Clinical trial results:
A phase IV, multicenter, single-arm and open-label study with omalizumab (Xolair®) in chronic spontaneous urticaria (CSU) patients who remain symptomatic despite antihistamine (H1) treatment

Summary

EudraCT number	2014-005424-97
Trial protocol	FR
Global end of trial date	11 January 2016

Results information

Result version number	v1 (current)
This version publication date	27 January 2017
First version publication date	27 January 2017

Trial information

Trial identification

Sponsor protocol code	CIGE025EFR02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02550106
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	11 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2016
Global end of trial reached?	Yes
Global end of trial date	11 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the proportion of patients with a urticaria control test (UCT) score ≥ 12 (indicating a well-controlled urticaria) at Week 12 in adult patients with chronic spontaneous urticaria (CSU) with inadequate response to H1 antihistamine treatment and treated by omalizumab 300 mg S.C. every 4 weeks.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 April 2015
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	France: 136
Worldwide total number of subjects	136
EEA total number of subjects	136

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	126
From 65 to 84 years	10

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Full Analysis Set

Pre-assignment

Screening details:

The study consisted of a screening period (Day -7 to Day -1), a treatment period of 12 weeks (Day 1 to Day 85) and an extension period up to commercial availability of omalizumab in France. Omalizumab was launched on the French market on 03-Nov-2015.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label, non-blinded study.

Arms

Arm title	OMALIZUMAB

Arm description:

sub cutaneous injections of 300 mg every 4 weeks until Week 8

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

Dosage and administration details:

300 mg S.C. every 4 weeks

Number of subjects in period 1	OMALIZUMAB
Started	136
Completed	124
Not completed	12
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Lack of efficacy	3
Protocol deviation	6

Baseline characteristics

Reporting groups	
Reporting group title	OMALIZUMAB
Reporting group description:	
sub cutaneous injections of 300 mg every 4 weeks until Week 8	

Reporting group values	OMALIZUMAB	Total	
Number of subjects	136	136	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	126	126	
From 65-84 years	10	10	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	44.4		
standard deviation	± 12.67	-	
Gender, Male/Female Units: Subjects			
Female	106	106	
Male	30	30	

End points

End points reporting groups

Reporting group title	OMALIZUMAB
Reporting group description: sub cutaneous injections of 300 mg every 4 weeks until Week 8	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until W8	
Subject analysis set title	OMALIZUMAB without angioedema
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneaous injections of 300 mg every 4 weeks until Week 8	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until Week 8	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until W8	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until W8	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until End Of Study (EOS)	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	

Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until EOS	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until Week 8	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until W8	
Subject analysis set title	OMALIZUMAB with ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until W8	
Subject analysis set title	OMALIZUMAB without ANGIOEDEMA
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneous injections of 300 mg every 4 weeks until W8	
Subject analysis set title	OMALIZUMAB Without angioedema
Subject analysis set type	Full analysis
Subject analysis set description: sub cutaneaous injections of 300 mg every 4 weeks until Week 8	

Primary: Percent of participants with an urticaria control test [UCT] score of greater than or equal to 12

End point title	Percent of participants with an urticaria control test [UCT] score of greater than or equal to 12[1]

End point description:

UCT number and percentage of patients with disease control, UCT score at least 12 at Week 12

No statistical analysis was planned for this primary outcome in this single-arm study

End point type	Primary

End point timeframe:

WEEK 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single-arm study

End point values	OMALIZUMAB			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: percent of participants				
number (confidence interval 95%)	75 (66.9 to 82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with UAS7≤6 (patients achieving disease control), in adult patients with CSU, with or without the presence of angioedema

End point title	Proportion of participants with UAS7≤6 (patients achieving disease control), in adult patients with CSU, with or without the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:

WEEK 12

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without angioedema		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	83	51		
Units: percent of participants				
number (confidence interval 95%)	69.6 (58.2 to 79.5)	63.8 (48.5 to 77.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: CSU disease activity using the urticaria activity score (UAS7), with or without the presence of angioedema

End point title	CSU disease activity using the urticaria activity score (UAS7), with or without the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:

WEEK 12

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	47		
Units: absolute value				
arithmetic mean (standard deviation)				
baseline	29.7 (± 7.32)	29.2 (± 6.72)		
at week 12	6.6 (± 10.08)	6.5 (± 9.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: control of the CSU using the UCT score, with or without the presence of angioedema

End point title	control of the CSU using the UCT score, with or without the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:

WEEK 12

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	50		
Units: absolute value				
arithmetic mean (standard deviation)				
baseline	3 (± 2.06)	3.6 (± 2.55)		
at week 12	13.1 (± 3.95)	12.9 (± 3.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: control of the CSU using the UCT score for patients in extension treatment period phase at week 16, with or without the presence of angioedema

End point title	control of the CSU using the UCT score for patients in extension treatment period phase at week 16, with or without

	the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:
week 16

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	42		
Units: absolute value				
arithmetic mean (standard deviation)	14.2 (± 2.96)	13.4 (± 3.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: control of the CSU using the UCT score for patients in extension treatment period phase at week 20, with or without the presence of angioedema

End point title	control of the CSU using the UCT score for patients in extension treatment period phase at week 20, with or without the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:
week 20

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	34		
Units: absolute value				
arithmetic mean (standard deviation)	14.4 (± 2.4)	13.3 (± 4.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: control of the CSU using the UCT score for patients in extension

treatment period phase at week 24, with or without the presence of angioedema	
End point title	control of the CSU using the UCT score for patients in extension treatment period phase at week 24, with or without the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:

week 24

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	12		
Units: absolute value				
arithmetic mean (standard deviation)	14.5 (± 2.14)	13.4 (± 3.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: control of the CSU using the UCT score for patients in extension treatment period phase at week 28, with or without the presence of angioedema	
End point title	control of the CSU using the UCT score for patients in extension treatment period phase at week 28, with or without the presence of angioedema

End point description:

End point type	Secondary

End point timeframe:

week 28

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	2		
Units: absolute value				
arithmetic mean (standard deviation)	13.5 (± 3.54)	12 (± 5.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: The quality of life using the chronic urticaria quality of life (CU-QoL) questionnaire

End point title	The quality of life using the chronic urticaria quality of life (CU-QoL) questionnaire

End point description:

End point type	Secondary

End point timeframe:
WEEK 12

End point values	OMALIZUMAB with ANGIOEDEMA	OMALIZUMAB without ANGIOEDEMA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	49		
Units: absolute value				
arithmetic mean (standard deviation)				
baseline	68.9 (± 15.64)	62.4 (± 17.76)		
at 12 weeks	32.5 (± 13.33)	33.3 (± 13.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: The angioedema quality of life (AE-QoL)

End point title	The angioedema quality of life (AE-QoL)

End point description:

End point type	Secondary

End point timeframe:
WEEK 12

End point values	OMALIZUMAB with ANGIOEDEMA			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: absolute value				
arithmetic mean (standard deviation)				
baseline	57.88 (± 22.474)			
at week 12	16.4 (± 20.074)			

Statistical analyses

No statistical analyses for this end point

Secondary: The dermatology life quality index (DLQI)

End point title	The dermatology life quality index (DLQI)

End point description:

End point type	Secondary

End point timeframe:

WEEK 12

End point values	OMALIZUMAB without ANGIOEDEMA	OMALIZUMAB Without angioedema		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	49		
Units: absolute value				
arithmetic mean (standard deviation)				
baseline	14.2 (± 5.39)	13.2 (± 6.67)		
at week 12	2.4 (± 3.95)	2.7 (± 5.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: angioedema activity using the angioedema activity score (AAS)

End point title	angioedema activity using the angioedema activity score (AAS)

End point description:

End point type	Secondary

End point timeframe:

WEEK 12

End point values	OMALIZUMAB with ANGIOEDEMA			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: absolute value				
arithmetic mean (standard deviation)				
baseline	32.7 (± 27.21)			
at week 12	3.7 (± 10.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Omalizumab 300 mg

Reporting group description:

Omalizumab 300 mg

Serious adverse events	Omalizumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 136 (6.62%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FRACTURED SACRUM			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
PHARYNGEAL OEDEMA			

subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
BLADDER DILATATION			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY INCONTINENCE			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
FOOT DEFORMITY			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SACROILIITIS			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
OBESITY			

subjects affected / exposed	1 / 136 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Omalizumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 136 (32.35%)		
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	7 / 136 (5.15%)		
occurrences (all)	7		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	22 / 136 (16.18%)		
occurrences (all)	33		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	23 / 136 (16.91%)		
occurrences (all)	33		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	12 / 136 (8.82%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported