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

Summary

EudraCT number	2018-000839-28
Trial protocol	FR HU DK ES DE SE AT GR CZ BG PL HR
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	CQGE031C2302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03580369
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	Study Director, Novartis Pharmaceuticals, 1 (862) 778-8300, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001811-PIP02-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 June 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:

The main purpose of this trial was to demonstrate that ligelizumab (72 mg q4w and/or 120 mg q4w) is superior to placebo and superior to omalizumab 300 mg q4w measured by 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	17 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	Austria: 10
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Poland: 52
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Argentina: 53
Country: Number of subjects enrolled	Brazil: 28
Country: Number of subjects enrolled	Canada: 39
Country: Number of subjects enrolled	Colombia: 13
Country: Number of subjects enrolled	Guatemala: 12
Country: Number of subjects enrolled	India: 42
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 99
Country: Number of subjects enrolled	Malaysia: 23
Country: Number of subjects enrolled	Oman: 8
Country: Number of subjects enrolled	Peru: 16
Country: Number of subjects enrolled	Singapore: 11
Country: Number of subjects enrolled	South Africa: 38
Country: Number of subjects enrolled	Thailand: 30
Country: Number of subjects enrolled	United States: 162
Country: Number of subjects enrolled	Czechia: 31

Country: Number of subjects enrolled	Germany: 118
Country: Number of subjects enrolled	Greece: 28
Country: Number of subjects enrolled	Bulgaria: 27
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	Croatia: 5
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Russian Federation: 97
Country: Number of subjects enrolled	Turkey: 40
Worldwide total number of subjects	1072
EEA total number of subjects	361

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)	38
Adults (18-64 years)	971
From 65 to 84 years	63
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

1,072 participants enrolled at 164 sites in 28 countries

Pre-assignment

Screening details:

There were 1,034 adult subjects and 38 adolescent subjects

Period 1

Period 1 title	Overall period (overall 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

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	QGE031
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

liquid in vial for subcutaneous injection

Arm title	Ligelizumab 120 mg

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	QGE031
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

liquid in vial for subcutaneous injection

Arm title	Omalizumab 300 mg

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:

liquid in vial for subcutaneous injection

Arm title	Placebo - QGE031 120mg

Arm description:

Placebo and 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	Placebo + drug
Investigational medicinal product code	placebo + QGE031
Other name	placebo + QGE031
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

liquid in vial for subcutaneous injection

Number of subjects in period 1	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg
Started	317	324	322
Completed	273	267	277
Not completed	44	57	45
Physician decision	4	5	1
Consent withdrawn by subject	19	17	17
Adverse event, non-fatal	7	15	6
Technical problems	-	-	1
No treatment due to mis-randomization	1	-	3
Pregnancy	2	3	2
Reason unknown	-	1	-
Lost to follow-up	2	2	3
Lack of efficacy	3	7	2
Protocol deviation	6	7	10

Number of subjects in period 1	Placebo - QGE031 120mg
Started	109
Completed	94
Not completed	15
Physician decision	-
Consent withdrawn by subject	7
Adverse event, non-fatal	1

Technical problems	2
No treatment due to mis-randomization	-
Pregnancy	-
Reason unknown	-
Lost to follow-up	1
Lack of efficacy	3
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Ligelizumab 72 mg
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
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
Reporting group description:	
Omalizumab 300 mg arm: 2 injections of 1.2 mL omalizumab q4w	
Reporting group title	Placebo - QGE031 120mg
Reporting group description:	
Placebo and Ligelizumab 120 mg arm: 1 injection of 1.0 mL ligelizumab + 1 injection of 1.0 mL ligelizumab placebo q4w	

Reporting group values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg
Number of subjects	317	324	322
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
<=18 years	10	12	13
Between 18 and 65 years	288	297	291
>=65 years	19	15	18
Age Continuous			
Units: Years			
arithmetic mean	43.3	42.3	42.2
standard deviation	± 13.12	± 13.48	± 13.19
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	217	226	218
Adolescent|Female	5	9	9
Adult|Male	90	86	91
Adolescent|Male	5	3	4
Race/Ethnicity, Customized			
All participants: Adult and Adolescent			
Units: Subjects			
Adult White	226	220	221
Adolescent White	8	8	8
Adult Black or African American	1	4	9
Adolescent Black or African American	0	1	0
Adult Asian	60	72	64
Adolescent Asian	0	3	2
Adult Native Hawaiian or Other Pacific Islander	0	1	0

Adolescent Native Hawaiian or Pacific Islander	0	0	0
Adult Native American	12	10	9
Adolescents Native American	2	0	3
Adult Multi-racial	6	4	6
Adolescent Multi-racial	0	0	0
Adult Race Not Reported	2	1	0
Adolescent Race Not Reported	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	15.1	14.6	14.7
standard deviation	± 1.62	± 2.01	± 1.65

Reporting group values	Placebo - QGE031 120mg	Total	
Number of subjects	109	1072	
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
<=18 years	3	38	
Between 18 and 65 years	95	971	
>=65 years	11	63	
Age Continuous			
Units: Years			
arithmetic mean	0		
standard deviation	± 0	-	
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	76	737	
Adolescent|Female	1	24	
Adult|Male	30	297	
Adolescent|Male	2	14	
Race/Ethnicity, Customized			
All participants: Adult and Adolescent			
Units: Subjects			
Adult White	80	747	
Adolescent White	2	26	
Adult Black or African American	1	15	
Adolescent Black or African American	0	1	
Adult Asian	22	218	
Adolescent Asian	0	5	
Adult Native Hawaiian or Other Pacific Islander	0	1	
Adolescent Native Hawaiian or Pacific Islander	0	0	
Adult Native American	3	34	
Adolescents Native American	1	6	
Adult Multi-racial	0	16	
Adolescent Multi-racial	0	0	
Adult Race Not Reported	0	3	
Adolescent Race Not Reported	0	0	

Age Continuous Units: Years arithmetic mean standard deviation	±	-	

Subject analysis sets

Subject analysis set title	Placebo
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
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
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
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	Placebo	Placebo	Placebo
Number of subjects	109	106	2
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
<=18 years	3		
Between 18 and 65 years	95		
>=65 years	11		
Age Continuous Units: Years			
arithmetic mean	43.2		
standard deviation	± 14.06	±	±
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female	76		
Adolescent|Female	2		
Adult|Male	30		
Adolescent|Male	1		

Race/Ethnicity, Customized			
All participants: Adult and Adolescent			
Units: Subjects			
Adult White	80		
Adolescent White	2		
Adult Black or African American	1		
Adolescent Black or African American	0		
Adult Asian	22		
Adolescent Asian	0		
Adult Native Hawaiian or Other Pacific Islander	0		
Adolescent Native Hawaiian or Pacific Islander	0		
Adult Native American	3		
Adolescents Native American	1		
Adult Multi-racial	0		
Adolescent Multi-racial	0		
Adult Race Not Reported	0		
Adolescent Race Not Reported	0		
Age Continuous			
Units: Years			
arithmetic mean	15.3		
standard deviation	± 2.08	±	±

Reporting group values	Placebo		
Number of subjects	3		
Age Categorical			
Adults (971+63=1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
<=18 years			
Between 18 and 65 years			
>=65 years			
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	±		
Sex: Female, Male			
Adults (1,034) + Adolescents (38) = Total (1,072)			
Units: Participants			
Adult|Female			
Adolescent|Female			
Adult|Male			
Adolescent|Male			
Race/Ethnicity, Customized			
All participants: Adult and Adolescent			
Units: Subjects			
Adult White			
Adolescent White			
Adult Black or African American			
Adolescent Black or African American			
Adult Asian			

Adolescent Asian Adult Native Hawaiian or Other Pacific Islander Adolescent Native Hawaiian or Pacific Islander Adult Native American Adolescents Native American Adult Multi-racial Adolescent Multi-racial Adult Race Not Reported Adolescent Race Not Reported			
Age Continuous Units: Years arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	Ligelizumab 72 mg

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

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

Reporting group description:

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

Reporting group title	Placebo - QGE031 120mg

Reporting group description:

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

Subject analysis set title	Placebo
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
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
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
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 (FAS) Within treatment

End point title	Mean change from baseline in UAS7 at Week 12 (Multiple imputation) of Adult subjects (FAS) Within treatment[1]

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. Possible range of weekly UAS7 score is 0 to 42. Complete UAS7 response is defined as UAS7 = 0.

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. 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) is on a scale of 0 to 3. Weekly score (ISS7) is derived by adding up average daily scores of the 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)

End point type	Primary

End point timeframe:

Week 12

Notes:

[1] - 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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	306	312	306	106
Units: score				
least squares mean (standard error)	-19.368 (± 0.668)	-19.330 (± 0.660)	-20.040 (± 0.663)	-11.366 (± 1.129)

Statistical analyses

Statistical analysis title	Ligelizumab 72 mg vs Placebo Adults

Statistical analysis description:

Treatment contrast in LS mean (change), Adults

Comparison groups	Ligelizumab 72 mg v Placebo
Number of subjects included in analysis	412
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-8.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.576
upper limit	-5.428
Variability estimate	Standard error of the mean
Dispersion value	1.313

Notes:

[2] - Linear mixed model with repeated measures (MMRM)

Statistical analysis title	Ligelizumab 72 mg, Omalizumab 300 mg

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	612
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.7628
Method	Mixed models analysis
Parameter estimate	LS mean
Point estimate	0.672
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.169
upper limit	2.513
Variability estimate	Standard error of the mean
Dispersion value	0.939

Notes:

[3] - Linear mixed model with repeated measures (MMRM)

Statistical analysis title	Ligelizumab 120 mg, Placebo

Statistical analysis description:

Treatment contrast in LS mean (change), Adults

Comparison groups	Ligelizumab 120 mg v Placebo
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-7.964
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.522
upper limit	-5.047
Variability estimate	Standard error of the mean
Dispersion value	1.305

Notes:

[4] - Linear mixed model with repeated measures (MMRM)

Statistical analysis title	Ligelizumab 120 mg, Omalizumab 300 mg

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	618
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.7768
Method	Mixed models analysis
Parameter estimate	LS mean
Point estimate	0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.118
upper limit	2.538
Variability estimate	Standard error of the mean
Dispersion value	0.933

Notes:

[5] - Linear mixed model with repeated measures (MMRM)

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

End point title	Mean change from baseline in UAS7 at Week 12 (observed data) of Adolescent subjects (FAS) Within treatment[6][7]

End point description:

UAS7 up to end of study (Observed data) for adolescents. No Statistical Analysis was planned for adolescent population.

UAS is the sum of the HSS and the ISS. UAS7 is the sum of the HSS7 and the ISS7 scores. Possible range of weekly UAS7 score is 0 to 42. Complete UAS7 response is defined as UAS7 = 0.

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. 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)

ISS is on a scale of 0 to 3. Weekly score (ISS7) is derived by adding up average daily scores of the 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).

End point type	Primary

End point timeframe:

Week 12

Notes:

[6] - 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 were planned.

[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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	10	12	2
Units: score				
arithmetic mean (standard deviation)	-17.39 (± 13.070)	-14.64 (± 14.662)	-13.84 (± 15.343)	-12.75 (± 18.738)

Statistical analyses

No statistical analyses for this end point

Secondary: Number and proportion of subjects with UAS7=0 response at Week 12

(Multiple imputation)	
End point title	Number and proportion of subjects with UAS7=0 response at Week 12 (Multiple imputation)[8]

End point description:

No Statistical analysis was planed for adolescent group.

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.

Complete absence of hives and itch at Week 12

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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	306	312	116	106
Units: Participants				
Adults	102	104	116	8
Adolescents	3	3	0	1

Statistical analyses

Statistical analysis title	Ligelizumab 72 mg, Placebo

Statistical analysis description:

Wald chi-square test based on logistic regression

Comparison groups	Ligelizumab 72 mg v Placebo
Number of subjects included in analysis	412
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.667
upper limit	12.095

Notes:

[9] - 95% confidence interval for the odds ratio

Statistical analysis title	Ligelizumab 72 mg vs Omalizumab 300 mg

Statistical analysis description:

Wald chi-square test based on logistic regression

Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.843
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.598
upper limit	1.18

Notes:

[10] - 95% confidence interval for the odds ratio

Statistical analysis title	Ligelizumab 120 mg vs Placebo
Statistical analysis description:	
Wald chi-square test based on logistic regression	
Comparison groups	Ligelizumab 120 mg v Placebo
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.734
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.694
upper limit	12.207

Notes:

[11] - 95% confidence interval for the odds ratio

Statistical analysis title	Ligelizumab 120 mg vs Omalizumab 300 mg
Statistical analysis description:	
Wald chi-square test based on logistic regression	
Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	428
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.8312
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.848

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.605
upper limit	1.188

Notes:

[12] - 95% confidence interval for the odds ratio

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)[13]

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)

End point type	Secondary

End point timeframe:

Week 12

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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	306	312	306	106
Units: score				
least squares mean (standard error)	-8.502 (± 0.305)	-8.532 (± 0.301)	-8.921 (± 0.302)	-5.402 (± 0.514)

Statistical analyses

Statistical analysis title	Ligelizumab 120 mg vs Placebo

Statistical analysis description:

Treatment contrast in LS mean (change), Adults

Comparison groups	Ligelizumab 120 mg v Placebo
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-3.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.271
upper limit	-1.929
Variability estimate	Standard error of the mean
Dispersion value	0.597

Notes:

[14] - Linear mixed model with repeated measures (MMRM)

Statistical analysis title	Ligelizumab 72 mg vs Placebo
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	612
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.8366
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	0.419
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.419
upper limit	1.258
Variability estimate	Standard error of the mean
Dispersion value	0.428

Notes:

[15] - Linear mixed model with repeated measures (MMRM)

Statistical analysis title	Ligelizumab 120 mg vs Placebo
Statistical analysis description:	
Treatment contrast in LS mean (change), Adults	
Comparison groups	Ligelizumab 120 mg v Placebo
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-3.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.295
upper limit	-1.966
Variability estimate	Standard error of the mean
Dispersion value	0.594

Notes:
[16] - Adults

Statistical analysis title	Ligelizumab 120 mg vs Omalizumab 300 mg

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	618
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.8201
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	0.389
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.444
upper limit	1.222
Variability estimate	Standard error of the mean
Dispersion value	0.425

Notes:
[17] - Linear mixed model with repeated measures (MMRM)

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)[18]

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)

No Statistical Analysis was planned for adolescent population.

End point type	Secondary

End point timeframe:
Week 12

Notes:
[18] - 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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	10	12	2
Units: score				
arithmetic mean (standard deviation)	-8.40 (± 6.779)	-6.82 (± 7.404)	-5.10 (± 7.153)	-7.00 (± 9.899)

Statistical analyses

No statistical analyses for this end point

Secondary: Number and Proportion of participants with DLQI score of 0 – 1 at Week 12 (no impact on subject's quality of life)

End point title	Number and Proportion of participants with DLQI score of 0 – 1 at Week 12 (no impact on subject's quality of life)[19]

End point description:

Assessed as percentage of subjects achieving DLQI = 0-1

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.
No statistical anaylsis was planned for adolescent group.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[19] - 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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	306	312	306	106
Units: Participants				
Adults	133	150	147	22
Adolescents	3	6	2	1

Statistical analyses

Statistical analysis title	Ligelizumab 72 mg vs Placebo

Statistical analysis description:

Wald chi-square test based on logistic regression

Comparison groups	Ligelizumab 72 mg v Placebo

Number of subjects included in analysis	412
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.747
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.621
upper limit	4.656

Notes:

[20] - 95% confidence interval for the odds ratio

Statistical analysis title	Ligelizumab 72 mg vs Omalizumab 300 mg
Statistical analysis description:	
Wald chi-square test based on logistic regression	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.8586
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.836
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.603
upper limit	1.159

Notes:

[21] - 95% confidence interval for the odds ratio

Statistical analysis title	Ligelizumab 120 mg vs Placebo
Statistical analysis description:	
Wald chi-square test based on logistic regression	
Comparison groups	Ligelizumab 120 mg v Placebo
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.261
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.929
upper limit	5.513

Notes:

[22] - 95% confidence interval for the odds ratio

Statistical analysis title	Ligelizumab 120 mg vs Omalizumab 300 mg

Statistical analysis description:

Wald chi-square test based on logistic regression

Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.519
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.992
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.717
upper limit	1.373

Notes:

[23] - 95% confidence interval for the odds ratio

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)[24]

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:

Week 12

Notes:

[24] - 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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	306	312	306	106
Units: Weeks				
least squares mean (standard error)	8.568 (± 0.235)	8.912 (± 0.239)	8.790 (± 0.239)	6.475 (± 0.327)

Statistical analyses

Statistical analysis title	Ligelizumab 72 mg vs Placebo
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Placebo
Number of subjects included in analysis	412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.323
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.183
upper limit	1.48

Statistical analysis title	Ligelizumab 120 mg vs Placebo
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Placebo
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.376
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	1.54

Statistical analysis title	Ligelizumab 120 mg vs Omalizumab 300 mg
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 120 mg v Omalizumab 300 mg
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3586
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	1.014

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.941
upper limit	1.092

Statistical analysis title	Ligelizumab 120 mg vs Omalizumab 300 mg
Statistical analysis description:	
Adults	
Comparison groups	Ligelizumab 72 mg v Omalizumab 300 mg
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7469
Method	Negative binomial regression model
Parameter estimate	Risk ratio (RR)
Point estimate	0.975
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.904
upper limit	1.051

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)[25]

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:

Week 12

Notes:

[25] - 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: No statistical analysis were planned.

End point values	Ligelizumab 72 mg	Ligelizumab 120 mg	Omalizumab 300 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	8	10	1
Units: Weeks				
least squares mean (standard error)	6.0 (± 4.94)	7.3 (± 5.44)	9.0 (± 3.50)	11.0 (± 0.00)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events (AEs) and Serious Adverse Events (SAEs) were collected after signature of the informed consent form until 30 days after last dose of study treatment, and up to 52 weeks.	
Adverse event reporting additional description:	
AEs and SAEs are any untoward sign or symptom that occurs during the study treatment period and up to 52 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	22 / 316 (6.96%)	32 / 324 (9.88%)	23 / 319 (7.21%)
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 salivary gland neoplasm			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Bladder cancer			

subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 316 (0.00%)	2 / 324 (0.62%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Abortion spontaneous			
subjects affected / exposed	1 / 316 (0.32%)	2 / 324 (0.62%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	1 / 316 (0.32%)	2 / 324 (0.62%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	0 / 319 (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
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Respiratory, thoracic and mediastinal disorders			
Paranasal cyst			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Investigations			
Weight increased			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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			
Clavicle fracture			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			

subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	2 / 319 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Joint dislocation			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Ligament sprain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Muscle strain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Pelvic fracture			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Road traffic accident			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Spinal column injury			

subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Tendon rupture			
subjects affected / exposed	1 / 316 (0.32%)	1 / 324 (0.31%)	0 / 319 (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
Toxicity to various agents			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Angina pectoris			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Atrial fibrillation			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Cardiomyopathy			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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

Coronary artery occlusion			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Myocardial infarction			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Headache			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Loss of consciousness			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	0 / 319 (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
Syncope			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Gastrointestinal disorders			
Abdominal adhesions			

subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Gastritis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Intestinal obstruction			
subjects affected / exposed	1 / 316 (0.32%)	1 / 324 (0.31%)	0 / 319 (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
Oesophagitis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Pancreatitis chronic			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Cholelithiasis			

subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 316 (0.32%)	2 / 324 (0.62%)	0 / 319 (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
Chronic spontaneous urticaria			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Urticaria			
subjects affected / exposed	1 / 316 (0.32%)	2 / 324 (0.62%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Intervertebral disc protrusion			
subjects affected / exposed	3 / 316 (0.95%)	0 / 324 (0.00%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoarthritis			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Osteonecrosis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Bronchitis			
subjects affected / exposed	0 / 316 (0.00%)	2 / 324 (0.62%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	0 / 316 (0.00%)	3 / 324 (0.93%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	2 / 319 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Gastrointestinal infection			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Kidney infection			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	0 / 319 (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
Nasopharyngitis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	0 / 319 (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
Paronychia			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Pneumonia			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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
Pneumonia bacterial			

subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Pyelonephritis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 324 (0.00%)	0 / 319 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	0 / 316 (0.00%)	0 / 324 (0.00%)	1 / 319 (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 respiratory tract infection			
subjects affected / exposed	0 / 316 (0.00%)	1 / 324 (0.31%)	0 / 319 (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
Urinary tract infection			
subjects affected / exposed	2 / 316 (0.63%)	1 / 324 (0.31%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	1 / 2	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	3 / 109 (2.75%)	4 / 102 (3.92%)	
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)			
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bladder cancer			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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			
Paranasal cyst			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight increased			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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			
Clavicle fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			

subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			

subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Coronary artery occlusion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 109 (0.92%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			

subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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			
Angioedema			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic spontaneous urticaria			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
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 / 102 (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	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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 / 102 (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 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (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	178 / 316 (56.33%)	182 / 324 (56.17%)	206 / 319 (64.58%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 316 (2.53%)	10 / 324 (3.09%)	5 / 319 (1.57%)
occurrences (all)	10	11	6
Blood creatinine increased			

subjects affected / exposed	6 / 316 (1.90%)	8 / 324 (2.47%)	11 / 319 (3.45%)
occurrences (all)	6	9	13
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 316 (1.90%)	8 / 324 (2.47%)	4 / 319 (1.25%)
occurrences (all)	7	9	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 316 (0.95%)	7 / 324 (2.16%)	4 / 319 (1.25%)
occurrences (all)	3	7	5
SARS-CoV-2 test negative			
subjects affected / exposed	2 / 316 (0.63%)	7 / 324 (2.16%)	7 / 319 (2.19%)
occurrences (all)	2	9	7
SARS-CoV-2 test positive			
subjects affected / exposed	5 / 316 (1.58%)	5 / 324 (1.54%)	8 / 319 (2.51%)
occurrences (all)	5	5	8
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	7 / 316 (2.22%)	1 / 324 (0.31%)	4 / 319 (1.25%)
occurrences (all)	11	1	5
Ligament sprain			
subjects affected / exposed	1 / 316 (0.32%)	3 / 324 (0.93%)	7 / 319 (2.19%)
occurrences (all)	1	3	8
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 316 (1.58%)	6 / 324 (1.85%)	8 / 319 (2.51%)
occurrences (all)	5	6	8
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 316 (3.80%)	8 / 324 (2.47%)	2 / 319 (0.63%)
occurrences (all)	15	20	2
Headache			
subjects affected / exposed	40 / 316 (12.66%)	30 / 324 (9.26%)	39 / 319 (12.23%)
occurrences (all)	66	68	61
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	4 / 316 (1.27%)	6 / 324 (1.85%)	8 / 319 (2.51%)
occurrences (all)	4	6	10
Injection site pain			
subjects affected / exposed	12 / 316 (3.80%)	10 / 324 (3.09%)	4 / 319 (1.25%)
occurrences (all)	35	24	10
Injection site erythema			
subjects affected / exposed	8 / 316 (2.53%)	14 / 324 (4.32%)	5 / 319 (1.57%)
occurrences (all)	17	29	9
Injection site reaction			
subjects affected / exposed	15 / 316 (4.75%)	15 / 324 (4.63%)	7 / 319 (2.19%)
occurrences (all)	23	21	9
Injection site swelling			
subjects affected / exposed	7 / 316 (2.22%)	8 / 324 (2.47%)	3 / 319 (0.94%)
occurrences (all)	14	16	8
Pyrexia			
subjects affected / exposed	13 / 316 (4.11%)	11 / 324 (3.40%)	12 / 319 (3.76%)
occurrences (all)	15	12	15
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 316 (0.32%)	6 / 324 (1.85%)	9 / 319 (2.82%)
occurrences (all)	2	7	13
Abdominal pain upper			
subjects affected / exposed	7 / 316 (2.22%)	5 / 324 (1.54%)	8 / 319 (2.51%)
occurrences (all)	10	5	8
Diarrhoea			
subjects affected / exposed	10 / 316 (3.16%)	9 / 324 (2.78%)	18 / 319 (5.64%)
occurrences (all)	10	11	19
Nausea			
subjects affected / exposed	8 / 316 (2.53%)	9 / 324 (2.78%)	10 / 319 (3.13%)
occurrences (all)	14	12	14
Toothache			
subjects affected / exposed	4 / 316 (1.27%)	9 / 324 (2.78%)	5 / 319 (1.57%)
occurrences (all)	7	10	5
Vomiting			

subjects affected / exposed	4 / 316 (1.27%)	2 / 324 (0.62%)	2 / 319 (0.63%)
occurrences (all)	4	2	2
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 316 (0.95%)	8 / 324 (2.47%)	6 / 319 (1.88%)
occurrences (all)	3	11	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 316 (3.16%)	12 / 324 (3.70%)	14 / 319 (4.39%)
occurrences (all)	10	15	18
Oropharyngeal pain			
subjects affected / exposed	9 / 316 (2.85%)	7 / 324 (2.16%)	18 / 319 (5.64%)
occurrences (all)	9	8	21
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 316 (0.95%)	8 / 324 (2.47%)	0 / 319 (0.00%)
occurrences (all)	3	8	0
Angioedema			
subjects affected / exposed	4 / 316 (1.27%)	9 / 324 (2.78%)	7 / 319 (2.19%)
occurrences (all)	10	16	22
Chronic spontaneous urticaria			
subjects affected / exposed	4 / 316 (1.27%)	6 / 324 (1.85%)	12 / 319 (3.76%)
occurrences (all)	7	19	14
Eczema			
subjects affected / exposed	6 / 316 (1.90%)	8 / 324 (2.47%)	11 / 319 (3.45%)
occurrences (all)	8	11	12
Dermatitis contact			
subjects affected / exposed	4 / 316 (1.27%)	4 / 324 (1.23%)	9 / 319 (2.82%)
occurrences (all)	5	4	9
Urticaria			
subjects affected / exposed	17 / 316 (5.38%)	15 / 324 (4.63%)	10 / 319 (3.13%)
occurrences (all)	20	20	12
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	9 / 316 (2.85%)	19 / 324 (5.86%)	16 / 319 (5.02%)
occurrences (all)	9	23	18
Back pain			
subjects affected / exposed	12 / 316 (3.80%)	9 / 324 (2.78%)	16 / 319 (5.02%)
occurrences (all)	15	13	17
Myalgia			
subjects affected / exposed	2 / 316 (0.63%)	5 / 324 (1.54%)	7 / 319 (2.19%)
occurrences (all)	2	5	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 316 (1.90%)	3 / 324 (0.93%)	7 / 319 (2.19%)
occurrences (all)	6	3	7
COVID-19			
subjects affected / exposed	9 / 316 (2.85%)	5 / 324 (1.54%)	12 / 319 (3.76%)
occurrences (all)	9	5	14
Gastroenteritis			
subjects affected / exposed	9 / 316 (2.85%)	5 / 324 (1.54%)	6 / 319 (1.88%)
occurrences (all)	10	5	6
Influenza			
subjects affected / exposed	6 / 316 (1.90%)	7 / 324 (2.16%)	11 / 319 (3.45%)
occurrences (all)	7	8	12
Nasopharyngitis			
subjects affected / exposed	35 / 316 (11.08%)	32 / 324 (9.88%)	38 / 319 (11.91%)
occurrences (all)	43	46	50
Sinusitis			
subjects affected / exposed	6 / 316 (1.90%)	8 / 324 (2.47%)	6 / 319 (1.88%)
occurrences (all)	6	8	7
Rhinitis			
subjects affected / exposed	1 / 316 (0.32%)	1 / 324 (0.31%)	7 / 319 (2.19%)
occurrences (all)	1	2	7
Upper respiratory tract infection			
subjects affected / exposed	20 / 316 (6.33%)	24 / 324 (7.41%)	28 / 319 (8.78%)
occurrences (all)	25	35	36
Urinary tract infection			
subjects affected / exposed	11 / 316 (3.48%)	10 / 324 (3.09%)	12 / 319 (3.76%)
occurrences (all)	14	15	14

Non-serious adverse events	Placebo only	Transitioned to QGE031 120mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 109 (34.86%)	43 / 102 (42.16%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 109 (0.00%)	3 / 102 (2.94%)	
occurrences (all)	0	4	
Blood creatinine increased			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 109 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	2	
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 109 (0.92%)	1 / 102 (0.98%)	
occurrences (all)	1	1	
Ligament sprain			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 109 (1.83%)	1 / 102 (0.98%)	
occurrences (all)	2	1	
Nervous system disorders			

Dizziness			
subjects affected / exposed	2 / 109 (1.83%)	1 / 102 (0.98%)	
occurrences (all)	5	1	
Headache			
subjects affected / exposed	6 / 109 (5.50%)	4 / 102 (3.92%)	
occurrences (all)	7	6	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	0 / 109 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	8	
Injection site erythema			
subjects affected / exposed	0 / 109 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	8	
Injection site reaction			
subjects affected / exposed	0 / 109 (0.00%)	6 / 102 (5.88%)	
occurrences (all)	0	9	
Injection site swelling			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	7	
Pyrexia			
subjects affected / exposed	4 / 109 (3.67%)	1 / 102 (0.98%)	
occurrences (all)	4	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	2 / 109 (1.83%)	2 / 102 (1.96%)	
occurrences (all)	2	2	
Diarrhoea			
subjects affected / exposed	4 / 109 (3.67%)	3 / 102 (2.94%)	
occurrences (all)	4	5	
Nausea			

subjects affected / exposed	1 / 109 (0.92%)	2 / 102 (1.96%)	
occurrences (all)	1	2	
Toothache			
subjects affected / exposed	1 / 109 (0.92%)	3 / 102 (2.94%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	0 / 109 (0.00%)	3 / 102 (2.94%)	
occurrences (all)	0	3	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 109 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 109 (0.92%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 109 (1.83%)	1 / 102 (0.98%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 109 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Angioedema			
subjects affected / exposed	2 / 109 (1.83%)	0 / 102 (0.00%)	
occurrences (all)	2	0	
Chronic spontaneous urticaria			
subjects affected / exposed	2 / 109 (1.83%)	2 / 102 (1.96%)	
occurrences (all)	2	2	
Eczema			
subjects affected / exposed	1 / 109 (0.92%)	1 / 102 (0.98%)	
occurrences (all)	1	1	
Dermatitis contact			
subjects affected / exposed	1 / 109 (0.92%)	1 / 102 (0.98%)	
occurrences (all)	1	1	
Urticaria			

subjects affected / exposed	2 / 109 (1.83%)	3 / 102 (2.94%)	
occurrences (all)	2	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 109 (0.92%)	5 / 102 (4.90%)	
occurrences (all)	1	6	
Back pain			
subjects affected / exposed	1 / 109 (0.92%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	3 / 109 (2.75%)	0 / 102 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 109 (0.92%)	1 / 102 (0.98%)	
occurrences (all)	1	1	
COVID-19			
subjects affected / exposed	1 / 109 (0.92%)	1 / 102 (0.98%)	
occurrences (all)	1	1	
Gastroenteritis			
subjects affected / exposed	3 / 109 (2.75%)	2 / 102 (1.96%)	
occurrences (all)	3	2	
Influenza			
subjects affected / exposed	1 / 109 (0.92%)	2 / 102 (1.96%)	
occurrences (all)	1	3	
Nasopharyngitis			
subjects affected / exposed	10 / 109 (9.17%)	8 / 102 (7.84%)	
occurrences (all)	12	9	
Sinusitis			
subjects affected / exposed	1 / 109 (0.92%)	1 / 102 (0.98%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	0 / 109 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	2	
Upper respiratory tract infection			

subjects affected / exposed	4 / 109 (3.67%)	1 / 102 (0.98%)	
occurrences (all)	5	3	
Urinary tract infection			
subjects affected / exposed	3 / 109 (2.75%)	5 / 102 (4.90%)	
occurrences (all)	4	5	

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
07 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. This amendment also introduced an interim analysis in order to perform the primary efficacy analysis once all adult patients have completed the treatment period (Week 52). Additional changes in this amendment include: 1) Instruction on Public Health Emergency mitigation procedures: a) Introduction of the use of local laboratory assessments, b) Introduction of remote PRO completion and c) Introduction of phone calls, virtual contacts to replace on-site study visit for the duration of the disruption, 4) 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 4 subjects between RAN (1034) vs FAS (1030) is due to mis-randomization of 4 subjects. These subjects did not receive Ligelizumab and hence rightfully not included in FAS (though included in RAN).

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Notes: