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Sponsor

Generic Drug Name

Ligelizumab solution for injection (120 mg/mL)

Trial Indication

Chronic Inducible Urticaria (CINDU)

Protocol Number

CQGE031E12301

Protocol Title

A multi-center, randomized, double-blind, placebo controlled study to investigate the efficacy and safety of ligelizumab (QGE031) in the treatment of Chronic Inducible Urticaria (CINDU) in adolescents and adults inadequately controlled with H1-antihistamines

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: November 16, 2021
Primary Completion Date: August 09, 2022
Study Completion Date: August 09, 2022

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Reason for Termination

Phase III PEARL studies (CQGE031C2302 and CQGE031C2303) with ligelizumab met their primary endpoint of superiority vs placebo at Week 12 for treatment of CSU, but not versus omalizumab. Decision to discontinue was not based on safety concerns.

Study Design/Methodology

This was a Phase III multicenter, randomized, double-blind, placebo-controlled study to demonstrate superiority of ligelizumab 72 mg and/or 120 mg sc q4w over placebo as an add-on therapy to H1-antihistamines at local-approved doses in adolescents and adults for the treatment of CINDU. The treatment duration was 40 Weeks, with the primary endpoint assessed at Week 12. Three subtypes of CINDU populations were planned to be assessed in three parallel cohorts: symptomatic dermographism, cold urticaria and cholinergic urticaria. The study population was planned to consist of both adolescents and adults.

Approximately 428 male and female participants aged ≥12 years diagnosed with symptomatic dermographism (n=168), cold urticaria (n=102) or cholinergic urticaria (n=158) and who remained symptomatic despite the use of H1-AH at the approved dose level, were planned to be enrolled.

The study design consisted of a 4 Week screening period, a 24 Week double-blinded treatment period, and a 12 Week follow-up period.

After undergoing screening procedures, on Day 1 (or Week 0, the start of the double-blinded treatment period), all eligible participants from the symptomatic dermographism and cold urticaria cohort were randomized in a 2:2:1:1 ratio to ligelizumab 120 mg q4w, ligelizumab 72 mg q4w, placebo to ligelizumab 120 mg and placebo to ligelizumab 72 mg. In the cholinergic urticaria cohort, all eligible participants were randomized in a 1:1 ratio to ligelizumab 120 mg q4w or placebo to ligelizumab 120 mg. Randomization was stratified by age group (adults and adolescents). Randomization of adults was further stratified by region. Participants received the study medication as per randomization.

At Weeks 0, 4, 8, 12, 24 and 36 participants from all cohorts underwent provocation tests in order to elicit symptoms. A positive response at Week 0 (Day 1) to the FricTest®4.0, TempTest®4.0 or Pulse Controlled Ergometry was required to be randomized to the symptomatic dermographism, cold urticaria or cholinergic urticaria cohorts, respectively. As thresholds were not defined in CINDU, it was left to the investigator's discretion to enroll only those participants with moderate or severe disease burden. Participants had to avoid taking any rescue medication in the 24 hours prior to the provocation test.

For both cold urticaria and symptomatic dermographism participants, the provocation test was applied to specific areas on the body e.g left volar forearm and upper back, symptoms were assessed for those specific areas. For cholinergic urticaria, due to the nature of the provocation test, symptoms were assessed over the whole body.

The 12 Week follow-up period was concluded with a follow-up visit (Week 36) corresponding to 16 Weeks after the last treatment dose. No study treatment was given during the posttreatment follow-up period; however, participants continued with the background medication and rescue medication as needed.

Study treatment discontinuation could be initiated by either the participant or the investigator for a participant for any reason. A participant was deemed to have discontinued the study when they permanently stopped receiving the study treatment and did not undergo further protocolrequired assessments or follow-up, for any reason.

Due to the early termination of the trial, screening was stopped, and all participants discontinued treatment and were then required to enter 12 Week treatment free follow up period.

Centers

24 centers in 9 countries: Hungary(3), Turkey(2), Australia(2), Spain(3), Russia(6), Slovakia (Slovak Republic)(2), United States(4), Greece(1), Taiwan(1)

Publication

No data identified.

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Objectives:

Objectives and endpoints

Objectives	Endpoints
Primary objective	**Endpoints for primary objective**

To demonstrate superiority of ligelizumab versus placebo with regards to the change from baseline in response to a standardized provocation test for each CINDU subtype	• Symptomatic Dermographism
	  • Change from baseline in Total Fric Score (TFS) at Week 12 in response to FricTest® 4.0
	• Cold Urticaria
	  • Change from baseline in critical temperature threshold (CTT) at Week 12 in response to the TempTest® 4.0

	• Cholinergic Urticaria • Change from baseline in itch numerical rating scale (NRS) at Week 12 in response to the pulse-controlled ergometry test.
Secondary objectives	**Endpoints for secondary objectives**

To demonstrate superiority of ligelizumab versus placebo with regard to proportion of participants with a complete response after standardized provocation test
 	
To demonstrate superiority of ligelizumab versus placebo in itch NRS following the provocation test
	• Symptomatic Dermographism
	Proportion of participants with complete response in FricTest® at Week 12
	
	• Change from baseline in itch NRS following provocation test at Week 12, in participants with itch NRS > 0 at baseline
	• Cold Urticaria
	  • Proportion of participants with complete response in TempTest® at Week 12
	  • Change from baseline in itch NRS following provocation test at Week 12, in participants with itch NRS > 0 at baseline
	• Cholinergic Urticaria
	  • Proportion of participants with itch NRS=0 following the pulse-controlled ergometry test at Week 12
	  • Proportion of participants with physician global assessment of severity of hives=0 following the pulse-controlled ergometry test at Week 12

To assess the safety of ligelizumab	Safety endpoints included but were not limited to: • Occurrence of treatment emergent adverse events (serious and non-serious) during the study • Occurrence of treatment emergent adverse events during the study leading to discontinuation of study treatment • Occurrence of treatment emergent adverse events of interest listed as either identified or potential risks, during the study • Changes in safety parameters

Test Products, Doses, and Modes of Administration

Ligelizumab 72 mg per 1 mL, Liquid in Vial (solution for injection) s.c.

Ligelizumab 120 mg per 1 mL, Liquid in Vial (solution for injection) s.c.

Statistical Methods

Analysis of the primary endpoint

No inferential statistical analysis was performed due to limited sample size. Listings are presented for change from baseline at Week 12 for symptomatic dermographism, cholinergic urticaria and Cold Urticaria

No participants completed Week 12 visit in symptomatic dermographism subtype, 2 participants completed Week 12 visit in cold urticaria subtype (1 each in ligelizumab 72 mg arm and ligelizumab 120 mg arm) and 1 participant in cholinergic urticaria. Hence listings for change from baseline (CFB) in response to provocation at Week 12 are presented for cold urticaria and cholinergic urticaria cohorts only.

Analysis of secondary endpoints

There were no statistical modeling, hypothesis testing, or methodology used for symptomatic dermographism, cold urticaria, cholinergic urticaria due to limited sample size.

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Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Confirmed CINDU diagnosis (as per guidelines) for symptomatic dermographism, cold urticaria or cholinergic urticaria for ≥ 4 months.
- Diagnosis of CINDU (symptomatic dermographism, cold urticaria or cholinergic urticaria) inadequately controlled with H1-AH at local label approved doses at the time of randomization, as defined by all of the following:
- Positive response (i.e development of symptoms) to triggers despite treatment with H1-AH
- Positive response (i.e. development of symptoms) to provocation test on day of randomization
- Participants must be able to physically perform the protocol defined provocation test specific to the participant's CINDU.
- Cholinergic urticaria participants must show sweating in performing the pulse-controlled ergometry test on day of randomization. Participants with anhidrosis must not be included.
  Willing and able to complete a daily symptom eDiary as per protocol requirement and adhere to the study visit schedules

Exclusion Criteria:

- History of hypersensitivity to any of the study drugs or its components or to drugs of similar chemical classes or to the provocation test or items used in provocation tests

  Participants who have concomitant CSU at screening
- Participants who have a familial form of the target CINDU that is being considered for the participant's inclusion in this study
- Participants having a more defined other form of inducible urticaria than the target CINDU that is being considered for the participant's inclusion in this study

- Diseases, other than chronic inducible urticaria, with urticarial or angioedema symptoms such as urticarial vasculitis, erythema multiforme, cutaneous mastocytosis (urticaria pigmentosa) and hereditary or acquired angioedema (eg, due to C1 inhibitor deficiency).

- Any other skin disease associated with chronic itching that might influence, in the investigator's opinion, the study evaluations and results (eg, atopic dermatitis, bullous pemphigoid, dermatitis herpetiformis, senile pruritus, etc.) or skin diseases associated with only wheals and no itch e.g asymptomatic dermographism

- Prior exposure to ligelizumab, omalizumab and or other anti-IgE therapies

Participant Flow Table

Treatment

	72 mg ligelizumab, symptomatic dermographism	**120 mg ligelizumab, symptomatic dermographism**	**Placebo - 72 mg ligelizumab, symptomatic dermographism**	**Placebo - 120 mg ligelizumab, symptomatic dermographism**	**72 mg ligelizumab cold urticaria**	**120 mg ligelizumab, cold urticaria**	**Placebo - 72 mg ligelizumab, cold urticaria**	**Placebo - 120 mg ligelizumab, cold urticaria**	**120 mg Ligelizumab, cholinergic urticaria**	**Placebo - 120 mg ligelizumab, cholinergic urticaria**	**Total**
Arm/Group Description	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	
Started	5	6	4	2	3	3	1	3	6	6	39
Completed	0	0	0	0	0	0	0	0	0	0	0

Not Completed	5	6	4	2	3	3	1	3	6	6	39
Study terminated by sponsor	5	6	4	2	3	3	1	3	6	6	39

Follow-up

	72 mg ligelizumab, symptomatic dermographism	**120 mg ligelizumab, symptomatic dermographism**	**Placebo - 72 mg ligelizumab, symptomatic dermographism**	**Placebo - 120 mg ligelizumab, symptomatic dermographism**	**72 mg ligelizumab cold urticaria**	**120 mg ligelizumab, cold urticaria**	**Placebo - 72 mg ligelizumab, cold urticaria**	**Placebo - 120 mg ligelizumab, cold urticaria**	**120 mg Ligelizumab, cholinergic urticaria**	**Placebo - 120 mg ligelizumab, cholinergic urticaria**	**Total**
Arm/Group Description	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	
Started	2	5	4	0	3	2	0	2	5	6	29
Completed	1	5	3	0	3	2	0	1	5	5	25
Not Completed	1	0	1	0	0	0	0	1	0	1	4
Withdrawal by Subject	1	0	1	0	0	0	0	1	0	1	4

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Baseline Characteristics

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria	Total
Arm/Group Description	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	
Number of Participants [units: participants]	5	6	4	2	3	3	1	3	6	6	39
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation											
	30.4±9.81	28.3±12.74	40.8±18.86	36.5±12.02	35.3±12.50	31.7±16.17	60.0±NA[1]	32.3±26.58	28.8±9.62	25.2±5.56	27.0±7.73
Age Categorical (units:) Analysis Population Type: Participants Count of Participants											
<=18 years	1	1	1	0	0	1	0	1	0	0	5

Between 18 and 65 years	4	5	3	2	3	2	1	2	6	6	34
>=65 years	0	0	0	0	0	0	0	0	0	0	0
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants											
Female	3	3	2	2	3	2	1	1	2	0	19
Male	2	3	2	0	0	1	0	2	4	6	20
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants Count of Participants											
White	4	6	4	2	3	3	1	3	5	5	36
Black or African American	1	0	0	0	0	0	0	0	0	1	2
Asian	0	0	0	0	0	0	0	0	1	0	1

Summary of Efficacy

Primary Outcome Results

Change from baseline in Total Fric Score in participants with symptomatic dermographism - Treatment period

Description Total Fric score (a scale from 0-4 where a positive response with all of the four pins is TFS = 4, while a positive response with only one pin - the largest pin is TFS

= 1)

Time Frame Baseline, Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo -120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg - ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0

Change from baseline in Total Fric Score in participants with symptomatic dermographism - Treatment period
(units: Score)

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Change from baseline in critical temperature threshold in participants with cold urticaria - Treatment period

Description: The Temptest is used to induce itch and hives in participants with cold urticaria. Critical temperature threshold (CTT), as measured by the Temptest, determines the highest temperature sufficient for inducing symptoms.

Time Frame: Baseline, Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0
Change from baseline in critical temperature threshold in participants with cold urticaria - Treatment period (units: Temperature)										
	0	0	0	0	0	0	0	0	0	0

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Change from baseline in itch numerical rating scale in participants with cholinergic urticaria in Treatment period

Description: Itch numerical rating scale, a scale from 0 to 10. Negative change from baseline indicates improvement. Patients were asked to rate itching severity based on the worst level of itching in the past 24 h using an 11-point scale from 0 (“no itch”) to 10 (“worst itch imaginable”)

Time Frame: Baseline, Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0
Change from baseline in itch numerical rating scale in participants with cholinergic urticaria in Treatment period (units: Scores on a scale)										

Secondary Outcome Results

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Proportion of participants with symptomatic dermographism with Total Fric score = 0 during Treatment period

Description: Total Fric score, a scale from 0-4 where a positive response with all of the four pins is TFS = 4, while a positive response with only one pin - the largest pin is TFS = 1

Time Frame: Baseline, Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0

Proportion of participants with symptomatic dermographism with Total Fric score = 0 during Treatment period
(units: Participants)

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Change from baseline in itch numerical rating scale in participants with symptomatic dermographism in Treatment period

Description: Itch numerical rating scale, a scale from 0-10

Time Frame: Baseline, Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg Ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab, cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0

Change from baseline in itch numerical rating scale in participants with symptomatic dermographism in Treatment period
(units: Scores on a scale)

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Proportion of participants with cold urticaria with complete response (no itch or hives) to the TempTest in Treatment period

Description The Temptest is used to induce itch and hives in participants with cold urticaria

Time Frame Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab, cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0

Proportion of participants with cold urticaria with complete response (no itch or hives) to the TempTest in Treatment period
(units: Participants)

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Change from baseline in itch numerical rating scale in participants with cold urticaria in Treatment period

Description: Itch numerical rating scale, a scale from 0-10

Time Frame: Baseline, Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo -120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0
	Change from baseline in itch numerical rating scale in participants with cold urticaria in Treatment period (units: Scores on a scale)									

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Proportion of participants with cholinergic urticaria with itch numerical rating scale =0 in Treatment period

Description: Itch numerical rating scale, a scale from 0-10

Time Frame: Week 12

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0

Proportion of participants with cholinergic urticaria with itch numerical rating scale =0 in Treatment period
(units: Scores on a scale)

	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Pleacebo - 120 mg ligelizumab, cold urticaria	120 mg ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria
Arm/Group Description	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with symptomatic dermographism	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	72 mg ligelizumab subcutaneous injection every 4 weeks in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria	120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0

Proportion of participants with cholinergic urticaria with physician global assessment of severity of hives (PGA - hive score) =0 in Treatment period
(units: Scores on a scale)

Proportion of participants with cholinergic urticaria with physician global assessment of severity of hives (PGA - hive score) =0 in Treatment period

Description: Physician global assessment of severity of hives PGA is an assessment of all lesions scored on a scale of 0–5 in both trials, with 0 representing clear skin, 1 almost clear skin, and 5 representing severe psoriasis

Time Frame: Week 12

NOVARTIS

Summary of Safety

Safety Results

Time Frame	Adverse Events (AEs) were collected after signature of the informed consent form until 30 days after last dose of study treatment. Treatment period was 12 weeks. Serious Adverse Events (SAEs) were collected after signature of the informed consent form until 30 days after last study visit.
Additional Description	An AE is any untoward medical occurrence, unfavorable, or unintended sign (including an abnormal laboratory finding), symptom, disease, or injury, temporally associated with the use of a marketed or investigational medicinal product, gene therapy, theragnostic product, or medical device, in patients, clinical-trial subjects, device users, or other persons, whether or not it is considered to be related to or due to the product.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Ligelizumab 72mg N = 8	**Ligelizumab 120mg N = 15**	**Placebo - Ligelizumab 72mg N = 5**	**Placebo - Ligelizumab 120mg N = 11**	**Total N = 39**
Arm/Group Description	QGE031 72mg	QGE031 120mg	Placebo - QGE031 72mg	Placebo - QGE031 120mg	Total
Total Number Affected	0	0	0	0	0
Total Number At Risk	8	15	5	11	39

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Serious Adverse Events

No data identified.

Other (Not Including Serious) Adverse Events

	Ligelizumab 72mg N = 8	Ligelizumab 120mg N = 15	Placebo - Ligelizumab 72mg N = 5	Placebo - Ligelizumab 120mg N = 11	Total N = 39
Arm/Group Description	QGE031 72mg	QGE031 120mg	Placebo - QGE031 72mg	Placebo - QGE031 120mg	Total
Total # Affected by any Other Adverse Event	3	6	3	1	13
Total # at Risk by any Other Adverse Event	8	15	5	11	39
Cardiac disorders					
Bradycardia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (2.56%)
Ear and labyrinth disorders					
Tinnitus	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Vertigo	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Endocrine disorders					
Hypopituitarism	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Gastrointestinal disorders					
Abdominal pain	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Nausea	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Infections and infestations					
COVID-19	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Herpes simplex	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)

Influenza	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Nasopharyngitis	0 (0.00%)	2 (13.33%)	0 (0.00%)	0 (0.00%)	2 (5.13%)
Peritonsillar abscess	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (2.56%)
Post-acute COVID-19 syndrome	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Respiratory tract infection	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Upper respiratory tract infection	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Urinary tract infection	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Metabolism and nutrition disorders					
Glucose tolerance impaired	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Hyperuricaemia	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Vitamin D deficiency	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Musculoskeletal and connective tissue disorders					
Arthralgia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (2.56%)
Groin pain	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Muscle spasms	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Myalgia	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Nervous system disorders					
Headache	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (2.56%)
Migraine	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	1 (2.56%)
Tension headache	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Respiratory, thoracic and mediastinal disorders					
Cough	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.56%)
Oropharyngeal pain	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.56%)

Conclusion:

The study was terminated due to a strategic company decision to stop the development of ligelizumab in chronic urticaria (CSU and CINDU). At the time of early study termination, a very small number of participants had completed the primary endpoint timepoint. The data collected in the study was very limited, hence meaningful efficacy or safety conclusion could not be drawn. Overall, safety was in line with that observed in ligelizumab CSU studies.

Date of Clinical Trial Report

19 Dec 2022