



Clinical trial results:

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

Summary

EudraCT number	2020-003018-11
Trial protocol	HU SK ES SI NL FR DE GR IT BG AT
Global end of trial date	09 August 2022

Results information

Result version number	v1
This version publication date	25 February 2023
First version publication date	25 February 2023

Trial information

Trial identification

Sponsor protocol code	CQGE031E12301
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05024058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma, AG, +41 6133241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma, AG, +41 6133241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 August 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 August 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

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.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 November 2021
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	Greece: 1
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	39
EEA total number of subjects	13

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)	5
Adults (18-64 years)	34
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

39 participants were randomized. None completed study.

Pre-assignment

Screening details:

Study terminated by sponsor.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	72 mg ligelizumab, symptomatic dermographism
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Arm description:

72 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism

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

Dosage and administration details:

72 mg per 0.6 mL

Arm title	120 mg ligelizumab, symptomatic dermographism
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Arm description:

120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermographism

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

Dosage and administration details:

120 mg per 1 mL

Arm title	Placebo - 72 mg ligelizumab, symptomatic dermographism
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Arm description:

Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism

Arm type	Placebo
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Investigational medicinal product name	Ligelizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 0 mg per 1 mL	
Arm title	Placebo - 120 mg ligelizumab, symptomatic dermographism
Arm description: Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermographism	
Arm type	Placebo
Investigational medicinal product name	Ligelizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 0 mg per 1 mL	
Arm title	72 mg ligelizumab cold urticaria
Arm description: 72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	
Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 72 mg per 0.6 mL	
Arm title	120 mg ligelizumab, cold urticaria
Arm description: 120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria	
Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 120 mg per 1 mL	
Arm title	Placebo - 72 mg ligelizumab, cold urticaria
Arm description: Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria	
Arm type	Placebo
Investigational medicinal product name	Ligelizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0 mg per 1 mL

Arm title	Placebo - 120 mg ligelizumab, cold urticaria
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Arm description:

Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria

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

Dosage and administration details:

0 mg per 1 mL

Arm title	120 mg Ligelizumab, cholinergic urticaria
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Arm description:

120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cholinergic urticaria

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

Dosage and administration details:

120 mg per 1 mL

Arm title	Placebo - 120 mg ligelizumab, cholinergic urticaria
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Arm description:

Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria

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

Dosage and administration details:

0 mg per 1 mL

Number of subjects in period 1	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism
Started	5	6	4
Completed Treatment	0	0	0
Started Follow-up	2	5	4

Completed Follow-up	1	5	3
Completed	0	0	0
Not completed	5	6	4
Study Terminated by Sponsor	5	6	4

Number of subjects in period 1	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria
Started	2	3	3
Completed Treatment	0	0	0
Started Follow-up	0	3	2
Completed Follow-up	0	3	2
Completed	0	0	0
Not completed	2	3	3
Study Terminated by Sponsor	2	3	3

Number of subjects in period 1	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg Ligelizumab, cholinergic urticaria
Started	1	3	6
Completed Treatment	0	0	0
Started Follow-up	0	2	5
Completed Follow-up	0	1	5
Completed	0	0	0
Not completed	1	3	6
Study Terminated by Sponsor	1	3	6

Number of subjects in period 1	Placebo - 120 mg ligelizumab, cholinergic urticaria
Started	6
Completed Treatment	0
Started Follow-up	6
Completed Follow-up	5
Completed	0
Not completed	6
Study Terminated by Sponsor	6

Baseline characteristics

Reporting groups

Reporting group title	72 mg ligelizumab, symptomatic dermatographism
Reporting group description:	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermatographism
Reporting group title	120 mg ligelizumab, symptomatic dermatographism
Reporting group description:	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermatographism
Reporting group title	Placebo - 72 mg ligelizumab, symptomatic dermatographism
Reporting group description:	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermatographism
Reporting group title	Placebo - 120 mg ligelizumab, symptomatic dermatographism
Reporting group description:	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermatographism
Reporting group title	72 mg ligelizumab cold urticaria
Reporting group description:	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria
Reporting group title	120 mg ligelizumab, cold urticaria
Reporting group description:	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria
Reporting group title	Placebo - 72 mg ligelizumab, cold urticaria
Reporting group description:	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria
Reporting group title	Placebo - 120 mg ligelizumab, cold urticaria
Reporting group description:	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria
Reporting group title	120 mg Ligelizumab, cholinergic urticaria
Reporting group description:	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cholinergic urticaria
Reporting group title	Placebo - 120 mg ligelizumab, cholinergic urticaria
Reporting group description:	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria

Reporting group values	72 mg ligelizumab, symptomatic dermatographism	120 mg ligelizumab, symptomatic dermatographism	Placebo - 72 mg ligelizumab, symptomatic dermatographism
Number of subjects	5	6	4
Age Categorical Units:			
<=18 years	1	1	1
Between 18 and 65 years	4	5	3
>=65 years	0	0	0

Age Continuous Units: years arithmetic mean standard deviation	30.4 ± 9.81	28.3 ± 12.74	40.8 ± 18.86
Sex: Female, Male Units: Participants			
Female	3	3	2
Male	2	3	2
Race/Ethnicity, Customized Units: Subjects			
White	4	6	4
Black or African American	1	0	0
Asian	0	0	0

Reporting group values	Placebo - 120 mg ligelizumab, symptomatic dermographism	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria
Number of subjects	2	3	3
Age Categorical Units:			
<=18 years	0	0	1
Between 18 and 65 years	2	3	2
>=65 years	0	0	0
Age Continuous Units: years arithmetic mean standard deviation	36.5 ± 12.02	35.3 ± 12.50	31.7 ± 16.17
Sex: Female, Male Units: Participants			
Female	2	3	2
Male	0	0	1
Race/Ethnicity, Customized Units: Subjects			
White	2	3	3
Black or African American	0	0	0
Asian	0	0	0

Reporting group values	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria	120 mg Ligelizumab, cholinergic urticaria
Number of subjects	1	3	6
Age Categorical Units:			
<=18 years	0	1	0
Between 18 and 65 years	1	2	6
>=65 years	0	0	0
Age Continuous Units: years arithmetic mean standard deviation	60.0 ± 9.99	32.3 ± 26.58	28.8 ± 9.62

Sex: Female, Male Units: Participants			
Female	1	1	2
Male	0	2	4
Race/Ethnicity, Customized Units: Subjects			
White	1	3	5
Black or African American	0	0	0
Asian	0	0	1

Reporting group values	Placebo - 120 mg ligelizumab, cholinergic urticaria	Total	
Number of subjects	6	39	
Age Categorical Units:			
<=18 years	0	5	
Between 18 and 65 years	6	34	
>=65 years	0	0	
Age Continuous Units: years			
arithmetic mean	25.2		
standard deviation	± 5.56	-	
Sex: Female, Male Units: Participants			
Female	0	19	
Male	6	20	
Race/Ethnicity, Customized Units: Subjects			
White	5	36	
Black or African American	1	2	
Asian	0	1	

End points

End points reporting groups

Reporting group title	72 mg ligelizumab, symptomatic dermatographism
Reporting group description:	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermatographism
Reporting group title	120 mg ligelizumab, symptomatic dermatographism
Reporting group description:	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with symptomatic dermatographism
Reporting group title	Placebo - 72 mg ligelizumab, symptomatic dermatographism
Reporting group description:	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with symptomatic dermatographism
Reporting group title	Placebo - 120 mg ligelizumab, symptomatic dermatographism
Reporting group description:	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with symptomatic dermatographism
Reporting group title	72 mg ligelizumab cold urticaria
Reporting group description:	72 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria
Reporting group title	120 mg ligelizumab, cold urticaria
Reporting group description:	120 mg ligelizumab subcutaneous injections every 4 weeks in participants with cold urticaria
Reporting group title	Placebo - 72 mg ligelizumab, cold urticaria
Reporting group description:	Placebo every 4 weeks until week 12 followed by 72 mg ligelizumab subcutaneous injections in participants with cold urticaria
Reporting group title	Placebo - 120 mg ligelizumab, cold urticaria
Reporting group description:	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cold urticaria
Reporting group title	120 mg Ligelizumab, cholinergic urticaria
Reporting group description:	120 mg ligelizumab subcutaneous injection every 4 weeks in participants with cholinergic urticaria
Reporting group title	Placebo - 120 mg ligelizumab, cholinergic urticaria
Reporting group description:	Placebo every 4 weeks until week 12 followed by 120 mg ligelizumab subcutaneous injections in participants with cholinergic urticaria

Primary: Change from baseline in Total Fric Score in participants with symptomatic dermatographism

End point title	Change from baseline in Total Fric Score in participants with symptomatic dermatographism ^{[1][2]}
End point description:	Total Fric score (a scale of 0-4 where 0= no linear hive ≥ 3mm in width, 1= one linear hive ≥ 3mm in width, 2= two linear hives ≥ 3mm in width, 3= three linear hives ≥ 3mm in width and 4 = four linear hives ≥ 3mm in width)
End point type	Primary
End point timeframe:	Baseline, Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	72 mg ligelizumab, symptomatic dermographism	120 mg ligelizumab, symptomatic dermographism	Placebo - 72 mg ligelizumab, symptomatic dermographism	Placebo - 120 mg ligelizumab, symptomatic dermographism
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[3]	0 ^[4]	0 ^[5]	0 ^[6]
Units: Scores on a scale				

Notes:

[3] - No subjects were analyzed since the study was prematurely terminated.

[4] - No subjects were analyzed since the study was prematurely terminated.

[5] - No subjects were analyzed since the study was prematurely terminated.

[6] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in critical temperature threshold in participants with cold urticaria

End point title	Change from baseline in critical temperature threshold in participants with cold urticaria ^{[7][8]}
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End point 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.

End point type	Primary
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End point timeframe:

Baseline, Week 12

Notes:

[7] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

[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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[9]	0 ^[10]	0 ^[11]	0 ^[12]
Units: Temperature				

Notes:

[9] - No subjects were analyzed since the study was prematurely terminated

[10] - No subjects were analyzed since the study was prematurely terminated

[11] - No subjects were analyzed since the study was prematurely terminated

[12] - No subjects were analyzed since the study was prematurely terminated

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in itch numerical rating scale in participants with cholinergic urticaria

End point title	Change from baseline in itch numerical rating scale in participants with cholinergic urticaria ^{[13][14]}
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End point 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 possible itch")

End point type	Primary
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End point timeframe:

Baseline, Week 12

Notes:

[13] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

[14] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	120 mg Ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[15]	0 ^[16]		
Units: Scores on a scale				

Notes:

[15] - No subjects were analyzed since the study was prematurely terminated.

[16] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with symptomatic dermographism with Total Fric score = 0

End point title	Proportion of participants with symptomatic dermographism with Total Fric score = 0 ^[17]
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End point description:

Total Fric score (a scale of 0-4 where 0= no linear hive \geq 3mm in width, 1= one linear hive \geq 3mm in width, 2= two linear hives \geq 3mm in width, 3= three linear hives \geq 3mm in width and 4 = four linear

hives \geq 3mm in width)

End point type	Secondary
End point timeframe:	
Week 12	

Notes:

[17] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	72 mg ligelizumab, symptomatic dermatographism	120 mg ligelizumab, symptomatic dermatographism	Placebo - 72 mg ligelizumab, symptomatic dermatographism	Placebo - 120 mg ligelizumab, symptomatic dermatographism
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[18]	0 ^[19]	0 ^[20]	0 ^[21]
Units: Proportion of participants				

Notes:

[18] - No subjects were analyzed since the study was prematurely terminated.

[19] - No subjects were analyzed since the study was prematurely terminated.

[20] - No subjects were analyzed since the study was prematurely terminated.

[21] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in itch numerical rating scale in participants with symptomatic dermatographism

End point title	Change from baseline in itch numerical rating scale in participants with symptomatic dermatographism ^[22]
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End point 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 possible itch")

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

Notes:

[22] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	72 mg ligelizumab, symptomatic dermatographism	120 mg ligelizumab, symptomatic dermatographism	Placebo - 72 mg ligelizumab, symptomatic dermatographism	Placebo - 120 mg ligelizumab, symptomatic dermatographism
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[23]	0 ^[24]	0 ^[25]	0 ^[26]

Units: Scores on a scale				
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Notes:

[23] - No subjects were analyzed since the study was prematurely terminated.

[24] - No subjects were analyzed since the study was prematurely terminated.

[25] - No subjects were analyzed since the study was prematurely terminated.

[26] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with cold urticaria with complete response (no itch or hives) to the TempTest

End point title	Proportion of participants with cold urticaria with complete response (no itch or hives) to the TempTest ^[27]
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End point 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.

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[27] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[28]	0 ^[29]	0 ^[30]	0 ^[31]
Units: Proportion of participants				

Notes:

[28] - No subjects were analyzed since the study was prematurely terminated.

[29] - No subjects were analyzed since the study was prematurely terminated.

[30] - No subjects were analyzed since the study was prematurely terminated.

[31] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in itch numerical rating scale in participants with cold urticaria

End point title	Change from baseline in itch numerical rating scale in participants with cold urticaria ^[32]
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End point 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 possible itch")

End point type	Secondary
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End point timeframe:

Baseline, Week 12

Notes:

[32] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	72 mg ligelizumab cold urticaria	120 mg ligelizumab, cold urticaria	Placebo - 72 mg ligelizumab, cold urticaria	Placebo - 120 mg ligelizumab, cold urticaria
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[33]	0 ^[34]	0 ^[35]	0 ^[36]
Units: Scores on a scale				

Notes:

[33] - No subjects were analyzed since the study was prematurely terminated.

[34] - No subjects were analyzed since the study was prematurely terminated.

[35] - No subjects were analyzed since the study was prematurely terminated.

[36] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with cholinergic urticaria with itch numerical rating scale =0

End point title	Proportion of participants with cholinergic urticaria with itch numerical rating scale =0 ^[37]
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End point 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 possible itch")

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[37] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	120 mg Ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[38]	0 ^[39]		
Units: Proportion of participants				

Notes:

[38] - No subjects were analyzed since the study was prematurely terminated.

[39] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with cholinergic urticaria with physician global assessment of severity of hives (PGA - hive score) =0

End point title	Proportion of participants with cholinergic urticaria with physician global assessment of severity of hives (PGA - hive score) =0 ^[40]
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End point description:

Physician global assessment of severity of hives

PGA is an assessment of all lesions scored on a scale from 0-5 (with 0= No hives and 5=Very severe hives)

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[40] - 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: Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

End point values	120 mg Ligelizumab, cholinergic urticaria	Placebo - 120 mg ligelizumab, cholinergic urticaria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[41]	0 ^[42]		
Units: Proportion of participants				

Notes:

[41] - No subjects were analyzed since the study was prematurely terminated.

[42] - No subjects were analyzed since the study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected after signature of the informed consent (ICF) form until after 16 weeks from last dose (12 wks from end of treatment). Treatment period was 24 wks.

SAEs were collected after signature of the ICF until after 16 wks from last dose.

Adverse event reporting additional description:

AE: Untoward medical occurrence, unfavorable/unintended sign, symptom, disease or injury, temporally assoc. with use of a marketed/investigational medicinal product, gene therapy, theragnostic product or medical device in patients, clinical-trial subjs, device users or other persons, whether or not considered to be related to or due to the product.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	QGE031 72mg
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Reporting group description:

QGE031 72mg

Reporting group title	QGE031 120mg
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Reporting group description:

QGE031 120mg

Reporting group title	Total
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Reporting group description:

Total

Reporting group title	Placebo - QGE031 120mg
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Reporting group description:

Placebo - QGE031 120mg

Reporting group title	Placebo - QGE031 72mg
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Reporting group description:

Placebo - QGE031 72mg

Serious adverse events	QGE031 72mg	QGE031 120mg	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 15 (0.00%)	0 / 39 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo - QGE031 120mg	Placebo - QGE031 72mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	QGE031 72mg	QGE031 120mg	Total
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 8 (37.50%)	6 / 15 (40.00%)	13 / 39 (33.33%)
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 15 (0.00%) 0	1 / 39 (2.56%) 1
Nervous system disorders Tension headache subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0	1 / 15 (6.67%) 1 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0	1 / 39 (2.56%) 1 1 / 39 (2.56%) 1 1 / 39 (2.56%) 3
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1 0 / 8 (0.00%) 0	0 / 15 (0.00%) 0 1 / 15 (6.67%) 1	1 / 39 (2.56%) 1 1 / 39 (2.56%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0 1 / 8 (12.50%) 1	1 / 15 (6.67%) 1 0 / 15 (0.00%) 0	1 / 39 (2.56%) 1 1 / 39 (2.56%) 1

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 15 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Infections and infestations			
Peritonsillar abscess			
subjects affected / exposed	0 / 8 (0.00%)	0 / 15 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Herpes simplex			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Influenza			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	2 / 15 (13.33%) 2	2 / 39 (5.13%) 2
Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 15 (0.00%) 0	1 / 39 (2.56%) 1
Post-acute COVID-19 syndrome subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1
Glucose tolerance impaired subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 15 (6.67%) 1	1 / 39 (2.56%) 1

Non-serious adverse events	Placebo - QGE031 120mg	Placebo - QGE031 72mg	
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 11 (9.09%)	3 / 5 (60.00%)	
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 5 (20.00%) 1	
Nervous system disorders			

Tension headache subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Migraine subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 5 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 5 (20.00%) 3	
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Endocrine disorders Hypopituitarism subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Groin pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Peritonsillar abscess			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Herpes simplex			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Post-acute COVID-19 syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Metabolism and nutrition disorders			
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	
Glucose tolerance impaired subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 5 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Study was terminated early with too few patients meeting the primary endpoint analysis timepoint to perform proper hypothesis testing.

Notes: