



Clinical trial results:

A multicenter, randomized, double-blind, placebo-controlled phase 2b dose-finding study to investigate the efficacy and safety of ligelizumab (QGE031) in adolescent patients with Chronic Spontaneous Urticaria (CSU)

Summary

EudraCT number	2017-004207-52
Trial protocol	DE ES BE HU EE
Global end of trial date	03 February 2021

Results information

Result version number	v1 (current)
This version publication date	13 August 2021
First version publication date	13 August 2021

Trial information

Trial identification

Sponsor protocol code	CQGE031C2202
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03437278
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 February 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Change in the Urticaria Activity Score (UAS7) between baseline and Week 24

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	01 August 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	India: 5
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Turkey: 7
Worldwide total number of subjects	49
EEA total number of subjects	19

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)	49
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 20 sites: Argentina (3), Belgium (1), Canada (2), Germany (2), Hungary (1), India (3), Russia (3), Spain (2), Taiwan (1) and Turkey (2).

Pre-assignment

Screening details:

Participants underwent a Screening period of up to 4 weeks.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ligelizumab 24 mg

Arm description:

Participants received a dose of ligelizumab 24 mg (low dose) which consisted of one injection of 0.2 ml of ligelizumab 120 mg/ 1 ml vial every 4 weeks from Day 1 to Week 20 (inclusive).

Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Ligelizumab comes in 120 mg per 1 ml liquid vials. Participants received one injection every 4 weeks at a dose of 24 mg, low dose.

Arm title	Ligelizumab 120 mg
------------------	--------------------

Arm description:

Participants received a dose of ligelizumab 120 mg (high dose) which consisted of one injection of 1 ml of ligelizumab 120 mg/ 1 ml vial every 4 weeks from Day 1 to Week 20 (inclusive).

Arm type	Experimental
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Ligelizumab comes in 120 mg per 1 ml liquid vials. Participants received one injection every 4 weeks at a dose of 120 mg, high dose.

Arm title	Placebo + Ligelizumab 120 mg
------------------	------------------------------

Arm description:

Participants received Placebo which consisted of one injection of 1 ml placebo every 4 weeks from Day 1 to Week 8 (inclusive). From week 12 to week 20 (inclusive), participants received a dose of ligelizumab 120 mg (high dose) which consisted of one injection of 1 ml of ligelizumab 120 mg/ 1 ml vial.

Arm type	Placebo
----------	---------

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details:	
Placebo 0 mg per 1 ml liquid injection once every 4 weeks.	
Investigational medicinal product name	Ligelizumab
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Ligelizumab comes in 120 mg per 1 ml liquid vials. Participants received one injection every 4 weeks at a dose of 120 mg, high dose.

Number of subjects in period 1	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg
Started	24	13	12
Completed	22	13	10
Not completed	2	0	2
Physician decision	1	-	1
Adverse event, non-fatal	-	-	1
Progressive disease	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Ligelizumab 24 mg
Reporting group description:	
Participants received a dose of ligelizumab 24 mg (low dose) which consisted of one injection of 0.2 ml of ligelizumab 120 mg/ 1 ml vial every 4 weeks from Day 1 to Week 20 (inclusive).	
Reporting group title	Ligelizumab 120 mg
Reporting group description:	
Participants received a dose of ligelizumab 120 mg (high dose) which consisted of one injection of 1 ml of ligelizumab 120 mg/ 1 ml vial every 4 weeks from Day 1 to Week 20 (inclusive).	
Reporting group title	Placebo + Ligelizumab 120 mg
Reporting group description:	
Participants received Placebo which consisted of one injection of 1 ml placebo every 4 weeks from Day 1 to Week 8 (inclusive). From week 12 to week 20 (inclusive), participants received a dose of ligelizumab 120 mg (high dose) which consisted of one injection of 1 ml of ligelizumab 120 mg/ 1 ml vial.	

Reporting group values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg
Number of subjects	24	13	12
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	24	13	12
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	14.9	15.2	14.4
standard deviation	± 1.94	± 1.41	± 1.51
Sex: Female, Male			
Units: Participants			
Female	10	9	9
Male	14	4	3
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	7	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	16	12	10
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	49		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	49		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	28		
Male	21		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	10		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	38		
More than one race	0		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Ligelizumab 24 mg
Reporting group description: Participants received a dose of ligelizumab 24 mg (low dose) which consisted of one injection of 0.2 ml of ligelizumab 120 mg/ 1 ml vial every 4 weeks from Day 1 to Week 20 (inclusive).	
Reporting group title	Ligelizumab 120 mg
Reporting group description: Participants received a dose of ligelizumab 120 mg (high dose) which consisted of one injection of 1 ml of ligelizumab 120 mg/ 1 ml vial every 4 weeks from Day 1 to Week 20 (inclusive).	
Reporting group title	Placebo + Ligelizumab 120 mg
Reporting group description: Participants received Placebo which consisted of one injection of 1 ml placebo every 4 weeks from Day 1 to Week 8 (inclusive). From week 12 to week 20 (inclusive), participants received a dose of ligelizumab 120 mg (high dose) which consisted of one injection of 1 ml of ligelizumab 120 mg/ 1 ml vial.	
Subject analysis set title	All participants with PK data
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants in the study (low dose, high dose and placebo+high dose) with available pharmacokinetic data	

Primary: Change from baseline of weekly Urticaria Activity Score (UAS7) at week 24

End point title	Change from baseline of weekly Urticaria Activity Score (UAS7) at week 24 ^[1]
-----------------	--

End point description:

UAS7 is a self-reported scoring system to evaluate urticaria signs and symptoms. UAS7 is the sum of daily urticaria activity scores (UAS) over a seven-day period. The possible range of UAS7 score is 0 to 42 (0 to 6 for daily UAS x 7 days). A higher urticaria activity score indicates more severe symptoms. A negative change score from baseline indicates improvement. Baseline was calculated using data from the 7 days prior to the first treatment date.

To handle the missing data, if a participant had at least 4 non-missing daily scores within the 7 days prior to a study visit, the weekly score was calculated as the sum of the available scores in that week, divided by the number of days with daily scores available, multiplied by 7. However, if there were less than 4 non-missing daily scores within the prior 7 days, then the weekly score was missing for the week.

No statistical analysis was planned for this primary outcome.

End point type	Primary
End point timeframe: Baseline, week 24	

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: Statistical analysis were not planned for this primary endpoint

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	13	11	
Units: Score on a scale				
arithmetic mean (standard deviation)	-20.36 (± 12.963)	-22.50 (± 13.503)	-21.26 (± 14.480)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of weekly Urticaria Activity Score (UAS7) at weeks 12 and 40

End point title	Change from baseline of weekly Urticaria Activity Score (UAS7) at weeks 12 and 40
-----------------	---

End point description:

UAS7 is a self-reported scoring system to evaluate urticaria signs and symptoms. UAS7 is the sum of daily urticaria activity scores (UAS) over a seven-day period. The possible range of UAS7 score is 0 to 42 (0 to 6 for daily UAS x 7 days). A higher urticaria activity score indicates more severe symptoms. A negative change score from baseline indicates improvement. Baseline was calculated using data from the 7 days prior to the first treatment date.

To handle the missing data, if a participant had at least 4 non-missing daily scores within the 7 days prior to a study visit, the weekly score was calculated as the sum of the available scores in that week, divided by the number of days with daily scores available, multiplied by 7. However, if there were less than 4 non-missing daily scores within the prior 7 days, then the weekly score was missing for the week.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, weeks 12 and 40

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=23, 13, 12)	-15.70 (± 10.867)	-18.38 (± 12.268)	-12.96 (± 13.043)	
Week 40 (n=22, 12, 10)	-17.50 (± 12.619)	-15.65 (± 11.096)	-19.43 (± 17.667)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with complete response in weekly Urticaria Activity Score (UAS7)

End point title	Percentage of participants with complete response in weekly Urticaria Activity Score (UAS7)
-----------------	---

End point description:

UAS7 is a self-reported scoring system to evaluate urticaria signs and symptoms. UAS7 is the sum of daily urticaria activity scores (UAS) over a seven-day period. The possible range of UAS7 score is 0 to 42 (0 to 6 for daily UAS x 7 days). A higher urticaria activity score indicates more severe symptoms. A complete UAS7 response is defined as UAS7=0, no wheals neither pruritus. Participants with post-baseline missing data were considered as non-responders.

End point type	Secondary
----------------	-----------

End point timeframe:

Weeks 12, 24 and 40

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Participants				
Week 12	4	5	2	
Week 24	8	8	4	
Week 40	3	2	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of weekly Itch Severity Score (ISS7)

End point title	Change from baseline of weekly Itch Severity Score (ISS7)
-----------------	---

End point description:

ISS7 is the sum of daily Itch Severity Score (ISS) over a seven-day period. The possible range of ISS7 score is 0-21 (0-3 for daily ISS x 7 days), where 0 is defined as complete ISS7 response (no itching) and 21 is the worst score. A negative change score from baseline indicates improvement. Baseline was calculated using data from the 7 days prior to the first treatment date.

To handle the missing data, if a participant had at least 4 non-missing daily scores within the 7 days prior to a study visit, the weekly score was calculated as the sum of the available scores in that week, divided by the number of days with daily scores available, multiplied by 7. However, if there were less than 4 non-missing daily scores within the prior 7 days, then the weekly score was missing for the week.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, weeks 12, 24 and 40

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Score on a scale				
arithmetic mean (standard deviation)				

Week 12 (n=23, 13, 12)	-7.66 (± 5.824)	-7.81 (± 6.047)	-6.34 (± 6.936)	
Week 24 (n=23, 13, 12)	-9.71 (± 7.049)	-9.85 (± 6.488)	-10.28 (± 7.811)	
Week 40 (n=22, 12, 10)	-8.73 (± 6.656)	-6.86 (± 5.848)	-9.88 (± 8.687)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with complete response in weekly Itch Severity Score (ISS7)

End point title	Percentage of participants with complete response in weekly Itch Severity Score (ISS7)
-----------------	--

End point description:

ISS7 is the sum of daily Itch Severity Score (ISS) over a seven-day period. The possible range of ISS7 score is 0-21 (0-3 for daily ISS x 7 days), where 0 is defined as complete ISS7 response (no itching) and 21 is the worst score. Participants with post-baseline missing data were considered as non-responders.

End point type	Secondary
----------------	-----------

End point timeframe:

Weeks 12, 24 and 40

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Participants				
Week 12	4	5	2	
Week 24	9	8	4	
Week 40	4	2	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of weekly Hives Severity Score (HSS7)

End point title	Change from baseline of weekly Hives Severity Score (HSS7)
-----------------	--

End point description:

HSS7 is the sum of daily Hives Severity Score (HSS) over a seven-day period. The possible range of HSS7 score is 0-21 (0-3 for daily HSS x 7 days), where 0 is defined as complete HSS7 response (no wheals) and 21 is the worst score. A negative change score from baseline indicates improvement. Baseline was calculated using data from the 7 days prior to the first treatment date.

To handle the missing data, if a participant had at least 4 non-missing daily scores within the 7 days prior to a study visit, the weekly score was calculated as the sum of the available scores in that week, divided by the number of days with daily scores available, multiplied by 7. However, if there were less

than 4 non-missing daily scores within the prior 7 days, then the weekly score was missing for the week.

End point type	Secondary
End point timeframe:	
Baseline, weeks 12, 24 and 40	

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=23, 13, 12)	-8.03 (± 6.307)	-10.58 (± 7.225)	-6.62 (± 6.385)	
Week 24 (n=23, 13, 11)	-10.65 (± 6.673)	-12.65 (± 7.785)	-10.98 (± 6.842)	
Week 40 (n=22, 12, 10)	-8.77 (± 6.770)	-8.78 (± 6.084)	-9.55 (± 9.197)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with complete response in weekly Hives Severity Score (HSS7)

End point title	Percentage of participants with complete response in weekly Hives Severity Score (HSS7)
End point description:	
HSS7 is the sum of daily Hives Severity Score (HSS) over a seven-day period. The possible range of HSS7 score is 0-21 (0-3 for daily HSS x 7 days), where 0 is defined as complete HSS7 response (no wheals) and 21 is the worst score. Participants with post-baseline missing data were considered as non-responders.	
End point type	Secondary
End point timeframe:	
Weeks 12, 24 and 40	

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Participants				
Week 12	6	6	2	
Week 24	10	9	4	
Week 40	5	2	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of the Children Dermatology Life Quality Index (CDLQI)

End point title	Change from baseline of the Children Dermatology Life Quality Index (CDLQI)
-----------------	---

End point description:

The children dermatology life quality index questionnaire is a 10-item dermatology- specific health-related quality of life measure designed for use in children. Participants rated their dermatology symptoms as well as the impact of their skin condition on various aspects of their lives. The CDLQI total score is a sum of all 10 item responses, each individual response ranging from 0 (not at all) to 3 (very much). Total score ranges from 0 to 30 with higher scores indicating greater health-related quality of life impairment. A negative change score from baseline indicates improvement. Baseline was defined as the last non-missing value prior to or on the first treatment date.

To handle the missing data, if a participant had only one item missing score per visit, then it was imputed to 0 and total score was calculated accordingly. If there were 2 or more item missing scores per visit, then the total score for the visit was considered as missing.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, weeks 12, 24 and 40

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=19, 13, 11)	-10.1 (± 4.88)	-6.6 (± 8.05)	-5.0 (± 6.23)	
Week 24 (n=21, 10, 11)	-11.5 (± 6.85)	-8.8 (± 10.43)	-10.1 (± 6.74)	
Week 40 (n=19, 11, 11)	-10.3 (± 6.86)	-5.5 (± 9.04)	-8.6 (± 8.54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total human immunoglobulin E (IgE)

End point title	Change from baseline in total human immunoglobulin E (IgE)
-----------------	--

End point description:

Change from baseline in IgE (free IgE plus IgE bound to ligelizumab) at weeks 12, 24 and 40 as a pharmacodynamic measurement.

End point type	Secondary
End point timeframe:	
Baseline, weeks 12, 24 and 40	

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: International units / millilitre				
arithmetic mean (standard deviation)				
Week 12 (n=17, 11, 9)	186 (± 160)	245 (± 291)	-43.1 (± 56.2)	
Week 24 (n=19, 12, 9)	169 (± 126)	328 (± 504)	325 (± 411)	
Week 40 (n=19, 13, 9)	30.4 (± 105)	-15.6 (± 118)	-22.0 (± 93.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F) of Ligelizumab estimated with PopPK model

End point title	Apparent Clearance (CL/F) of Ligelizumab estimated with PopPK model
End point description:	
Model-based estimate of apparent clearance (CL/F) was derived using compartmental pharmacokinetic population (PopPK) modelling using non-linear mixed effects model for ligelizumab. Apparent clearance population estimate was derived through fitting individual drug administration history and collected ligelizumab concentrations at the specified data points (listed in Time Frame).	
End point type	Secondary
End point timeframe:	
Weeks 0 (baseline), 4, 8, 12, 16, 20 (all pre-dose) and weeks 24, 32 and 40	

End point values	All participants with PK data			
Subject group type	Subject analysis set			
Number of subjects analysed	47			
Units: Liters / day				
median (inter-quartile range (Q1-Q3))	0.66 (0.44 to 1.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent volume of distribution of Ligelizumab estimated with a PopPK model

End point title	Apparent volume of distribution of Ligelizumab estimated with a PopPK model
-----------------	---

End point description:

Model-based estimate of apparent volume of distribution was derived using compartmental pharmacokinetic population (PopPK) modelling using non-linear mixed effects model for ligelizumab. Apparent volume of distribution population estimate was derived through fitting individual drug administration history and collected ligelizumab concentrations at the specified data points (listed in Time Frame).

End point type	Secondary
----------------	-----------

End point timeframe:

Weeks 0 (baseline), 4, 8, 12, 16, 20 (all pre-dose) and weeks 24, 32 and 40

End point values	All participants with PK data			
Subject group type	Subject analysis set			
Number of subjects analysed	47			
Units: Liters				
median (inter-quartile range (Q1-Q3))	14.5 (11.02 to 16.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with adverse events (AEs) and serious adverse events (SAEs)
-----------------	--

End point description:

Number of participants with AEs and SAEs, including significant changes from baseline in vital signs (blood pressure, pulse rate), electrocardiograms and laboratory values qualifying and reported as AEs. The number of participants in each category is reported in the table.

End point type	Secondary
----------------	-----------

End point timeframe:

From the start of treatment to 20 weeks after end of treatment, assessed up to maximum duration of 40 weeks

End point values	Ligelizumab 24 mg	Ligelizumab 120 mg	Placebo + Ligelizumab 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	12	
Units: Participants				
AEs	18	11	9	
Treatment related AEs	6	5	2	

SAEs	1	0	1	
SAEs leading to treatment discontinuation	0	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the start of treatment until 20 weeks after end of treatment, assessed up to maximum duration of 40 weeks

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	23.1
--------------------	------

Reporting groups

Reporting group title	Ligelizumab 24 mg q4w
-----------------------	-----------------------

Reporting group description:

Ligelizumab 24 mg q4w

Reporting group title	Ligelizumab 120 mg q4w
-----------------------	------------------------

Reporting group description:

Ligelizumab 120 mg q4w

Reporting group title	Placebo - Ligelizumab 120 mg q4w
-----------------------	----------------------------------

Reporting group description:

Placebo - Ligelizumab 120 mg q4w

Reporting group title	Total
-----------------------	-------

Reporting group description:

Total

Serious adverse events	Ligelizumab 24 mg q4w	Ligelizumab 120 mg q4w	Placebo - Ligelizumab 120 mg q4w
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	0 / 13 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Pulmonary valve incompetence			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tricuspid valve incompetence			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			

subjects affected / exposed	1 / 24 (4.17%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 49 (4.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Pulmonary valve incompetence			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tricuspid valve incompetence			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ligelizumab 24 mg q4w	Ligelizumab 120 mg q4w	Placebo - Ligelizumab 120 mg q4w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 24 (75.00%)	11 / 13 (84.62%)	9 / 12 (75.00%)
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Arthropod bite			

subjects affected / exposed	0 / 24 (0.00%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Face injury			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 24 (8.33%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Headache			
subjects affected / exposed	5 / 24 (20.83%)	1 / 13 (7.69%)	4 / 12 (33.33%)
occurrences (all)	7	2	11
Intercostal neuralgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 24 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	6	0
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	0 / 24 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Injection site erythema			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	1 / 24 (4.17%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Injection site reaction			
subjects affected / exposed	0 / 24 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	2 / 24 (8.33%)	2 / 13 (15.38%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Eye disorders			

Eye pruritus subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 9	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	0 / 13 (0.00%) 0	2 / 12 (16.67%) 5
Gastritis subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	3 / 13 (23.08%) 3	1 / 12 (8.33%) 1
Odynophagia subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Vomiting subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	3 / 13 (23.08%) 3	0 / 12 (0.00%) 0
Reproductive system and breast disorders			
Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	1 / 12 (8.33%) 2
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Hepatobiliary disorders			

Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 3	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Skin and subcutaneous tissue disorders Angioedema subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 5	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Chronic spontaneous urticaria subjects affected / exposed occurrences (all)	5 / 24 (20.83%) 10	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Onycholysis subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 5	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 4	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Fibromyalgia subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0

Medial tibial stress syndrome subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Muscle spasms subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 2
Infections and infestations			
Gastrointestinal infection subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	1 / 12 (8.33%) 1
Influenza subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 4	1 / 13 (7.69%) 1	2 / 12 (16.67%) 2
Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 24 (29.17%) 14	4 / 13 (30.77%) 9	4 / 12 (33.33%) 6
Pharyngitis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Post procedural infection subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Respiratory tract infection viral subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	2 / 13 (15.38%) 2	0 / 12 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 5	2 / 13 (15.38%) 3	0 / 12 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	2 / 13 (15.38%) 5	1 / 12 (8.33%) 1
Viral infection			

subjects affected / exposed	0 / 24 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 49 (77.55%)		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Arthropod bite			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Face injury			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	10 / 49 (20.41%)		
occurrences (all)	20		
Intercostal neuralgia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	6		
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	2		
Injection site erythema			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		

Injection site pain subjects affected / exposed occurrences (all)	3 / 49 (6.12%) 3		
Injection site reaction subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Pyrexia subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 4		
Eye disorders Eye pruritus subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 10		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 7		
Gastritis subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Nausea subjects affected / exposed occurrences (all)	5 / 49 (10.20%) 5		
Odynophagia subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Vomiting			

subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 4		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all) Menstruation irregular subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 3 1 / 49 (2.04%) 1		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 4		
Skin and subcutaneous tissue disorders Angioedema subjects affected / exposed occurrences (all) Chronic spontaneous urticaria subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Onycholysis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	3 / 49 (6.12%) 6 5 / 49 (10.20%) 10 1 / 49 (2.04%) 1 1 / 49 (2.04%) 1 1 / 49 (2.04%) 1 1 / 49 (2.04%) 1		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	4		
Fibromyalgia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Medial tibial stress syndrome			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	2		
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	5 / 49 (10.20%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	15 / 49 (30.61%)		
occurrences (all)	29		
Pharyngitis			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Post procedural infection			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Rhinitis			

subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	5 / 49 (10.20%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	7		
Viral infection			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		

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

None reported