adult Asian	66		67
Adolescent Asian	0	2	0
Adult Native Hawaiian or Other Pacific Islander	0	0	0
Adolescent Native Hawaiian or Pacific Islander	0	0	0
Adult Native American	7	0	4
Adolescents Native American	0	4	0
Adult Multi-racial	2	0	3
Adolescent Multi-racial	0	0	0
Adult Race Not Reported	0	0	0
Adolescent Race Not Reported	0	0	0
Age Continuous Units: Years			
arithmetic mean	41.7	14.3	43.0
standard deviation	± 13.42	± 1.39	± 14.11

Reporting group values	Ligelizumab 120 mg - Adolescents	Omalizumab 300 mg - Adults	Omalizumab 300 mg - Adolescents
Number of subjects	19	309	14
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adults|<=18 years	0	0	0
Adolescents|<=18 years	19	0	14
Adults|Between 18 and 65 years	0	286	0
Adolescents|Between 18 and 65 years	0	0	0
Adults|>=65 years	0	23	0
Adolescents|>=65 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	15.1	44.1	15.9
standard deviation	± 1.56	± 14.11	± 1.17
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	0	225	0
Adolescent|Female	12	0	10

Adult|Male	0	84	0
Adolescent|Male	7	0	4

Race/Ethnicity, Customized Units: Subjects			
Adult White	0	228	0
Adolescent White	15	0	10
Adult Black or African American	0	9	0
Adolescent Black or African American	0	0	0
Adult Asian	0	63	0
Adolescent Asian	2	0	4
Adult Native Hawaiian or Other Pacific Islander	0	0	0
Adolescent Native Hawaiian or Pacific Islander	0	0	0
Adult Native American	0	6	0
Adolescents Native American	2	0	0
Adult Multi-racial	0	3	0
Adolescent Multi-racial	0	0	0
Adult Race Not Reported	0	0	0
Adolescent Race Not Reported	0	0	0
Age Continuous Units: Years			
arithmetic mean	15.1	44.1	15.9
standard deviation	± 1.56	± 14.11	± 1.17

Reporting group values	Placebo - Ligelizumab 120mg - Adults	Placebo - Ligelizumab 120mg - Adolescents	Total
Number of subjects	103	6	1078
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adults|<=18 years	0	0	0
Adolescents|<=18 years	0	6	55
Adults|Between 18 and 65 years	96	0	948
Adolescents|Between 18 and 65 years	0	0	0
Adults|>=65 years	7	0	75
Adolescents|>=65 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	42.9	14.8	
standard deviation	± 13.01	± 1.47	-
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	80	0	743
Adolescent|Female	0	4	36
Adult|Male	23	0	280
Adolescent|Male	0	2	19

Race/Ethnicity, Customized Units: Subjects			
Adult White	79	0	752
Adolescent White	0	5	39
Adult Black or African American	1	0	27
Adolescent Black or African American	0	0	1
Adult Asian	19	0	215
Adolescent Asian	0	0	8
Adult Native Hawaiian or Other Pacific Islander	0	0	0
Adolescent Native Hawaiian or Pacific Islander	0	0	0
Adult Native American	3	0	20
Adolescents Native American	0	1	7
Adult Multi-racial	1	0	9
Adolescent Multi-racial	0	0	0
Adult Race Not Reported	0	0	0
Adolescent Race Not Reported	0	0	0
Age Continuous Units: Years			
arithmetic mean	42.9	15.0	
standard deviation	± 13.01	± 1.50	-

Subject analysis sets

Subject analysis set title	Ligelizumab 72 mg
Subject analysis set type	Full analysis
Subject analysis set description: Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Subject analysis set title	Ligelizumab 72 mg
Subject analysis set type	Full analysis
Subject analysis set description: Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Subject analysis set title	Ligelizumab 120 mg
Subject analysis set type	Full analysis
Subject analysis set description: Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Subject analysis set title	Ligelizumab 120 mg
Subject analysis set type	Full analysis
Subject analysis set description: Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Subject analysis set title	Omalizumab 300 mg
Subject analysis set type	Full analysis
Subject analysis set description: Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Subject analysis set title	Omalizumab 300 mg
Subject analysis set type	Full analysis
Subject analysis set description: Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	

Subject analysis set title	Placebo - QGE031 120mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48

Subject analysis set title	Placebo - QGE031 120mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48

Reporting group values	Ligelizumab 72 mg	Ligelizumab 72 mg	Ligelizumab 120 mg
Number of subjects	307	16	304
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adults|<=18 years	0	16	0
Adolescents|<=18 years	0	16	0
Adults|Between 18 and 65 years	288	0	278
Adolescents|Between 18 and 65 years	0	0	0
Adults|>=65 years	19	0	26
Adolescents|>=65 years	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	41.7	14.3	43.0
standard deviation	± 13.42	± 1.39	± 14.11
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	227	0	211
Adolescent|Female	0	10	12
Adult|Male	80	0	93
Adolescent|Male	6	6	7
Race/Ethnicity, Customized			
Units: Subjects			
Adult White	227	0	218
Adolescent White	0	9	15
Adult Black or African American	5	0	12
Adolescent Black or African American	0	1	0
Adult Asian	66	0	67
Adolescent Asian	0	2	0
Adult Native Hawaiian or Other Pacific Islander	0	0	0
Adolescent Native Hawaiian or Pacific Islander	0	0	0
Adult Native American	7	0	4
Adolescents Native American	0	4	0
Adult Multi-racial	2	0	3
Adolescent Multi-racial	0	0	0
Adult Race Not Reported	0	0	0

Adolescent Race Not Reported	0	0	0

Age Continuous			
Units: Years			
arithmetic mean	41.7	14.3	43.0
standard deviation	± 13.2	± 1.39	± 14.11

Reporting group values	Ligelizumab 120 mg	Omalizumab 300 mg	Omalizumab 300 mg
Number of subjects	19	309	14
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adults|<=18 years	19	0	14
Adolescents|<=18 years	0	0	0
Adults|Between 18 and 65 years	0	286	0
Adolescents|Between 18 and 65 years	0	0	0
Adults|>=65 years	0	23	0
Adolescents|>=65 years	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	15.1	44.1	15.9
standard deviation	± 1.56	± 14.11	± 1.17
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	0	225	0
Adolescent|Female	12	10	10
Adult|Male	0	84	0
Adolescent|Male	7	4	4
Race/Ethnicity, Customized			
Units: Subjects			
Adult White	0	228	0
Adolescent White	15	0	10
Adult Black or African American	0	9	0
Adolescent Black or African American	0	0	0
Adult Asian	0	63	0
Adolescent Asian	2	0	4
Adult Native Hawaiian or Other Pacific Islander	0	0	0
Adolescent Native Hawaiian or Pacific Islander	0	0	0
Adult Native American	0	6	0
Adolescents Native American	2	0	0
Adult Multi-racial	0	3	
Adolescent Multi-racial	0	0	0
Adult Race Not Reported	0	0	
Adolescent Race Not Reported	0	0	0

Age Continuous			
Units: Years			
arithmetic mean	15.1	44.1	15.9
standard deviation	± 1.56	± 14.11	± 1.17

Reporting group values	Placebo - QGE031 120mg	Placebo - QGE031 120mg	
Number of subjects	103	6	
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adults|<=18 years	0	0	
Adolescents|<=18 years	6	6	
Adults|Between 18 and 65 years	96	0	
Adolescents|Between 18 and 65 years	0	0	
Adults|>=65 years	7	0	
Adolescents|>=65 years	0	0	
Age Continuous			
Units: Years			
arithmetic mean	42.9	15.0	
standard deviation	± 13.01	± 1.50	
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	80	0	
Adolescent|Female	4	4	
Adult|Male	23	0	
Adolescent|Male	2	2	
Race/Ethnicity, Customized			
Units: Subjects			
Adult White	79	0	
Adolescent White	5	5	
Adult Black or African American	1	0	
Adolescent Black or African American	0	0	
Adult Asian	19	0	
Adolescent Asian	0	0	
Adult Native Hawaiian or Other Pacific Islander	0	0	
Adolescent Native Hawaiian or Pacific Islander	0	0	
Adult Native American	3	0	
Adolescents Native American	0	1	
Adult Multi-racial	0	0	
Adolescent Multi-racial	0	0	
Adult Race Not Reported	0	0	
Adolescent Race Not Reported	0	0	
Age Continuous			
Units: Years			
arithmetic mean	42.9	15.0	
standard deviation	± 13.01	± 1.50	

End points reporting groups

Reporting group title	Ligelizumab 72 mg - Adults
Reporting group description:	
Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 72 mg - Adolescents
Reporting group description:	
Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 120 mg - Adults
Reporting group description:	
Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 120 mg - Adolescents
Reporting group description:	
Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Omalizumab 300 mg - Adults
Reporting group description:	
Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Reporting group title	Omalizumab 300 mg - Adolescents
Reporting group description:	
Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Reporting group title	Placebo - Ligelizumab 120mg - Adults
Reporting group description:	
2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48	
Reporting group title	Placebo - Ligelizumab 120mg - Adolescents
Reporting group description:	
2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48	
Reporting group title	Ligelizumab 72 mg - Adults
Reporting group description:	
Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 72 mg - Adolescents
Reporting group description:	
Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 120 mg - Adults
Reporting group description:	
Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Ligelizumab 120 mg - Adolescents
Reporting group description:	
Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	
Reporting group title	Omalizumab 300 mg - Adults
Reporting group description:	
Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Reporting group title	Omalizumab 300 mg - Adolescents

Reporting group description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Reporting group title	Placebo - Ligelizumab 120mg - Adults

Reporting group description:

This is when patients switched to Ligelizumab: 2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48

Reporting group title	Placebo - Ligelizumab 120mg - Adolescents

Reporting group description:

2 injections of 1.0 mL of ligelizumab placebo q4w from Week 0 to Week 20; 1.0 mL of ligelizumab 120 mg + 1.0 mL of ligelizumab placebo q4w from Week 24 through Week 48

Subject analysis set title	Ligelizumab 72 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Subject analysis set title	Ligelizumab 72 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ligelizumab 72 mg arm: 1 injection of 0.6 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Subject analysis set title	Ligelizumab 120 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Subject analysis set title	Ligelizumab 120 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w

Subject analysis set title	Omalizumab 300 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Subject analysis set title	Omalizumab 300 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w

Subject analysis set title	Placebo - QGE031 120mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48

Subject analysis set title	Placebo - QGE031 120mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo-ligelizumab arm: 2 injections of 1.0mL of ligelizumab placebo from Week 0 through Week 20; 1 injection of 1.0mL of ligelizumab 120 mg + 1 injection of 1.0 mL ligelizumab placebo from Week 24 through Week 48

Primary: Mean change from baseline in UAS7 at Week 12 (Multiple imputation) of Adult subjects

End point title	Mean change from baseline in UAS7 at Week 12 (Multiple imputation) of Adult subjects

End point description:

The Urticaria Activity Score (UAS) is sum of the Hive Severity Score (HSS) and the Itch Severity Score (ISS). UAS7 is sum of the HSS7 and the ISS7 scores. Possible range of weekly UAS7 score is 0 to 42. Complete UAS7 response is UAS7 = 0. Hives Severity Score (HSS) scale is 0 to 3. A weekly score (HSS7) is derived by adding up the average daily scores of the 7 days preceding the visit. Possible range of the weekly score is therefore 0 to 21. Hives Severity Score scale: 0 - None 1 - Mild (1-6 hives/12 hours) 2 - Moderate (7-12 hives/12 hours) 3 - Severe (>12 hives/12 hours). Itch Severity Score (ISS) scale is 0 to 3. Score (ISS7) is derived by adding up average daily scores of 7 days preceding visit. Possible range of weekly score is therefore 0 to 21. Itch Severity Score scale: 0 - None 1 - Mild (minimal awareness, easily tolerated) 2 - Moderate (definite awareness, bothersome but tolerable) 3 - Severe (difficult to tolerate). Negative change from baseline indicates improvement

End point type	Primary

End point timeframe:

Baseline, Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	307	303	307	103
Units: Score				
least squares mean (standard error)	-19.218 (± 0.651)	-20.312 (± 0.654)	-19.632 (± 0.652)	-9.221 (± 1.135)

Statistical analyses

Statistical analysis title	Change in UAS7 at week 12

Statistical analysis description:

Treatment contrast in LS mean (change), Adults

Comparison groups	Ligelizumab 72 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-9.997
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.554
upper limit	-7.439
Variability estimate	Standard error of the mean
Dispersion value	1.305

Statistical analysis title	Change in UAS7 at week 12
Statistical analysis description:	
Treatment contrast in LS mean (change), Adults	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6735
Method	Mixed models analysis
Parameter estimate	LS mean
Point estimate	0.414
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.392
upper limit	2.221
Variability estimate	Standard error of the mean
Dispersion value	0.922

Statistical analysis title	Change in UAS7 at week 12
Statistical analysis description:	
Treatment contrast in LS mean (change), Adults	
Comparison groups	Ligelizumab 120 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-11.091
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.664
upper limit	-8.518
Variability estimate	Standard error of the mean
Dispersion value	1.313

Statistical analysis title	Change in UAS7 at week 12
Statistical analysis description:	
Treatment contrast in LS mean (change), Adults	
Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg

Number of subjects included in analysis	610
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2305
Method	Mixed models analysis
Parameter estimate	LS mean
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.489
upper limit	1.128
Variability estimate	Standard error of the mean
Dispersion value	0.923

Primary: Mean change from baseline in UAS7 at Week 12 (observed data) of Adolescent subjects (FAS)

End point title	Mean change from baseline in UAS7 at Week 12 (observed data) of Adolescent subjects (FAS)[1]

End point description:

The Urticaria Activity Score (UAS) is sum of the Hive Severity Score (HSS) and the Itch Severity Score (ISS). UAS7 is sum of the HSS7 and the ISS7 scores. Possible range of weekly UAS7 score is 0 to 42. Complete UAS7 response is UAS7 = 0. Hives Severity Score (HSS) scale is 0 to 3. A weekly score (HSS7) is derived by adding up the average daily scores of the 7 days preceding the visit. Possible range of the weekly score is therefore 0 to 21. Hives Severity Score scale: 0 - None 1 - Mild (1-6 hives/12 hours) 2 - Moderate (7-12 hives/12 hours) 3 - Severe (>12 hives/12 hours). Itch Severity Score (ISS) scale is 0 to 3. Score (ISS7) is derived by adding up average daily scores of 7 days preceding visit. Possible range of weekly score is therefore 0 to 21. Itch Severity Score scale: 0 - None 1 - Mild (minimal awareness, easily tolerated) 2 - Moderate (definite awareness, bothersome but tolerable) 3 - Severe (difficult to tolerate). Negative change from baseline indicates improvement

End point type	Primary

End point timeframe:

Baseline, Week 12

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 analysis was planned for this outcome

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	19	14	6
Units: score				
arithmetic mean (standard deviation)	-14.92 (± 13.479)	-24.83 (± 12.640)	-18.16 (± 10.246)	-11.94 (± 14.278)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in ISS7 at Week 12 (Multiple Imputation) of Adult subjects (FAS)

End point title	Mean change from baseline in ISS7 at Week 12 (Multiple Imputation) of Adult subjects (FAS)

End point description:

Improvement of severity of itch assessed as absolute change from baseline in ISS7 score at Week 12 Itch Severity Score (ISS) is on a scale of 0 to 3. A weekly score (ISS7) is derived by adding up the average daily scores of the 7 days preceding the visit. The possible range of the weekly score is therefore 0 to 21. Itch Severity Score scale: 0 - None 1 - Mild (minimal awareness, easily tolerated) 2 - Moderate (definite awareness, bothersome but tolerable) 3 - Severe (difficult to tolerate) Negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	307	303	307	103
Units: score				
least squares mean (standard error)	-8.632 (± 0.298)	-9.023 (± 0.300)	-8.733 (± 0.300)	-4.527 (± 0.522)

Statistical analyses

Statistical analysis title	Change in ISS7 at week 12

Statistical analysis description:

Adults

Comparison groups	Ligelizumab 72 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-4.105
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.281
upper limit	-2.929
Variability estimate	Standard error of the mean
Dispersion value	0.6

Statistical analysis title	Change in ISS7 at week 12

Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5943
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	0.101
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.727
upper limit	0.928
Variability estimate	Standard error of the mean
Dispersion value	0.422

Statistical analysis title	Change in ISS7 at week 12
Comparison groups	Ligelizumab 120 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-4.496
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.678
upper limit	-3.314
Variability estimate	Standard error of the mean
Dispersion value	0.603

Notes:

[2] - Adults

Statistical analysis title	Change in ISS7 at week 12
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	610
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2467
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.29

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.423

Secondary: Mean change from baseline in ISS7 at Week 12 (observed data) of Adolescent subjects, (FAS)

End point title	Mean change from baseline in ISS7 at Week 12 (observed data) of Adolescent subjects, (FAS)

End point description:

Improvement of severity of itch assessed as absolute change from baseline in ISS7 score at Week 12 Itch Severity Score (ISS) is on a scale of 0 to 3. A weekly score (ISS7) is derived by adding up the average daily scores of the 7 days preceding the visit. The possible range of the weekly score is therefore 0 to 21. Itch Severity Score scale: 0 - None 1 - Mild (minimal awareness, easily tolerated) 2 - Moderate (definite awareness, bothersome but tolerable) 3 - Severe (difficult to tolerate) Negative change from baseline indicates improvement.. No Statistical Analysis was planned for adolescent population.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	19	14	6
Units: score				
arithmetic mean (standard deviation)	-6.38 (± 6.994)	-12.04 (± 6.264)	-8.56 (± 4.935)	-6.97 (± 7.904)

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of weeks of AAS7=0 up to week 12 (Multiple Imputation) of Adult subjects (FAS)

End point title	Cumulative number of weeks of AAS7=0 up to week 12 (Multiple Imputation) of Adult subjects (FAS)

End point description:

Cumulative number of weeks that subjects achieve AAS7 = 0 responses between baseline and Week 12 Angioedema Activity Score (AAS7) is a measure of the frequency and intensity of angioedema episodes. The total possible range of scores over 7 days is 0-15 (mean day sum score) where higher scores indicate increased angioedema activity.

End point type	Secondary

End point timeframe:
Baseline, Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	307	303	307	103
Units: Weeks				
least squares mean (standard error)	8.668 (± 0.241)	8.897 (± 0.246)	8.427 (± 0.237)	6.242 (± 0.331)

Statistical analyses

Statistical analysis title	Number of weeks of AAS7 = 0
Statistical analysis description: Adults	
Comparison groups	Ligelizumab 72 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.389
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.235
upper limit	1.561

Statistical analysis title	Number of weeks of AAS7 = 0
Statistical analysis description: Adults	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2369
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.029

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.952
upper limit	1.111

Statistical analysis title	Number of weeks of AAS7 = 0
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.425
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.268
upper limit	1.603

Statistical analysis title	Number of weeks of AAS7 = 0
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	610
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.083
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.056
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.978
upper limit	1.14

Secondary: Cumulative number of weeks of AAS7=0 up to week 12 (observed data) of Adolescent subjects (FAS)

End point title	Cumulative number of weeks of AAS7=0 up to week 12 (observed data) of Adolescent subjects (FAS)

End point description:

Cumulative number of weeks that subjects achieve AAS7 = 0 responses between baseline and Week 12 Angioedema Activity Score (AAS7) is a measure of the frequency and intensity of angioedema episodes. The total possible range of scores over 7 days is 0-15 (mean day sum score) where higher scores indicate increased angioedema activity. No Statistical Analysis was planned.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	19	14	6
Units: Weeks				
least squares mean (standard error)	6.8 (± 4.90)	8.6 (± 4.60)	10.2 (± 3.01)	9.2 (± 4.92)

Statistical analyses

No statistical analyses for this end point

Secondary: Number and proportion of subjects with UAS7=0 response at Week 12 (Multiple imputation - adults, observed data for adolescents)

End point title	Number and proportion of subjects with UAS7=0 response at Week 12 (Multiple imputation - adults, observed data for adolescents)

End point description:

The Urticaria Activity Score (UAS) is the sum of the Hive Severity Score (HSS) and the Itch Severity Score (ISS). UAS7 is the sum of the HSS7 and the ISS7 scores. The possible range of the weekly UAS7 score is 0 to 42. Complete UAS7 response is defined as UAS7 = 0. No Statistical analysis was planned for adolescent group.

End point type	Secondary

End point timeframe:

Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	307	303	307	103
Units: Participants				
Adults	88	103	94	4
Adolescents	4	8	5	0

Statistical analyses

Statistical analysis title	Number of those with UAS7 = 0
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.029
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.183
upper limit	25.615

Notes:

[3] - Wald chi-square test based on logistic regression

Statistical analysis title	Number of those with UAS7 = 0
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.6646
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.926
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.319

Notes:

[4] - Wald chi-square test based on logistic regression

Statistical analysis title	Number of those with UAS7 = 0
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.508

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.058
upper limit	32.638

Notes:

[5] - Wald chi-square test based on logistic regression

Statistical analysis title	Number of those with UAS7 = 0

Statistical analysis description:

Adults

Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	610
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.173
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	1.181
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.836
upper limit	1.667

Notes:

[6] - Wald chi-square test based on logistic regression

Secondary: Number and Proportion of participants with DLQI score of 0 – 1 at Week 12 (Multiple imputation - adults, observed data for adolescents)

End point title	Number and Proportion of participants with DLQI score of 0 – 1 at Week 12 (Multiple imputation - adults, observed data for adolescents)

End point description:

Assessed as percentage of subjects achieving DLQI = 0-1, which means No impact on subjects quality of life at Week 12 The Dermatology life Quality Index (DLQI) score range is 0 to 30, with 0 (meaning no impact of skin disease on quality of life) to 30 (meaning maximum impact on quality of life). No statistical anaylsis was planned for adolescent group.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo - QGE031 120mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	307	303	307	103
Units: Participants				
Adults	134	153	147	18
Adolescents	4	9	5	0

Statistical analyses

Statistical analysis title	Number of those with DLQI = 0-1
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Placebo - QGE031 120mg
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.443
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.955
upper limit	6.063

Notes:

[7] - Wald chi-square test based on logistic regression

Statistical analysis title	Number of those with DLQI = 0-1
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.8524
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.838
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.602
upper limit	1.167

Notes:

[8] - Wald chi-square test based on logistic regression

Statistical analysis title	Number of those with DLQI = 0-1
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Placebo - QGE031 120mg

Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.542
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.577
upper limit	8.004

Notes:

[9] - Wald chi-square test based on logistic regression

Statistical analysis title	Number of those with DLQI = 0-1

Statistical analysis description:

Adults

Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	610
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.2764
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.106
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.794
upper limit	1.54

Notes:

[10] - Wald chi-square test based on logistic regression

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event (AE) monitoring was continued for at least 30 days following the last dose of study treatment or end of study visit (64 weeks), whichever is longer.	
Adverse event reporting additional description:	
AEs and SAEs are any untoward sign or symptom that occurs during the study treatment and up to 16 weeks.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	QGE031 72mg
Reporting group description:	
QGE031 72mg	
Reporting group title	QGE031 120mg
Reporting group description:	
QGE031 120mg	
Reporting group title	Omalizumab 300mg
Reporting group description:	
Omalizumab 300mg	
Reporting group title	Placebo only
Reporting group description:	
Placebo only	
Reporting group title	Transitioned to QGE031 120mg
Reporting group description:	
Transitioned to QGE031 120mg	

Serious adverse events	QGE031 72mg	QGE031 120mg	Omalizumab 300mg
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 320 (5.63%)	14 / 325 (4.31%)	12 / 321 (3.74%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Brain neoplasm benign			

subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Breast cancer recurrent			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Carcinoid tumour			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Cervix carcinoma			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Haematoma			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Peripheral artery stenosis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unintended pregnancy			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Uterine cyst			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Uterine haemorrhage			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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			
Atelectasis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Completed suicide			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Depression			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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

Homicidal ideation			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Suicidal ideation			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Injury, poisoning and procedural complications			
Foreign body in throat			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Humerus fracture			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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

Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Large intestine polyp			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Hepatobiliary disorders			
Hepatic cyst			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pemphigoid			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	1 / 321 (0.31%)
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			
Acute kidney injury			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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 pain			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Ureterolithiasis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 321 (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
Spinal pain			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 321 (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
Spondylitis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 321 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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
Appendicitis perforated			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacterial urethritis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 321 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 320 (0.31%)	2 / 325 (0.62%)	0 / 321 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	2 / 321 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 321 (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
Pyelonephritis			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 321 (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

Serious adverse events	Placebo only	Transitioned to QGE031 120mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 109 (3.67%)	3 / 96 (3.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm benign			

subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unintended pregnancy			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cyst			

subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Homicidal ideation			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Foreign body in throat			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic cyst			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal pain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (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			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bacterial urethritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	QGE031 72mg	QGE031 120mg	Omalizumab 300mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	184 / 320 (57.50%)	192 / 325 (59.08%)	175 / 321 (54.52%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	4 / 320 (1.25%)	3 / 325 (0.92%)	10 / 321 (3.12%)
occurrences (all)	4	4	16
SARS-CoV-2 test negative			
subjects affected / exposed	7 / 320 (2.19%)	2 / 325 (0.62%)	4 / 321 (1.25%)
occurrences (all)	11	2	7
Vascular disorders			

Hypertension			
subjects affected / exposed	11 / 320 (3.44%)	10 / 325 (3.08%)	9 / 321 (2.80%)
occurrences (all)	13	10	9
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 320 (2.19%)	3 / 325 (0.92%)	7 / 321 (2.18%)
occurrences (all)	12	3	8
Headache			
subjects affected / exposed	39 / 320 (12.19%)	46 / 325 (14.15%)	39 / 321 (12.15%)
occurrences (all)	105	92	73
Migraine			
subjects affected / exposed	1 / 320 (0.31%)	4 / 325 (1.23%)	3 / 321 (0.93%)
occurrences (all)	1	4	6
Somnolence			
subjects affected / exposed	3 / 320 (0.94%)	4 / 325 (1.23%)	3 / 321 (0.93%)
occurrences (all)	7	4	8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 320 (1.25%)	5 / 325 (1.54%)	8 / 321 (2.49%)
occurrences (all)	4	6	10
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 320 (3.13%)	9 / 325 (2.77%)	7 / 321 (2.18%)
occurrences (all)	16	11	10
Injection site erythema			
subjects affected / exposed	8 / 320 (2.50%)	12 / 325 (3.69%)	0 / 321 (0.00%)
occurrences (all)	21	18	0
Injection site pain			
subjects affected / exposed	7 / 320 (2.19%)	6 / 325 (1.85%)	5 / 321 (1.56%)
occurrences (all)	10	7	7
Injection site reaction			
subjects affected / exposed	5 / 320 (1.56%)	9 / 325 (2.77%)	3 / 321 (0.93%)
occurrences (all)	19	17	10
Injection site swelling			
subjects affected / exposed	6 / 320 (1.88%)	6 / 325 (1.85%)	1 / 321 (0.31%)
occurrences (all)	6	16	1

Injection site urticaria			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	1 / 321 (0.31%)
occurrences (all)	0	3	1
Pyrexia			
subjects affected / exposed	8 / 320 (2.50%)	9 / 325 (2.77%)	10 / 321 (3.12%)
occurrences (all)	8	10	13
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	11 / 320 (3.44%)	10 / 325 (3.08%)	7 / 321 (2.18%)
occurrences (all)	15	12	12
Abdominal pain upper			
subjects affected / exposed	11 / 320 (3.44%)	4 / 325 (1.23%)	2 / 321 (0.62%)
occurrences (all)	11	5	2
Diarrhoea			
subjects affected / exposed	12 / 320 (3.75%)	11 / 325 (3.38%)	8 / 321 (2.49%)
occurrences (all)	16	11	9
Gastritis			
subjects affected / exposed	4 / 320 (1.25%)	4 / 325 (1.23%)	1 / 321 (0.31%)
occurrences (all)	4	4	1
Gastrooesophageal reflux disease			
subjects affected / exposed	7 / 320 (2.19%)	2 / 325 (0.62%)	3 / 321 (0.93%)
occurrences (all)	7	2	4
Nausea			
subjects affected / exposed	15 / 320 (4.69%)	11 / 325 (3.38%)	9 / 321 (2.80%)
occurrences (all)	25	13	13
Toothache			
subjects affected / exposed	4 / 320 (1.25%)	5 / 325 (1.54%)	8 / 321 (2.49%)
occurrences (all)	4	6	10
Vomiting			
subjects affected / exposed	11 / 320 (3.44%)	7 / 325 (2.15%)	4 / 321 (1.25%)
occurrences (all)	11	7	4
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 320 (0.31%)	9 / 325 (2.77%)	4 / 321 (1.25%)
occurrences (all)	2	13	4
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	7 / 320 (2.19%)	12 / 325 (3.69%)	6 / 321 (1.87%)
occurrences (all)	12	15	6
Oropharyngeal pain			
subjects affected / exposed	13 / 320 (4.06%)	10 / 325 (3.08%)	5 / 321 (1.56%)
occurrences (all)	14	11	6
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 320 (0.94%)	10 / 325 (3.08%)	6 / 321 (1.87%)
occurrences (all)	3	10	8
Angioedema			
subjects affected / exposed	14 / 320 (4.38%)	6 / 325 (1.85%)	8 / 321 (2.49%)
occurrences (all)	27	8	13
Chronic spontaneous urticaria			
subjects affected / exposed	9 / 320 (2.81%)	8 / 325 (2.46%)	4 / 321 (1.25%)
occurrences (all)	14	11	4
Dermatitis contact			
subjects affected / exposed	5 / 320 (1.56%)	9 / 325 (2.77%)	3 / 321 (0.93%)
occurrences (all)	5	9	3
Eczema			
subjects affected / exposed	12 / 320 (3.75%)	12 / 325 (3.69%)	12 / 321 (3.74%)
occurrences (all)	16	15	14
Urticaria			
subjects affected / exposed	13 / 320 (4.06%)	17 / 325 (5.23%)	12 / 321 (3.74%)
occurrences (all)	22	21	14
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 320 (2.50%)	15 / 325 (4.62%)	14 / 321 (4.36%)
occurrences (all)	11	22	16
Back pain			
subjects affected / exposed	19 / 320 (5.94%)	21 / 325 (6.46%)	15 / 321 (4.67%)
occurrences (all)	23	25	16
Myalgia			
subjects affected / exposed	6 / 320 (1.88%)	9 / 325 (2.77%)	1 / 321 (0.31%)
occurrences (all)	6	10	1
Infections and infestations			

Bronchitis			
subjects affected / exposed	8 / 320 (2.50%)	4 / 325 (1.23%)	9 / 321 (2.80%)
occurrences (all)	8	5	9
COVID-19			
subjects affected / exposed	17 / 320 (5.31%)	18 / 325 (5.54%)	12 / 321 (3.74%)
occurrences (all)	17	18	12
Gastroenteritis			
subjects affected / exposed	9 / 320 (2.81%)	6 / 325 (1.85%)	7 / 321 (2.18%)
occurrences (all)	11	6	8
Influenza			
subjects affected / exposed	16 / 320 (5.00%)	13 / 325 (4.00%)	9 / 321 (2.80%)
occurrences (all)	17	16	9
Nasopharyngitis			
subjects affected / exposed	44 / 320 (13.75%)	39 / 325 (12.00%)	40 / 321 (12.46%)
occurrences (all)	60	53	55
Oral herpes			
subjects affected / exposed	1 / 320 (0.31%)	5 / 325 (1.54%)	4 / 321 (1.25%)
occurrences (all)	1	5	5
Pharyngitis			
subjects affected / exposed	4 / 320 (1.25%)	4 / 325 (1.23%)	3 / 321 (0.93%)
occurrences (all)	4	5	4
Sinusitis			
subjects affected / exposed	3 / 320 (0.94%)	5 / 325 (1.54%)	8 / 321 (2.49%)
occurrences (all)	3	5	10
Tonsillitis			
subjects affected / exposed	2 / 320 (0.63%)	4 / 325 (1.23%)	7 / 321 (2.18%)
occurrences (all)	2	4	8
Upper respiratory tract infection			
subjects affected / exposed	17 / 320 (5.31%)	19 / 325 (5.85%)	15 / 321 (4.67%)
occurrences (all)	22	23	21
Urinary tract infection			
subjects affected / exposed	4 / 320 (1.25%)	11 / 325 (3.38%)	18 / 321 (5.61%)
occurrences (all)	6	13	27

Non-serious adverse events	Placebo only	Transitioned to QGE031 120mg	
Total subjects affected by non-serious adverse events			

subjects affected / exposed	41 / 109 (37.61%)	39 / 96 (40.63%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 109 (1.83%)	0 / 96 (0.00%)	
occurrences (all)	2	0	
SARS-CoV-2 test negative			
subjects affected / exposed	1 / 109 (0.92%)	1 / 96 (1.04%)	
occurrences (all)	1	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	7 / 109 (6.42%)	6 / 96 (6.25%)	
occurrences (all)	13	6	
Migraine			
subjects affected / exposed	0 / 109 (0.00%)	3 / 96 (3.13%)	
occurrences (all)	0	15	
Somnolence			
subjects affected / exposed	3 / 109 (2.75%)	0 / 96 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 109 (0.92%)	2 / 96 (2.08%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 109 (0.92%)	1 / 96 (1.04%)	
occurrences (all)	1	1	
Injection site erythema			
subjects affected / exposed	1 / 109 (0.92%)	2 / 96 (2.08%)	
occurrences (all)	1	2	
Injection site pain			

subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences (all)	1	0	
Injection site reaction			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences (all)	0	2	
Injection site swelling			
subjects affected / exposed	1 / 109 (0.92%)	3 / 96 (3.13%)	
occurrences (all)	1	5	
Injection site urticaria			
subjects affected / exposed	0 / 109 (0.00%)	2 / 96 (2.08%)	
occurrences (all)	0	4	
Pyrexia			
subjects affected / exposed	0 / 109 (0.00%)	2 / 96 (2.08%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 109 (3.67%)	1 / 96 (1.04%)	
occurrences (all)	4	1	
Abdominal pain upper			
subjects affected / exposed	2 / 109 (1.83%)	0 / 96 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	1 / 109 (0.92%)	3 / 96 (3.13%)	
occurrences (all)	1	4	
Gastritis			
subjects affected / exposed	0 / 109 (0.00%)	2 / 96 (2.08%)	
occurrences (all)	0	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	2 / 109 (1.83%)	0 / 96 (0.00%)	
occurrences (all)	3	0	
Toothache			
subjects affected / exposed	4 / 109 (3.67%)	2 / 96 (2.08%)	
occurrences (all)	4	4	

Vomiting			
subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 109 (1.83%)	2 / 96 (2.08%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 109 (1.83%)	0 / 96 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 109 (1.83%)	2 / 96 (2.08%)	
occurrences (all)	2	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences (all)	0	1	
Angioedema			
subjects affected / exposed	1 / 109 (0.92%)	1 / 96 (1.04%)	
occurrences (all)	2	1	
Chronic spontaneous urticaria			
subjects affected / exposed	1 / 109 (0.92%)	2 / 96 (2.08%)	
occurrences (all)	1	2	
Dermatitis contact			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	4 / 109 (3.67%)	2 / 96 (2.08%)	
occurrences (all)	4	2	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 109 (0.92%)	3 / 96 (3.13%)	
occurrences (all)	1	3	
Back pain			
subjects affected / exposed	2 / 109 (1.83%)	2 / 96 (2.08%)	
occurrences (all)	2	2	
Myalgia			
subjects affected / exposed	1 / 109 (0.92%)	2 / 96 (2.08%)	
occurrences (all)	1	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 109 (0.92%)	1 / 96 (1.04%)	
occurrences (all)	1	1	
COVID-19			
subjects affected / exposed	1 / 109 (0.92%)	4 / 96 (4.17%)	
occurrences (all)	1	4	
Gastroenteritis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 96 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 109 (0.92%)	3 / 96 (3.13%)	
occurrences (all)	1	3	
Nasopharyngitis			
subjects affected / exposed	7 / 109 (6.42%)	7 / 96 (7.29%)	
occurrences (all)	8	9	
Oral herpes			
subjects affected / exposed	3 / 109 (2.75%)	1 / 96 (1.04%)	
occurrences (all)	3	1	
Pharyngitis			
subjects affected / exposed	1 / 109 (0.92%)	2 / 96 (2.08%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	2 / 109 (1.83%)	0 / 96 (0.00%)	
occurrences (all)	2	0	
Tonsillitis			

subjects affected / exposed	0 / 109 (0.00%)	0 / 96 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 109 (0.92%)	1 / 96 (1.04%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	0 / 109 (0.00%)	1 / 96 (1.04%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2019	This amendment provided the following clarifications: 1- A urine dipstick assessment had to be done at Week 24 (and a urine sample sent to central lab for urinalysis if indicated) 2- If subjects were administered omalizumab in the follow-up phase, they had to be discontinued from the study 3- Inclusion of levocetirizine and desloratadine as allowed H1-AH rescue medications
05 January 2021	This amendment introduced measures to mitigate the impact of COVID-19 on trial integrity by amending the hierarchical testing strategy to include pooled analysis of secondary endpoints against active comparator and adding COVID-19 related intercurrent events to the primary estimand. 1- This amendment also introduced an interim analysis in order to perform the primary efficacy analysis once all adult patients had completed the treatment period (Week 52). Additional changes in this amendment include: 2- Instruction on Public Health Emergency mitigation procedures: 3- Introduction of the use of local laboratory assessments, 4- Introduction of remote PRO completion and 5- Introduction of phone calls, virtual contacts to replace on-site study visit for the duration of the disruption, 6- Clarification of subject discontinuation: If a subject missed more than 3 consecutive dosing visits then the subject was to be discontinued from the study treatment

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 difference of 3 subjects between RAN (1034) vs FAS (1030) is due to mis-randomization of 3 subjects. These subjects did not receive Ligelizumab and hence rightfully not included in FAS (though included in RAN).

Notes: