NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Ligelizumab

Trial Indication(s)

Chronic spontaneous urticaria

Protocol Number

CQGE031C2201

Protocol Title

A multi-center, 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)

Clinical Trial Phase

Phase 2

Phase of Drug Development

IIb

Study Start/End Dates

Study Start Date: July 2015 (Actual)
Primary Completion Date: November 2016 (Actual)
Study Completion Date: June 2017 (Actual)

Reason for Termination (If applicable)

NA

Study Design/Methodology

This was a Phase IIb dose-finding, multicenter, randomized, double-blind, active and placebo-controlled, parallel-group study to establish a dose-response relationship of QGE031, and evaluate its efficacy and safety compared to placebo and omalizumab administered subcutaneously (s.c.) as an add-on therapy for the treatment of adult patients diagnosed with refractory CSU who remained symptomatic despite H1-AH at approved or increased doses alone or in combination with H2-AH and/or a leukotriene receptor antagonist (LTRA).

Centers

85 centers in 10 countries: Greece(3), Australia(5), Canada(3), United States(26), Japan(11), Germany(7), Spain(17), United Kingdom(3), Taiwan(3), Russia(7)

Objectives:

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.

Secondary objectives were:

- To evaluate the efficacy of ligelizumab (based on the selected dose-response model) compared to omalizumab 300 mg with respect to achievement of complete hives response at Week 12 in patients with CSU when added to H1-AH alone or in combination with H2-AH and/or a LTRA.
- To evaluate the efficacy of individual ligelizumab doses of 24 mg, 72 mg and 240 mg s.c. compared to omalizumab 300 mg with respect to achievement of complete hives response at Week 20 in patients with CSU when added to H1-AH alone or in combination with H2-AH and/or a LTRA.
- To evaluate the efficacy of ligelizumab doses of 24 mg, 72 mg and 240 mg s.c. versus placebo and omalizumab 300 mg in patients with CSU, in terms of:
    - Change from Baseline in Hives Severity Score (HSS7) at Week 12 and 20
    - Change from Baseline in Itch Severity Score (ISS7) at Week 12 and 20
    - Change from Baseline in Urticaria Activity Score (UAS7) at Week 12 and 20

- To evaluate the safety (including immunogenicity) and tolerability of ligelizumab (doses of 24 mg, 72 mg and 240 mg s.c. every 4 weeks) versus placebo and omalizumab 300 mg in patients with CSU particularly in regards to electrocardiogram (ECG), adverse events, vital signs and clinical laboratory evaluation during 20 weeks of treatment and 24 weeks of follow-up.

Test Product (s), Dose(s), and Mode(s) of Administration

The test product was QGE031 120 mg per 1 mL, liquid in vial for subcutaneous administration (s.c.). Ligelizumab was administered at doses of 24 mg, 72 mg and 240 mg every 4 weeks and ligelizumab 120 mg single dose.

Statistical Methods

This was a 44 week, Phase IIb dose-finding, multicenter, randomized, double-blind, active and placebo-controlled, parallel-group study in CSU patients. Patients were randomized to one of six treatment arms i.e. four doses of ligelizumab 24 mg, 72 mg, 240 mg (every 4 weeks), 120 mg single dose and active comparator (omalizumab 300 mg) and placebo (0 mg) every 4 weeks.

The study comprised:

- Screening epoch, Day −14 to Day 1: Duration of up to 2 weeks in which patients who have given informed consent were assessed for study eligibility.
- Treatment epoch, Day 1 to Day 141 (20 weeks): Double-blind treatment epoch during which patients were seen in the clinic every 4 weeks.
- Post-treatment follow-up epoch, Day 141 to Day 309 (24 weeks): Follow-up epoch consisted of 6 visits (every 4 weeks) with the final visit occurring up to 24 weeks after the last treatment visit or when patients relapsed within the follow-up epoch from Week 32 onwards.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
-Diagnosis of chronic spontaneous urticaria for at least 6 months
-Diagnosis of chronic spontaneous urticaria refractory to standard of care at time of randomization

Exclusion Criteria:
-Clearly defined underlying etiology for chronic urticaria other than chronic spontaneous urticaria
-Evidence of parasitic infection
-Any other skin disease with chronic itching
-Previous treatment with omalizumab or QGE031
-Contraindications to or hypersensitivity to fexofenadine, loratadine, cetirizine, or epinephrine
-History of anaphylaxis

-History or current diagnosis of ECG abnormalities indicating significant risk of safety for patients participating in the study
-History of hypersensitivity to any of the study drugs or its components of similar chemical classes
-Pregnant or nursing (lactating) women

Other protocol defined inclusion/exclusion criteria may apply.

Participant Flow Table

Overall Study

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w	Placebo s.c. q4w	QGE031 120 mg s.c. s.d.
Started	43	84	85	85	43	42
Completed	40	77	73	72	39	37
Not Completed	3	7	12	13	4	5
Adverse Event	0	1	1	2	1	2
Lack of Efficacy	1	2	1	2	1	1
Non-compliance with study treatment	0	1	2	0	0	0
Pregnancy	0	0	0	1	0	0
Protocol Violation	2	0	3	3	1	1
Technical problems	0	0	1	0	0	0
Lost to Follow-up	0	0	2	0	0	0

Physician Decision	0	0	1	3	0	1
Withdrawal by Subject	0	3	1	2	1	0

Baseline Characteristics

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w	Placebo s.c. q4w	QGE031 120 mg s.c. s.d.	Total
Number of Participants [units: participants]	43	84	85	85	43	42	382
Age Continuous (units: years) Mean ± Standard Deviation							
	44.1±14.36	44.3±12.38	42.9±10.51	41.8±13.06	45.4±11.22	42.4±14.54	43.3±12.49
Age Categorical (units: participants) Count of Participants (Not Applicable)							
<=18 years	0	0	0	0	0	0	0
Between 18 and 65 years	39	77	85	81	41	37	360
>=65 years	4	7	0	4	2	5	22
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)							
Female	31	61	67	66	31	30	286
Male	12	23	18	19	12	12	96

Summary of Efficacy

Primary Outcome Result(s)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w	Placebo s.c. q4w	QGE031 120 mg s.c. s.d.
Number of Participants Analyzed [units: participants]	43	84	85	85	43	42
Dose response relationship with respect to achievement of complete hives response (HSS7=0) (units: percentage of participants) Number (95% Confidence Interval)						
Week 12	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)	0 (0.0 to 8.2)	19.0 (8.6 to 34.1)

Statistical Analysis

Groups	QGE031 24 mg s.c. q4w, QGE031 72 mg s.c. q4w, QGE031 240 mg s.c. q4w, Omalizumab 300 mg s.c. q4w	
P Value	0	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.
Method	Regression, Logistic	Target dose was based on this estimated dose response. The 60% CI included the 20 - 80th percentile of target dose estimated in the bootstrap samples.
Other Estimated target dose	32.5	Min dose with effect size >15%
60 % Confidence Interval 2-Sided	27.5 to 42.5	

Secondary Outcome Result(s)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	43	84	85	85
Complete hives response (HSS7=0) rate at Week 12 measured over 7 days (units: Odds Ratio) Number (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	40	81	78	77
Change from baseline in Hives Severity Score (HSS7) at Week 12 measured over 7 days (units: Hodges-Lehmann median) Median (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	43	84	85	85
HSS7=0 response: comparison between treatment groups at Week 20 measured over 7 days (units: Odds ratio) Number (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	39	78	74	73
Change from baseline in Hives Severity Score (HSS7) at Week 20 measured over 7 days (units: Hodges-Lehmann median) Median (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	40	81	78	77
Change from baseline in Itch Severity Score (ISS7) at Week 12 measured over 7 days (units: Hodges-Lehmann median) Median (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	39	78	74	73
Change from baseline in Itch Severity Score (ISS7) at Week 20 measured over 7 days (units: Hodges-Lehmann median) Median (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	40	81	78	77
Change from baseline in Urticaria Activity Score (UAS7) at Week 12 measured over 7 days (units: Hodges-Lehmann median) Median (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	39	78	74	73
Change from baseline in Urticaria Activity Score (UAS7) at Week 20 measured over 7 days (units: Hodges-Lehmann median) Median (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	43	84	85	85
Complete Urticaria Activity Score Response (UAS7=0) rate at Week 12 measured over 7 days (units: Odds ratio) Number (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	43	84	85	85
UAS7=0 response: comparison between treatment groups at Week 20 measured over 7 days (units: Odds ratio) Number (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	43	84	85	85
Complete Itch Response (ISS7=0) rate at Week 12 measured over 7 days (units: Odds Ratio) Number (95% Confidence Interval)				
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)

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

	QGE031 24 mg s.c. q4w	QGE031 72 mg s.c. q4w	QGE031 240 mg s.c. q4w	Omalizumab 300 mg s.c. q4w
Number of Participants Analyzed [units: participants]	43	84	85	85
ISS7=0 response: comparison between treatment groups at Week 20 measured over 7 days (units: Odds ratio) Number (95% Confidence Interval)				
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)

Summary of Safety

Safety Results

All-Cause Mortality

QGE031 24 mg s.c. q4w N = 43	QGE031 72 mg s.c. q4w N = 84	QGE031 240 mg s.c. q4w N = 85	Omalizumab 300 mg s.c. q4w N = 85	Placebo s.c. q4w N = 43	QGE031 120 mg s.c. s.d. N = 42

Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Timeframe for AE
Additional Description	AE additional description
Source Vocabulary for Table Default	MedDRA (20.0)
Assessment Type for Table Default	Systematic Assessment

	QGE031 24 mg s.c. q4w N = 43	QGE031 72 mg s.c. q4w N = 84	QGE031 240 mg s.c. q4w N = 85	Omalizumab 300 mg s.c. q4w N = 85	Placebo s.c. q4w N = 43	QGE031 120 mg s.c. s.d. N = 42
Total participants affected	3 (6.98%)	2 (2.38%)	2 (2.35%)	3 (3.53%)	4 (9.30%)	4 (9.52%)
Cardiac disorders						
Angina pectoris	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Gastrointestinal disorders						
Abdominal distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Colon dysplasia	0 (0.00%)	0 (0.00%)	1 (1.18%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diverticular perforation	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Inguinal hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)
Large intestine polyp	0 (0.00%)	0 (0.00%)	1 (1.18%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Subileus	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.18%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions						
Chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Hepatobiliary disorders						
Cholelithiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Hepatic cyst	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Hepatitis acute	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations						
Diverticulitis	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pilonidal cyst	0 (0.00%)	0 (0.00%)	1 (1.18%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)
Injury, poisoning and procedural complications						
Fractured coccyx	0 (0.00%)	1 (1.19%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Radius fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.18%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders						
Intervertebral disc protrusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Sjogren's syndrome	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Benign lung neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)

Breast cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)
Breast neoplasm	0 (0.00%)	1 (1.19%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemangioma of liver	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Papillary thyroid cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Skin and subcutaneous tissue disorders						
Angioedema	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Prurigo	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.18%)	0 (0.00%)	0 (0.00%)
Urticaria	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Timeframe for AE
Additional Description	AE additional description
Source Vocabulary for Table Default	MedDRA (20.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	QGE031 24 mg s.c. q4w N = 43	QGE031 72 mg s.c. q4w N = 84	QGE031 240 mg s.c. q4w N = 85	Omalizumab 300 mg s.c. q4w N = 85	Placebo s.c. q4w N = 43	QGE031 120 mg s.c. s.d. N = 42
Total participants affected	24 (55.81%)	45 (53.57%)	46 (54.12%)	44 (51.76%)	30 (69.77%)	28 (66.67%)
Gastrointestinal disorders						
Diarrhoea	2 (4.65%)	4 (4.76%)	5 (5.88%)	6 (7.06%)	2 (4.65%)	2 (4.76%)

Gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (7.14%)
Nausea	1 (2.33%)	1 (1.19%)	2 (2.35%)	5 (5.88%)	2 (4.65%)	1 (2.38%)
General disorders and administration site conditions						
Injection site erythema	0 (0.00%)	2 (2.38%)	5 (5.88%)	0 (0.00%)	0 (0.00%)	1 (2.38%)
Injection site reaction	0 (0.00%)	3 (3.57%)	6 (7.06%)	0 (0.00%)	1 (2.33%)	0 (0.00%)
Infections and infestations						
Bronchitis	1 (2.33%)	1 (1.19%)	0 (0.00%)	5 (5.88%)	1 (2.33%)	0 (0.00%)
Influenza	1 (2.33%)	4 (4.76%)	4 (4.71%)	5 (5.88%)	1 (2.33%)	1 (2.38%)
Upper respiratory tract infection	7 (16.28%)	7 (8.33%)	10 (11.76%)	10 (11.76%)	6 (13.95%)	9 (21.43%)
Urinary tract infection	0 (0.00%)	5 (5.95%)	4 (4.71%)	5 (5.88%)	0 (0.00%)	2 (4.76%)
Viral upper respiratory tract infection	7 (16.28%)	13 (15.48%)	17 (20.00%)	17 (20.00%)	13 (30.23%)	10 (23.81%)
Investigations						
Blood creatinine increased	1 (2.33%)	3 (3.57%)	3 (3.53%)	2 (2.35%)	4 (9.30%)	1 (2.38%)
Musculoskeletal and connective tissue disorders						
Arthralgia	1 (2.33%)	6 (7.14%)	1 (1.18%)	2 (2.35%)	1 (2.33%)	1 (2.38%)
Back pain	0 (0.00%)	1 (1.19%)	0 (0.00%)	1 (1.18%)	1 (2.33%)	3 (7.14%)
Nervous system disorders						
Dizziness	2 (4.65%)	5 (5.95%)	2 (2.35%)	2 (2.35%)	4 (9.30%)	0 (0.00%)
Headache	7 (16.28%)	9 (10.71%)	7 (8.24%)	12 (14.12%)	7 (16.28%)	1 (2.38%)

Skin and subcutaneous tissue disorders						
Eczema	1 (2.33%)	5 (5.95%)	4 (4.71%)	2 (2.35%)	1 (2.33%)	3 (7.14%)
Urticaria	1 (2.33%)	9 (10.71%)	3 (3.53%)	4 (4.71%)	5 (11.63%)	7 (16.67%)
Vascular disorders						
Hypertension	1 (2.33%)	5 (5.95%)	2 (2.35%)	2 (2.35%)	3 (6.98%)	3 (7.14%)

Other Relevant Findings

NA

Conclusion:

This phase II study showed:

- A clear dose response relationship with respect to HSS7=0 response rates at Week 12;
- Efficacy of ligelizumab added to standard of care treatment in patients with moderate to severe CSU. A statistically significant superiority over omalizumab was noted at Week 12 for HSS7=0 and was maintained throughout the treatment period; and
- No new identified safety signals

Date of Clinical Trial Report

12-Mar-2018