Clinical trial results:
A Phase III, Randomized, Multicenter, Double-blind, Placebo-controlled Clinical Trial of Omalizumab in Patients with Chronic Rhinosinusitis with Nasal Polyps

Summary

EudraCT number	2017-001718-28
Trial protocol	BE HU ES FI PL FR
Global end of trial date	07 March 2019

Results information

Result version number	v2 (current)
This version publication date	05 April 2020
First version publication date	01 March 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GA39855

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03280537
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4070
Public contact	F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.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	07 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 March 2019
Global end of trial reached?	Yes
Global end of trial date	07 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy and safety of omalizumab compared with placebo in adult patients with chronic rhinosinusitis with nasal polyps who have had an inadequate response to standard-of-care treatments.

Protection of trial subjects:

This study was conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. All study subjects were required to read and sign and informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 23
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Ukraine: 22
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Spain: 23
Worldwide total number of subjects	127
EEA total number of subjects	75

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	112
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

At the first visit of the 5-week screening/run-in period, participants were asked to standardize their nasal corticosteroids to a regimen of mometasone, 200 micrograms twice a day (BID). If intolerant to a BID regimen, then they remained on a stable dosage of mometasone once a day (QD) during the run-in period and throughout the treatment period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received matching placebo as a subcutaneous injection once every 2 weeks or once every 4 weeks. The dose and dosing frequency was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.

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

Dosage and administration details:

Placebo was administered subcutaneously every 2 or 4 weeks by qualified personnel who were not involved with conducting safety or efficacy evaluations using a disposable
25-gauge needle in the deltoid region of the right or left arm. Alternatively, the injections could have been administered in the thigh, if medically significant reasons precluded administration in the deltoid region. Because the solution is slightly viscous, the injection may have taken 5-10 seconds to administer. The dose (mg) and dosing frequency were determined by serum total IgE level (IU/mL) (measured before the start of treatment via central laboratory) and body weight (kg). Assignment of the study drug dose was determined by using the study drug-dosing table. The placebo equivalent of doses of greater than (>) 150 mg were divided among more than one injection site to limit injections to no more than 150 mg per site.

Arm title	Omalizumab

Arm description:

Participants received omalizumab as a subcutaneous injection once every 2 weeks (q2w) or once every 4 weeks (q4w). The dose (from 75 mg up to 600 mg) and dosing frequency (q2w or q4w) was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.

Arm type	Experimental

Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	Xolair IGE025 RO5489789
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab was administered subcutaneously every 2 or 4 weeks by qualified personnel who were not involved with conducting safety or efficacy evaluations using a disposable 25-gauge needle in the deltoid region of the right or left arm. Alternatively, the injections could have been administered in the thigh, if medically significant reasons precluded administration in the deltoid region. Because the solution is slightly viscous, the injection may have taken 5-10 seconds to administer. The dose (mg) and dosing frequency were determined by serum total IgE level (IU/mL) (measured before the start of treatment via central laboratory) and body weight (kg). Assignment of the study drug dose was determined by using the study drug-dosing table. Doses of greater than (>) 150 mg were divided among more than one injection site to limit injections to no more than 150 mg per site.

Number of subjects in period 1	Placebo	Omalizumab
Started	65	62
Completed	63	58
Not completed	2	4
Consent withdrawn by subject	2	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo as a subcutaneous injection once every 2 weeks or once every 4 weeks. The dose and dosing frequency was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.	
Reporting group title	Omalizumab
Reporting group description:	
Participants received omalizumab as a subcutaneous injection once every 2 weeks (q2w) or once every 4 weeks (q4w). The dose (from 75 mg up to 600 mg) and dosing frequency (q2w or q4w) was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.	

Reporting group values	Placebo	Omalizumab	Total
Number of subjects	65	62	127
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)	56	56	112
From 65-84 years	9	6	15
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	51.0	49.0	
standard deviation	± 12.0	± 11.9	-
Sex: Female, Male Units: participants			
Female	21	23	44
Male	44	39	83
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	65	61	126
More than one race	0	0	0
Unknown or Not Reported	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	3	5	8
Not Hispanic or Latino	61	56	117
Unknown or Not Reported	1	1	2
Geographic Region of Enrollment Units: Subjects			
North America	14	12	26
ex-North America	51	50	101
Participants with Asthma Comorbidity and Aspirin Sensitivity			
Asthma comorbidity was defined as asthma history at screening and having used medication for asthma or received a prescription for any asthma medication in the last 12 months prior to screening.			
Units: Subjects			
Asthmatic and Aspirin Sensitive	18	21	39
Asthmatic and Not Aspirin Sensitive	21	17	38
Not Asthmatic	26	24	50
Mometasone Prescribed Daily Dose at Baseline Units: Subjects			
200 micrograms	5	2	7
400 micrograms	60	60	120
Average Daily Nasal Congestion Score at Baseline			
The Nasal Congestion Score (NCS) was assessed daily by the participant via an electronic diary as the response to the following question: Is your nose blocked? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0 = Not at all; 1 = Mild; 2 = Moderate; and 3 = Severe. Baseline was defined as the average of the daily values recorded during the 7-day interval ending on the latest day prior to randomization such that the prior 7-day interval includes a recorded value on at least 4 of the 7 days of that interval.			
Units: Score on a scale			
arithmetic mean	2.3	2.3	
standard deviation	± 0.6	± 0.7	-
Nasal Polyp Score (NPS) at Baseline			
Total NPS ranges from 0 to 8 (sum of 0-4 for left and right nasal passage scores per the following criteria), with a lower score indicating smaller-sized nasal polyps: 0 = No polyps; 1 = Small polyps in middle meatus not reaching below inferior border of the middle turbinate; 2 = Polyps reaching below lower border of the middle turbinate; 3 = Large polyps reaching lower border of the inferior turbinate or polyps medial to the middle turbinate; and 4 = Large polyps causing complete obstruction of the inferior nasal cavity. Baseline was the last assessment on or before the date of randomization.			
Units: Score on a scale			
arithmetic mean	6.1	6.4	
standard deviation	± 0.9	± 0.9	-
Average Daily Total Nasal Symptom Score (TNSS) at Baseline			
The Total Nasal Symptom Score (TNSS) was defined as the sum of the four individual scores for Nasal Congestion Score, Anterior Rhinorrhea Score, Posterior Rhinorrhea Score, and Sense of Smell Score, ranging from 0 (no symptoms) to 12 (most severe symptoms), assessed daily by the participant via an electronic diary. Baseline was defined as the average of the daily values recorded during the 7-day interval ending on the latest day prior to randomization such that the prior 7-day interval includes a recorded value on at least 4 of the 7 days of that interval.			
Units: Score on a scale			
arithmetic mean	8.7	8.4	
standard deviation	± 2.3	± 2.6	-
Average Daily Sense of Smell Score at Baseline			
The Sense of Smell Score was assessed daily by the participant via an electronic diary as the response to the following question: Is your sense of smell reduced? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0 = Not at all; 1 = Mild; 2 = Moderate; and 3 = Severe. Baseline was defined as the average of the daily values recorded during the 7-day interval ending on the latest day prior to randomization such that the prior 7-day interval includes a recorded			

value on at least 4 of the 7 days of that interval.			
Units: Score on a scale			
arithmetic mean	2.8	2.6	
standard deviation	± 0.6	± 0.8	-
Average Daily Posterior Rhinorrhea Score at Baseline			
The Posterior Rhinorrhea Score was assessed daily by the participant via an electronic diary as the response to the following question: Do you feel dripping at the back of the nose? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0=Not at all; 1=Mild; 2=Moderate; and 3=Severe. Baseline was defined as the average of the daily values recorded during the 7-day interval ending on the latest day prior to randomization such that the prior 7-day interval includes a recorded value on at least 4 of the 7 days of that interval.			
Units: Score on a scale			
arithmetic mean	1.8	1.6	
standard deviation	± 0.9	± 0.9	-
Average Daily Anterior Rhinorrhea Score at Baseline			
The Anterior Rhinorrhea Score was assessed daily by the participant via an electronic diary as the response to the following question: Do you have a runny nose? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0=Not at all; 1=Mild; 2=Moderate; and 3=Severe. Baseline was defined as the average of the daily values recorded during the 7-day interval ending on the latest day prior to randomization such that the prior 7-day interval includes a recorded value on at least 4 of the 7 days of that interval.			
Units: Score on a scale			
arithmetic mean	1.9	1.9	
standard deviation	± 0.8	± 0.9	-
Total Sino-Nasal Outcome Test-22 (SNOT-22) Score at Baseline			
The SNOT-22 Questionnaire, a disease specific HRQoL measure, comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant was asked to rate how severe each problem had been for them over the past 2 weeks on a scale from 0 (no problem at all) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0 to 110, with a lower score indicating less disease and better HRQoL. Baseline was defined as the last assessment on or before the date of randomization.			
Units: Score on a scale			
arithmetic mean	59.8	59.2	
standard deviation	± 18.2	± 20.5	-
University of Pennsylvania Smell Identification Test (UPSIT) Score at Baseline			
The UPSIT is a 40-question instrument that measures an individual’s ability to detect odors and ranges from 0 to 40, with a higher score indicating a better sense of smell. It is a self-administered "scratch-and-sniff" test provided in booklets that have 40 microencapsulated odorants, each with a multiple-choice option for the response. The number of correct responses is summed to provide a total score. Baseline was defined as the last assessment on or before the date of randomization.			
Units: Score on a scale			
arithmetic mean	13.1	12.8	
standard deviation	± 7.3	± 7.6	-

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo as a subcutaneous injection once every 2 weeks or once every 4 weeks. The dose and dosing frequency was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.

Reporting group title	Omalizumab

Reporting group description:

Participants received omalizumab as a subcutaneous injection once every 2 weeks (q2w) or once every 4 weeks (q4w). The dose (from 75 mg up to 600 mg) and dosing frequency (q2w or q4w) was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.

Subject analysis set title	Placebo (Safety Analysis Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Placebo safety analysis set consisted of all participants who received only (and at least one) placebo injections (i.e., no active treatment) during the treatment period. One participant in the Placebo arm received incorrectly one dose of omalizumab and was therefore included in the Omalizumab arm in the safety analysis set.

Subject analysis set title	Omalizumab (Safety Analysis Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Omalizumab safety analysis set consisted of all participants who received at least one omalizumab injection during the treatment period. One participant in the Placebo arm received incorrectly one dose of omalizumab and was therefore included in the Omalizumab arm in the safety analysis set.

Primary: Change From Baseline in Nasal Polyp Score (NPS) at Week 24

End point title	Change From Baseline in Nasal Polyp Score (NPS) at Week 24

End point description:

Total NPS ranges from 0 to 8 (sum of 0-4 for left and right nasal passage scores per the following criteria), with a lower score indicating smaller-sized nasal polyps: 0 = No polyps; 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2 = Polyps reaching below the lower border of the middle turbinate (modified to accommodate those with a middle turbinectomy, such that polyp must have reached the top of the inferior turbinate.); 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; and 4 = Large polyps causing complete obstruction of the inferior nasal cavity. Two blinded primary independent expert readers reviewed every post-screening recorded video endoscopy for a given participant to determine total NPS. A third reader chose one of the two scores to be used for analysis in cases where there was any discrepancy in total NPS assigned between the two primary readers.

End point type	Primary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.31 (-0.63 to 0.01)	-0.90 (-1.23 to -0.57)		

Statistical analyses

Statistical analysis title	Change from Baseline in NPS at Week 24

Statistical analysis description:

The primary analysis tested the null hypothesis that no treatment group difference existed for change from baseline in NPS at Week 24. As NPS and NCS are co-primary outcome measures, both null hypotheses for NPS and NCS must be rejected, with parameter estimates indicating a benefit of omalizumab over placebo, for the study to be deemed positive.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.014 [1]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[1] - Tested at the two-sided 0.05 level. There was no adjustment for multiplicity for the co-primary outcome measures.

Primary: Change From Baseline in Average Daily Nasal Congestion Score (NCS) at Week 24

End point title	Change From Baseline in Average Daily Nasal Congestion Score (NCS) at Week 24

End point description:

The Nasal Congestion Score (NCS) was assessed daily by the participant via an electronic diary as the response to the following question: Is your nose blocked? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0 = Not at all; 1 = Mild; 2 = Moderate; and 3 = Severe. For each study day, a score was calculated using an average of the prior 7 days among the available days within the pre-specified window (For Week 24: Study Days 155 to 186), excluding the study day itself, if a value had been recorded by the participant on at least 4 of the prior 7 days; otherwise, the 7-day prior average for that study day was to be considered missing. One calculated (non-missing) 7-day prior average was selected for analysis according to the study day with nearest proximity to Week 24 (Study Day 168), with the earlier selected in the case of a tie. Baseline was defined as the (non-missing) 7-day interval ending on the latest day prior to randomization.

End point type	Primary

End point timeframe:

Baseline, Week 24 (Study Days 155 to 186)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.20 (-0.42 to 0.01)	-0.70 (-0.92 to -0.48)		

Statistical analyses

Statistical analysis title	Change from Baseline in Avg Daily NCS at Week 24

Statistical analysis description:

The primary analysis tested the null hypothesis that no treatment group difference existed for change from baseline in average daily NCS at Week 24. As NPS and NCS are co-primary outcome measures, both null hypotheses for NPS and NCS must be rejected, with parameter estimates indicating a benefit of omalizumab over placebo, for the study to be deemed positive.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0017 [2]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[2] - Tested at the two-sided 0.05 level. There was no adjustment for multiplicity for the co-primary outcome measures.

Secondary: Change From Baseline in Average Daily Sense of Smell Score at Week 24

End point title	Change From Baseline in Average Daily Sense of Smell Score at Week 24

End point description:

The Sense of Smell Score was assessed daily by the participant via an electronic diary as the response to the following question: Is your sense of smell reduced? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0 = Not at all; 1 = Mild; 2 = Moderate; and 3 = Severe. For each study day, a score was calculated using an average of the prior 7 days among the available days within the pre-specified window (For Week 24: Study Days 155 to 186), excluding the study day itself, if a value had been recorded by the participant on at least 4 of the prior 7 days; otherwise, the 7-day prior average for that study day was to be considered missing. One calculated (non-missing) 7-day prior average was selected for analysis according to the study day with nearest proximity to Week 24 (Study Day 168), with the earlier selected in the case of a tie. Baseline was defined as the (non-missing) 7-day interval ending on the latest day prior to randomization.

End point type	Secondary

End point timeframe:

Baseline, Week 24 (Study Days 155 to 186)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.13 (-0.33 to 0.06)	-0.58 (-0.78 to -0.38)		

Statistical analyses

Statistical analysis title	Change from Baseline in Avg Daily SSS at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the average daily Sense of Smell Score (SSS) at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0024 [3]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[3] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Average Daily Posterior Rhinorrhea Score at Week 24

End point title	Change From Baseline in Average Daily Posterior Rhinorrhea Score at Week 24

End point description:

The Posterior Rhinorrhea Score was assessed daily by the participant via an electronic diary as the response to the following question: Do you feel dripping at the back of the nose? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0=Not at all; 1=Mild; 2=Moderate; and 3=Severe. For each study day, a score was calculated using an average of the prior 7 days among available days within a pre-specified window (For Week 24: Study Days 155 to 186), excluding the study day itself, if a value had been recorded by the participant on at least 4 of the prior 7 days, otherwise the 7-day prior average for that study day was to be considered missing. One calculated (non-missing) 7-day prior average was selected for analysis according to the study day with nearest proximity to Week 24 (Study Day 168), with the earlier selected in the case of a tie. Baseline was defined as the (non-missing) 7-day interval ending on the latest day prior to randomization.

End point type	Secondary

End point timeframe:

Baseline, Week 24 (Study Days 155 to 186)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.00 (-0.19 to 0.18)	-0.55 (-0.74 to -0.35)		

Statistical analyses

Statistical analysis title	Change from Baseline in Avg Daily PRS at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the average daily Posterior Rhinorrhea Score (PRS) at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001 [4]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[4] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Nasal Polyp Score (NPS) at Week 16

End point title	Change From Baseline in Nasal Polyp Score (NPS) at Week 16

End point description:

Total NPS ranges from 0 to 8 (sum of 0-4 for left and right nasal passage scores per the following criteria), with a lower score indicating smaller-sized nasal polyps: 0 = No polyps; 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2 = Polyps reaching below the lower border of the middle turbinate (modified to accommodate those with a middle turbinectomy, such that polyp must have reached the top of the inferior turbinate.); 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; and 4 = Large polyps causing complete obstruction of the inferior nasal cavity. Two blinded primary independent expert readers reviewed every post-screening recorded video endoscopy for a given participant to determine total NPS. A third reader chose one of the two scores to be used for analysis in cases where there was any discrepancy in total NPS assigned between the two primary readers.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	58		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.29 (-0.61 to 0.04)	-1.20 (-1.54 to -0.86)		

Statistical analyses

Statistical analysis title	Change from Baseline in NPS at Week 16

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the NPS at Week 16.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 [5]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.44
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[5] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Average Daily Nasal Congestion Score (NCS) at Week 16

End point title	Change From Baseline in Average Daily Nasal Congestion Score (NCS) at Week 16

End point description:

The Nasal Congestion Score (NCS) was assessed daily by the participant via an electronic diary as the response to the following question: Is your nose blocked? The four available response options, scored from 0 (no symptoms) to 3 (severe symptoms) were: 0 = Not at all; 1 = Mild; 2 = Moderate; and 3 = Severe. For each study day, a score was calculated using an average of the prior 7 days among the available days within the pre-specified window (For Week 16: Study Days 99 to 126), excluding the study day itself, if a value had been recorded by the participant on at least 4 of the prior 7 days; otherwise, the 7-day prior average for that study day was to be considered missing. One calculated (non-missing) 7-day prior average was selected for analysis according to the study day with nearest proximity to Week 24 (Study Day 112), with the earlier selected in the case of a tie. Baseline was defined as the (non-missing) 7-day interval ending on the latest day prior to randomization.

End point type	Secondary

End point timeframe:

Baseline, Week 16 (Study Days 99 to 126)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	61		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.21 (-0.41 to -0.01)	-0.80 (-1.00 to -0.59)		

Statistical analyses

Statistical analysis title	Change from Baseline in Avg Daily NCS at Week 16

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the average daily NCS at Week 16.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [6]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least-Squares Means
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[6] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Participant Reported Health-Related Quality of Life (HRQoL) as Assessed by the Total Sino-Nasal Outcome Test (SNOT)-22 Questionnaire at Week 24

End point title	Change From Baseline in Participant Reported Health-Related Quality of Life (HRQoL) as Assessed by the Total Sino-Nasal Outcome Test (SNOT)-22 Questionnaire at Week 24

End point description:

The SNOT-22 Questionnaire, a disease specific HRQoL measure, comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant was asked to rate how severe each problem had been for them over the past 2 weeks on a scale from 0 (no problem at all) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0 to 110, with a lower score indicating less disease and better HRQoL. A negative score indicates a decrease (or improvement) from the baseline score.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-6.55 (-10.88 to -2.23)	-21.59 (-26.05 to -17.14)		

Statistical analyses

Statistical analysis title	Change from Baseline in SNOT-22 Score at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the SNOT-22 score at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [7]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-15.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.26
upper limit	-8.82
Variability estimate	Standard error of the mean
Dispersion value	3.14

Notes:

[7] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Average Daily Anterior Rhinorrhea Score at Week 24

End point title	Change From Baseline in Average Daily Anterior Rhinorrhea Score at Week 24

End point description:

The Anterior Rhinorrhea Score was assessed daily by the participant via an electronic diary as the response to the following question: Do you have a runny nose? The four available response options were scored from 0 (no symptoms) to 3 (severe symptoms): 0=Not at all; 1=Mild; 2=Moderate; and 3=Severe. For each study day, a score was calculated using an average of the prior 7 days among available days within a pre-specified window (For Week 24: Study Days 155 to 186), excluding the study day itself, if a value had been recorded by the participant on at least 4 of the prior 7 days, otherwise the 7-day prior average for that study day was to be considered missing. One calculated (non-missing) 7-day prior average was selected for analysis according to the study day with nearest proximity to Week 24 (Study Day 168), with the earlier selected in the case of a tie. Baseline was defined as the (non-missing) 7-day interval ending on the latest day prior to randomization.

End point type	Secondary

End point timeframe:

Baseline, Week 24 (Study Days 155 to 186)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.08 (-0.27 to 0.11)	-0.70 (-0.90 to -0.51)		

Statistical analyses

Statistical analysis title	Change from Baseline in Avg Daily ARS at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the average daily Anterior Rhinorrhea Score (ARS) at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [8]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[8] - Tested at the two-sided 0.05 significance level.

Secondary: Number of Participants Requiring Rescue Medication (Systemic Corticosteroids for ≥3 Consecutive Days) Through Week 24

End point title	Number of Participants Requiring Rescue Medication (Systemic Corticosteroids for ≥3 Consecutive Days) Through Week 24

End point description:

A participant was considered to have had the event of requiring rescue medication if they had taken systemic corticosteroids for 3 or more consecutive days at any point between randomization and Week 24; if the participant had greater than 155 days of follow-up on study and had not taken systemic corticosteroids for 3 or more consecutive days, then they did not have the event. Participants with less than 155 days of follow-up on the study were classified as having had the event if they discontinued study drug due to adverse event, progressive disease, or lack of efficacy and remained missing; if the participant had less than 155 days of follow-up on study and had not already met these criteria, they were classified as having a missing outcome. The null hypothesis was to be assessed by the Wald Chi-square test of the treatment term in the logistic regression model. If model convergence was an issue,

then Fisher’s Exact test was to be used.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Participants	5	1		

Statistical analyses

Statistical analysis title	Requiring Rescue Medication Through Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for requirement of rescue medication through Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1594 [9]
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	1.89

Notes:

[9] - Tested at the two-sided 0.05 significance level.

Secondary: Number of Participants Having Had Surgery for Nasal Polyps Through Week 24

End point title	Number of Participants Having Had Surgery for Nasal Polyps Through Week 24

End point description:

A participant was considered to have had the event of surgery for nasal polyps if they underwent the procedure at any point between randomization and Week 24; if the participant had greater than 155 days of follow-up on study and had not undergone surgery for nasal polyps, then they did not have the event. Participants with less than 155 days of follow-up on the study were classified as having had the event if they discontinued study drug due to adverse event, progressive disease, or lack of efficacy and remained missing; if the participant had less than 155 days of follow-up on study and had not already met these criteria, they were classified as having a missing outcome. The null hypothesis was to be assessed by the Wald Chi-square test of the treatment term in the logistic regression model. If model convergence was an issue, then Fisher’s Exact test was to be used.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Participants	1	0		

Statistical analyses

Statistical analysis title	Having Had Nasal Polypectomy Through Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for having had surgery for nasal polyps through Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 1 [10]
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	20.61

Notes:

[10] - Tested at the two-sided 0.05 significance level.

Secondary: Number of Participants with a Change From Baseline at Week 24 in Asthma Quality of Life Questionnaire (AQLQ) of ≥0.5 in Participants with Comorbid Asthma Only

End point title	Number of Participants with a Change From Baseline at Week 24 in Asthma Quality of Life Questionnaire (AQLQ) of ≥0.5 in Participants with Comorbid Asthma Only

End point description:

The AQLQ is a 32-item participant-reported measure of asthma-related quality of life (QoL) with a total score (the mean of all 32 responses) ranging from 1 (severely impaired) to 7 (not impaired at all); a higher score indicates a better QoL. An increase of at least 0.5 points in the AQLQ score was considered the minimal important difference for improvement in QoL. The analysis was conducted only in the subgroup of participants with comorbid asthma at screening and AQLQ assessments at Baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	35		
Units: Participants	12	20		

Statistical analyses

Statistical analysis title	Change from Baseline in AQLQ of ≥0.5 at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for number of participants with a change from baseline in AQLQ score of ≥0.5 at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0396
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	4.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	15.25

Secondary: Number of Participants Requiring Rescue Treatment (Systemic Corticosteroids For ≥3 Consecutive Days or Having Had Surgery for Nasal Polyps) Through Week 24

End point title	Number of Participants Requiring Rescue Treatment (Systemic Corticosteroids For ≥3 Consecutive Days or Having Had Surgery for Nasal Polyps) Through Week 24

End point description:

A participant was considered to have had the event of requiring rescue treatment if they had taken systemic corticosteroids for 3 or more consecutive days or had nasal polypectomy at any point between randomization and Week 24; if the participant had greater than 155 days of follow-up on study and had not received rescue treatment, then they did not have the event. Participants with less than 155 days of follow-up on the study were classified as having had the event if they discontinued study drug due to adverse event, progressive disease, or lack of efficacy and remained missing; if the participant had less than 155 days of follow-up on study and had not already met these criteria, they were classified as having a missing outcome. The null hypothesis was to be assessed by the Wald Chi-square test of the treatment term in the logistic regression model. If model convergence was an issue, then Fisher's Exact test was to be used.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Participants	5	1		

Statistical analyses

Statistical analysis title	Requiring Rescue Treatment Through Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for requirement of rescue treatment through Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1594 [11]
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	1.89

Notes:

[11] - Tested at the two-sided 0.05 significance level.

Secondary: Number of Participants With Reduction in the Need for Surgery for Nasal Polyps by Week 24, as Defined by an NPS of ≤4 (Unilateral Score of ≤2 on Each Side) and Improvement in SNOT-22 Score of ≥8.9

End point title	Number of Participants With Reduction in the Need for Surgery for Nasal Polyps by Week 24, as Defined by an NPS of ≤4 (Unilateral Score of ≤2 on Each Side) and Improvement in SNOT-22 Score of ≥8.9

End point description:

A participant was considered to have had the event of reduction in the need for surgery for nasal polyps if they had a Nasal Polyp Score (NPS) of ≤4 and an improvement in the SNOT-22 score of ≥8.9 (minimal important difference) without rescue treatment at Week 24; if the participant had received rescue treatment or had discontinued study drug due to adverse event, progressive disease, or lack of efficacy and remained missing, then they did not have the event. Participants without an intercurrent event and without valid Week 24 assessments of both NPS and SNOT-22 were classified as having a missing outcome. The null hypothesis was to be assessed by the Wald Chi-square test of the treatment term in the logistic regression model. If model convergence was an issue, then Fisher's Exact test was to be used.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	59		
Units: Participants	2	10		

Statistical analyses

Statistical analysis title	Reduction in Need for Nasal Polypectomy by Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in reduction in the need for surgery for nasal polyps by Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0139 [12]
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	6.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	60.23

Notes:

[12] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Average Daily Total Nasal Symptom Score (TNSS) at Week 24

End point title	Change From Baseline in Average Daily Total Nasal Symptom Score (TNSS) at Week 24

End point description:

The Total Nasal Symptom Score (TNSS) was defined as the sum of the four individual scores for Nasal Congestion Score, Anterior Rhinorrhea Score, Posterior Rhinorrhea Score, and Sense of Smell Score, ranging from 0 (no symptoms) to 12 (most severe symptoms), assessed daily by the participant via an electronic diary. For each study day, a score was calculated using an average of the prior 7 days among the available days within the pre-specified window (For Week 24: Study Days 155 to 186), excluding the study day itself, if a value had been recorded by the participant on at least 4 of the prior 7 days; otherwise, the 7-day prior average for that study day was to be considered missing. One calculated (non-missing) 7-day prior average was selected for analysis according to the study day with nearest proximity to Week 24 (Study Day 168), with the earlier selected in the case of a tie. Baseline was defined as the (non-missing) 7-day interval ending on the latest day prior to randomization.

End point type	Secondary

End point timeframe:

Baseline, Week 24 (Study Days 155 to 186)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.44 (-1.07 to 0.19)	-2.53 (-3.18 to -1.89)		

Statistical analyses

Statistical analysis title	Change from Baseline in Avg Daily TNSS at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the average daily Total Nasal Symptom Score (TNSS) at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [13]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	-2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1.18
Variability estimate	Standard error of the mean
Dispersion value	0.46

Notes:

[13] - Tested at the two-sided 0.05 significance level.

Secondary: Change From Baseline in Sense of Smell, as Assessed by The University of Pennsylvania Smell Identification Test (UPSIT) Score at Week 24

End point title	Change From Baseline in Sense of Smell, as Assessed by The University of Pennsylvania Smell Identification Test (UPSIT) Score at Week 24

End point description:

The UPSIT is a 40-question instrument that measures an individual’s ability to detect odors and ranges from 0 to 40, with a higher score indicating a better sense of smell. It is a self-administered "scratch-and-sniff" test provided in booklets that have 40 microencapsulated odorants, each with a multiple-choice option for the response. The number of correct responses is summed to provide a total score.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: Score on a scale				
arithmetic mean (confidence interval 95%)	0.44 (-1.15 to 2.04)	4.31 (2.66 to 5.95)		

Statistical analyses

Statistical analysis title	Change from Baseline in UPSIT Score at Week 24

Statistical analysis description:

The null hypothesis was that no difference exists between the treatment groups for change from baseline in the UPSIT score at Week 24.

Comparison groups	Placebo v Omalizumab
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0011 [14]
Method	Mixed-Effect Model of Repeated Measures
Parameter estimate	Difference in Least Squares Means
Point estimate	3.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	6.15
Variability estimate	Standard error of the mean
Dispersion value	1.16

Notes:

[14] - Tested at the two-sided 0.05 significance level.

Secondary: Number of Participants who Experienced at Least One Adverse Event by Greatest Severity

End point title	Number of Participants who Experienced at Least One Adverse Event by Greatest Severity

End point description:

All adverse events (AE) were treatment emergent AEs, defined as any new AE or any worsening of an existing condition with an onset date on or after the first study drug administration date. AEs were assessed for severity according to the following grading scale: mild (discomfort noticed, but no disruption of normal daily activity), moderate (discomfort sufficient to reduce or affect normal daily activity), or severe (incapacitating with inability to work or to perform normal daily activity). The terms "severe" and "serious" are not synonymous; regardless of severity, some events may have also met seriousness criteria. Multiple occurrences of the same AE in one individual are counted once at the greatest intensity.

End point type	Secondary

End point timeframe:

Up to Week 28

End point values	Placebo (Safety Analysis Set)	Omalizumab (Safety Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	63		
Units: Participants				
AEs of Any Severity	35	32		
Mild AEs	19	18		
Moderate AEs	13	10		
Severe AEs	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced at Least One Serious Adverse Event

End point title	Number of Participants who Experienced at Least One Serious Adverse Event

End point description:

A serious adverse event was defined as any adverse event that met any of the following criteria: was fatal; was life-threatening; required or prolonged inpatient hospitalization; resulted in persistent or significant disability/incapacity; was a congenital anomaly/birth defect in a neonate/infant born to a mother exposed to the study drug; or, was a significant medical event in the investigator's judgment. Multiple occurrences of the same serious adverse event in one individual were counted once.

End point type	Secondary

End point timeframe:

Up to Week 28

End point values	Placebo (Safety Analysis Set)	Omalizumab (Safety Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	63		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events Leading to Omalizumab/Placebo Discontinuation

End point title	Number of Participants with Adverse Events Leading to

	Omalizumab/Placebo Discontinuation

End point description:

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Placebo (Safety Analysis Set)	Omalizumab (Safety Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	63		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Abnormalities by Highest Grade Post-Baseline

End point title	Number of Participants with Laboratory Abnormalities by Highest Grade Post-Baseline

End point description:

Clinical laboratory tests for serum chemistry and hematology parameters were performed at laboratories; any abnormal values (High or Low) were based on laboratory normal ranges. Laboratory abnormalities are presented by the highest grade according to the World Health Organization (WHO) grade for Adverse Events, except for eosinophils and white blood cells that were graded according to the FDA Toxicity Grading Scale for Healthy Volunteers. Not every abnormal laboratory value qualified as an adverse event, only if it met any of the following criteria: clinically significant (per investigator); accompanied by clinical symptoms; resulted in a change in study treatment; or required a change in concomitant therapy. Abs. = absolute count; SGPT/ALT = serum glutamic-pyruvic transaminase/alanine aminotransferase; SGOT/AST = serum glutamic-oxaloacetic transaminase/aspartate aminotransferase

End point type	Secondary

End point timeframe:

Up to Week 28

End point values	Placebo (Safety Analysis Set)	Omalizumab (Safety Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	63		
Units: Participants				
Alkaline Phosphatase-High, Any Grade(Gr.)(n=62,60)	0	0		
SGPT/ALT - High, Any Gr. (n=62,60)	4	1		
SGPT/ALT - High, Gr. 1 (n=62,60)	4	1		
SGOT/AST - High, Any Gr. (n=61,60)	2	0		
SGOT/AST - High, Gr. 1 (n=61,60)	2	0		

Creatinine - High, Any Gr. (n=62,60)	0	0		
Eosinophils, Abs. - High, Any Gr. (n=63,62)	17	8		
Eosinophils, Abs. - High, Gr. 1 (n=63,62)	17	8		
Hemoglobin - Low, Any Gr. (n=63,62)	0	0		
Hemoglobin - High, Any Gr. (n=63,62)	0	0		
Neutrophils, Segmented(Abs.)-Low, Any Gr.(n=63,62)	2	2		
Neutrophils, Segmented(Abs.)-Low, Gr. 1(n=63,62)	2	2		
Platelet - Low, Any Gr. (n=63,62)	0	0		
Potassium - Low, Any Gr. (n=62,60)	0	0		
Potassium - High, Any Gr. (n=62,60)	1	1		
Potassium - High, Gr. 1 (n=62,60)	1	1		
Sodium - Low, Any Gr. (n=62,60)	0	0		
Sodium - High, Any Gr. (n=62,60)	2	2		
Sodium - High, Gr. 1 (n=62,60)	2	2		
Bilirubin - High, Any Gr. (n=62,58)	2	2		
Bilirubin - High, Gr. 1 (n=62,58)	1	1		
Bilirubin - High, Gr. 2 (n=62,58)	1	1		
Total Leukocyte Count - Low, Any Gr. (n=63,62)	2	0		
Total Leukocyte Count - Low, Gr. 1 (n=63,62)	2	0		
Total Leukocyte Count - High, Any Gr. (n=63,62)	4	0		
Total Leukocyte Count - High, Gr. 1 (n=63,62)	3	0		
Total Leukocyte Count - High, Gr. 2 (n=63,62)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Serum Concentration of Omalizumab at Specified Timepoints

End point title	Mean Serum Concentration of Omalizumab at Specified Timepoints

End point description:

Serum concentrations of omalizumab were quantified using an enzyme-linked immunoabsorbent assay (ELISA) with a lower limit of quantification (LLOQ) of 28.0 nanograms per millilitre (ng/mL). According to the analysis plan, values below the lower limit of quantification (BLQ) were set to 14 ng/mL (i.e. half of LLOQ value). If one-third or fewer of participants had results that were BLQ, then all summary statistics were to be calculated. However, if more than one-third of participants had results that were BLQ, then the mean and standard deviation were non-reportable and only the median and maximum were to be calculated for that timepoint. The value '9999999' indicates that per the analysis plan, the mean and standard deviation at Day 1 (before dosing) were non-reportable because more than one-third of participants (all except for one) had results that were below the lower limit of quantification.

End point type	Secondary

End point timeframe:

Predose on Day 1, Week 16, Week 24, Unscheduled Visit (outside of planned study visits, as clinically indicated), Dosing Termination/Early Termination Visit (up to 28 weeks)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[15]	61		
Units: nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=0,60)	()	9999999 (± 9999999)		
Week 16 (n=0,58)	()	33600 (± 25000)		
Week 24 (n=0,57)	()	36500 (± 27200)		
Unscheduled Visit (n=0,2)	()	44600 (± 49700)		
Dosing Termination/Early Termination Visit (n=0,2)	()	34800 (± 29600)		

Notes:

[15] - Only omalizumab-treated participants at each timepoint were included in this analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Median Serum Concentration of Omalizumab at Specified Timepoints

End point title	Median Serum Concentration of Omalizumab at Specified Timepoints

End point description:

Serum concentrations of omalizumab were quantified using an enzyme-linked immunoabsorbent assay (ELISA) with a lower limit of quantification (LLOQ) of 28.0 nanograms per millilitre (ng/mL). According to the analysis plan, values below the lower limit of quantification (BLQ) were set to 14 ng/mL (i.e. half of LLOQ value). If one-third or fewer of participants had results that were BLQ, then all summary statistics were to be calculated. However, if more than one-third of participants had results that were BLQ, then the mean and standard deviation were non-reportable and only the median and maximum were to be calculated for that timepoint. The value '-9999999' indicates that per the analysis plan, the minimum at Day 1 (before dosing) were non-reportable because more than one-third of participants (all except for one) had results that were below the lower limit of quantification.

End point type	Secondary

End point timeframe:

Predose on Day 1, Week 16, Week 24, Unscheduled Visit (outside of planned study visits, as clinically indicated), Dosing Termination/Early Termination Visit (up to 28 weeks)

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	61		
Units: nanograms per millilitre (ng/mL)				
median (full range (min-max))				
Day 1 (n=0,60)	(to)	0.00 (-9999999 to 49.5)		

Week 16 (n=0,58)	(to)	25000 (6820 to 133000)		
Week 24 (n=0,57)	(to)	26300 (8930 to 130000)		
Unscheduled Visit (n=0,2)	(to)	44600 (9420 to 79700)		
Dosing Termination/Early Termination Visit (n=0,2)	(to)	34800 (13900 to 55700)		

Notes:

[16] - Only omalizumab-treated participants at each timepoint were included in this analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Serum Concentration of Total and Free Immunoglobulin E (IgE) at Specified Timepoints

End point title	Mean Serum Concentration of Total and Free Immunoglobulin E (IgE) at Specified Timepoints

End point description:

Serum concentrations of total immunoglobulin E (IgE) and free IgE were measured throughout the 24-week blinded treatment period, as target engagement biomarkers of omalizumab, using validated quantitative immunoassays with lower limits of quantification of 2 and 0.83 International Units per millilitre (IU/mL), respectively, and upper limits of quantification (ULQ) of 5000 and 62.5 IU/mL, respectively. The free IgE assay had limited range to measure circulating levels of free IgE in the presence of complexes of omalizumab-IgE. According to the analysis plan for the free IgE assay, results above ULQ were set to 62.5 IU/mL. If results for one-third or fewer of participants were greater than (>) the ULQ, then all summary statistics were to be reported. However, if results for more than one-third of participants were >ULQ, then only the median, interquartile range and minimum were calculated, and the mean, standard deviation, and maximum were non-reportable (as indicated by '999999').

End point type	Secondary

End point timeframe:

Predose on Day 1, Week 16, Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: IU/mL				
arithmetic mean (standard deviation)				
Total IgE - Day 1 (n=63,60)	230 (± 235)	218 (± 220)		
Total IgE - Week 16 (n=60,59)	215 (± 172)	695 (± 608)		
Total IgE - Week 24 (n=59,58)	253 (± 319)	641 (± 559)		
Free IgE - Day 1 (n=63,61)	999999 (± 999999)	999999 (± 999999)		
Free IgE - Week 16 (n=60,59)	999999 (± 999999)	11.7 (± 13.9)		
Free IgE - Week 24 (n=60,58)	999999 (± 999999)	11.6 (± 13.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Serum Concentration of Total and Free Immunoglobulin E (IgE) at Specified Timepoints

End point title	Median Serum Concentration of Total and Free Immunoglobulin E (IgE) at Specified Timepoints

End point description:

Serum concentrations of total immunoglobulin E (IgE) and free IgE were measured throughout the 24-week blinded treatment period, as target engagement biomarkers of omalizumab, using validated quantitative immunoassays with lower limits of quantification of 2 and 0.83 International Units per millilitre (IU/mL), respectively, and upper limits of quantification (ULQ) of 5000 and 62.5 IU/mL, respectively. The free IgE assay had limited range to measure circulating levels of free IgE in the presence of complexes of omalizumab-IgE. According to the analysis plan for the free IgE assay, results above ULQ were set to 62.5 IU/mL. If results for one-third or fewer of the participants were greater than the ULQ, then all summary statistics were to be reported. However, if the results for more than one-third of participants were greater than the ULQ, then only the median, interquartile range and minimum were calculated, and the mean, standard deviation, and maximum were non-reportable.

End point type	Secondary

End point timeframe:

Predose on Day 1, Week 16, Week 24

End point values	Placebo	Omalizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: IU/mL				
median (inter-quartile range (Q1-Q3))				
Total IgE - Day 1 (n=63,60)	147 (82.0 to 333)	135 (80.0 to 277)		
Total IgE - Week 16 (n=60,59)	141 (83.0 to 320)	437 (292 to 1030)		
Total IgE - Week 24 (n=59,58)	147 (74.0 to 315)	440 (279 to 742)		
Free IgE - Day 1 (n=63,61)	62.5 (29.9 to 62.5)	62.5 (26.2 to 62.5)		
Free IgE - Week 16 (n=60,59)	59.6 (31.3 to 62.5)	7.58 (4.71 to 11.9)		
Free IgE - Week 24 (n=60,58)	59.6 (17.7 to 62.5)	7.65 (5.46 to 10.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline until end of safety follow-up (up to 28 weeks)

Adverse event reporting additional description:

The safety analysis set consisted of all participants who received at least one dose of study drug, grouped according to treatment received during the treatment period. One participant in the placebo arm received incorrectly one dose of omalizumab and was therefore included in the omalizumab arm in the safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Omalizumab

Reporting group description:

Participants received omalizumab as a subcutaneous injection once every 2 weeks (q2w) or once every 4 weeks (q4w). The dose (from 75 mg up to 600 mg) and dosing frequency (q2w or q4w) was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo as a subcutaneous injection once every 2 weeks or once every 4 weeks. The dose and dosing frequency was determined by serum total IgE level and body weight using the study-drug dosing table. All participants were also treated during the entire study with intranasal corticosteroids (mometasone nasal spray) as background therapy.

Serious adverse events	Omalizumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 63 (4.76%)	1 / 64 (1.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Snake bite			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Asthma			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Omalizumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 63 (26.98%)	20 / 64 (31.25%)	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 63 (11.11%)	3 / 64 (4.69%)	
occurrences (all)	14	7	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	5 / 63 (7.94%)	2 / 64 (3.13%)	
occurrences (all)	8	4	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 63 (1.59%)	5 / 64 (7.81%)	
occurrences (all)	1	8	
Epistaxis			
subjects affected / exposed	4 / 63 (6.35%)	1 / 64 (1.56%)	
occurrences (all)	5	1	
Nasal polyps			
subjects affected / exposed	1 / 63 (1.59%)	4 / 64 (6.25%)	
occurrences (all)	1	5	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 8	9 / 64 (14.06%) 10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2017	The key changes in Protocol version 2 are summarized: -An additional exclusion criterion was added to exclude subjects with a history of myocardial infarction, unstable angina, cerebrovascular accident, or transient ischemic attack or a known history of a hypercoagulable disorder.; -The inclusion criteria were updated to specify acceptable methods of contraception. Barrier methods with use of spermicides allowed under Protocol version 1 were not permitted and acceptable methods included surgical sterilization, hormonal contraception, and intrauterine device. Also, four additional urine pregnancy tests were added to the treatment period.; -Viral serologies for HIV, hepatitis B, and hepatitis C were added during screening at Day -35.; -Additional specifications were added to the section on the management of subjects who experienced specific AEs. While liver injury had not been described as a risk associated with omalizumab, this new section specified how study drug should be managed for subjects who experienced drug induced liver injury.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported