Clinical trial results:
A 26-week randomized, double-blind, placebo-controlled, multi-center study to evaluate the effect of omalizumab on markers of asthma impairment in patients with persistent allergic asthma

Summary

EudraCT number	2017-001799-41
Trial protocol	Outside EU/EEA
Global end of trial date	17 March 2010

Results information

Result version number	v1 (current)
This version publication date	25 October 2017
First version publication date	25 October 2017

Trial information

Trial identification

Sponsor protocol code	CIGE025AUS33

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00870584
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, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 March 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 March 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the effect of omalizumab on markers of impairment, as measured by the Asthma Control Test (ACT) scores at Week 24 of treatment, in patients with inadequately controlled persistent allergic asthma on Step 4 or above therapy, as defined
in the 2007 National Heart, Lung, and Blood Institute (NHLBI) guidelines. Inadequately controlled was defined as not well controlled or very poorly controlled.

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	09 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	United States: 271
Worldwide total number of subjects	271
EEA total number of subjects	0

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)	19
Adults (18-64 years)	239
From 65 to 84 years	13

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Approximately 266 patients from an estimated 50 centers were to be randomized to receive omalizumab or placebo, in a 1:1 ratio (133 patients per treatment group), as add-on therapy to their current asthma maintenance therapy.

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, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Omalizumab

Arm description:

The determined dose (at least 0.016 mg/kg/IgE (IU/mL) was administered subcutaneously every 2 weeks or every 4 weeks. Dose and dosing interval were determined based on patient body weight and pre-treatment serum IgE level; a dosing table was used.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	IGE025
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab was supplied as a lyophilized, sterile powder in a single-use, 5 mL vial. The vial was designed to deliver 150 mg (1.2 mL) of omalizumab for subcutaneous (s.c.) administration after reconstitution with 1.4 mL sterile water for injection. Doses of more than 150 mg were divided among multiple injection sites to limit injections to not more than 150 mg per site

Arm title	Placebo

Arm description:

Placebo was administered subcutaneously every 2 weeks or every 4 weeks depending on the dosing schedule in the protocol.

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

Dosage and administration details:

Placebo was supplied as a lyophilized, sterile powder in a single-use, 5 mL vial. The vial was designed to deliver 150 mg (1.2 mL) of omalizumab for subcutaneous (s.c.) administration after reconstitution with 1.4 mL sterile water for injection. Doses of more than 150 mg were divided among multiple injection sites to limit injections to not more than 150 mg per site

Number of subjects in period 1	Omalizumab	Placebo
Started	136	135
Completed	120	122
Not completed	16	13
Consent withdrawn by subject	6	7
Adverse event, non-fatal	3	3
Protocol Deviation	2	2
Lost to follow-up	5	1

Baseline characteristics

Reporting groups	
Reporting group title	Omalizumab
Reporting group description:	
The determined dose (at least 0.016 mg/kg/IgE (IU/mL) was administered subcutaneously every 2 weeks or every 4 weeks. Dose and dosing interval were determined based on patient body weight and pre-treatment serum IgE level; a dosing table was used.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered subcutaneously every 2 weeks or every 4 weeks depending on the dosing schedule in the protocol.	

Reporting group values	Omalizumab	Placebo	Total
Number of subjects	136	135	271
Age categorical			
Units: Subjects			
Adolescents (12-17)	10	10	20
Adults (18-64)	123	124	247
From 65 Years	3	1	4
Age Continuous			
Units: years			
arithmetic mean	41.9	40.7	
standard deviation	± 14.6	± 14.85	-
Gender, Male/Female			
Units: Subjects			
Female	93	87	180
Male	43	48	91

End points

End points reporting groups

Reporting group title	Omalizumab
Reporting group description:	
The determined dose (at least 0.016 mg/kg/IgE (IU/mL) was administered subcutaneously every 2 weeks or every 4 weeks. Dose and dosing interval were determined based on patient body weight and pre-treatment serum IgE level; a dosing table was used.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered subcutaneously every 2 weeks or every 4 weeks depending on the dosing schedule in the protocol.	

Primary: Change from baseline in Asthma Control Test (ACT) after 24 weeks of treatment

End point title	Change from baseline in Asthma Control Test (ACT) after 24 weeks of treatment
End point description:	
The Asthma Control Test (ACT) is a validated tool to assess overall asthma control over the last 4 weeks in patients aged >= 12 years old. It is a 1 page questionnaire consisting of 5 simple questions assessing: asthma symptoms, use of rescue medications, and the impact of asthma on everyday functioning. All questions are scored on a 5-point Likert scale, with a higher score indicating better control. All scores are added together to calculate a total score. Total score ranges from 5 to 25. A positive change indicates improvement.	
End point type	Primary
End point timeframe:	
Baseline and 24 weeks	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	123		
Units: Score on a scale				
arithmetic mean (standard deviation)	5.2 (± 4.37)	4.7 (± 4.01)		

Statistical analyses

Statistical analysis title	Change in ACT total score from baseline
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	241
Analysis specification	Post-hoc
Analysis type	
P-value	= 0.1779
Method	ANCOVA

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.59

Secondary: Investigator Global Evaluation of Treatment Effectiveness (IGETE) at 24 weeks

End point title	Investigator Global Evaluation of Treatment Effectiveness (IGETE) at 24 weeks

End point description:

The IGETE is an assessment of asthma symptom control in response to asthma treatment. It consists of the question "What is the investigator's overall impression of the study medication and its effect on the typical symptoms of allergic asthma during the study?" The scale is: excellent, good, moderate, poor, and worsening. A good or excellent response is suggested as a means of defining a patient who has responded to treatment.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	135		
Units: participants				
Excellent	26	19		
Good	44	44		
Moderate	29	30		
Poor	27	36		
Worsening	1	2		
Missing	9	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	Omalizumab
Reporting group description:	
Omalizumab	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	Omalizumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 136 (2.21%)	5 / 135 (3.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Leukocytosis			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 136 (0.74%)	1 / 135 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 136 (0.00%)	1 / 135 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 136 (0.00%)	2 / 135 (1.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis bacterial			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	0 / 136 (0.00%)	1 / 135 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bites			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 136 (0.00%)	1 / 135 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection pseudomonas			
subjects affected / exposed	0 / 136 (0.00%)	1 / 135 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 136 (0.74%)	0 / 135 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Omalizumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 136 (38.24%)	51 / 135 (37.78%)	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 136 (5.15%)	9 / 135 (6.67%)	
occurrences (all)	7	9	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	20 / 136 (14.71%)	25 / 135 (18.52%)	
occurrences (all)	20	25	
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 136 (5.15%)	9 / 135 (6.67%)	
occurrences (all)	7	9	
Sinusitis			
subjects affected / exposed	13 / 136 (9.56%)	9 / 135 (6.67%)	
occurrences (all)	13	9	
Upper respiratory tract infection			
subjects affected / exposed	15 / 136 (11.03%)	18 / 135 (13.33%)	
occurrences (all)	15	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2008	Amendment 1 -issued prior to study start included the following key changes:- Specified that inclusion criteria events documenting uncontrolled asthma should have occurred, on average, during the 4 weeks preceding screening. -Deleted duplicate exclusion criterion for patients who had previously received anti-IgE therapy. -Clarified patient number assignment and IVRS randomization process. -Clarified that patients were required to remain on their current asthma maintenance therapy throughout study participation, with no changes in this therapy during the study. -Added a definition for asthma exacerbation. -Changed the administration of the ACT from every scheduled visit to Visits 1, 6, 10, and 14. -Changed the administration of the WPAI-A from Visits 2 through 14 to Visits 2, 6, 10, and 14. -Included a review of concomitant medications at all study visits (assessment added to Visits 3-5, 7-9, and 11-13). -Eliminated urinalysis from the end-of-study visit (Visit 14). -In keeping with the International Conference on Harmonisation E9 guidance, changed the terminology for the safety and intent-to-treat populations to the Safety and Full Analysis Sets, respectively, and added a Randomized Set.
21 July 2009	Amendment 2 issues prior to database lock, clarified how health care utilization was captured. All health care utilization resulting from an asthma exacerbation, rather than only outpatient or inpatient hospitalization, was captured on the Health Care Utilization CRF. Amendment 2 also clarified that if an exacerbation occurred within the double-blind treatment period, patients were to attend their regularly scheduled study visit and receive study medication. Efficacy assessments, including administration of the ACT, were not to be performed until at least 28 days after the last dose of systemic steroid burst. The changes in Amendments 1 and 2 were not felt to affect the interpretation of study results, as the changes in Amendment 1 occurred before the first patient entered the study and the changes in Amendment 2 occurred before database lock and were minor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported