Clinical trial results:
A 24 Week, Open Label, Multi-center Evaluation of Pharmacokinetics and Pharmacodynamics, Efficacy and Safety of Omalizumab in Japanese Children (6 - 15 Years) With Inadequately Controlled Allergic Asthma Despite Current Recommended Treatment

Summary

EudraCT number	2015-003534-27
Trial protocol	Outside EU/EEA
Global end of trial date	17 February 2012

Results information

Result version number	v1 (current)
This version publication date	04 January 2017
First version publication date	04 January 2017

Trial information

Trial identification

Sponsor protocol code	CIGE025B1301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01155700
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals 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	17 February 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To examine whether the geometric mean of serum free IgE level at 24 weeks of the treatment period in Japanese pediatric patients reaches under 25 ng/mL (target level).

Protection of trial subjects:

Patients were permitted to use any rescue medication for asthma attacks/exacerbations on an as needed (prn) basis during the treatment period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2010
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	Japan: 38
Worldwide total number of subjects	38
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)	21
Adolescents (12-17 years)	17
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 38 patients were treated and completed the study therefore no patients discontinued the study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Omalizumab

Arm description:

Omalizumab treatment

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

Dosage and administration details:

Omalizumab 75 to 375 mg was administered subcutaneously every 2 or 4 weeks. Doses (mg) and dosing frequency were determined from dosing tables based on the patient' serum total IgE level (IU/mL) and body weight (kg) measured at Visit 1 (run-in period).

Number of subjects in period 1	Omalizumab
Started	38
Completed	38

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	38	38	
Age categorical Units: Subjects			
Children (2-11 years)	21	21	
Adolescents (12-17 years)	17	17	
Age continuous Units: years			
arithmetic mean	10.7		
standard deviation	± 2.46	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	23	23	

End points

End points reporting groups

Reporting group title	Omalizumab
Reporting group description: Omalizumab treatment	

Primary: Geometric mean of serum free IgE level at 24 weeks

End point title	Geometric mean of serum free IgE level at 24 weeks[1]
End point description: To evaluate whether the geometric mean of serum free IgE level at 24 weeks of the treatment period in Japanese pediatric patients reaches under 25 ng/mL (target level).	
End point type	Primary
End point timeframe: 24 weeks	

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: No statistical analyses have been specified for this primary end point.

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	38[2]			
Units: ng/ml				
geometric mean (confidence interval 95%)	15.551 (13.844 to 17.469)			

Notes:

[2] - Pharmacokinetic set:received study medication and and provided drug concentration data

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in peak expiratory flow (PEF)

End point title	Change from baseline in peak expiratory flow (PEF)
End point description: PEF was measured at almost the same time in the morning and evening each day during the run-in and treatment period. The measurements were performed, using a Peak Flow Meter provided to the patients at Visit 1, within 15 minutes of wakening in the morning prior to rescue and asthma control medication use. The evening PEF was also measured prior to rescue and asthma control medication use.	
End point type	Secondary
End point timeframe: Baseline and 24 weeks	

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	38[3]			
Units: L/min				
arithmetic mean (standard deviation)				
Morning PEF - Baseline	246.2 (± 72.22)			
Morning PEF - 24 weeks	269.3 (± 95.59)			
Morning PEF - Change from baseline	22.4 (± 60.59)			
Evening PEF - Baseline	255.4 (± 69.45)			
Evening PEF - 24 weeks	276.9 (± 93.38)			
Evening PEF - Change from baseline	21.5 (± 60.95)			

Notes:

[3] - Full analysis set- n = 37, 38, 37, 38, 38, 38

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FEV1 at 24 weeks

End point title	Change from baseline in FEV1 at 24 weeks

End point description:

FEV1 was measured at almost the same time in the morning and evening each day during the run-in and treatment period. The measurements were performed, using a Peak Flow Meter provided to the patients at Visit 1, within 15 minutes of wakening in the morning prior to rescue and asthma control medication use. The evening FEV1 was also measured prior to rescue and asthma control medication use.

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	38[4]			
Units: Liter				
arithmetic mean (standard deviation)				
FEV1 - Baseline	1.841 (± 0.4438)			
FEV1 - 24 weeks	1.928 (± 0.5479)			
FEV1 - Change from baseline	0.087 (± 0.3314)			

Notes:

[4] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in asthma symptom score, daily activity score, nocturnal sleep score at 24 weeks

End point title	Change from baseline in asthma symptom score, daily activity score, nocturnal sleep score at 24 weeks

End point description:

The asthma symptoms and the cough were measured three times a day. The daily activity and the nocturnal sleep were measured once a day. From these measurements, asthma symptom score, daily activity score and nocturnal sleep score were calculated according to the rating standard of the Japanese Society of Allergology. The asthma symptom score in a day (possible range 0 to 30) was calculated by summing symptom scores (ranges 0 to 9) and cough scores (ranges 0 or 1) in the morning, the afternoon and the evening as recorded on the diary. The total activity score (ranges 0 to 27) was calculated as the total of daily activity score (ranges 0 to 18) and nocturnal sleep score (ranges 0 to 9).

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	38[5]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Asthma symptom score - Baseline	21.9 (± 20.27)			
Asthma symptom score - 24 weeks	8.3 (± 11.48)			
Asthma symptom score - Change from baseline	-13.6 (± 19.23)			
Daily activity score - Baseline	21 (± 17.87)			
Daily activity score - 24 weeks	3.9 (± 7.98)			
Daily activity score - Change from baseline	-17.1 (± 17.9)			
Nocturnal sleep score - Baseline	9.2 (± 9.82)			
Nocturnal sleep score - 24 weeks	2.8 (± 6.39)			
Nocturnal sleep score - Change from baseline	-6.4 (± 11.29)			

Notes:

[5] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in number of puffs/tablets of asthma rescue medication at 24 weeks

End point title	Change from baseline in number of puffs/tablets of asthma rescue medication at 24 weeks

End point description:

The use of asthma rescue medication taken in a day was calculated by summing the number of puffs/tablets taken in the morning, noon and evening.

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	38[6]			
Units: Number of puffs				
arithmetic mean (standard deviation)				
Baseline	6.6 (± 11.17)			
24 weeks	2.2 (± 4.82)			
Change from baseline	-4.4 (± 7.7)			

Notes:

[6] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in quality of life score at 24 weeks

End point title	Change from baseline in quality of life score at 24 weeks

End point description:

Quality of life questionnaires for pediatric patients with bronchial asthma and their parents or caregivers were administered to all patients/their parents or guardians at Visits 2, 7 and 9 (or at discontinuation). The questionnaires was completed prior to any other visit assessments and study drug administration to avoid influencing the responses.

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	37[7]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
24 weeks vs baseline - Baseline	23 (± 5.01)			
24 weeks vs baseline - Post-baseline	26.2 (± 5.19)			
Emotional - Baseline	15.1 (± 3.08)			
Emotional - Post-baseline	17.3 (± 3.04)			
Overall - Baseline	38.1 (± 7.33)			
Overall - Post-baseline	43.5 (± 7.55)			

Notes:

[7] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Investigators Global Evaluation of Treatment Effectiveness (GETE)s and patients GETEs at 24 weeks

End point title	Investigators Global Evaluation of Treatment Effectiveness (GETE)s and patients GETEs at 24 weeks

End point description:

The global evaluation of the treatment effectiveness performed by the investigator and the patient and evaluated based on the following scale:
1. Excellent (complete control of asthma)
2. Good (marked improvement of asthma)
3. Moderate (discernible, but limited improvement in asthma)
4. Poor (no appreciable change in asthma)
5. Worsening of asthma

End point type	Secondary

End point timeframe:

24 weeks /the last assessment

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	38[8]			
Units: percent				
number (not applicable)				
Investigators GETE - Excellent	7.9			
Investigators GETE - Good	68.4			
Investigators GETE - Moderate	23.7			
Investigators GETE - Poor	0			
Investigators GETE - Worsening	0			
Patients GETE - Excellent	31.6			
Patients GETE - Good	47.4			
Patients GETE - Moderate	15.8			
Patients GETE - Poor	5.3			
Patients GETE - Worsening	0			

Notes:

[8] - Full analysis set

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	14.1

Reporting groups

Reporting group title	Omalizumab

Reporting group description:

Omalizumab

Serious adverse events	Omalizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 38 (15.79%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 38 (13.16%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Omalizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 38 (94.74%)		
Injury, poisoning and procedural complications			

Contusion subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	5 / 38 (13.16%) 7		
General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Injection site swelling subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 2 / 38 (5.26%) 3 3 / 38 (7.89%) 7 2 / 38 (5.26%) 3 2 / 38 (5.26%) 3 3 / 38 (7.89%) 3		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all)	 4 / 38 (10.53%) 5 3 / 38 (7.89%) 3 4 / 38 (10.53%) 4		
Respiratory, thoracic and mediastinal disorders Asthma			

subjects affected / exposed	4 / 38 (10.53%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Urticaria			
subjects affected / exposed	4 / 38 (10.53%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	4		
Myalgia			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 38 (13.16%)		
occurrences (all)	9		
Gastroenteritis			
subjects affected / exposed	8 / 38 (21.05%)		
occurrences (all)	9		
Influenza			
subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	10 / 38 (26.32%)		
occurrences (all)	13		
Pharyngitis			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Sinusitis			

subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2 10 / 38 (26.32%) 14		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 2 / 38 (5.26%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2011	• Changed the bioanalytical CRO for total IgE analysis from Phadia to Atlanbio due to business considerations. • Updated information on storage condition of reconstituted study medication due to the technical change. • Added an alternative instruction for calibration of spirometers due to the technical change. • Deleted the process of obvious errors correction and corrected the way to change the database after it is locked.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported