Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Multicenter, Dose-ranging, Phase 2b Study to Evaluate Efficacy and Safety of Tezepelumab for the Treatment of Chronic Spontaneous Urticaria

Summary

EudraCT number	2020-002759-39
Trial protocol	GR FR IT ES PL
Global end of trial date	13 April 2023

Results information

Result version number	v1 (current)
This version publication date	12 April 2024
First version publication date	12 April 2024

Trial information

Trial identification

Sponsor protocol code	20190194

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04833855
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the effect of tezepelumab on improvement in the Urticaria Activity Score over 7 days (UAS7).

Protection of trial subjects:

The study was conducted in accordance with the protocol and with consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Conference on Harmonisation (ICH) Good Clinical Practice Guidelines, and applicable ICH laws and regulations.

Background therapy:

Participants maintained a stable dose of second generation H1-antihistamines (sgAH) as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

Evidence for comparator: -

Actual start date of recruitment	15 April 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 13
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	United States: 38
Country: Number of subjects enrolled	Canada: 26
Worldwide total number of subjects	183
EEA total number of subjects	65

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)	0
Adults (18-64 years)	168
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 56 study centers in Japan, Republic of Korea, France, Germany, Greece, Italy, Poland, Spain, Canada, and the United States, and participated from 15 April 2021 to 13 April 2023.

Pre-assignment

Screening details:

Participants with chronic spontaneous urticaria (CSU) and symptomatic despite treatment with sgAH were randomized based on if they were previously treated with anti-immunoglobulin E (IgE) therapies or were anti-IgE naïve.

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, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants with and without previous anti-IgE therapy experience were randomized to receive placebo subcutaneously (SC) every 2 weeks (Q2W) for 16 weeks.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

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

Dosage and administration details:

Participants received placebo SC Q2W for 16 weeks.

Arm title	Omalizumab 300 mg SC Q4W

Arm description:

Participants without previous anti-IgE experience were randomized to receive omalizumab 300 mg SC every 4 weeks (Q4W) for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

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

Dosage and administration details:

Participants received placebo SC Q4W at intervening study visits for 16 weeks, to ensure participants received an injection Q2W.

Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	Xolair®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received omalizumab 300 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W.

Arm title	Tezepelumab 210 mg SC Q4W

Arm description:

Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 210 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

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

Dosage and administration details:

Participants received placebo SC Q4W at intervening study visits for 16 weeks, to ensure participants received an injection Q2W.

Investigational medicinal product name	Tezepelumab
Investigational medicinal product code	AMG 157
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received tezepelumab 210 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W.

Arm title	Tezepelumab 420 mg SC Q2W

Arm description:

Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 420 mg SC Q2W for 16 weeks.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

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

Dosage and administration details:

Participants received tezepelumab 420 mg SC Q4W for 16 weeks.

Number of subjects in period 1	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W
Started	48	31	52
Completed	43	29	45
Not completed	5	2	7
Consent withdrawn by subject	4	1	3
Protocol specified criteria	-	-	2
Lost to follow-up	1	-	2
Decision by sponsor	-	1	-

Number of subjects in period 1	Tezepelumab 420 mg SC Q2W
Started	52
Completed	48
Not completed	4
Consent withdrawn by subject	1
Protocol specified criteria	1
Lost to follow-up	2
Decision by sponsor	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants with and without previous anti-IgE therapy experience were randomized to receive placebo subcutaneously (SC) every 2 weeks (Q2W) for 16 weeks. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	
Reporting group title	Omalizumab 300 mg SC Q4W
Reporting group description:	
Participants without previous anti-IgE experience were randomized to receive omalizumab 300 mg SC every 4 weeks (Q4W) for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	
Reporting group title	Tezepelumab 210 mg SC Q4W
Reporting group description:	
Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 210 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	
Reporting group title	Tezepelumab 420 mg SC Q2W
Reporting group description:	
Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 420 mg SC Q2W for 16 weeks. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	

Reporting group values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W
Number of subjects	48	31	52
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)	0	0	0
Adults (18-64 years)	44	30	47
From 65-84 years	4	1	5
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	42.8	39.8	45.0
standard deviation	± 15.2	± 13.1	± 14.7
Gender Categorical Units: Subjects			
Female	37	23	35
Male	11	8	17

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	2	3
Not Hispanic or Latino	45	29	49
Unknown or Not Reported	0	0	0
Race, Customized Units: Subjects			
Asian	18	12	16
Black or African American	1	2	2
Multiple	0	0	0
White	29	17	34
Other	0	0	0

Reporting group values	Tezepelumab 420 mg SC Q2W	Total	
Number of subjects	52	183	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	47	168	
From 65-84 years	5	15	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	42.9		
standard deviation	± 14.5	-	
Gender Categorical Units: Subjects			
Female	39	134	
Male	13	49	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	14	
Not Hispanic or Latino	46	169	
Unknown or Not Reported	0	0	
Race, Customized Units: Subjects			
Asian	14	60	
Black or African American	2	7	
Multiple	1	1	
White	34	114	
Other	1	1	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants with and without previous anti-IgE therapy experience were randomized to receive placebo subcutaneously (SC) every 2 weeks (Q2W) for 16 weeks. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	
Reporting group title	Omalizumab 300 mg SC Q4W
Reporting group description:	
Participants without previous anti-IgE experience were randomized to receive omalizumab 300 mg SC every 4 weeks (Q4W) for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	
Reporting group title	Tezepelumab 210 mg SC Q4W
Reporting group description:	
Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 210 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	
Reporting group title	Tezepelumab 420 mg SC Q2W
Reporting group description:	
Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 420 mg SC Q2W for 16 weeks. Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).	

Primary: Change from Baseline in UAS7 at Week 16

End point title	Change from Baseline in UAS7 at Week 16
End point description:	
The UAS is a CSU-specific patient-reported outcome measure with 2 components: Hives Severity Score (HSS) for number of wheals and an Itch Severity Score (ISS) for itch intensity, and are each scored from 0 (no wheals, no itch) to 3 (>50 wheals, severe itch) for the previous 24 hours. The HSS and ISS are combined to give a daily UAS ranging from 0 to 6. The sum of the daily UAS over a 7-day period provides the UAS7, from 0 (no symptoms) to 42 (severe urticaria). The least squares mean (LSM) estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline UAS7, treatment, study week and the interaction between treatment and study week. A negative change from baseline indicates an improvement in urticaria activity. The full analysis set (FAS) included all randomized participants who received at least 1 dose of investigational product.	
End point type	Primary
End point timeframe:	
Baseline and Week 16	

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-13.6 (± 1.6)	-18.4 (± 2.0)	-13.5 (± 1.6)	-14.7 (± 1.5)

Statistical analyses

Statistical analysis title	Tezepelumab 420 mg SC Q2W - Placebo
Comparison groups	Placebo v Tezepelumab 420 mg SC Q2W
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6 [1]
Method	Repeated measure model
Parameter estimate	LSM difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	3.1
Variability estimate	Standard error of the mean
Dispersion value	2.2

Notes:

[1] - Nominal p-value. Model parameters: stratification factor (prior anti-IgE status), baseline UAS7, treatment, study week, interaction between treatment and study week.

Statistical analysis title	Tezepelumab 210 mg SC Q4W - Placebo
Comparison groups	Placebo v Tezepelumab 210 mg SC Q4W
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99 [2]
Method	Repeated measure model
Parameter estimate	LSM difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	4.4
Variability estimate	Standard error of the mean
Dispersion value	2.2

Notes:

[2] - Nominal p-value. Model parameters: stratification factor (prior anti-IgE status), baseline UAS7, treatment, study week, interaction between treatment and study week.

Secondary: Change from Baseline in ISS over 7 Days (ISS7) at Week 16

End point title	Change from Baseline in ISS over 7 Days (ISS7) at Week 16

End point description:

The ISS is a component of the UAS, a CSU-specific patient-reported outcome measure and assessed itch intensity, with daily scores ranging from 0 (no itch) to 3 (severe itch) for the previous 24 hours. The sum of daily ISS over a 7-day period provides the ISS7, from 0 (no symptoms) to 21 (severe itch). The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline ISS7, treatment, study week and the interaction between treatment and study week. A negative change from baseline indicates an improvement in urticaria activity. The FAS included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-7.7 (± 0.8)	-9.6 (± 1.0)	-7.3 (± 0.8)	-8.0 (± 0.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a UAS7 of ≤ 6 (Minimal Residual Disease) at Week 16

End point title	Number of Participants with a UAS7 of ≤ 6 (Minimal Residual Disease) at Week 16

End point description:

The sum of the daily UAS over a 7-day period provides the UAS7, from 0 (no symptoms) to 42 (severe urticaria). Minimal residual disease in UAS7 was defined as a score ≤ 6 and indicates well-controlled urticaria and a good response to treatment. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	8	14	10	13

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HSS over 7 Days (HSS7) at Week 16

End point title	Change from Baseline in HSS over 7 Days (HSS7) at Week 16

End point description:

The HSS is a component of the UAS, a CSU-specific patient-reported outcome measure and assessed the number of wheals, with daily scores ranging from 0 (no wheals) to 3 (>50 wheals) for the previous 24 hours. The sum of daily HSS over a 7-day period provides the HSS7, from 0 (no symptoms) to 21 (severe wheals). The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline HSS7, treatment, study week and the interaction between treatment and study week. A negative change from baseline indicates an improvement in urticaria activity. The FAS included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-5.8 (± 0.8)	-8.8 (± 1.1)	-6.3 (± 0.8)	-6.7 (± 0.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a UAS7 = 0 at Week 16 (Complete Response)

End point title	Number of Participants with a UAS7 = 0 at Week 16 (Complete Response)

End point description:

The sum of the daily UAS over a 7-day period provides the UAS7, from 0 (no symptoms) to 42 (severe urticaria). A complete response was defined as UAS7 = 0 at Week 16. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	4	11	7	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Change from Baseline in UAS7 of ≤ -10 (Minimal Important Difference)

End point title	Number of Participants with a Change from Baseline in UAS7 of ≤ -10 (Minimal Important Difference)

End point description:

The sum of the daily UAS over a 7-day period provides the UAS7, from 0 (no symptoms) to 42 (severe urticaria). Minimal important difference in UAS7 was defined as a change from baseline of ≤ -10. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	28	20	27	32

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ISS7 = 0 at Week 16 (Complete Resolution)

End point title	Number of Participants with ISS7 = 0 at Week 16 (Complete Resolution)

End point description:

The sum of daily ISS over a 7-day period provides the ISS7, from 0 (no symptoms) to 21 (severe itch). An ISS7 = 0 indicates a complete resolution of itch. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	4	12	7	9

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with HSS7 = 0 at Week 16 (Complete Resolution)

End point title	Number of Participants with HSS7 = 0 at Week 16 (Complete Resolution)

End point description:

The sum of daily HSS over a 7-day period provides the HSS7, from 0 (no symptoms) to 21 (severe wheals). An HSS7 = 0 indicates a complete resolution of hives. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	6	11	8	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Change from Baseline in ISS7 of ≤ -5 (Minimal Important Difference)

End point title	Number of Participants with a Change from Baseline in ISS7 of ≤ -5 (Minimal Important Difference)

End point description:

The sum of daily ISS over a 7-day period provides the ISS7, from 0 (no symptoms) to 21 (severe itch). Minimal important difference in ISS7 was defined as a change from baseline of ≤ -5. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	29	20	28	34

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Change from Baseline in HSS7 of ≤ -5.5 (Minimal Important Difference)

End point title	Number of Participants with a Change from Baseline in HSS7 of ≤ -5.5 (Minimal Important Difference)

End point description:

The sum of daily HSS over a 7-day period provides the HSS7, from 0 (no symptoms) to 21 (severe wheals). Minimal important difference in HSS7 was defined as a change from baseline of ≤ -5.5. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	25	39	48
Units: participants	23	19	24	31

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Weekly Sleep Interference Score (SIS7) at Week 16

End point title	Change from Baseline in Weekly Sleep Interference Score (SIS7) at Week 16

End point description:

The SIS is part of the Urticaria Patient Daily Diary and was assessed by the participant using the electronic diary once daily in the morning. Participants scored sleep interference on a scale of 0 (no interference) to 3 (substantial, woke up often, severe interference with sleep). The SIS7 was a sum of the daily scores over 7 days. The LSM estimates were based on the repeated measure model with stratification factor (prior anti-IgE status), baseline SIS7, treatment, study week and the interaction between treatment and study week. A negative change from baseline indicates an improvement in sleep interference. The FAS included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-8.4 (± 0.7)	-6.5 (± 0.9)	-7.4 (± 0.7)	-7.8 (± 0.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SQS7: Sum of Average Daily Q1 - Q3 at Week 16

End point title	Change from Baseline in SQS7: Sum of Average Daily Q1 - Q3 at Week 16

End point description:

The SQS was assessed by the participant through 3 questions relating to falling asleep (Q1), wakefulness (Q2), and feeling rested in the morning (Q3). The sum of average daily Q1 - Q3 score was generated by averaging 3 daily sleep quality items and then summing the daily average over 7 days with a score ranging from 0 (good quality sleep) to 21 (poor quality sleep) (sum of the average daily Q1 - Q3). The LSM estimates were based on the repeated measure model with stratification factor (prior anti-IgE status), baseline SQS7 - sum of average daily Q1 - Q3, treatment, study week and the interaction between treatment and study week. A negative change from baseline indicates an improvement in sleep quality.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-6.5 (± 0.6)	-5.6 (± 0.8)	-6.1 (± 0.6)	-5.7 (± 0.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Weekly Sleep Quality Score (SQS7): Sum of Daily SQS at Week 16

End point title	Change from Baseline in Weekly Sleep Quality Score (SQS7): Sum of Daily SQS at Week 16

End point description:

The SQS was assessed by the participant through 3 questions relating to falling asleep (Q1), wakefulness (Q2), and feeling rested in the morning (Q3). The sum of the 3 daily sleep quality items over 7 days, ranged from 0 (good quality sleep) to 63 (poor quality sleep). The LSM estimates were based on the repeated measure model with stratification factor (prior anti-IgE status), baseline SQS7 - sum of SQS, treatment, study week and the interaction between treatment and study week. A negative change from baseline indicates an improvement in sleep quality. The FAS included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-19.5 (± 1.8)	-16.7 (± 2.3)	-18.3 (± 1.7)	-17.1 (± 1.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Urticaria Control Test (UCT) Score at Week 16

End point title	Change from Baseline in Urticaria Control Test (UCT) Score at Week 16

End point description:

The UCT assesses disease control in participants with CSU through a retrospective validated scoring system, evaluating the physical symptoms of chronic urticaria (itch, hives and/or angioedema) and the effectiveness of treatment over 4 weeks. It consists of 4 questions with 5 answer options, scored from 0 to 4, and the UCT score is the sum of all 4 questions, with total score ranging from 0 (no control) to 16 (complete control). A score of ≥ 12 indicates well-controlled urticaria and a score of ≤ 11 points indicates poor disease control. A positive change from baseline indicates an improvement in disease control. The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline UCT score, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational

product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	29	48	49
Units: score on a scale				
least squares mean (standard error)	4.1 (± 0.6)	6.3 (± 0.8)	4.9 (± 0.6)	5.9 (± 0.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Weekly Angioedema Activity Score (AAS7) at Week 16

End point title	Change from Baseline in Weekly Angioedema Activity Score (AAS7) at Week 16

End point description:

The AAS is a 5-item patient-reported outcome measure used to determine angioedema activity. Participants retrospectively documented the presence or absence of angioedema in the past 24 hours, and the AAS daily score ranged from 0 to 15 points, assessing 5 key factors when angioedema is present, including duration, physical discomfort, impact on daily activities, impact on appearance, and overall severity). The daily AAS scores are summed for 7 days to form the AAS7 with a range of 0 (not present) to 105 (most severe angioedema activity). Negative changes from baseline indicate an improvement in angioedema activity. The LSM estimates were based on the repeated measure model with stratification factor (prior anti-IgE status), baseline AAS7, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: score on a scale				
least squares mean (standard error)	-19.0 (± 2.7)	-18.7 (± 3.5)	-20.8 (± 2.7)	-15.6 (± 2.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Cumulative Weeks that Participants Achieved AAS7 = 0 at Week 16 (Angioedema Occurrence Free)

End point title	Number of Cumulative Weeks that Participants Achieved AAS7 = 0 at Week 16 (Angioedema Occurrence Free)

End point description:

The AAS is a 5-item patient-reported outcome measure used to determine angioedema activity. Participants retrospectively documented the presence or absence of angioedema in the past 24 hours, and the AAS daily score ranged from 0 to 15 points, assessing 5 key factors when angioedema is present, including duration, physical discomfort, impact on daily activities, impact on appearance, and overall severity). The daily AAS scores are summed for 7 days to form the AAS7 with a range of 0 (not present) to 105 (most severe angioedema activity). Angioedema occurrence free was defined as AAS7 = 0. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	26	44	37
Units: weeks				
arithmetic mean (standard deviation)	10.8 (± 5.2)	11.3 (± 4.9)	9.9 (± 5.8)	11.5 (± 5.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) at Week 16

End point title	Change from Baseline in the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) at Week 16

End point description:

The CU-Q2oL is a 23-item, self-reported urticaria-specific measure to evaluate 6 dimensions of quality of life (QoL): pruritus, impact on life activities, sleep problems, limitations, looks, and swelling. The total score is transformed to a linear scale of 0 to 100 with a higher CU-Q2oL score indicating a higher QoL impairment. A negative change from baseline indicates an improvement in QoL. The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline CU-Q2oL score, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	25	41	44
Units: score on a scale				
least squares mean (standard error)	-19.6 (± 2.1)	-19.8 (± 2.8)	-19.3 (± 2.2)	-18.7 (± 2.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Angioedema Control Test (AECT) Score at Week 16

End point title	Change from Baseline in the Angioedema Control Test (AECT) Score at Week 16

End point description:

The AECT is a patient-reported outcome measure to evaluate disease control in the domains of signs and symptoms, QoL, anxiety/fear, and effectiveness of therapy. The total AECT score ranges from 0 to 16, with higher scores indicating better controlled disease. A positive change from baseline indicates an improvement in angioedema control. The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline AECT score, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with angioedema presence at baseline and at least 1 non-missing AECT record were included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	7	15	16
Units: score on a scale				
least squares mean (standard error)	4.2 (± 1.2)	3.9 (± 2.2)	4.6 (± 1.3)	2.3 (± 1.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Angioedema Quality of Life Questionnaire (AE-QoL) at Week 16

End point title	Change from Baseline in the Angioedema Quality of Life Questionnaire (AE-QoL) at Week 16

End point description:

The AE-QoL is a validated angioedema QoL questionnaire for participants with angioedema. It consists of 17 questions evaluating 4 domains including functioning, fatigue/mood, fear/shame, and food with a

recall period of 4 weeks. The total score is transformed to a linear scale ranging from 0 to 100, with a higher score indicating a worse impairment in QoL. A negative change from baseline indicates an improvement in QoL. The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline AE-QoL score, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with angioedema presence at baseline and at least 1 non-missing AE-QoL record were included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	7	15	16
Units: score on a scale				
least squares mean (standard error)	-29.2 (± 6.0)	-24.1 (± 10.9)	-24.6 (± 6.4)	-13.1 (± 7.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Dermatology Life Quality Index (DLQI) at Week 16

End point title	Change from Baseline in the Dermatology Life Quality Index (DLQI) at Week 16

End point description:

The DLQI is a 10-item, participant-completed, health-related QoL assessment with content specific to those with dermatology conditions. The DLQI evaluates participant perceptions including dermatology-related symptoms and feelings, impacts on daily activities, leisure, work or school, personal relationships, and side effects of treatment. The recall period was 1 week. The DLQI total score ranges from 0 to 30 with a higher score indicating a greater QoL impairment. A negative change from baseline indicates an improvement in QoL. The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline DLQI score, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	25	41	44
Units: score on a scale				
least squares mean (standard error)	-7.4 (± 0.9)	-7.3 (± 1.2)	-7.0 (± 0.9)	-7.0 (± 0.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an AECT Score = 16 at Week 16 (Complete Control)

End point title	Number of Participants with an AECT Score = 16 at Week 16 (Complete Control)

End point description:

The total AECT score ranges from 0 to 16, with higher scores indicating better controlled disease. Complete control was defined as AECT score = 16. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data at Week 16 and angioedema presence at baseline and at least 1 non-missing AECT record were included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	14	14
Units: participants	3	2	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Work Productivity and Activity Impairment Questionnaire: Chronic Urticaria (WPAI-CU) Score at Week 16

End point title	Change from Baseline in the Work Productivity and Activity Impairment Questionnaire: Chronic Urticaria (WPAI-CU) Score at Week 16

End point description:

The WPAI-CU is a questionnaire that assesses the impact of an intervention on work productivity, evaluating 4 areas including absenteeism, presenteeism, work productivity loss, and activity impairment over the past 7 days. Each of the areas is scored separately as a percentage, with higher numbers indicating greater impairment and less productivity. A negative change from baseline indicates an improvement. The LSM estimates are based on the repeated measure model with stratification factor (prior anti-IgE status), baseline WPAI-CU score, treatment, study week and the interaction between treatment and study week. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with observed data were included for each question.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	25	41	44
Units: score on a scale				
least squares mean (standard error)				
Absenteeism (n=33, 20, 28, 26)	-4.7 (± 2.5)	0.3 (± 3.0)	-7.5 (± 2.5)	-2.3 (± 2.7)
Presenteeism (n=32, 19, 27, 24)	-19.9 (± 5.2)	-18.3 (± 6.6)	-20.3 (± 5.3)	-17.8 (± 5.7)
Work productivity loss (n=32, 19, 27, 24)	-20.0 (± 5.4)	-13.3 (± 6.7)	-23.5 (± 5.5)	-17.5 (± 5.9)
Activity impairment (n=44, 25, 41, 44)	-28.5 (± 4.2)	-30.3 (± 5.6)	-27.2 (± 4.3)	-24.1 (± 4.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Cumulative Days of sgAH Rescue Medication Use from Baseline to Week 16

End point title	Number of Cumulative Days of sgAH Rescue Medication Use from Baseline to Week 16

End point description:

Participants recorded any need of sgAH rescue medication in their daily electronic diary. The FAS included all randomized participants who received at least 1 dose of investigational product. Participants with data available are included.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	19	31	25
Units: days				
least squares mean (standard deviation)	49.5 (± 39.0)	31.6 (± 42.7)	46.1 (± 39.3)	32.7 (± 33.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Tezepelumab

End point title	Serum Concentration of Tezepelumab[3]

End point description:

The lower limit of quantification was 10 ng/mL, and values below this limit were set to zero.
The pharmacokinetic analysis set included participants who received tezepelumab and had at least 1 sample with a measurable serum concentration. Participants with data available at each time point are included.

End point type	Secondary

End point timeframe:

Week 1 pre-dose, Weeks 2, 4, 8, 12, 16, 24, and 32

Notes:

[3] - 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: The pre-specified endpoint is for the serum concentration of tezepelumab in the tezepelumab 210 mg SC Q4W and tezepelumab 420 mg SC Q2W treatment arms only.

End point values	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	52		
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 1 (n=51, 52)	0.00 (± 0.00)	0.00 (± 0.00)		
Week 2 (n=51, 48)	20.1 (± 6.93)	41.3 (± 12.4)		
Week 4 (n=46, 47)	14.2 (± 5.78)	71.3 (± 20.8)		
Week 8 (n=41, 43)	21.2 (± 8.54)	101 (± 30.5)		
Week 12 (n=38, 43)	24.8 (± 9.67)	123 (± 44.1)		
Week 16 (n= 39, 41)	27.1 (± 10.7)	136 (± 43.4)		
Week 24 (n=37, 39)	6.95 (± 5.65)	37.3 (± 21.1)		
Week 32 (n=40, 42)	1.73 (± 1.73)	11.0 (± 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical study participant irrespective of a causal relationship with study treatment. TEAEs were AEs that started on or after the first dose of investigational product up to the end of study (Week 32). A serious AE (SAE) was defined as any untoward medical occurrence that met at least 1 of the following serious criteria: immediately life-threatening, required hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or other medically important serious event. The safety analysis set consisted of all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Day 1 Week 1 to Week 32

End point values	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W	Tezepelumab 420 mg SC Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	52	52
Units: participants				
TEAEs	23	24	29	28
SAEs	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deaths collected from enrollment to the end of study visit, up to 38 weeks. SAEs and other AEs were collected from Day 1 up to Week 32, up to 32 weeks.

Adverse event reporting additional description:

Final Analysis

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants with and without previous anti-IgE therapy experience were randomized to receive placebo SC Q2W for 16 weeks.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

Reporting group title	Omalizumab 300 mg SC Q4W

Reporting group description:

Participants without previous anti-IgE experience were randomized to receive omalizumab 300 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

Reporting group title	Tezepelumab 210 mg SC Q4W

Reporting group description:

Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 210 mg SC Q4W for 16 weeks. Participants received placebo SC at intervening study visits to ensure all participants received an injection Q2W.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

Reporting group title	Tezepelumab 420 mg SC Q2W

Reporting group description:

Participants with and without previous anti-IgE therapy experience were randomized to receive tezepelumab 420 mg SC Q2W for 16 weeks.
Participants maintained a stable dose of sgAH as background medication from screening Visit 2 (Day -14) to the end of the Safety Follow-up Period (up to Week 32).

Serious adverse events	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	1 / 31 (3.23%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			

subjects affected / exposed	0 / 48 (0.00%)	0 / 31 (0.00%)	1 / 52 (1.92%)
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			
Intentional self-injury			
subjects affected / exposed	0 / 48 (0.00%)	1 / 31 (3.23%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Tezepelumab 420 mg SC Q2W		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Intentional self-injury			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Omalizumab 300 mg SC Q4W	Tezepelumab 210 mg SC Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 48 (29.17%)	7 / 31 (22.58%)	19 / 52 (36.54%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 48 (4.17%)	1 / 31 (3.23%)	5 / 52 (9.62%)
occurrences (all)	3	1	15
General disorders and administration site conditions			

Injection site pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 31 (0.00%)	4 / 52 (7.69%)
occurrences (all)	8	0	9
Pyrexia			
subjects affected / exposed	1 / 48 (2.08%)	3 / 31 (9.68%)	3 / 52 (5.77%)
occurrences (all)	1	3	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 48 (0.00%)	0 / 31 (0.00%)	2 / 52 (3.85%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	3 / 48 (6.25%)	1 / 31 (3.23%)	2 / 52 (3.85%)
occurrences (all)	3	1	3
Urticaria			
subjects affected / exposed	4 / 48 (8.33%)	0 / 31 (0.00%)	4 / 52 (7.69%)
occurrences (all)	5	0	5
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 31 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 48 (6.25%)	2 / 31 (6.45%)	8 / 52 (15.38%)
occurrences (all)	3	2	8
Nasopharyngitis			
subjects affected / exposed	2 / 48 (4.17%)	1 / 31 (3.23%)	1 / 52 (1.92%)
occurrences (all)	4	1	1

Non-serious adverse events	Tezepelumab 420 mg SC Q2W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 52 (38.46%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	8		
General disorders and administration			

site conditions Injection site pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 1 / 52 (1.92%) 1 2 / 52 (3.85%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 3 / 52 (5.77%) 3		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 0 / 52 (0.00%) 0 3 / 52 (5.77%) 4		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 3 / 52 (5.77%) 3		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 5 / 52 (9.62%) 5 3 / 52 (5.77%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2021	- To incorporate regulatory authority recommendations, to align with international treatment guidelines, to reduce patient burden, and improve study experience by reducing the frequency of select eDiary data collection. - Updated schedule of activities to reduce frequency of chronic urticaria QoL questionnaire, DLQI assessment, work productivity, and activity impairment questionnaire (chronic urticaria); and urticaria severity score was removed. - The washout period for prior use of biologics was reduced. - Excluded treatments, medical devices, and/or procedures were updated to clarify the use of systemic corticosteroids, and to exclude H2 antagonists and leukotriene receptor antagonists. - Updated primary objectives and endpoints to clarify the definition of intercurrent events, to add a secondary objective to evaluate the effect of tezepelumab on participants achieving complete control of angioedema disease, and to clarify minimal residual disease endpoints. - The grading scale for adverse events was updated, and laboratory test results were updated to align for grading intensity. - Covariates were updated to clarify the analysis of primary and key secondary endpoints using the baseline score of endpoint. - Updated handling of missing and incomplete data to clarify addressing missing data in binary efficacy endpoints. - Exclusion criteria were updated to clarify QuantiFERON-tuberculosis Gold Plus test requirements and hepatitis-B core antibody testing, only where required by the local country or region.
30 September 2021	The error in the study schema was rectified.
26 April 2022	- Number of anti-IgE experienced participants was reduced and interim analysis 2 was added for administrative decision making purposes. The original interim analysis 2, which was a futility analysis was removed. The total number of participants in the primary analysis was reduced. - The number of participants for the anti-IgE experienced cohort was reduced due to limited source of participants. - Objectives and endpoints language was updated in response to regulatory advice regarding HSS7 and ISS7 assessments. - The exclusion criteria were updated to clarify that COVID-19 vaccines were allowed provided that the vaccine was not administered within 7 days before or after any study dosing visit. - Clarified that participants were required to document both HSS and ISS daily with a recall period over 24 hours, and to define that a weekly UAS score represented the sum over a period of 7 days. - Statistical considerations were updated to accommodate changes in number of participants, and to relocate the key secondary endpoints, as well as changes to the multiple testing strategy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported