Clinical trial results:
A Phase II, Multicenter, Randomized, Double-Blind, Placebo- Controlled Dose-Ranging Study of Xolair (Omalizumab) in Patients with Chronic Idiopathic Urticaria (CIU) Who Remain Symptomatic with Antihistamine Treatment (H1)

Summary

EudraCT number	2009-009498-87
Trial protocol	DE
Global end of trial date	07 January 2010

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	Q4577g

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00866788
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 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, 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 January 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 January 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of single doses of omalizumab compared with placebo in participants with refractory chronic idiopathic urticaria (CIU) receiving concomitant H1 antihistamine therapy. The secondary objectives were to evaluate the safety and efficacy of different dose levels of omalizumab in participants with refractory CIU, to evaluate the efficacy of omalizumab in participants with refractory CIU on the participant-reported, quality-of-life-related outcome measures and to evaluate the pharmacokinetics and pharmacodynamics of omalizumab in participants with refractory CIU.

Protection of trial subjects:

This study was conducted in accordance with the United States Food and Drug Administration (U.S. FDA) regulations, the International Conference on Harmonisation E6 Guideline for Good Clinical Practice, and applicable local, state, and federal laws, as well as other applicable country laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 2009
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	Germany: 13
Country: Number of subjects enrolled	United States: 77
Worldwide total number of subjects	90
EEA total number of subjects	13

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	5

Adults (18-64 years)	80
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were screened from Week -2 to Week -1.

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	Investigator, Data analyst, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a single subcutaneous placebo injection on Day 0 of the study. Participants remained on stable doses of their preallocation a chronic idiopathic urticaria (CIU) H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

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:

Participants received a single subcutaneous placebo injection on Day 0 of the study.

Arm title	Omalizumab 75 milligrams (mg)

Arm description:

Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	Xolair®
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

75 mg of omalizumab (Xolair) was administered subcutaneously on Day 0 of the study.

Arm title	Omalizumab 300 mg

Arm description:

Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Arm type	Experimental

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

Dosage and administration details:

300 mg of omalizumab (Xolair) was administered subcutaneously on Day 0 of the study.

Arm title	Omalizumab 600 mg

Arm description:

Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	Xolair®
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg of omalizumab (Xolair) was administered subcutaneously on Day 0 of the study.

Number of subjects in period 1	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg
Started	21	23	25
Completed Week 4	20	18	23
Completed	15	17	23
Not completed	6	6	2
Consent withdrawn by subject	2	1	-
Physician decision	-	-	1
Disease progression	3	1	1
Pregnancy	-	1	-
Adverse event	-	2	-
Lost to follow-up	1	1	-

Number of subjects in period 1	Omalizumab 600 mg
Started	21
Completed Week 4	20
Completed	16
Not completed	5
Consent withdrawn by subject	1
Physician decision	1
Disease progression	-
Pregnancy	-
Adverse event	1

Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a single subcutaneous placebo injection on Day 0 of the study. Participants remained on stable doses of their preallocation a chronic idiopathic urticaria (CIU) H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	
Reporting group title	Omalizumab 75 milligrams (mg)
Reporting group description:	
Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	
Reporting group title	Omalizumab 300 mg
Reporting group description:	
Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	
Reporting group title	Omalizumab 600 mg
Reporting group description:	
Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	

Reporting group values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg
Number of subjects	21	23	25
Age categorical Units: Subjects			
12-<18 years	2	2	1
18-<40 years	7	10	12
>=40 years	12	11	12
Gender categorical Units: Subjects			
Female	17	15	17
Male	4	8	8

Reporting group values	Omalizumab 600 mg	Total	
Number of subjects	21	90	
Age categorical Units: Subjects			
12-<18 years	0	5	
18-<40 years	11	40	
>=40 years	10	45	
Gender categorical Units: Subjects			
Female	12	61	
Male	9	29	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a single subcutaneous placebo injection on Day 0 of the study. Participants remained on stable doses of their preallocation a chronic idiopathic urticaria (CIU) H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	
Reporting group title	Omalizumab 75 milligrams (mg)
Reporting group description:	
Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	
Reporting group title	Omalizumab 300 mg
Reporting group description:	
Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	
Reporting group title	Omalizumab 600 mg
Reporting group description:	
Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.	

Primary: Change in Urticaria Activity Score 7 (UAS7) From Baseline to Week 4

End point title	Change in Urticaria Activity Score 7 (UAS7) From Baseline to Week 4
End point description:	
The UAS is a composite diary-recorded score, which is the sum of the numeric severity intensity ratings (0 = none to 3 = intense) for 1) the number of wheals (hives) and 2) the intensity of the pruritus (itch). The UAS7 is the sum of the daily average UAS (morning and evening values) for 7 days. The maximum UAS7 score is 42. Intent-to-Treat population (all randomized participants). The last observation carried forward value was used if a participant's Week 4 diary data were completely missing. One participant from the omalizumab 600-mg group did not have any post-baseline data and was excluded from the primary analysis.	
End point type	Primary
End point timeframe:	
Baseline (based on the 7 days prior to randomization) and 4 weeks (Days 21-27)	

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	20
Units: scores on a scale				
arithmetic mean (standard deviation)	-6.91 (± 9.84)	-9.79 (± 11.75)	-19.93 (± 12.38)	-14.56 (± 10.17)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Omalizumab 75 milligrams (mg)
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1601 [1]
Method	van Elteren test

Notes:

[1] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 [2]
Method	van Elteren test

Notes:

[2] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Omalizumab 600 mg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0473 [3]
Method	van Elteren test

Notes:

[3] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Secondary: Change in the Weekly Pruritus Score From Baseline to Week 4

End point title	Change in the Weekly Pruritus Score From Baseline to Week 4

End point description:

The pruritus (itch) score was recorded by participants twice daily (morning and evening) based on the severity of itch over the last 12 hours, using a scale from 0 (none) to 3 (severe). The weekly pruritus score was the sum of average daily pruritus scores over the previous 7 days. The range of the weekly score is 0-21. Intent-to-Treat population (all randomized participants). The last observation carried forward value was used if a participant's Week 4 diary data were completely missing. One participant from the omalizumab 600-mg group did not have any post-baseline data and was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline (based on the 7 days prior to randomization) and 4 weeks (Days 21-27)

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	20
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.45 (± 5.22)	-4.5 (± 5.84)	-9.22 (± 5.98)	-6.46 (± 5.63)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Omalizumab 75 milligrams (mg)
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.164 [4]
Method	van Elteren test

Notes:

[4] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005 [5]
Method	van Elteren test

Notes:

[5] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Omalizumab 600 mg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0558 [6]
Method	van Elteren test

Notes:

[6] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Secondary: Change in the Weekly Score for Number of Hives From Baseline to Week 4

End point title	Change in the Weekly Score for Number of Hives From Baseline to Week 4

End point description:

The number of hives was recorded by participants twice daily (morning and evening) using a scale from 0 (no hives) to 3 (more than 12 hives). The weekly score of number of hives was the sum of the average daily scores over the previous 7 days, and ranged from 0 to 21. Intent-to-Treat population (all randomized patients). The last observation carried forward value was used if a patient's Week 4 diary data were completely missing. One subject from the omalizumab 600-mg group did not have any post-baseline data and was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline (based on the 7 days prior to randomization) and 4 weeks (Days 21-27)

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	20
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.46 (± 5.17)	-5.28 (± 6.91)	-10.71 (± 6.75)	-8.1 (± 6)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Omalizumab 75 milligrams (mg) v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1411 [7]
Method	van Elteren test

Notes:

[7] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 [8]
Method	van Elteren test

Notes:

[8] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Omalizumab 600 mg

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0248 [9]
Method	van Elteren test

Notes:

[9] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Secondary: Change in the Weekly Score for Sleep Interference From Baseline to Week 4

End point title	Change in the Weekly Score for Sleep Interference From Baseline to Week 4

End point description:

The extent to which hives or itch interfered with participants' sleep was recorded once daily in the patient diary using a scale from 0 (no interference) to 3 (substantial interference, waking often). The weekly score of sleep interference was the sum of the daily scores over the previous 7 days, and ranged from 0 to 21. Intent-to-Treat population (all randomized patients). The last observation carried forward value was used if a patient's Week 4 diary data were completely missing. One subject from the omalizumab 600-mg group did not have any post-baseline data and was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline (based on the 7 days prior to randomization) and 4 weeks (Days 21-27)

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	20
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.23 (± 5.93)	-3.9 (± 5.03)	-5.81 (± 5.36)	-6.85 (± 6.23)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Omalizumab 75 milligrams (mg)
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5507 [10]
Method	van Elteren test

Notes:

[10] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Omalizumab 300 mg

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1525 [11]
Method	van Elteren test

Notes:

[11] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Omalizumab 600 mg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0449 [12]
Method	van Elteren test

Notes:

[12] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Secondary: Change in the Weekly Score for the Amount of Rescue Medication From Baseline to Week 4

End point title	Change in the Weekly Score for the Amount of Rescue Medication From Baseline to Week 4

End point description:

Diphenhydramine 25mg was provided and used on an as-needed basis (maximum 3 times/day) as rescue medication. The weekly score for the amount of rescue medication is the sum of the daily scores for the amount of rescue medication used at each day in the week, and ranged from 0 to 21. Intent-to-Treat population (all randomized patients). The last observation carried forward value was used if a patient's Week 4 diary data were completely missing. One subject from the omalizumab 600-mg group did not have any post-baseline data and was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline (based on the 7 days prior to randomization) and 4 weeks (Days 21-27)

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	20
Units: pills				
arithmetic mean (standard deviation)	-1.38 (± 4.39)	-1.74 (± 4.48)	-2.64 (± 5.17)	-1.69 (± 3.56)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Omalizumab 75 milligrams (mg)

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7261 [13]
Method	van Elteren test

Notes:

[13] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Omalizumab 300 mg
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.162 [14]
Method	van Elteren test

Notes:

[14] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Omalizumab 600 mg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6504 [15]
Method	van Elteren test

Notes:

[15] - The p-value was based on the van Elteren test (stratified by baseline weight ≥ 80 or < 80 kg).

Secondary: Number of Patients With Adverse Events by Severity

End point title	Number of Patients With Adverse Events by Severity

End point description:

The severity (i.e. intensity) of each Adverse Event (AE) was graded according to the following scale: Mild: Symptoms causing no or minimal interference with usual social and functional activities. Moderate: Symptoms causing greater than minimal interference with usual social and functional activities. Severe: Symptoms causing inability to perform usual social and functional activities. Additional AE data is provided in the AE section below. The terms "severe" and "serious" are not synonymous. Severity refers to the intensity of an AE. A "Serious" AE is defined below. Safety-Evaluable Population, which included all randomized participants who received any study drug. number (n) equals (=) number of participants analyzed in the specified category.

End point type	Secondary

End point timeframe:

16 weeks overall (data reported separately for "up to 4 weeks" and "Weeks 5 to 16")

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	21
Units: participants				
number (not applicable)				
4 Weeks - Any Adverse Event (n=21,23,25,21)	10	8	12	10
4 Weeks - Mild (n=21,23,25,21)	8	4	6	7
4 Weeks - Moderate (n=21,23,25,21)	2	3	5	2
4 Weeks - Severe (n=21,23,25,21)	0	1	1	1
Follow-up period-Any adverse event (n=20,18,23,20)	7	9	12	5
Follow-up period-Mild (n=20,18,23,20)	4	5	4	3
Follow-up period-Moderate (n=20,18,23,20)	2	2	6	1
Follow-up period-Severe (n=20,18,23,20)	1	2	2	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Immunogenicity

End point title	Number of Participants With Immunogenicity

End point description:

Immunogenicity was measured by detection of anti-therapeutic antibodies (anti-omalizumab antibodies) using a fragment enzyme-linked immunosorbent assay (ELISA). Analysis was performed on safety-evaluable population.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	23	25	21
Units: participants				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) of Omalizumab

End point title	Maximum Observed Concentration (Cmax) of Omalizumab[16]

End point description:

Cmax is the maximum (or peak) concentration of omalizumab in serum. The analysis was performed on Pharmacokinetic-Evaluable Population which included all randomized participants who received omalizumab and had pharmacokinetic data available. Here, number of participants analyzed = participants with available data for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose on Days 0 and 3 of Week 0, Weeks 1, 2, 3, 4, 8, 12, 16 or early termination (up to Week 16)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo group did not receive any omalizumab, therefore Cmax is not applicable.

End point values	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	23	20	
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)	11.4 (± 16.4)	33.1 (± 10.4)	67 (± 26.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Concentration (Tmax) of Omalizumab

End point title	Time to Maximum Concentration (Tmax) of Omalizumab[17]

End point description:

Tmax is the time to maximum concentration of omalizumab. Here, number of participants analyzed = participants with available data for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose on Days 0 and 3 of Week 0, Weeks 1, 2, 3, 4, 8, 12, 16 or early termination (up to Week 16)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo group did not receive any omalizumab, therefore Tmax is not applicable.

End point values	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	23	20	
Units: days				
arithmetic mean (standard deviation)	7.37 (± 3.72)	8.01 (± 5.54)	6.24 (± 3.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Curve from Time of Dosing Extrapolated to Infinity (AUC-Inf)

End point title	Area Under the Concentration-time Curve from Time of Dosing Extrapolated to Infinity (AUC-Inf)[18]

End point description:

AUCinf is the area under the concentration-time curve from time of dosing extrapolated to infinity. AUCinf was measured in microgram times day per milliliter (µg*day/mL). The analysis was performed on Pharmacokinetic-Evaluable Population. Here, number of participants analyzed = participants with available data for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose on Days 0 and 3 of Week 0, Weeks 1, 2, 3, 4, 8, 12, 16 or early termination (up to Week 16)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo group did not receive any omalizumab, therefore AUC-Inf is not applicable.

End point values	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	22	19	
Units: µg*day/mL				
arithmetic mean (standard deviation)	317 (± 99.6)	1260 (± 580)	2800 (± 1140)	

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-Life (t1/2) of Omalizumab

End point title	Terminal Half-Life (t1/2) of Omalizumab[19]

End point description:

Terminal Half-Life (t1/2) is the time required for the serum concentration of omalizumab to decrease by half in the final stage of its elimination. The analysis was performed on Pharmacokinetic−Evaluable Population. Here, number of participants analyzed = participants with available data for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose on Days 0 and 3 of Week 0, Weeks 1, 2, 3, 4, 8, 12, 16 or early termination (up to Week 16)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo group did not receive any omalizumab, therefore t1/2 is not applicable.

End point values	Omalizumab 75 milligrams (mg)	Omalizumab 300 mg	Omalizumab 600 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	22	19	
Units: days				
arithmetic mean (standard deviation)	18.2 (± 4.76)	17.1 (± 4.41)	22.5 (± 5.9)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were recorded from Day -7 until end of study at 16 weeks

Adverse event reporting additional description:

A Serious AE is any AE that is either: fatal, life threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, a congenital anomaly/birth defect in a neonate/infant born to a mother exposed to the study treatment or considered a significant medical event by the investigator.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received a single subcutaneous placebo injection on Day 0 of the study. Participants remained on stable doses of their preallocation a CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Reporting group title	Omalizumab 75 mg

Reporting group description:

Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Reporting group title	Omalizumab 300 mg

Reporting group description:

Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Reporting group title	Omalizumab 600 mg

Reporting group description:

Omalizumab (Xolair) was administered subcutaneously on Day 0 of the study. Participants remained on stable doses of their preallocation CIU H1 antihistamine treatment throughout the study, and were provided diphenhydramine as rescue medication for pruritus relief on an as-needed basis.

Serious adverse events	Placebo	Omalizumab 75 mg	Omalizumab 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 23 (0.00%)	1 / 25 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 23 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Omalizumab 600 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 21 (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 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 21 (23.81%)	9 / 23 (39.13%)	11 / 25 (44.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 21 (4.76%)	0 / 23 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	4
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	2 / 23 (8.70%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 23 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Skin and subcutaneous tissue disorders			
Idiopathic urticaria			
subjects affected / exposed	0 / 21 (0.00%)	1 / 23 (4.35%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 23 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0

Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)	4 / 23 (17.39%)	3 / 25 (12.00%)
occurrences (all)	4	5	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	2 / 23 (8.70%)	3 / 25 (12.00%)
occurrences (all)	0	2	3

Non-serious adverse events	Omalizumab 600 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 21 (38.10%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Idiopathic urticaria			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2009	Study Q4577g was amended to consolidate the two CIU protocols for Germany and the United States into one single protocol covering both countries, per recommendation by Genentech's Product Development Regulatory.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported