Clinical trial results:
Multicenter double- blinded, placebo- controlled randomized cross-over (2x2) trial, to assess efficacy and safety of a new indication for Omalizumab (Xolair®, Novartis) in autoimmune and no autoimmune chronic urticaria.

Summary

EudraCT number	2010-024113-31
Trial protocol	ES
Global end of trial date	13 May 2014

Results information

Result version number	v1 (current)
This version publication date	19 September 2021
First version publication date	19 September 2021
Summary attachment (see zip file)	FINAL REPORT (SPANISH) (Informe final CUN-OMAL-CU-2010.pdf)

Trial information

Trial identification

Sponsor protocol code	CUN-OMAL-CU-2010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01713725
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clínica Universidad de Navarra
Sponsor organisation address	Avda. Pío XII, 36, Pamplona, Spain, 31008
Public contact	UCICEC, Clínica Universidad de Navarra, 34 948 255 400, ucicec@unav.es
Scientific contact	UCICEC, Clínica Universidad de Navara, 34 948 255 400, ucicec@unav.es

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	01 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2014
Global end of trial reached?	Yes
Global end of trial date	13 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1.To evaluate the efficacy of omalizumab in a new indication: patients with chronic urticaria.
2.To evaluate the safety of omalizumab in a new indication: patients with chronic urticaria.
3.To evaluate whether the efficacy and safety of omalizumab is different in patients with autoimmune and non-autoimmune chronic urticaria.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2012
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	Spain: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with autoimmune and non-autoimmune chronic urticaria who do not respond to approved doses of antihistamines will be included. These patients will be invited to participate in the allergology departments of the participating hospitals.

Pre-assignment

Screening details:

Adult patients of both sexes, with UAS 7 Severity Scale greater than or equal to 28.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Arm A (treatment group)

Arm description:

This is a crossover design in which there are two groups of patients. Group I patients start in arm A, administered 5 doses of Omalizumab, and after a 4-week washout period, move to arm B, where they are administered 5 doses of placebo. Group II patients start in arm B (5 doses of placebo) and after a 4-week washout period move to arm A (5 doses of Omalizumab).

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	R03DX05
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector
Routes of administration	Subcutaneous use

Dosage and administration details:

It is administered subcutaneously in the deltoid region of the arm. The dose is 300mg. It is administered as two subcutaneous injections of 150mg in 1ml each. A total of 5 doses are administered. The first two doses are administered every 2 weeks and the next 3 doses every 4 weeks. This is followed by a 4-week washout period.

Arm title	Arm B (placebo group)

Arm description:

This is a crossover design in which there are two groups of patients. Group I patients start in arm A, administered 5 doses of Omalizumab, and after a 4-week washout period, move to arm B, where they are administered 5 doses of placebo. Group II patients start in arm B (5 doses of placebo) and after a 4-week washout period move to arm A (5 doses of Omalizumab).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector
Routes of administration	Subcutaneous use

Dosage and administration details:

2ml of Physiological Saline is administered as two injections of 1ml each, subcutaneously in the deoltoid region of the upper arm. The volume to be administered is the same as that of the active treatment. A total of 5 doses are administered. The first two doses are administered every 2 weeks and the next 3 doses every 4 weeks.

Number of subjects in period 1	Arm A (treatment group)	Arm B (placebo group)
Started	10	10
Completed	7	10
Not completed	3	0
Protocol deviation	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	
Gender categorical Units: Subjects			
Female	10	10	
Male	10	10	

End points

End points reporting groups

Reporting group title	Arm A (treatment group)

Reporting group description:

This is a crossover design in which there are two groups of patients. Group I patients start in arm A, administered 5 doses of Omalizumab, and after a 4-week washout period, move to arm B, where they are administered 5 doses of placebo. Group II patients start in arm B (5 doses of placebo) and after a 4-week washout period move to arm A (5 doses of Omalizumab).

Reporting group title	Arm B (placebo group)

Reporting group description:

This is a crossover design in which there are two groups of patients. Group I patients start in arm A, administered 5 doses of Omalizumab, and after a 4-week washout period, move to arm B, where they are administered 5 doses of placebo. Group II patients start in arm B (5 doses of placebo) and after a 4-week washout period move to arm A (5 doses of Omalizumab).

Primary: Efficacy of Omalizumab

End point title	Efficacy of Omalizumab

End point description:

Effectiveness is evaluated by the difference between basal mean values of Urticaria Activity Score scale (UAS), life questionary CU-Q2oL and Visual Activity Scale (VAS) and post-treatment and post-placebo mean values of these three scales.
The basal values in UAS scale are 3(2;6) and the basal values in VAS scale are 60 (25;75), values expressed as a median (25 percentile; 75 percentile).
On the UAS scale, a statistically significant difference is found when comparing baseline to post-treatment values. No significant difference is found when comparing baseline to post-placebo values.
The same is observed when comparing the values of the CU-Q2oL scale and VAS scale. There are no statistically significant differences between patients with an autoimmune mechanism and those without.

End point type	Primary

End point timeframe:

Effectiveness is assessed in each study visit.

End point values	Arm A (treatment group)	Arm B (placebo group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: NA				
median (inter-quartile range (Q1-Q3))				
Urticaria Activity Score scale (UAS)	0 (0 to 2)	2 (0 to 3)		
Visual Activity Scale (VAS)	10 (1 to 29)	27 (4 to 60)		

Statistical analyses

Statistical analysis title	Comparison of means
Comparison groups	Arm A (treatment group) v Arm B (placebo group)

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious unexpected adverse reactions are reported within 15 days of knowledge of the reaction or within 7 days if death or life threatening has occurred. Patient who develops an adverse event will be followed until resolution.

Adverse event reporting additional description:

None of the patients included had AEs and 12 of them had 139 AEs, of which 77% were of mild intensity and the rest of moderate intensity. Of the 139 AEs, 8 of them (5.8%) showed a possible relationship with the drug administered, 1 (0.7%) showed a probable relationship, 10 (7.2%) showed a remote relationship and 93 (66.9%) had no relationship.

Assessment type	Systematic

Dictionary used

Dictionary name	CTM
Dictionary version	NA

Reporting groups

Reporting group title	All the patients

Reporting group description:

Adverse effects are assessed and monitored for all trial participants.

Serious adverse events	All the patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	All the patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 20 (60.00%)		
Nervous system disorders			
vasovagal syncope			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Headache			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	13		

aphonia subjects affected / exposed occurrences (all) fever subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Ear and labyrinth disorders ear infection subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Eye disorders Rhinoconjunctivitis subjects affected / exposed occurrences (all) Eye oedema subjects affected / exposed occurrences (all) eye angioedema subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 2 2 / 20 (10.00%) 10 1 / 20 (5.00%) 5		
Social circumstances bad night´s rest subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Gastrointestinal disorders diarrhea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 1 2 / 20 (10.00%) 4		
Respiratory, thoracic and mediastinal disorders Rhinitis subjects affected / exposed occurrences (all) Rhinorrea	 1 / 20 (5.00%) 8 		

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
dyspnea with wheezing			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	6		
breathlessness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	11		
cold			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
nasal pruritus			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
tonge angioedema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Lip oedema			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	11		
lip angioedema			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
facial oedema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	3		
tongue sores			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin hyperpigmentation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Dermatitis subjects affected / exposed occurrences (all) odontalgia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Psychiatric disorders Anxiety disorder subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2		
Musculoskeletal and connective tissue disorders cervical pain subjects affected / exposed occurrences (all) Costodorsal pain subjects affected / exposed occurrences (all) Muscular pain subjects affected / exposed occurrences (all) artritis subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 7 2 / 20 (10.00%) 2 3 / 20 (15.00%) 4 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 2 / 20 (10.00%) 8 1 / 20 (5.00%) 12		
Infections and infestations amygdalitis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2011	Change from single-blinded design with blinded evaluator to double-blinded.
02 March 2012	Add two more blood draws, one after each period.
20 June 2012	Change of promoter Addition of an inclusion criterion Changes to clarify procedures Change in permitted medication Changes in the calendar Correction of errors
26 July 2013	Decrease in n Sample donation Biobank

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported