Clinical trial results:
A multicenter, randomized, double-blind, placebo and active-controlled phase 2b dose-finding study of QGE031 as add-on therapy to investigate the efficacy and safety in patients with chronic spontaneous urticaria (CSU)

Summary

EudraCT number	2014-005559-16
Trial protocol	DE ES GB GR
Global end of trial date	12 June 2017

Results information

Result version number	v1
This version publication date	22 June 2018
First version publication date	22 June 2018

Trial information

Trial identification

Sponsor protocol code	CQGE031C2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02477332
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to establish the dose-response relationship of ligelizumab with respect to achievement of complete hives response at Week 12 in patients with chronic spontaneous urticaria (CSU) when added to H1-antihistamines (H1-AH) alone or in combination with H2-antihistamines (H2-AH) and/or a leukotriene receptor antagonist (LTRA).

Note: Complete hives response is defined as a Hive Severity Score (HSS7) of 0. Analogously, complete itch response and complete urticaria response are defined as an itch severity score (ISS7) and an urticaria activity score (UAS7) of 0, respectively.

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:

H1-AH at approved or increased doses alone or in combination with H2-AH and/or a leukotriene receptor antagonist (LTRA).

Evidence for comparator: -

Actual start date of recruitment	15 July 2015
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: 33
Country: Number of subjects enrolled	Canada: 28
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Greece: 8
Country: Number of subjects enrolled	Japan: 36
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	Spain: 61
Country: Number of subjects enrolled	Taiwan: 35
Country: Number of subjects enrolled	United States: 83
Worldwide total number of subjects	382
EEA total number of subjects	129

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)	360
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

574 subjects screened; 382 subjects randomized; 338 (88.5%) subjects completed treatment epoch; 349 (91.4%) subjects entered follow-up phase and 320 (83.8%) completed the follow-up epoch

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	QGE031 24 mg s.c. q4w

Arm description:

ligelizumab 24 mg injection subcutaneous every 4 weeks

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:

ligelizumab 24 mg injection subcutaneous every 4 weeks

Arm title	QGE031 72 mg s.c. q4w

Arm description:

ligelizumab 72 mg injection subcutaneous every 4 weeks

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:

ligelizumab 72 mg injection subcutaneous every 4 weeks

Arm title	QGE031 240 mg s.c. q4w

Arm description:

ligelizumab 240 mg injection subcutaneous every 4 weeks

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: ligelizumab 240 mg injection subcutaneous every 4 weeks	

Arm title	Omalizumab 300 mg s.c. q4w
Arm description: omalizumab 300 mg injection subcutaneous every 4 weeks	
Arm type	Active comparator
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: omalizumab 300 mg injection subcutaneous every 4 weeks	
Arm title	Placebo s.c. q4w
Arm description: placebo injection subcutaneous every 4 weeks	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: placebo injection subcutaneous every 4 weeks	
Arm title	QGE031 120 mg s.c. s.d.
Arm description: ligelizumab 120 mg injection subcutaneous single dose	
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: ligelizumab 120 mg injection subcutaneous single dose	

Number of subjects in period 1	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w
Started	43	84	85
Completed	40	77	73
Not completed	3	7	12
Consent withdrawn by subject	-	3	1
Physician decision	-	-	1
Adverse event, non-fatal	-	1	1

Technical problems	-	-	1
Non-compliance with study treatment	-	1	2
Pregnancy	-	-	-
Lost to follow-up	-	-	2
Lack of efficacy	1	2	1
Protocol deviation	2	-	3

Number of subjects in period 1	Omalizumab 300 mg s.c. q4w	Placebo s.c. q4w	QGE031 120 mg s.c. s.d.
Started	85	43	42
Completed	72	39	37
Not completed	13	4	5
Consent withdrawn by subject	2	1	-
Physician decision	3	-	1
Adverse event, non-fatal	2	1	2
Technical problems	-	-	-
Non-compliance with study treatment	-	-	-
Pregnancy	1	-	-
Lost to follow-up	-	-	-
Lack of efficacy	2	1	1
Protocol deviation	3	1	1

Baseline characteristics

Reporting groups	
Reporting group title	QGE031 24 mg s.c. q4w
Reporting group description:	
ligelizumab 24 mg injection subcutaneous every 4 weeks	
Reporting group title	QGE031 72 mg s.c. q4w
Reporting group description:	
ligelizumab 72 mg injection subcutaneous every 4 weeks	
Reporting group title	QGE031 240 mg s.c. q4w
Reporting group description:	
ligelizumab 240 mg injection subcutaneous every 4 weeks	
Reporting group title	Omalizumab 300 mg s.c. q4w
Reporting group description:	
omalizumab 300 mg injection subcutaneous every 4 weeks	
Reporting group title	Placebo s.c. q4w
Reporting group description:	
placebo injection subcutaneous every 4 weeks	
Reporting group title	QGE031 120 mg s.c. s.d.
Reporting group description:	
ligelizumab 120 mg injection subcutaneous single dose	

Reporting group values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w
Number of subjects	43	84	85
Age Categorical Units: Subjects			
<18 years	0	0	0
>=18 and <65 years	39	77	85
>=65 years	4	7	0
Age Continuous Units: years			
arithmetic mean	44.1	44.3	42.9
standard deviation	± 14.36	± 12.38	± 10.51
Sex: Female, Male Units: Subjects			
Female	31	61	67
Male	12	23	18

Reporting group values	Omalizumab 300 mg s.c. q4w	Placebo s.c. q4w	QGE031 120 mg s.c. s.d.
Number of subjects	85	43	42
Age Categorical Units: Subjects			
<18 years	0	0	0
>=18 and <65 years	81	41	37
>=65 years	4	2	5
Age Continuous Units: years			
arithmetic mean	41.8	45.4	42.4

standard deviation	± 13.06	± 11.22	± 14.54

Sex: Female, Male Units: Subjects			
Female	66	31	30
Male	19	12	12

Reporting group values	Total		
Number of subjects	382		
Age Categorical Units: Subjects			
<18 years	0		
>=18 and <65 years	360		
>=65 years	22		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Subjects			
Female	286		
Male	96		

End points

End points reporting groups

Reporting group title	QGE031 24 mg s.c. q4w
Reporting group description: ligelizumab 24 mg injection subcutaneous every 4 weeks	
Reporting group title	QGE031 72 mg s.c. q4w
Reporting group description: ligelizumab 72 mg injection subcutaneous every 4 weeks	
Reporting group title	QGE031 240 mg s.c. q4w
Reporting group description: ligelizumab 240 mg injection subcutaneous every 4 weeks	
Reporting group title	Omalizumab 300 mg s.c. q4w
Reporting group description: omalizumab 300 mg injection subcutaneous every 4 weeks	
Reporting group title	Placebo s.c. q4w
Reporting group description: placebo injection subcutaneous every 4 weeks	
Reporting group title	QGE031 120 mg s.c. s.d.
Reporting group description: ligelizumab 120 mg injection subcutaneous single dose	

Primary: Dose response relationship with respect to achievement of complete hives response (HSS7=0)

End point title	Dose response relationship with respect to achievement of complete hives response (HSS7=0)

End point description:

The primary objective was to establish the dose-response relationship of ligelizumab (24, 72 and 240 mg every 4 weeks) with respect to achievement of complete hives response (HSS7=0) at Week 12 and select an appropriate dose (or range of doses) which is likely to be superior to omalizumab at the highest approved dose (300 mg every 4 weeks). Hives Severity Score (HSS) is on a scale of 0 to 3. A weekly score (HSS7) is derived by adding up the average daily scores of the preceding 7 days, with a possible range of 0 - 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)

To confirm an overall dose-response signal based on MCP-Mod, and to estimate the minimal ligelizumab dose that shows a relevant superior effect over omalizumab, based on the selected dose response model, the lowest ligelizumab dose that provides a response rate 15% higher than the response of omalizumab 300 mg.

End point type	Primary

End point timeframe:

Week 12

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: percentage of participants				
number (confidence interval 95%)	30.2 (17.2 to 46.1)	51.2 (40.0 to 62.3)	42.4 (31.7 to 53.6)	25.9 (17.0 to 36.5)

End point values	Placebo s.c. q4w	QGE031 120 mg s.c. s.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 8.2)	19.0 (8.6 to 34.1)		

Statistical analyses

Statistical analysis title	Dose response Analysis
Statistical analysis description:	
Dose response relationship with respect to achievement of complete hives response. (HSS7=0)	
Comparison groups	QGE031 24 mg s.c. q4w v QGE031 72 mg s.c. q4w v QGE031 240 mg s.c. q4w v Omalizumab 300 mg s.c. q4w
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	
P-value	= 0 [1]
Method	Regression, Logistic
Parameter estimate	Estimated target dose
Point estimate	32.5
Confidence interval	
level	Other: 60 %
sides	2-sided
lower limit	27.5
upper limit	42.5

Notes:

[1] - The max statistic exceeds critical value (at the one-sided 5% alpha level), a dose response curve for the HSS7=0 at Week 12 was confirmed.

Secondary: Complete hives response (HSS7=0) rate at Week 12 measured over 7 days

End point title	Complete hives response (HSS7=0) rate at Week 12 measured over 7 days[2]

End point description:

Hives Severity Score (HSS) is on a scale of 0 to 3. A weekly score (HSS7) 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. Complete hives response defined as HSS7 = 0.

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)

End point type	Secondary

End point timeframe:

Week 12

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: Odds Ratio				
number (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	1.22 (0.54 to 2.74)	2.90 (1.52 to 5.55)	2.06 (1.08 to 3.95)	0 (0 to 0)
vs. Placebo|	39.13 (2.20 to 695.36)	93.03 (5.45 to 1586.70)	66.14 (3.88 to 1128.70)	32.07 (1.86 to 551.78)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Hives Severity Score (HSS7) at Week 12 measured over 7 days

End point title	Change from baseline in Hives Severity Score (HSS7) at Week 12 measured over 7 days[3]

End point description:

Hives Severity Score (HSS) is on a scale of 0 to 3. A weekly score (HSS7) 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.

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)

The median is for the treatment group difference.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	81	78	77
Units: Hodges-Lehmann median				
median (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	1.25 (-1.50 to 4.00)	-2.63 (-5.25 to 0.00)	-2.63 (-5.00 to -0.25)	0.00 (0.00 to 0.00)
vs placebo|	-1.75 (-5.00 to 1.50)	-5.50 (-8.50 to -2.50)	-5.75 (-8.25 to -3.25)	-3.00 (-6.00 to 0.00)

Statistical analyses

No statistical analyses for this end point

Secondary: HSS7=0 response: comparison between treatment groups at Week 20 measured over 7 days

End point title	HSS7=0 response: comparison between treatment groups at Week 20 measured over 7 days[4]

End point description:

Hives Severity Score (HSS) is on a scale of 0 to 3. A weekly score (HSS7) 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. Complete hives response defined as HSS7 = 0.

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)

End point type	Secondary

End point timeframe:

Week 20

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: Odds ratio				
number (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	0.64 (0.28 to 1.47)	2.00 (1.07 to 3.75)	1.56 (0.83 to 2.93)	0 (0 to 0)
vs. Placebo|	3.48 (1.00 to 12.12)	10.82 (3.51 to 33.32)	8.44 (2.74 to 26.03)	5.41 (1.74 to 16.81)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Hives Severity Score (HSS7) at Week 20 measured over 7 days

End point title	Change from baseline in Hives Severity Score (HSS7) at Week 20 measured over 7 days[5]

End point description:

Hives Severity Score (HSS) is on a scale of 0 to 3. A weekly score (HSS7) 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.

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)

The median is for the treatment group difference.

End point type	Secondary

End point timeframe:

Week 20

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	78	74	73
Units: Hodges-Lehmann median				
median (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	1.75 (-1.00 to 4.50)	-3.00 (-5.50 to -0.50)	-2.59 (-5.19 to 0.00)	0.0 (0.0 to 0.0)
vs. placebo|	-1.25 (-4.50 to 2.00)	-5.88 (-8.50 to -3.25)	-5.50 (-8.00 to -3.00)	-2.75 (-5.50 to 0.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Itch Severity Score (ISS7) at Week 12 measured over 7 days

End point title	Change from baseline in Itch Severity Score (ISS7) at Week 12 measured over 7 days[6]

End point description:

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) The median is for the treatment group difference.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	81	78	77
Units: Hodges-Lehmann median				
median (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	0.00 (-2.38 to 2.38)	-2.00 (-4.00 to 0.00)	-1.29 (-3.08 to 0.50)	0.00 (0.00 to 0.00)
vs. placebo|	-2.06 (-5.00 to 0.88)	-3.79 (-6.00 to -1.58)	-3.29 (-5.58 to -1.00)	-2.25 (-4.50 to 0.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Itch Severity Score (ISS7) at Week 20 measured over 7 days

End point title	Change from baseline in Itch Severity Score (ISS7) at Week 20 measured over 7 days[7]

End point description:

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)

The median is for the treatment group difference.

End point type	Secondary

End point timeframe:

Week 20

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	78	74	73
Units: Hodges-Lehmann median				
median (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	1.63 (-0.75 to 4.00)	-1.89 (-3.77 to 0.00)	-1.50 (-3.50 to 0.50)	0.00 (0.00 to 0.00)
vs. placebo|	-1.00 (-3.50 to 1.50)	-4.42 (-6.50 to -2.33)	-4.00 (-6.25 to -1.75)	-2.42 (-4.83 to 0.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Urticaria Activity Score (UAS7) at Week 12 measured over 7 days

End point title	Change from baseline in Urticaria Activity Score (UAS7) at Week 12 measured over 7 days[8]

End point description:

UAS7 is the sum of the HSS7 and the ISS7 scores. The possible range of the weekly UAS7 score is 0 to 42. The median is for the treatment group difference.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	81	78	77
Units: Hodges-Lehmann median				
median (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	1.50 (-4.00 to 7.00)	-4.50 (-8.50 to -0.50)	-4.00 (-8.00 to 0.00)	0.0 (0.0 to 0.0)
vs. placebo|	-3.88 (-10.00 to 2.25)	-9.75 (-14.75 to -4.75)	-9.50 (-14.00 to -5.00)	-5.13 (-10.00 to -0.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Urticaria Activity Score (UAS7) at Week 20 measured over 7 days

End point title	Change from baseline in Urticaria Activity Score (UAS7) at

	Week 20 measured over 7 days[9]

End point description:

UAS7 is the sum of the HSS7 and the ISS7 scores. The possible range of the weekly UAS7 score is 0 to 42. The median is for the treatment group difference.

End point type	Secondary

End point timeframe:

Week 20

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	78	74	73
Units: Hodges-Lehmann median				
median (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	3.75 (-1.50 to 9.00)	-5.00 (-9.00 to -1.00)	-3.96 (-8.00 to 0.08)	0.00 (0.00 to 0.00)
vs. Placebo|	-2.00 (-7.50 to 3.50)	-10.63 (-15.75 to -5.50)	-9.48 (-14.00 to -4.96)	-5.00 (-10.00 to 0.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Urticaria Activity Score Response (UAS7=0) rate at Week 12 measured over 7 days

End point title	Complete Urticaria Activity Score Response (UAS7=0) rate at Week 12 measured over 7 days[10]

End point description:

UAS7 is the sum of the HSS7 and the ISS7 scores. The possible range of the weekly UAS7 score is 0 to 42. Complete urticaria activity response is defined as UAS7 = 0.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: Odds ratio				
number (confidence interval 95%)				

vs. Omalizumab 300 mg s.c. q4w|	1.22 (0.54 to 2.75)	2.19 (1.14 to 4.19)	1.88 (0.98 to 3.61)	0.00 (0.0 to 0.00)
vs. placebo|	39.37 (2.21 to 700.09)	70.56 (4.13 to 1204.52)	60.62 (3.55 to 1035.53)	32.27 (1.87 to 555.57)

Statistical analyses

No statistical analyses for this end point

Secondary: UAS7=0 response: comparison between treatment groups at Week 20 measured over 7 days

End point title	UAS7=0 response: comparison between treatment groups at Week 20 measured over 7 days[11]

End point description:

UAS7 is the sum of the HSS7 and the ISS7 scores. The possible range of the weekly UAS7 score is 0 to 42. Complete urticaria activity response is defined as UAS7 = 0.

End point type	Secondary

End point timeframe:

Week 20

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: Odds ratio				
number (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	0.50 (0.20 to 1.25)	1.44 (0.76 to 2.75)	1.51 (0.79 to 2.87)	0.00 (0.00 to 0.00)
vs. Placebo|	4.86 (0.96 to 24.68)	13.90 (3.11 to 62.07)	14.52 (3.25 to 64.80)	9.64 (2.14 to 43.35)

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Itch Response (ISS7=0) rate at Week 12 measured over 7 days

End point title	Complete Itch Response (ISS7=0) rate at Week 12 measured over 7 days[12]

End point description:

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. Complete itch response defined as ISS7 = 0.

Itch Severity Score scale:

0 - None
1 - Mild (minimal awareness, easily tolerated)
2 - Moderate (definite awareness, bothersome but tolerable)
3 - Severe (difficult to tolerate)

End point type	Secondary

End point timeframe:

Week 12

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: Odds Ratio				
number (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	1.54 (0.71 to 3.33)	2.15 (1.14 to 4.06)	1.75 (0.92 to 3.31)	0 (0 to 0)
vs. Placebo|	13.60 (2.88 to 64.22)	19.02 (4.29 to 84.33)	15.46 (3.48 to 68.59)	8.85 (1.97 to 39.72)

Statistical analyses

No statistical analyses for this end point

Secondary: ISS7=0 response: comparison between treatment groups at Week 20 measured over 7 days

End point title	ISS7=0 response: comparison between treatment groups at Week 20 measured over 7 days[13]

End point description:

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. Complete itch response defined as ISS7 = 0.

Itch Severity Score scale:
0 - None
1 - Mild (minimal awareness, easily tolerated)
2 - Moderate (definite awareness, bothersome but tolerable)
3 - Severe (difficult to tolerate)

End point type	Secondary

End point timeframe:

Week 20

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the ligelizumab 120 mg single dose treatment arm were not included in this analysis.

End point values	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	84	85	85
Units: Odds ratio				
number (confidence interval 95%)				
vs. Omalizumab 300 mg s.c. q4w|	0.45 (0.18 to 1.12)	1.43 (0.76 to 2.70)	1.48 (0.79 to 2.80)	0 (0 to 0)
vs. Placebo|	3.13 (0.76 to 12.86)	9.86 (2.79 to 34.81)	10.25 (2.90 to 36.18)	6.91 (1.94 to 24.57)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	QGE031 24 mg q4w
Reporting group description:	
ligelizumab 24 mg injection subcutaneous every 4 weeks	
Reporting group title	QGE031 72 mg q4w
Reporting group description:	
ligelizumab 72 mg injection subcutaneous every 4 weeks	
Reporting group title	QGE031 240 mg q4w
Reporting group description:	
ligelizumab 240 mg injection subcutaneous every 4 weeks	
Reporting group title	Omalizumab 300 mg q4w
Reporting group description:	
omalizumab 300 mg injection subcutaneous every 4 weeks	
Reporting group title	Placebo q4w
Reporting group description:	
placebo injection subcutaneous every 4 weeks	
Reporting group title	QGE031 120 mg s.d.
Reporting group description:	
ligelizumab 120 mg injection subcutaneous single dose	

Serious adverse events	QGE031 24 mg q4w	QGE031 72 mg q4w	QGE031 240 mg q4w
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 43 (6.98%)	2 / 84 (2.38%)	2 / 85 (2.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign lung neoplasm			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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 neoplasm			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 85 (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
Haemangioma of liver			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fractured coccyx			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 85 (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
Radius fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Abdominal pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Colon dysplasia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (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
Inguinal hernia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Hepatic cyst			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Hepatitis acute			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (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
Prurigo			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Urticaria			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (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
Sjogren's syndrome			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (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

Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (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
Pilonidal cyst			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 85 (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

Serious adverse events	Omalizumab 300 mg q4w	Placebo q4w	QGE031 120 mg s.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 85 (3.53%)	4 / 43 (9.30%)	4 / 42 (9.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign lung neoplasm			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast neoplasm			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Haemangioma of liver			

subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fractured coccyx			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Radius fracture			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	0 / 42 (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			
Angina pectoris			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Abdominal pain			

subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Colon dysplasia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Diverticular perforation			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Inguinal hernia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Subileus			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	0 / 42 (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			
Cholelithiasis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Hepatic cyst			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Hepatitis acute			

subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Prurigo			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	0 / 42 (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
Urticaria			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (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
Sjogren's syndrome			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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			
Diverticulitis			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Pilonidal cyst			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	0 / 42 (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

Pneumonia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	QGE031 24 mg q4w	QGE031 72 mg q4w	QGE031 240 mg q4w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 43 (55.81%)	45 / 84 (53.57%)	46 / 85 (54.12%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	3 / 85 (3.53%)
occurrences (all)	1	3	3
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 43 (2.33%)	5 / 84 (5.95%)	2 / 85 (2.35%)
occurrences (all)	1	5	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 43 (4.65%)	5 / 84 (5.95%)	2 / 85 (2.35%)
occurrences (all)	2	6	2
Headache			
subjects affected / exposed	7 / 43 (16.28%)	9 / 84 (10.71%)	7 / 85 (8.24%)
occurrences (all)	12	11	10
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	5 / 85 (5.88%)
occurrences (all)	0	2	7
Injection site reaction			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	6 / 85 (7.06%)
occurrences (all)	0	4	9
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 43 (4.65%)	4 / 84 (4.76%)	5 / 85 (5.88%)
occurrences (all)	2	4	5
Gastritis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	2 / 85 (2.35%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 43 (2.33%)	5 / 84 (5.95%)	4 / 85 (4.71%)
occurrences (all)	1	6	4
Urticaria			
subjects affected / exposed	1 / 43 (2.33%)	9 / 84 (10.71%)	3 / 85 (3.53%)
occurrences (all)	2	10	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 43 (2.33%)	6 / 84 (7.14%)	1 / 85 (1.18%)
occurrences (all)	1	6	3
Back pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 85 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	4 / 85 (4.71%)
occurrences (all)	1	4	4
Upper respiratory tract infection			
subjects affected / exposed	7 / 43 (16.28%)	7 / 84 (8.33%)	10 / 85 (11.76%)
occurrences (all)	8	8	12
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)	5 / 84 (5.95%)	4 / 85 (4.71%)
occurrences (all)	0	6	4
Viral upper respiratory tract infection			
subjects affected / exposed	7 / 43 (16.28%)	13 / 84 (15.48%)	17 / 85 (20.00%)
occurrences (all)	12	19	20

Non-serious adverse events	Omalizumab 300 mg q4w	Placebo q4w	QGE031 120 mg s.d.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 85 (51.76%)	30 / 43 (69.77%)	28 / 42 (66.67%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 85 (2.35%)	4 / 43 (9.30%)	1 / 42 (2.38%)
occurrences (all)	3	5	1
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 85 (2.35%)	3 / 43 (6.98%)	3 / 42 (7.14%)
occurrences (all)	2	4	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 85 (2.35%)	4 / 43 (9.30%)	0 / 42 (0.00%)
occurrences (all)	4	5	0
Headache			
subjects affected / exposed	12 / 85 (14.12%)	7 / 43 (16.28%)	1 / 42 (2.38%)
occurrences (all)	14	20	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 85 (7.06%)	2 / 43 (4.65%)	2 / 42 (4.76%)
occurrences (all)	6	3	2
Gastritis			
subjects affected / exposed	0 / 85 (0.00%)	0 / 43 (0.00%)	3 / 42 (7.14%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	5 / 85 (5.88%)	2 / 43 (4.65%)	1 / 42 (2.38%)
occurrences (all)	5	2	1
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	2 / 85 (2.35%)	1 / 43 (2.33%)	3 / 42 (7.14%)
occurrences (all)	2	1	4
Urticaria			
subjects affected / exposed	4 / 85 (4.71%)	5 / 43 (11.63%)	7 / 42 (16.67%)
occurrences (all)	4	19	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 85 (2.35%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	2	1	1
Back pain			
subjects affected / exposed	1 / 85 (1.18%)	1 / 43 (2.33%)	3 / 42 (7.14%)
occurrences (all)	1	1	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 85 (5.88%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	5	1	0
Influenza			
subjects affected / exposed	5 / 85 (5.88%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	5	1	1
Upper respiratory tract infection			
subjects affected / exposed	10 / 85 (11.76%)	6 / 43 (13.95%)	9 / 42 (21.43%)
occurrences (all)	13	9	13
Urinary tract infection			
subjects affected / exposed	5 / 85 (5.88%)	0 / 43 (0.00%)	2 / 42 (4.76%)
occurrences (all)	5	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	17 / 85 (20.00%)	13 / 43 (30.23%)	10 / 42 (23.81%)
occurrences (all)	24	18	15

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2015	This amendment was generated to correct a typographical error of the EUDRACT number on the cover page of the protocol.
24 March 2015	This amendment was generated to update barrier methods of contraception in the exclusion criteria to reflect the latest recommendations related to acceptable forms of contraception in the study.
09 February 2016	This amendment: a. introduced a futility analysis prior to Week 12 analysis, b. clarified the dosing scheme for H1- antihistamine, receptor blockers in accordance to local health authority guidance, c. included updated generic SAE reporting language per clinical trial protocol template change, d. also included removal of multiple biomarkers assays and other editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported