



## Clinical trial results:

### **A 1 Year, Randomized, Double-blind, Parallel-group, Placebo-controlled, Multicenter Evaluation of Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Omalizumab in Children (6 - < 12 Years) With Moderate-severe, Persistent, Inadequately Controlled Allergic Asthma**

#### Summary

EudraCT number	2015-003538-28
Trial protocol	Outside EU/EEA
Global end of trial date	03 March 2008

#### 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	CIGE025AIA05
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	03 March 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 March 2008
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary safety objective was to confirm the safety of omalizumab during the 52 week double-blind treatment period and 16 week follow-up period. The primary efficacy objective was to demonstrate the effect of omalizumab on the clinically significant asthma exacerbation rate during the 24 week double-blind fixed steroid treatment.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 April 2004
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 290
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Brazil: 26
Country: Number of subjects enrolled	Argentina: 131
Country: Number of subjects enrolled	Colombia: 86
Country: Number of subjects enrolled	Poland: 69
Worldwide total number of subjects	628
EEA total number of subjects	69

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)	628
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 87 centers in 7 countries (Argentina - 8, Brazil - 3, Canada - 6, Colombia - 5, Poland - 6, United States - 58, and South Africa - 1).

### Pre-assignment

Screening details:

Of 1433 subjects screened subjects, 805 subjects excluded: unacceptable medical history/concomitant diagnosis(22), Intercurrent medical event(20), unacceptable laboratory values (73), Unacceptable test procedure results(358), not met diagnostic/severity criteria (213), Unacceptable medication use (32), consent withdrawal(93), unknown(3), other(28).

### Period 1

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

Blinding implementation details:

Unblinding was only to occur in the case of subjects emergencies and at the conclusion of the study and final data review.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Omalizumab

Arm description:

Omalizumab 75 to 375 mg was administered subcutaneously (sc) every 2 or 4 weeks depending on the dose. Omalizumab dose was individualized for each subject, based on their body weight and total serum IgE level at screening visit.

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

Dosage and administration details:

Omalizumab 75 to 375 mg was administered sc every 2 or 4 weeks depending on the dose. Omalizumab was supplied as a sterile, freeze-dried preparation that was reconstituted using sterile water for injection (WFI) to a final omalizumab concentration of 150 mg.

<b>Arm title</b>	Placebo
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Arm description:

Placebo solution was administered every 2 or 4 weeks.

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

Dosage and administration details:

Placebo solution was administered every 2 or 4 weeks.

<b>Number of subjects in period 1</b>	Omalizumab	Placebo
Started	421	207
Completed	352	175
Not completed	69	32
Consent withdrawn by subject	21	7
Adverse event, non-fatal	2	1
Unsatisfactory therapeutic effect	1	2
Administrative problems	22	11
Subject's condition no longer requires study drug	3	-
Lost to follow-up	12	5
Protocol deviation	8	6

## Baseline characteristics

### Reporting groups

Reporting group title	Omalizumab
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Reporting group description:

Omalizumab 75 to 375 mg was administered subcutaneously (sc) every 2 or 4 weeks depending on the dose. Omalizumab dose was individualized for each subject, based on their body weight and total serum IgE level at screening visit.

Reporting group title	Placebo
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Reporting group description:

Placebo solution was administered every 2 or 4 weeks.

Reporting group values	Omalizumab	Placebo	Total
Number of subjects	421	207	628
Age categorical			
Units: Subjects			
6 years to 9 years	254	143	397
10 years to 11 years	167	64	231
Age continuous			
Units: years			
arithmetic mean	8.7	8.4	
standard deviation	± 1.7	± 1.7	-
Gender categorical			
Units: Subjects			
Female	134	69	203
Male	287	138	425

## End points

### End points reporting groups

Reporting group title	Omalizumab
Reporting group description: Omalizumab 75 to 375 mg was administered subcutaneously (sc) every 2 or 4 weeks depending on the dose. Omalizumab dose was individualized for each subject, based on their body weight and total serum IgE level at screening visit.	
Reporting group title	Placebo
Reporting group description: Placebo solution was administered every 2 or 4 weeks.	

### Primary: Rate of clinically significant asthma exacerbations in the 24-week double-blind fixed steroid period

End point title	Rate of clinically significant asthma exacerbations in the 24-week double-blind fixed steroid period
End point description: A clinically significant asthma exacerbation was defined as worsening of asthma symptoms based on investigator's discretion as subjects requiring doubling of the baseline inhaled corticosteroid dose for at least 3 days and/or treatment with rescue systemic (oral or intravenous) corticosteroids. The initiation of the corticosteroid regimens marks the start of an asthma exacerbation and cessation of the additional corticosteroid regimens marks the end of an exacerbation. The analysis was performed in Modified Intent-to-treat (MITT) population defined as all subjects excluding subjects from GCP non-compliant sites who were randomized and were analyzed according to the randomized treatment. Subjects who discontinued prematurely were included in the analysis using an imputed number of clinically significant asthma exacerbation episodes. Here, 'Number of subjects analysed' signifies subjects evaluable for this parameter at defined time-frame for each arm, respect	
End point type	Primary
End point timeframe: Baseline to Week 25 (24 Week treatment period)	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	192		
Units: Exacerbation rate				
number (not applicable)	0.45	0.64		

### Statistical analyses

Statistical analysis title	Asthma exacerbations during 24 week
Comparison groups	Omalizumab v Placebo

Number of subjects included in analysis	576
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Poisson regression
Parameter estimate	Rate ratio
Point estimate	0.693
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.533
upper limit	0.903

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**Primary: Number of subjects with adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation and who died**

End point title	Number of subjects with adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation and who died <sup>[1]</sup>
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End point description:

AEs are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards. The analysis was performed on safety set population defined as all subjects who received at least one of the study treatment and had at least one post-baseline safety assessment.

End point type	Primary
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End point timeframe:

From start of study treatment to Week 52 (52 week treatment period), Follow-up period (16 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: Only descriptive summary statistics was planned for this outcome measure.

<b>End point values</b>	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	207		
Units: Subjects				
AEs	380	194		
SAEs	17	17		
Discontinuation due to AEs	2	1		
Discontinuation due to SAEs	1	1		
Deaths	0	0		

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Change from baseline in nocturnal clinical symptom score during 24**

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**week double-blind fixed steroid treatment period**

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End point title	Change from baseline in nocturnal clinical symptom score during 24 week double-blind fixed steroid treatment period
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End point description:

Patient diary was used to evaluate nocturnal clinical symptom using a question 'How did you sleep last night?' in morning. The responses were scored between 0 to 4 based on awakening during last night as score 0 = no awakening due to breathing problem; 1 = awoke once because of breathing problems but no rescue medication used; 2 = awoke once because of breathing problems but rescue medication controlled symptoms; 3 = awoke more than once because of breathing problems but rescue medication controlled symptoms; 4 = difficulty sleeping because of breathing problems even after use of rescue medication controlled symptoms. Subjects who discontinued prematurely were included in the analysis using an imputed number of clinically significant asthma exacerbation episodes. The analysis was performed in MITT population. Here, 'Number of subjects analysed' signifies subjects evaluable for this parameter at defined time-frame for each arm, respectively.

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End point type	Secondary
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End point timeframe:

Baseline to end of the 24-week (mean of 4 weeks prior to week 24 or early discontinuation)

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End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	382	191		
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.63 (± 0.72)	-0.5 (± 0.71)		

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Clinically significant asthma exacerbation rate during 52 week double-blind treatment period**

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End point title	Clinically significant asthma exacerbation rate during 52 week double-blind treatment period
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End point description:

A clinically significant asthma exacerbation was defined as worsening of asthma symptoms based on investigator's discretion as subjects requiring doubling of the baseline inhaled corticosteroid dose for at least 3 days and/or treatment with rescue systemic (oral or intravenous) corticosteroids. The initiation of the corticosteroid regimens marks the start of an asthma exacerbation and cessation of the additional corticosteroid regimens marks the end of an exacerbation. The analysis was performed in MITT population. Subjects who discontinued prematurely were included in the analysis using an imputed number of clinically significant asthma exacerbation episodes. Here, 'Number of subjects analysed' signifies subjects evaluable for this parameter at defined time-frame for each arm, respectively.

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End point type	Secondary
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End point timeframe:

Baseline to Week 52

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<b>End point values</b>	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	192		
Units: Exacerbation rate				
number (not applicable)	0.78	1.36		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in rescue medication use to 24 week double-blind fixed steroid treatment period

End point title	Change from baseline in rescue medication use to 24 week double-blind fixed steroid treatment period
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End point description:

$\beta$ 2-agonist rescue medication was used in inadequately controlled subjects defined as subjects who were partly controlled or uncontrolled according to Global Initiative for Asthma (GINA) guidelines (2007). Subjects who discontinued prematurely were included in the analysis using an imputed number of clinically significant asthma exacerbation episodes. The analysis was performed in MITT population. Here, 'Number of subjects analysed' signifies subjects evaluable for this parameter at defined time-frame for each arm, respectively.

End point type	Secondary
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End point timeframe:

Baseline to end of the 24-week (mean of 4 weeks prior to week 24 or early discontinuation)

<b>End point values</b>	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	381	191		
Units: Number of puffs				
arithmetic mean (standard deviation)	-1.3 ( $\pm$ 2.84)	-1 ( $\pm$ 2.5)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in quality of life score at the end of the 24-week fixed steroid treatment period

End point title	Change from baseline in quality of life score at the end of the 24-week fixed steroid treatment period
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End point description:

Self-administered standardized Pediatric Asthma Quality of Life Questionnaire (PAQLQ) was administered to subjects regardless of age to evaluate QoL. The PAQLQ (Standardized version) was designed to measure the problems that children experienced as a result of their asthma. It comprises of 23 items in 3 domains symptoms (5 items), activity limitations (10 items), emotional function(8 items), each scored on a scale of 1 (severely affected) to 7 (unaffected). Final score ranges from 1–7 for each domain and for the whole instrument, where higher scores indicated better QoL. The analysis was performed in MITT population. Subjects who discontinued prematurely were included in the analysis

using an imputed number of clinically significant asthma exacerbation episodes. Here, 'Number of subjects analysed' signifies subjects evaluable for this parameter at defined time-frame for each arm, respectively.

End point type	Secondary
End point timeframe:	
Baseline to end of the 24-week (mean of 4 weeks prior to week 24 or early discontinuation)	

<b>End point values</b>	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	187		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Activities	0.8 (± 1.31)	0.8 (± 1.33)		
Emotions	0.9 (± 1.38)	0.9 (± 1.35)		
Symptoms	1 (± 1.33)	0.9 (± 1.34)		
Overall	0.9 (± 1.21)	0.9 (± 1.2)		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until LSLV.

Adverse event reporting additional description:

On-treatment Period

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo solution was administered every 2 or 4 weeks.

Reporting group title	Omalizumab
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Reporting group description:

Omalizumab 75 to 375 mg was administered sc every 2 or 4 weeks depending on the dose. Omalizumab dose was individualized for each subject, based on their body weight and total serum IgE level at screening visit.

<b>Serious adverse events</b>	Placebo	Omalizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 207 (12.56%)	27 / 421 (6.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Medulloblastoma			
subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			

subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 207 (0.48%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope vasovagal			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			

subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Respiratory, thoracic and mediastinal disorders</b>			
Asthma			
subjects affected / exposed	18 / 207 (8.70%)	17 / 421 (4.04%)	
occurrences causally related to treatment / all	0 / 23	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Psychiatric disorders</b>			
Bipolar disorder			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tic			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Acute sinusitis			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 207 (0.48%)	3 / 421 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchitis			
subjects affected / exposed	1 / 207 (0.48%)	2 / 421 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis shigella			
subjects affected / exposed	0 / 207 (0.00%)	2 / 421 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 207 (2.90%)	3 / 421 (0.71%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Sinusitis</b>			
subjects affected / exposed	1 / 207 (0.48%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Upper respiratory tract infection</b>			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Upper respiratory tract infection bacterial</b>			
subjects affected / exposed	2 / 207 (0.97%)	0 / 421 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Metabolism and nutrition disorders</b>			
<b>Dehydration</b>			
subjects affected / exposed	0 / 207 (0.00%)	1 / 421 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Placebo	Omalizumab	
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	194 / 207 (93.72%)	374 / 421 (88.84%)	
<b>Nervous system disorders</b>			
<b>Headache</b>			
subjects affected / exposed	33 / 207 (15.94%)	58 / 421 (13.78%)	
occurrences (all)	60	96	
<b>General disorders and administration site conditions</b>			
<b>Pyrexia</b>			
subjects affected / exposed	20 / 207 (9.66%)	59 / 421 (14.01%)	
occurrences (all)	30	78	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	12 / 207 (5.80%)	23 / 421 (5.46%)	
occurrences (all)	21	27	
Diarrhoea			
subjects affected / exposed	12 / 207 (5.80%)	20 / 421 (4.75%)	
occurrences (all)	12	24	
Vomiting			
subjects affected / exposed	24 / 207 (11.59%)	34 / 421 (8.08%)	
occurrences (all)	26	41	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	170 / 207 (82.13%)	290 / 421 (68.88%)	
occurrences (all)	975	1526	
Cough			
subjects affected / exposed	25 / 207 (12.08%)	44 / 421 (10.45%)	
occurrences (all)	31	56	
Pharyngolaryngeal pain			
subjects affected / exposed	16 / 207 (7.73%)	33 / 421 (7.84%)	
occurrences (all)	18	42	
Rhinitis allergic			
subjects affected / exposed	19 / 207 (9.18%)	35 / 421 (8.31%)	
occurrences (all)	23	45	
Infections and infestations			
Bronchitis			
subjects affected / exposed	29 / 207 (14.01%)	36 / 421 (8.55%)	
occurrences (all)	33	41	
Ear infection			
subjects affected / exposed	11 / 207 (5.31%)	22 / 421 (5.23%)	
occurrences (all)	13	23	
Gastroenteritis			
subjects affected / exposed	15 / 207 (7.25%)	19 / 421 (4.51%)	
occurrences (all)	15	23	
Gastroenteritis viral			
subjects affected / exposed	7 / 207 (3.38%)	23 / 421 (5.46%)	
occurrences (all)	7	31	

Influenza		
subjects affected / exposed	28 / 207 (13.53%)	51 / 421 (12.11%)
occurrences (all)	53	79
Nasopharyngitis		
subjects affected / exposed	56 / 207 (27.05%)	117 / 421 (27.79%)
occurrences (all)	98	202
Pharyngitis		
subjects affected / exposed	18 / 207 (8.70%)	36 / 421 (8.55%)
occurrences (all)	24	38
Pharyngitis streptococcal		
subjects affected / exposed	13 / 207 (6.28%)	19 / 421 (4.51%)
occurrences (all)	17	26
Rhinitis		
subjects affected / exposed	20 / 207 (9.66%)	25 / 421 (5.94%)
occurrences (all)	34	36
Sinusitis		
subjects affected / exposed	38 / 207 (18.36%)	70 / 421 (16.63%)
occurrences (all)	57	91
Tonsillitis		
subjects affected / exposed	11 / 207 (5.31%)	7 / 421 (1.66%)
occurrences (all)	15	7
Upper respiratory tract infection		
subjects affected / exposed	46 / 207 (22.22%)	68 / 421 (16.15%)
occurrences (all)	62	95
Viral upper respiratory tract infection		
subjects affected / exposed	26 / 207 (12.56%)	34 / 421 (8.08%)
occurrences (all)	39	41

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2004	The aim of this amendment was to: <ul style="list-style-type: none"><li>• adjust the regression model used for statistical analysis of the primary efficacy variable</li><li>• make some minor adjustments to the inclusion and exclusion criteria</li><li>• clarify study procedure in the event of a low platelet count</li><li>• make adjustment to the statistical analysis including regarding the handling of missing values, censoring of observations, and treatment of data from subjects who discontinued (e.g. imputation procedure for exacerbation episodes)</li><li>• Safety parameters ( malignancies, platelet decreases and SAEs) originally planned to be included in the Data Safety Monitoring Board (DSMB) review were to be reviewed in an ongoing manner by Novartis personnel.</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported