



## Clinical trial results:

**An open label, single arm study to assess the safety and immunogenicity of omalizumab liquid administered subcutaneously in a pre-filled safety syringe (75 mg or 150 mg) over a period of 6 months to male and female adolescents and adults with moderate to severe persistent allergic asthma.**

### Summary

EudraCT number	2006-005917-36
Trial protocol	ES DE
Global end of trial date	22 September 2008

### Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	06 August 2015

### Trial information

#### Trial identification

Sponsor protocol code	CIGE025C2303
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00500539
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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 September 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 September 2008
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to assess the immunogenic potential of omalizumab liquid when administered over a period of 6 months (24 weeks) to omalizumab naive, moderate to severe persistent allergic asthma subjects aged 12 years or older.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed and that are consistent with Good Clinical Practice and applicable regulations. Rescue medication, as recommended by the treating physician based on asthma management standard of care, was permitted. Systemic corticosteroids were permitted after the screening visit for the treatment of asthma exacerbations during the study.

Background therapy:

Patients were allowed to continue using their own standard of care for asthma management.

Evidence for comparator: -

Actual start date of recruitment	05 July 2007
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	United States: 112
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Germany: 42
Worldwide total number of subjects	155
EEA total number of subjects	43

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)	13
Adults (18-64 years)	135
From 65 to 84 years	7
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 42 centres in 3 countries.

### Pre-assignment

Screening details:

A total of 266 subjects were screened, out of which 155 subjects were enrolled and treated with the study drug. The most common reasons for screening failures were unacceptable test procedure results and unacceptable laboratory values.

### 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:

As the current study was an open label study, this section was not applicable.

### Arms

Arm title	Omalizumab
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Arm description:

Subjects received omalizuamab (150 milligrams (mg); 225 mg; 300 mg or 375 mg) through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Subjects with body-weight between 90-150 kilograms (kg), received 300 mg of omalizumab for 4 weeks (if pre-treatment IgE level was between 30-100 international units per millilitres [IU/mL]) and for 2 weeks (if pre-treatment IgE level was between 200-300 IU/mL).

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	IGE025
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab 150 mg, 225mg, 300 mg or 375 mg was administered in pre-filled syringes containing either 75 mg/0.5 mL or 150 mg/1.0 mL.

Number of subjects in period 1	Omalizumab
Started	155
Completed	140
Not completed	15
Consent withdrawn by subject	1
Adverse event, non-fatal	4
Unsatisfactory therapeutic effect	1
Administrative problems	2
Lost to follow-up	2
Protocol deviation	5



## Baseline characteristics

### Reporting groups

Reporting group title	Overall study
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Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	155	155	
Age categorical			
Units: Subjects			
12-17 years	13	13	
18-54 years	108	108	
55-64 years	27	27	
65 years and older	7	7	
Age continuous			
Units: years			
arithmetic mean	42.7		
standard deviation	± 14.32	-	
Gender categorical			
Units: Subjects			
Female	95	95	
Male	60	60	

## End points

### End points reporting groups

Reporting group title	Omalizumab
Reporting group description:	
Subjects received omalizumab (150 milligrams (mg); 225 mg; 300 mg or 375 mg) through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Subjects with body-weight between 90-150 kilograms (kg), received 300 mg of omalizumab for 4 weeks (if pre-treatment IgE level was between 30-100 international units per millilitres [IU/mL]) and for 2 weeks (if pre-treatment IgE level was between 200-300 IU/mL).	

### Primary: Number of subjects with human anti-human antibody (HAHA) positive result at the end of 16 week follow-up period

End point title	Number of subjects with human anti-human antibody (HAHA) positive result at the end of 16 week follow-up period <sup>[1]</sup>
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End point description:

Immunogenic potential of liquid omalizumab injection was assessed based on the results of HAHA assay. HAHA was assessed using two parameters; Fab and Fc and the subjects were considered potentially HAHA positive if either Fab or Fc was greater than (>) 2.0 titer. All values more than 2.0 titer were re-assayed to obtain a confirmatory result. Confirmatory results were used to determine those subjects who were HAHA positive. The analysis was performed in safety set, defined as all subjects who received at least one dose of study drug and had at least one post-baseline safety assessment.

End point type	Primary
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End point timeframe:

End of 16 week follow up period (Week 41)

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: Only descriptive summary statistics was planned for this primary outcome measure.

<b>End point values</b>	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	136 <sup>[2]</sup>			
Units: Number of subjects				
Fab HAHA Positive	0			
Fc HAHA Positive	0			
Fab and/or Fc HAHA Positive	0			

Notes:

[2] - Number of subjects who had follow-up HAHA sample.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with adverse events (AEs), treatment related AEs, AEs leading to discontinuation, AEs by severity, serious adverse events (SAEs), SAEs leading to discontinuation and death during treatment period

End point title	Number of subjects with adverse events (AEs), treatment related AEs, AEs leading to discontinuation, AEs by severity, serious adverse events (SAEs), SAEs leading to discontinuation and death during treatment period
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**End point description:**

An AE was defined as any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study drug, whether or not related to study drug. A SAE was defined as an event which was fatal or life threatening, required or prolonged hospitalization, was significantly or permanently disabling or incapacitating, constituted a congenital anomaly or a birth defect, or encompassed any other clinically significant event that could jeopardize the subject or require medical or surgical intervention to prevent one of the aforementioned outcomes. Based on the severity, AEs were categorised into 3 types as mild, moderate and severe. Treatment related AEs or SAEs were defined as AEs or SAEs that were suspected to be related to study treatment as per investigator. Death was a fatal event leading to permanent cessations of all vital functions of the body. The analysis was performed in safety set.

End point type	Secondary
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**End point timeframe:**

24 weeks treatment period + 4 weeks for following up participants

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Number of subjects				
AEs	124			
Mild AEs	25			
Moderate AEs	76			
Severe AEs	23			
AEs suspected to be related to study drug	22			
AEs not suspected to be related to study drug	102			
SAEs	14			
Deaths	1			
Discontinued due to AEs	4			
Discontinued due to SAEs (included also in AEs)	2			

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects with adverse events (AEs), treatment related AEs, AEs leading to discontinuation, AEs by severity, serious adverse events (SAEs), SAEs leading to discontinuation and death during follow-up period**

End point title	Number of subjects with adverse events (AEs), treatment related AEs, AEs leading to discontinuation, AEs by severity, serious adverse events (SAEs), SAEs leading to discontinuation and death during follow-up period
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**End point description:**

An AE was defined as any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study drug, whether or not related to study drug. A SAE was defined as an event which was fatal or life threatening, required or prolonged hospitalization, was significantly or permanently disabling or incapacitating, constituted a congenital anomaly or a birth defect, or encompassed any other clinically significant event that could jeopardize the subject or require medical or surgical intervention to prevent one of the aforementioned outcomes. Based on the severity, AEs were categorised into 3 types as mild, moderate and severe. Treatment related AEs or SAEs were defined as AEs or SAEs that were suspected to be related to study treatment as per investigator. Death was a fatal



event leading to permanent cessations of all vital functions of the body. The analysis was performed in safety set.

End point type	Secondary
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End point timeframe:

Last 12 weeks of the follow-up period (initial 4 weeks of the follow-up period were included in the treatment period for AE reporting)

<b>End point values</b>	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	148			
Units: Number of subjects				
AEs	51			
Mild AEs	11			
Moderate AEs	37			
Severe AEs	3			
AEs suspected to be related to study drug	0			
AEs not suspected to be related to study drug	51			
SAEs	1			
Deaths	0			
Discontinued due to AEs	1			
Discontinued due to SAEs	0			

## 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

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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### Reporting groups

Reporting group title	Omalizumab
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Reporting group description:

Subjects received omalizuamab (150 mg; 225 mg; 300 mg or 375 mg) through s.c route for 2-4 weeks based on their body weight and IgE levels. Subjects with body-weight between 90-150 kg, received 300 mg of omalizumab for 4 weeks (if pre-treatment IgE level was between 30-100 IU/mL) and for 2 weeks (if pre-treatment IgE level was between 200-300 IU/mL).

Serious adverse events	Omalizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 155 (9.03%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural swelling			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina unstable			

subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 155 (2.58%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Laryngeal inflammation			

subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiectasis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 155 (0.65%)		
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 %

<b>Non-serious adverse events</b>	Omalizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 155 (47.74%)		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 155 (8.39%)		
occurrences (all)	28		
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	24 / 155 (15.48%)		
occurrences (all)	27		
Cough			
subjects affected / exposed	9 / 155 (5.81%)		
occurrences (all)	11		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 155 (9.68%)		
occurrences (all)	22		
Gastroenteritis viral			
subjects affected / exposed	8 / 155 (5.16%)		
occurrences (all)	8		
Sinusitis			
subjects affected / exposed	27 / 155 (17.42%)		
occurrences (all)	34		
Upper respiratory tract infection			
subjects affected / exposed	18 / 155 (11.61%)		
occurrences (all)	21		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2007	1. Study procedures were modified to include instructions for use of omalizumab safety syringe and skin prick testing procedures 2. Pharmacokinetic evaluation at the end of the treatment period, prior to the final dosing was added and an electrocardiogram evaluation before first dosing was included.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported