Clinical trial results:
A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of Xolair (Omalizumab) in Patients With Chronic Idiopathic Urticaria (CIU) Who Remain Symptomatic Despite Antihistamine Treatment (H1)

Summary

EudraCT number	2010-022782-99
Trial protocol	FR DE DK IT ES
Global end of trial date	17 October 2012

Results information

Result version number	v1
This version publication date	15 July 2016
First version publication date	08 August 2015

Trial information

Trial identification

Sponsor protocol code	GA00887 (Q4881g)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01287117
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124., Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +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	17 October 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a global, Phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of omalizumab administered subcutaneously as an add-on therapy for the treatment of adolescent and adult participants aged 12 to 75 years who have been diagnosed with refractory CIU and who remain symptomatic despite standard dosed H1 antihistamine treatment.

Protection of trial subjects:

This study was conducted in accordance with the U.S. Food and Drug Administration (FDA) regulations, the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP), Declaration of Helsinki, and applicable local, state, and federal laws, as well as other applicable country laws. The Clinical Study Protocol (CSP) and the Informed Consent Forms (ICFs) were reviewed and approved by an Independent Ethics Committee (IEC).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 17
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	Turkey: 2
Country: Number of subjects enrolled	United States: 220
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	319
EEA total number of subjects	97

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)	18
Adults (18-64 years)	285
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Randomized population: All randomized participants regardless of whether they received any study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo subcutaneously every 4 weeks during the 24-week double-blind treatment period.

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

Dosage and administration details:

Participants received placebo administered by SC injection every 4 weeks during the 24-week double-blind treatment period.

Arm title	Omalizumab 75 mg

Arm description:

Participants received omalizumab 75 milligrams (mg) subcutaneously every 4 weeks during the 24-week double-blind treatment period.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for cutaneous solution
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received SC omalizumab at doses of 75, 150, or 300 mg every 4 weeks during the 24-week, double-blind treatment period.

Arm title	Omalizumab 150 mg

Arm description:

Participants received omalizumab 150 mg subcutaneously every 4 weeks during the 24-week double-blind treatment period.

Arm type	Experimental

Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for cutaneous solution
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received SC omalizumab at doses of 75, 150, or 300 mg every 4 weeks during the 24-week, double-blind treatment period.

Arm title	Omalizumab 300 mg

Arm description:

Participants received omalizumab 300 mg subcutaneously every 4 weeks during the 24-week double-blind treatment period.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for cutaneous solution
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received SC omalizumab at doses of 75, 150, or 300 mg every 4 weeks during the 24-week, double-blind treatment period.

Number of subjects in period 1	Placebo	Omalizumab 75 mg	Omalizumab 150 mg
Started	80	78	80
Received Treatment	80	77	80
Completed	65	64	64
Not completed	15	14	16
Physician decision	-	1	1
Disease progression	10	5	6
Adverse event, non-fatal	2	1	1
Lost to follow-up	1	1	-
Participant/Legal Guardian's decision	2	6	8

Number of subjects in period 1	Omalizumab 300 mg
Started	81
Received Treatment	81
Completed	69
Not completed	12
Physician decision	1
Disease progression	5
Adverse event, non-fatal	1
Lost to follow-up	-
Participant/Legal Guardian's decision	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneously every 4 weeks during the 24-week double-blind treatment period.	
Reporting group title	Omalizumab 75 mg
Reporting group description:	
Participants received omalizumab 75 milligrams (mg) subcutaneously every 4 weeks during the 24-week double-blind treatment period.	
Reporting group title	Omalizumab 150 mg
Reporting group description:	
Participants received omalizumab 150 mg subcutaneously every 4 weeks during the 24-week double-blind treatment period.	
Reporting group title	Omalizumab 300 mg
Reporting group description:	
Participants received omalizumab 300 mg subcutaneously every 4 weeks during the 24-week double-blind treatment period.	

Reporting group values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg
Number of subjects	80	78	80
Age categorical			
Units: Subjects			

Age continuous			
Modified Intent-to-Treat (mITT) Population: All participants randomized in the study who received at least 1 dose of study drug. One participant (randomized to omalizumab 75 mg) did not receive study drug and was not included in the mITT Population.			
Units: years			
arithmetic mean	40.4	41.1	41.1
standard deviation	± 15.6	± 15.6	± 14
Gender categorical			
Units: Subjects			
Female	52	56	64
Male	28	22	16

Reporting group values	Omalizumab 300 mg	Total	
Number of subjects	81	319	
Age categorical			
Units: Subjects			

Age continuous			
Modified Intent-to-Treat (mITT) Population: All participants randomized in the study who received at least 1 dose of study drug. One participant (randomized to omalizumab 75 mg) did not receive study drug and was not included in the mITT Population.			
Units: years			
arithmetic mean	42.4		
standard deviation	± 13.2	-	

Gender categorical Units: Subjects			
Female	60	232	
Male	21	87	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneously every 4 weeks during the 24-week double-blind treatment period.	
Reporting group title	Omalizumab 75 mg
Reporting group description:	
Participants received omalizumab 75 milligrams (mg) subcutaneously every 4 weeks during the 24-week double-blind treatment period.	
Reporting group title	Omalizumab 150 mg
Reporting group description:	
Participants received omalizumab 150 mg subcutaneously every 4 weeks during the 24-week double-blind treatment period.	
Reporting group title	Omalizumab 300 mg
Reporting group description:	
Participants received omalizumab 300 mg subcutaneously every 4 weeks during the 24-week double-blind treatment period.	

Primary: Change From Baseline to Week 12 in the Weekly Itch Severity Score

End point title	Change From Baseline to Week 12 in the Weekly Itch Severity Score
End point description:	
The weekly itch severity score is the sum of the daily itch severity scores over 7 days and ranges from 0 to 21. The daily itch severity score is the average of the morning and evening scores on a scale of 0 (none) to 3 (severe). The Baseline weekly itch severity score is the sum of the daily itch severity scores over the 7 days prior to the first treatment. A higher itch severity score indicates more severe itching. A negative change score indicates improvement. mITT Population: All randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: units on a scale				
arithmetic mean (standard deviation)				
Change From Baseline to Week 12 in the Weekly Itch	-3.63 (± 5.22)	-6.46 (± 6.14)	-6.66 (± 6.28)	-9.4 (± 5.73)

Statistical analyses

Statistical analysis title	Change From Baseline to Week 12 in the Weekly Itch

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups.

Comparison groups	Omalizumab 75 mg v Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.001 [2]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.71
upper limit	-1.21

Notes:

[1] - Covariates included in the analysis were baseline weekly itch severity score (less than [<] 13 verses [vs] ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[2] - A multiplicity type I error control plan was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided).

Statistical analysis title	Change From Baseline to Week 12 in the Weekly Itch

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0012 [4]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.72
upper limit	-1.18

Notes:

[3] - Covariates included in the analysis were baseline weekly itch severity score (<13 vs ≥13) and baseline weight (<80 kg vs ≥80 kg).
[4] - A multiplicity type I error control plan was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided).

Statistical analysis title	Change From Baseline to Week 12 in the Weekly Itch

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg

Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0001 [6]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.49
upper limit	-4.1

Notes:

[5] - Covariates included in the analysis were baseline weekly itch severity score (<13 vs ≥13) and baseline weight (<80 kg vs ≥80 kg).
[6] - A multiplicity type I error control plan was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided).

Secondary: Change From Baseline to Week 12 in the Urticaria Activity Score Over 7 Days (UAS7)

End point title	Change From Baseline to Week 12 in the Urticaria Activity Score Over 7 Days (UAS7)

End point description:

The UAS7 is the sum of the daily urticarial activity scores over 7 days and ranges from 0 to 42. The daily urticarial activity score is the average of the morning and evening urticarial activity scores and ranges from 0 to 6. The urticarial activity score is the sum of ratings on a scale of 0 to 3 (0 is equal to [=] none to 3 = intense/severe) for (1) the number of wheals (hives) and (2) itch intensity over the previous 12 hours, ranges from 0 to 6, and is measured twice daily (morning and evening). The Baseline score is the sum of the daily urticarial activity scores over the 7 days prior to the first treatment. A higher urticarial activity score indicates more urticaria activity. A negative change score indicates improvement. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change From Baseline to Week 12 in the UAS7	-8.01 (± 11.47)	-13.82 (± 13.26)	-14.44 (± 12.95)	-20.75 (± 12.17)

Statistical analyses

Statistical analysis title	Change From Baseline to Week 12 in the UAS7

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.0035 [8]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-5.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.59
upper limit	-1.92

Notes:

[7] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[8] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline to Week 12 in the UAS7

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.0008 [10]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-6.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.33
upper limit	-2.75

Notes:

[9] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[10] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline to Week 12 in the UAS7

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg

Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.0001 [12]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.44
upper limit	-9.16

Notes:

[11] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[12] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Change From Baseline to Week 12 in the Weekly Number of Hives Score

End point title	Change From Baseline to Week 12 in the Weekly Number of Hives Score

End point description:

The weekly hives score is the sum of the daily hives scores over 7 days and ranges from 0 to 21. The number of hives is measured twice daily (morning and evening) on a scale of 0 (none) to 3 (> 12 hives per 12 hours). The daily hives score is the average of the morning and evening scores. The Baseline score is the sum of the daily hives scores over the 7 days prior to the first treatment. A higher score indicates more hives. A negative change score indicates improvement. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: Units on a scale				
arithmetic mean (standard deviation)	-4.37 (± 6.6)	-7.36 (± 7.52)	-7.78 (± 7.08)	-11.35 (± 7.25)

Statistical analyses

Statistical analysis title	Change From Baseline in Hives Score at Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups.

Comparison groups	Placebo v Omalizumab 75 mg

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.0149 [14]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.95
upper limit	-0.54

Notes:

[13] - Covariates included in the analysis were baseline weekly number of hives score (< median vs ≥ median) and baseline weight (< 80 kg vs ≥ 80 kg).
[14] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline in Hives Score at Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.0017 [16]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.57
upper limit	-1.32

Notes:

[15] - Covariates included in the analysis were baseline weekly number of hives score (< median vs ≥ median) and baseline weight (< 80 kg vs ≥ 80 kg).
[16] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline in Hives Score at Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	< 0.0001 [18]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-6.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	-4.76

Notes:

[17] - Covariates included in the analysis were baseline weekly number of hives score (< median vs ≥ median) and baseline weight (< 80 kg vs ≥ 80 kg).
[18] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Time to Minimally Important Difference (MID) Response in the Weekly Itch Severity Score by Week 12

End point title	Time to Minimally Important Difference (MID) Response in the Weekly Itch Severity Score by Week 12

End point description:

The time to the MID response is the number of weeks from the start of treatment (Baseline) until the time point at which the first MID response occurs. The MID response is defined as a reduction ≥ 5 points from Baseline in the weekly itch severity score. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	57	66	76
Units: Weeks				
median (confidence interval 95%)	4 (2 to 6)	3 (2 to 5)	2 (2 to 3)	1 (1 to 2)

Statistical analyses

Statistical analysis title	Time to MID Response in Weekly Itch Severity Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.0879 [20]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.03

Notes:

[19] - Covariates included in the analysis were baseline weekly itch severity score (< 13 vs ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[20] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Time to MID Response in Weekly Itch Severity Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.0301 [22]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.14

Notes:

[21] - Covariates included in the analysis were baseline weekly itch severity score (< 13 vs ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[22] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Time to MID Response in Weekly Itch Severity Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	< 0.0001 [24]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	3.36

Notes:

[23] - Covariates included in the analysis were baseline weekly itch severity score (< 13 vs ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[24] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Percentage of Participants With a UAS7 Score ≤ 6 at Week 12

End point title	Percentage of Participants With a UAS7 Score ≤ 6 at Week 12

End point description:

The UAS7 is the sum of the daily urticarial activity scores over 7 days and ranges from 0 to 42. The daily urticarial activity score is the average of the morning and evening urticarial activity scores and ranges from 0 to 6. The urticarial activity score is the sum of ratings on a scale of 0 to 3 (0 = none to 3 = intense/severe) for (1) the number of wheals (hives) and (2) itch intensity over the previous 12 hours, ranges from 0 to 6, and is measured twice daily (morning and evening). The Baseline score is the sum of the daily urticarial activity scores over the 7 days prior to the first treatment. A higher urticarial activity score indicates more urticaria activity. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: Percentage of participants				
number (not applicable)	11.3	26	40	51.9

Statistical analyses

Statistical analysis title	Percentage of Participants With a UAS7 Score ≤6

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.0148 [26]
Method	Cochran-Mantel-Haenszel

Notes:

[25] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (< 80 kg vs ≥ 80 kg).
[26] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Percentage of Participants With a UAS7 Score ≤6

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.0001 [28]
Method	Cochran-Mantel-Haenszel

Notes:

[27] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (< 80 kg vs ≥ 80 kg).
[28] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Percentage of Participants With a UAS7 Score ≤6

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	< 0.0001 [30]
Method	Cochran-Mantel-Haenszel

Notes:

[29] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (< 80 kg vs ≥ 80 kg).
[30] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Percentage of Weekly Itch Severity Score MID Responders at Week 12

End point title	Percentage of Weekly Itch Severity Score MID Responders at Week 12

End point description:

The percentage of participants with an itch severity score at 12 Weeks at least 5 points lower than at Baseline. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: Percentage of participants				
number (not applicable)	36.3	55.8	56.3	75.3

Statistical analyses

Statistical analysis title	% of Weekly Itch Severity Score MID Responders

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.0118 [32]
Method	Cochran-Mantel-Haenszel

Notes:

[31] - Covariates included in the analysis were baseline weekly itch severity score (< 13 vs ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[32] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	% of Weekly Itch Severity Score MID Responders

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	= 0.0226 [34]
Method	Cochran-Mantel-Haenszel

Notes:

[33] - Covariates included in the analysis were baseline weekly itch severity score (< 13 vs ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[34] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	% of Weekly Itch Severity Score MID Responders

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	< 0.0001 [36]
Method	Cochran-Mantel-Haenszel

Notes:

[35] - Covariates included in the analysis were baseline weekly itch severity score (< 13 vs ≥ 13) and baseline weight (< 80 kg vs ≥ 80 kg).
[36] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Change From Baseline to Week 12 in the Weekly Size of the Largest Hive Score

End point title	Change From Baseline to Week 12 in the Weekly Size of the Largest Hive Score

End point description:

The weekly size of the largest hive score is the sum of the daily size of the largest hive scores over 7 days and ranges from 0 to 21. The daily size of the largest hive score is assessed twice daily (morning and evening) on a scale of 0 (none) to 3 (> 2.5 cm). The daily size of the largest hive score is the average of the morning and evening scores. The Baseline weekly size of the largest hive score is calculated over the 7 days prior to the first treatment. A higher score indicates larger hives. A negative change score indicates a reduction in hive size. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: Units on a scale				
arithmetic mean (standard deviation)	-3.93 (± 5.44)	-6.2 (± 6.29)	-6.96 (± 6.68)	-9.79 (± 6.66)

Statistical analyses

Statistical analysis title	Change From Baseline in Largest Hive Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	= 0.0124 [38]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.17
upper limit	-0.51

Notes:

[37] - Covariates included in the analysis were baseline weekly size of largest hive score (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).

[38] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline in Largest Hive Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg

Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	= 0.0012 [40]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.05
upper limit	-1.27

Notes:

[39] - Covariates included in the analysis were baseline weekly size of largest hive score (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[40] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline in Largest Hive Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[41]
P-value	< 0.0001 [42]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-5.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.59
upper limit	-3.87

Notes:

[41] - Covariates included in the analysis were baseline weekly size of largest hive score (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[42] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Change From Baseline in the Overall Dermatology Life Quality Index (DLQI) Score at Week 12

End point title	Change From Baseline in the Overall Dermatology Life Quality Index (DLQI) Score at Week 12

End point description:

The DLQI is a 10-item dermatology-specific health-related quality of life measure. Participants rated their dermatology symptoms as well as the impact of their skin condition on various aspects of their lives on a scale of 0 (Not at all) to 3 (Very much). The overall DLQI is the sum of the responses to the 10 items and ranges from 0 to 30. A lower score indicates a better quality of life. A negative change score indicates improvement.mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62[43]	66[44]	63[45]	72[46]
Units: Units on a scale				
arithmetic mean (standard deviation)	-6.13 (± 6.25)	-6.33 (± 6.08)	-8 (± 7.24)	-10.29 (± 7.23)

Notes:

[43] - n (number) = participants with values at both Baseline and Week 12 were included in the analysis.

[44] - n (number) = participants with values at both Baseline and Week 12 were included in the analysis.

[45] - n (number) = participants with values at both Baseline and Week 12 were included in the analysis.

[46] - n (number) = participants with values at both Baseline and Week 12 were included in the analysis.

Statistical analyses

Statistical analysis title	Change From Baseline in the Overall DLQI Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	= 0.7956 [48]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	2.28

Notes:

[47] - Covariates included in the analysis were baseline overall DLQI score (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).

[48] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline in the Overall DLQI Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups.

Comparison groups	Placebo v Omalizumab 150 mg

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority[49]
P-value	= 0.2286 [50]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.46
upper limit	0.84

Notes:

[49] - Covariates included in the analysis were baseline overall DLQI score (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[50] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	Change From Baseline in the Overall DLQI Score

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority[51]
P-value	< 0.0001 [52]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-4.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.96
upper limit	-2.2

Notes:

[51] - Covariates included in the analysis were baseline overall DLQI score (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[52] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Percentage of Angioedema-free Days From Week 4 to Week 12

End point title	Percentage of Angioedema-free Days From Week 4 to Week 12

End point description:

The percentage of angioedema-free days from Weeks 4 to 12 was defined as the number of days for which a participant responded "No" to the angioedema question in the daily diary divided by the total number of days with a non-missing diary entry, starting at the Week 4 visit and ending the day prior to the Week 12 visit. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 4 to Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66[53]	69[54]	70[55]	74[56]
Units: Percentage				
arithmetic mean (standard deviation)	88.2 (± 19.4)	86.5 (± 28.4)	89.6 (± 20.6)	96.1 (± 11.3)

Notes:

[53] - n (number) = participants with nonmissing values at Week 4 and Week 12 were included in the analysis
[54] - n (number) = participants with nonmissing values at Week 4 and Week 12 were included in the analysis
[55] - n (number) = participants with nonmissing values at Week 4 and Week 12 were included in the analysis
[56] - n (number) = participants with nonmissing values at Week 4 and Week 12 were included in the analysis

Statistical analyses

Statistical analysis title	% of Angioedema-free Days From Week 4 to Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 75 mg
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority[57]
P-value	= 0.4867 [58]
Method	Stratified Wilcoxon

Notes:

[57] - Stratification variables included in the analysis were presence of angioedema at baseline (yes vs no) and baseline weight (< 80 kg vs ≥ 80 kg).
[58] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	% of Angioedema-free Days From Week 4 to Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate
control plan.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority[59]
P-value	= 0.1747 [60]
Method	Stratified Wilcoxon

Notes:

[59] - Stratification variables included in the analysis were presence of angioedema at baseline (yes vs no) and baseline weight (< 80 kg vs ≥ 80 kg).
[60] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of

0.05 (2-sided) within each dose.

Statistical analysis title	% of Angioedema-free Days From Week 4 to Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate
control plan.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority[61]
P-value	< 0.0001 [62]
Method	Stratified Wilcoxon

Notes:

[61] - Stratification variables included in the analysis were presence of angioedema at baseline (yes vs no) and baseline weight (< 80 kg vs ≥ 80 kg).
[62] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Secondary: Percentage of Complete Responders (UAS7 = 0) at Week 12

End point title	Percentage of Complete Responders (UAS7 = 0) at Week 12

End point description:

A complete responder was defined as a participant with a UAS7 score = 0 at Week 12. mITT Population: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Omalizumab 75 mg	Omalizumab 150 mg	Omalizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	77	80	81
Units: Percentage of participants				
number (not applicable)	8.8	11.7	15	35.8

Statistical analyses

Statistical analysis title	% of Complete Responders (UAS7 = 0) at Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 75 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 75 mg

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[63]
P-value	= 0.458 [64]
Method	Cochran-Mantel-Haenszel

Notes:

[63] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[64] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	% of Complete Responders (UAS7 = 0) at Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 150 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 150 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[65]
P-value	= 0.2087 [66]
Method	Cochran-Mantel-Haenszel

Notes:

[65] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[66] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Statistical analysis title	% of Complete Responders (UAS7 = 0) at Week 12

Statistical analysis description:

The null hypothesis was that there was no difference between the placebo and the omalizumab 300 mg groups. The p-value was not evaluated for statistical significance in accordance with the type I error rate control plan.

Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[67]
P-value	< 0.0001 [68]
Method	Cochran-Mantel-Haenszel

Notes:

[67] - Covariates included in the analysis were baseline UAS7 (< median vs ≥ median) and baseline weight (<80 kg vs ≥80 kg).
[68] - A pre-specified hierarchical order of testing was employed to adjust for the comparison of multiple omalizumab groups to the placebo group in order to maintain an overall type I error rate of 0.05 (2-sided) within each dose.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported starting with the first dose of study drug through the end of the study (up to 40 weeks).

Adverse event reporting additional description:

Safety population: All randomized participants who received at least 1 dose of study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo subcutaneously every 4 weeks during the 24 week treatment period.

Reporting group title	Omalizumab 75 mg

Reporting group description:

Participants received omalizumab 75 mg subcutaneously every 4 weeks during the 24 week treatment period.

Reporting group title	Omalizumab 150 mg

Reporting group description:

Participants received omalizumab 150 mg subcutaneously every 4 weeks during the 24 week treatment period.

Reporting group title	Omalizumab 300 mg

Reporting group description:

Participants received omalizumab 300 mg subcutaneously every 4 weeks during the 24 week treatment period.

Serious adverse events	Placebo	Omalizumab 75 mg	Omalizumab 150 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 80 (6.25%)	2 / 70 (2.86%)	5 / 87 (5.75%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 80 (1.25%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 80 (0.00%)	1 / 70 (1.43%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 80 (1.25%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	0 / 80 (0.00%)	1 / 70 (1.43%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic urticaria			
subjects affected / exposed	1 / 80 (1.25%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Shock hypoglycaemic			
subjects affected / exposed	0 / 80 (0.00%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 80 (1.25%)	0 / 70 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Omalizumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 81 (2.47%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			

subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angioedema			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Idiopathic urticaria			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Shock hypoglycaemic			

subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 81 (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 75 mg	Omalizumab 150 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 80 (45.00%)	37 / 70 (52.86%)	45 / 87 (51.72%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 80 (3.75%)	5 / 70 (7.14%)	12 / 87 (13.79%)
occurrences (all)	3	5	12
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 80 (5.00%)	1 / 70 (1.43%)	4 / 87 (4.60%)
occurrences (all)	7	1	5
Oropharyngeal pain			
subjects affected / exposed	4 / 80 (5.00%)	2 / 70 (2.86%)	5 / 87 (5.75%)
occurrences (all)	4	2	6
Cough			
subjects affected / exposed	3 / 80 (3.75%)	4 / 70 (5.71%)	3 / 87 (3.45%)
occurrences (all)	3	4	3
Skin and subcutaneous tissue disorders			
Idiopathic urticaria			
subjects affected / exposed	4 / 80 (5.00%)	10 / 70 (14.29%)	6 / 87 (6.90%)
occurrences (all)	4	13	8
Urticaria			
subjects affected / exposed	8 / 80 (10.00%)	8 / 70 (11.43%)	7 / 87 (8.05%)
occurrences (all)	15	9	7
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 80 (0.00%)	3 / 70 (4.29%)	5 / 87 (5.75%)
occurrences (all)	0	4	9
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	16 / 80 (20.00%)	5 / 70 (7.14%)	14 / 87 (16.09%)
occurrences (all)	17	5	16
Sinusitis			
subjects affected / exposed	5 / 80 (6.25%)	6 / 70 (8.57%)	7 / 87 (8.05%)
occurrences (all)	5	6	10
Upper respiratory tract infection			
subjects affected / exposed	3 / 80 (3.75%)	6 / 70 (8.57%)	4 / 87 (4.60%)
occurrences (all)	3	8	7
Bronchitis			
subjects affected / exposed	6 / 80 (7.50%)	5 / 70 (7.14%)	2 / 87 (2.30%)
occurrences (all)	6	5	2
Urinary tract infection			
subjects affected / exposed	3 / 80 (3.75%)	3 / 70 (4.29%)	7 / 87 (8.05%)
occurrences (all)	3	3	7

Non-serious adverse events	Omalizumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 81 (49.38%)		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		

Skin and subcutaneous tissue disorders			
Idiopathic urticaria			
subjects affected / exposed	11 / 81 (13.58%)		
occurrences (all)	13		
Urticaria			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	5		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 81 (12.35%)		
occurrences (all)	12		
Sinusitis			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	7		
Upper respiratory tract infection			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2011	• The number of weeks that a participant must have had chronic idiopathic urticaria (CIU) symptoms despite being on H1 antihistamines was increased from 6 to 8 weeks. • The secondary objectives were clarified to indicate that a goal of this study was to provide information regarding the recurrence of disease/symptoms after withdrawal of omalizumab in participants with refractory CIU. Secondary and exploratory endpoints were modified as a result. • Procedures regarding the use of excluded therapy were modified in an effort to continue to follow participants for safety evaluation after they had discontinued study drug treatment. • The washout period required after regular doxepin use prior to enrollment was reduced from 6 weeks to 14 days. • The criterion for women of childbearing potential and pregnancy was clarified. Additionally, nursing women were excluded from study participation. • Contraindications to diphenydramine were added. • The in-clinic urticaria activity score terminology was corrected. • The start of the screening period was modified from 14−18 to 12−18 days prior to Day 1. • The difference between discontinuation from study treatment and discontinuation from the study was clarified. • The Medical Monitor was replaced.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported