



Clinical trial results:

Multicentric, Open-label, Randomized, Parallel-group Study to Evaluate the Efficacy and Safety of Omalizumab in a 12-Month Period, in Patients with Severe IgE-mediated Asthma Inadequately Controlled with High Doses of Corticosteroids. MEXIC Study

Summary

EudraCT number	2016-004315-13
Trial protocol	Outside EU/EEA
Global end of trial date	08 January 2016

Results information

Result version number	v1 (current)
This version publication date	16 June 2018
First version publication date	16 June 2018

Trial information

Trial identification

Sponsor protocol code	CIGE025AMX02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01912872
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Novartis Pharmaceuticals AG Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Novartis Pharmaceuticals AG 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	08 January 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 January 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy and safety of omalizumab treatment during 12 months in order to reduce the use of inhaled corticosteroid (ICS) in pediatric and adult patients with severe IgE-mediated asthma inadequately controlled with high doses of corticosteroids.)

Protection of trial subjects:

The use of rescue medication (salbutamol and steroids) was allowed throughout the study in the event of asthma exacerbation defined as a sudden progressive increase in shortness of breath, cough, wheezing or chest tightness or a combination of these signs and symptoms. Under this situation, the patient was instructed to take rescue medication, but if the asthma exacerbation was not controlled, the patient was instructed to notify the Investigator and attend its office, where the Investigator decided whether to treat the patient at the office or send to the emergency service.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2013
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	Mexico: 112
Worldwide total number of subjects	112
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)	16
Adolescents (12-17 years)	17
Adults (18-64 years)	79
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study population consisted of male and female patients aged between 6 to 55 years with moderate to severe uncontrolled IgE-mediated asthma recruited from outpatient private clinics in Mexico.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pediatric Patients: Omalizumab + Budesonide and Formoterol

Arm description:

Participants received omalizumab injection for s.c. use 2 or 4 weeks according to the IgE level and body weight and budesonide + formoterol administered through an inhaler device.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection dose according to the IgE level and body weight.

Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

Budesonide (400 µg, 200 µg or 100 µg). Patients were instructed to take the inhaled budesonide doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.

Investigational medicinal product name	Formoterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

Formoterol 12ug. Patients were instructed to take the inhaled formoterol doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.

Arm title	Pediatric Patients: Budesonide and Formoterol
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Arm description:

Participants received budesonide + formoterol administered through an inhaler device.

Arm type	Active comparator
Investigational medicinal product name	Formoterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

Formoterol 12ug. Patients were instructed to take the inhaled formoterol doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.

Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

Budesonide (400 µg, 200 µg or 100 µg). Patients were instructed to take the inhaled budesonide doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.

Arm title	Adult Patients: Omalizumab + Budesonide and Formoterol
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Arm description:

Participants received Omalizumab every 2 or 4 weeks as a subcutaneous injection dose according to the IgE level and body weight. Participants also received and budesonide + formoterol administered through an inhaler device.

Arm type	Experimental
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection dose according to the IgE level and body weight.

Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

Budesonide (400 µg, 200 µg or 100 µg). Patients were instructed to take the inhaled budesonide doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.

Investigational medicinal product name	Formoterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

Formoterol 12ug. Patients were instructed to take the inhaled formoterol doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.

Arm title	Adult Patients: Budesonide and Formoterol
Arm description:	
Participants receive budesonide + formoterol administered through an inhaler device.	
Arm type	Active comparator
Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use
Dosage and administration details:	
Budesonide (400 µg, 200 µg or 100 µg). Patients were instructed to take the inhaled budesonide doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.	
Investigational medicinal product name	Formoterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use
Dosage and administration details:	
Formoterol 12ug. Patients were instructed to take the inhaled formoterol doses every 12 hours following the specific administration instructions as per the manufactures' prescription information.	

Number of subjects in period 1	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol
Started	16	17	40
Completed	11	13	30
Not completed	5	4	10
Consent withdrawn by subject	-	-	1
Other unspecified	3	1	3
Unsatisfactory therapeutic effect	-	-	-
Protocol Violation	-	-	1
Lost to follow-up	2	3	5
Non-compliance with lab inc/exclusion	-	-	-
Missing	-	-	-
Withdrawal of study medication	-	-	-

Number of subjects in period 1	Adult Patients: Budesonide and Formoterol
Started	39
Completed	27
Not completed	12
Consent withdrawn by subject	1
Other unspecified	-

Unsatisfactory therapeutic effect	2
Protocol Violation	-
Lost to follow-up	5
Non-compliance with lab inc/exclusion	1
Missing	1
Withdrawal of study medication	2

Baseline characteristics

Reporting groups

Reporting group title	Pediatric Patients: Omalizumab + Budesonide and Formoterol
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Reporting group description:

Participants received omalizumab injection for s.c. use 2 or 4 weeks according to the IgE level and body weight and budesonide + formoterol administered through an inhaler device.

Reporting group title	Pediatric Patients: Budesonide and Formoterol
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Reporting group description:

Participants received budesonide + formoterol administered through an inhaler device.

Reporting group title	Adult Patients: Omalizumab + Budesonide and Formoterol
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Reporting group description:

Participants received Omalizumab every 2 or 4 weeks as a subcutaneous injection dose according to the IgE level and body weight. Participants also received and budesonide + formoterol administered through an inhaler device.

Reporting group title	Adult Patients: Budesonide and Formoterol
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Reporting group description:

Participants receive budesonide + formoterol administered through an inhaler device.

Reporting group values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol
Number of subjects	16	17	40
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	11	5	0
Adolescents (12-17 years)	5	12	0
Adults (18-64 years)	0	0	40
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	11.1	12.4	37.6
standard deviation	± 3.32	± 1.80	± 10.01
Gender categorical			
Units: Subjects			
Female	6	8	28
Male	10	9	12

Reporting group values	Adult Patients: Budesonide and Formoterol	Total	
Number of subjects	39	112	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	16	
Adolescents (12-17 years)	0	17	
Adults (18-64 years)	39	79	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	38.7		
standard deviation	± 10.30	-	
Gender categorical Units: Subjects			
Female	28	70	
Male	11	42	

End points

End points reporting groups

Reporting group title	Pediatric Patients: Omalizumab + Budesonide and Formoterol
Reporting group description: Participants received omalizumab injection for s.c. use 2 or 4 weeks according to the IgE level and body weight and budesonide + formoterol administered through an inhaler device.	
Reporting group title	Pediatric Patients: Budesonide and Formoterol
Reporting group description: Participants received budesonide + formoterol administered through an inhaler device.	
Reporting group title	Adult Patients: Omalizumab + Budesonide and Formoterol
Reporting group description: Participants received Omalizumab every 2 or 4 weeks as a subcutaneous injection dose according to the IgE level and body weight. Participants also received and budesonide + formoterol administered through an inhaler device.	
Reporting group title	Adult Patients: Budesonide and Formoterol
Reporting group description: Participants receive budesonide + formoterol administered through an inhaler device.	

Primary: Prescribed Budesonide Dose (µg) at Baseline

End point title	Prescribed Budesonide Dose (µg) at Baseline ^[1]
End point description: Data for primary efficacy variable was captured by recording at each visit the actual weekly or every 2 weeks dose of omalizumab and daily dose of budesonide/formoterol each participant received since the last visit. Baseline summaries presented only due to early termination of the trial. Pediatric and Adult intent-to-treat (ITT) and per protocol (PP) populations. ITT population received at least one dose of study drug and one post-baseline assessment of the primary/secondary efficacy variables. PP population was participants that completed 12 months of treatment, had a valid assessment of the primary efficacy variable at Week 24.	
End point type	Primary
End point timeframe: Baseline	
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 performed/reported for this primary end point.	

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16 ^[2]	17 ^[3]	40 ^[4]	39 ^[5]
Units: µg				
arithmetic mean (standard deviation)				
ITT	337.5 (± 95.74)	270.6 (± 98.52)	580.0 (± 201.53)	533.3 (± 248.50)

PP	363.6 (± 80.90)	250.0 (± 90.45)	575.0 (± 201.61)	533.3 (± 258.20)
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Notes:

[2] - Pediatric intent-to-treat (ITT) and per protocol (PP) populations.

N = 16, 11

[3] - Pediatric intent-to-treat (ITT) and per protocol (PP) populations.

N = 17, 12

[4] - Adult intent-to-treat (ITT) and per protocol (PP) populations.

N= 40, 32

[5] - Adult intent-to-treat (ITT) and per protocol (PP) populations.

N= 39, 33

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Hospital Admissions Due to Asthma Exacerbation

End point title	Number of Hospital Admissions Due to Asthma Exacerbation
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End point description:

A hospital admission is defined as admissions to hospital involving a stay of at least 24 hours.

End point type	Secondary
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End point timeframe:

12 month treatment duration

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16 ^[6]	17 ^[7]	40 ^[8]	39 ^[9]
Units: hospital admissions				
number (not applicable)	0	1	0	0

Notes:

[6] - ITT population

[7] - ITT population

[8] - ITT population

[9] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Days Missed in School/Work Due to Asthma Exacerbation Episodes

End point title	Days Missed in School/Work Due to Asthma Exacerbation Episodes
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End point description:

Participants /parent/legal guarding reported number of missed days of school or work at each study visit via diaries.

End point type	Secondary
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End point timeframe:
12 month treatment duration

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16 ^[10]	17 ^[11]	40 ^[12]	39 ^[13]
Units: days				
number (not applicable)				
Missed school days	2	3	1	0
Missed work days	0	1	0	1

Notes:

[10] - ITT population

[11] - ITT population

[12] - ITT population

[13] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Control of Asthma Symptoms- Daytime Symptoms

End point title	Control of Asthma Symptoms- Daytime Symptoms
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End point description:

The clinical control of asthma was defined according to the following criteria (GINA 2012):

Daytime symptoms: none or less than twice a week

Limitations of daily activities: none

Nocturnal symptoms or awakening because of asthma: none

Need of relief or rescue medication: none or less than twice a week

Lung function (PEF or FEV1) without administration of bronchodilator: normal

End point type	Secondary
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End point timeframe:

12 month treatment duration

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16 ^[14]	17 ^[15]	40 ^[16]	39 ^[17]
Units: percentage of participants				
number (not applicable)	62.5	70.6	82.5	71.8

Notes:

[14] - ITT population

[15] - ITT population

[16] - ITT population

[17] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Control of Asthma Symptoms

End point title	Control of Asthma Symptoms
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End point description:

The clinical control of asthma was defined according to the following criteria (GINA 2012):

Daytime symptoms: none or less than twice a week

Limitations of daily activities: none

Nocturnal symptoms or awakening because of asthma: none

Need of relief or rescue medication: none or less than twice a week

Lung function (PEF or FEV1) without administration of bronchodilator: normal

End point type	Secondary
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End point timeframe:

12 month treatment duration

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16 ^[18]	17 ^[19]	40 ^[20]	39 ^[21]
Units: Number of days				
arithmetic mean (standard deviation)				
Wheezing	15.4 (± 23.43)	21.1 (± 32.84)	25.4 (± 28.89)	29.0 (± 36.30)
Night time cough	12.8 (± 7.75)	20.8 (± 27.24)	20.6 (± 22.09)	32.3 (± 42.50)

Notes:

[18] - ITT population

N= 11, 13

[19] - ITT population

N= 15, 17

[20] - ITT population

N= 32, 33

[21] - ITT population

N= 35, 33

Statistical analyses

No statistical analyses for this end point

Secondary: Control of Asthma Symptoms- Rescue Medication Use

End point title	Control of Asthma Symptoms- Rescue Medication Use
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End point description:

The clinical control of asthma was defined according to the following criteria (GINA 2012):

Daytime symptoms: none or less than twice a week
 Limitations of daily activities: none
 Nocturnal symptoms or awakening because of asthma: none
 Need of relief or rescue medication: none or less than twice a week
 Lung function (PEF or FEV1) without administration of bronchodilator: normal

End point type	Secondary
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End point timeframe:

12 month treatment duration

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16 ^[22]	17 ^[23]	40 ^[24]	39 ^[25]
Units: participants				
number (not applicable)	9	15	34	33

Notes:

[22] - ITT population

[23] - ITT population

[24] - ITT population

[25] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Participants Requiring Oral Systemic Corticosteroids During the 12 Month Study Duration

End point title	Participants Requiring Oral Systemic Corticosteroids During the 12 Month Study Duration
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End point description:

Number of days of concomitant medications use reported by participants at all visits via diaries.

End point type	Secondary
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End point timeframe:

12 month treatment duration

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 ^[26]	2 ^[27]	5 ^[28]	9 ^[29]
Units: days				
arithmetic mean (standard deviation)	7.3 (± 4.62)	16.5 (± 19.09)	28.0 (± 35.67)	16.3 (± 17.35)

Notes:

[26] - Number of patients requiring oral systemic corticosteroids within the ITT Pediatric population.

[27] - Number of patients requiring oral systemic corticosteroids within the ITT Pediatric population.

[28] - Number of patients requiring oral systemic corticosteroids within the ITT Adult population.

[29] - Number of patients requiring oral systemic corticosteroids within the ITT Adult population.

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Control Questionnaire (ACQ) at Baseline

End point title	Asthma Control Questionnaire (ACQ) at Baseline
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End point description:

The Asthma Control Questionnaire (ACQ) has six questions to be answered by the participants, each with a 7 point scale (0-good control, 6-poor control), and one question where the actual pre-bronchodilator Forced expiratory volume in 1 second (FEV1) value expressed in % of predicted FEV1 was classified to scores from 0 (> 95% of predicted) to 6 (< 50% of predicted). The overall score is the average of the 7 questions; a minimum overall score of 0 = good control of asthma whereas a maximum overall score of 6 = poor control of asthma.

Baseline summaries are presented only due to early termination of the trial. Participant responses to five ACQ questions were used in the calculations. Patient responses to ACQ questions 6 and 7 were not available for analysis.

End point type	Secondary
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End point timeframe:

Baseline

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15 ^[30]	17 ^[31]	40 ^[32]	39 ^[33]
Units: scores on a scale				
arithmetic mean (standard deviation)	3.3 (± 1.31)	3.3 (± 1.26)	3.6 (± 1.09)	3.3 (± 1.35)

Notes:

[30] - Number of participants with a baseline measurement within the ITT Pediatric population.

[31] - Number of participants with a baseline measurement within the ITT Pediatric population.

[32] - Number of participants with a baseline measurement within the ITT Adult population.

[33] - Number of participants with a baseline measurement within the ITT Adult population.

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Quality of Life Questionnaire (AQLQ) at Baseline

End point title	Asthma Quality of Life Questionnaire (AQLQ) at Baseline
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End point description:

The quality of life will be measured by the standardized version of the Asthma Quality of Life Questionnaire (AQLQ[S]) score for adults and the pediatric version of the AQLQ(S) for pediatric

participants (PAQLQ[S]) . The AQLQ(S) and PAQLQ(S) contain 4 domains (activity limitations, symptoms, emotional function, and environmental stimuli), with a total of 32 items; each item is measured in a 7-point Likert scale of 1 to 7 (1 = severe impairment, 7 = no impairment). All items are weighted equally. Mean score is calculated across all items within each domain and the overall score is the mean score of the 32 items.

Note: Environment domain is non-existent for pediatric population.

Baseline summaries are presented only due to early termination of the trial.

End point type	Secondary
End point timeframe:	
Baseline	

End point values	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol	Adult Patients: Budesonide and Formoterol
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15 ^[34]	17 ^[35]	40 ^[36]	39 ^[37]
Units: scores on a scale				
arithmetic mean (standard deviation)				
Overall	3.2 (± 1.21)	3.4 (± 1.54)	2.9 (± 1.04)	3.4 (± 1.25)
Symptoms domain	3.2 (± 1.49)	3.3 (± 1.48)	2.8 (± 1.16)	3.5 (± 1.37)
Activity limitations domain	3.2 (± 1.18)	3.3 (± 1.47)	3.2 (± 1.07)	3.5 (± 1.25)
Emotional functions domain	3.2 (± 1.47)	3.6 (± 1.76)	2.5 (± 1.16)	3.2 (± 1.49)
Environmental stimuli domain	0 (± 0)	0 (± 0)	2.7 (± 1.24)	3.1 (± 1.47)

Notes:

[34] - Number of participants with a baseline measurement within the ITT Pediatric population.

[35] - Number of participants with a baseline measurement within the ITT Pediatric population.

[36] - Number of participants with a baseline measurement within the ITT Adult population.

[37] - Number of participants with a baseline measurement within the ITT Adult population.

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 .

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	na

Reporting groups

Reporting group title	Pediatric Patients: Omalizumab + Budesonide and Formoterol
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Reporting group description:

Participants received omalizumab injection for s.c. use 2 or 4 weeks according to the IgE level and body weight and budesonide + formoterol administered through an inhaler device.

Reporting group title	Pediatric Patients: Budesonide and Formoterol
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Reporting group description:

Participants received budesonide + formoterol administered through an inhaler device.

Reporting group title	Adult Patients: Omalizumab + Budesonide and Formoterol
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Reporting group description:

Participants received Omalizumab every 2 or 4 weeks as a subcutaneous injection dose according to the IgE level and body weight. Participants also received and budesonide + formoterol administered through an inhaler device.

Reporting group title	Adult Patients: Budesonide and Formoterol
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Reporting group description:

Participants receive budesonide + formoterol administered through an inhaler device.

Serious adverse events	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	2 / 17 (11.76%)	2 / 40 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Maternal exposure during pregnancy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food allergy			

subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic inflammatory disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Expired product administered			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Adult Patients: Budesonide and Formoterol		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 39 (2.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Maternal exposure during pregnancy			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Immune system disorders Food allergy subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0		
Reproductive system and breast disorders Pelvic inflammatory disease subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0		
Hepatobiliary disorders Hepatic steatosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0		
Product issues Expired product administered subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 39 (0.00%) 0 / 0 0 / 0		

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

Non-serious adverse events	Pediatric Patients: Omalizumab + Budesonide and Formoterol	Pediatric Patients: Budesonide and Formoterol	Adult Patients: Omalizumab + Budesonide and Formoterol
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 16 (68.75%)	7 / 17 (41.18%)	27 / 40 (67.50%)
Injury, poisoning and procedural complications Pruritus - injection site reaction			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	2 / 40 (5.00%) 2
Sea food allergy subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 40 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	2 / 40 (5.00%) 2
Head trauma subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 40 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	3 / 17 (17.65%) 3	5 / 40 (12.50%) 5
Insomnia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	1 / 40 (2.50%) 1
Lipothymia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	2 / 40 (5.00%) 2
General disorders and administration site conditions			
Adynamia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	1 / 40 (2.50%) 1
Anxiety subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	5 / 40 (12.50%) 5
Asthenia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	1 / 40 (2.50%) 1
Fatigue subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	2 / 40 (5.00%) 2
Fever			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	3 / 40 (7.50%) 3
Pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	2 / 40 (5.00%) 2
Palpitations subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	4 / 40 (10.00%) 4
Tachycardia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	4 / 40 (10.00%) 4
Eye disorders Burning in the eye subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	1 / 40 (2.50%) 1
Conjunctivitis - bacterial subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 40 (0.00%) 0
Pruritus - ocular subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 40 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 40 (0.00%) 0
Abdominal pain -localized subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 40 (0.00%) 0
Colitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	0 / 40 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	1 / 40 (2.50%) 1
Epigastric pain - food-related			

subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
Gastroenteritis - acute			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Hepatic steatosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences (all)	1	0	1
Pyelonephritis - acute			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Allergic asthma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Asthma exacerbation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	4 / 40 (10.00%)
occurrences (all)	1	0	4
CRUP syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Cough - dry			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Cough - with sputum			

subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Dyspnea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Flu illness			
subjects affected / exposed	1 / 16 (6.25%)	1 / 17 (5.88%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	3 / 40 (7.50%)
occurrences (all)	0	1	3
Nasal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Nose bleeding			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Odinofagia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	5 / 40 (12.50%)
occurrences (all)	1	0	5
Otorhinolaryngological examination			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Rhinitis - acute			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Rhinitis - allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	4 / 40 (10.00%)
occurrences (all)	0	0	4
Rhinorrhea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	5 / 40 (12.50%)
occurrences (all)	1	0	5
Rhinosinusitis			

subjects affected / exposed	1 / 16 (6.25%)	1 / 17 (5.88%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Runny nose			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	4 / 40 (10.00%)
occurrences (all)	0	1	4
Sneezing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Sore throat			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	5 / 40 (12.50%)
occurrences (all)	0	1	5
Sputum			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	5 / 40 (12.50%)
occurrences (all)	0	1	5
Sputum increase			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	5 / 40 (12.50%)
occurrences (all)	0	0	5
Skin and subcutaneous tissue disorders			
Pruritus - allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Endocrine disorders			
Increased hunger			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	4 / 40 (10.00%)
occurrences (all)	0	0	4
Musculoskeletal and connective tissue disorders			
Hands tremor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Lower Limb cramp			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Muscle cramp			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Muscle pain - localized			

subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Pain - leg			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Pain - localized			
subjects affected / exposed	2 / 16 (12.50%)	0 / 17 (0.00%)	5 / 40 (12.50%)
occurrences (all)	2	0	5
Tremor			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Infections and infestations			
Diarrhea - Acute			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
External Otitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Flu - common			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Influenza virus infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Pharyngitis - Acute			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences (all)	1	0	1
Pharyngitis - bacterial			
subjects affected / exposed	2 / 16 (12.50%)	1 / 17 (5.88%)	1 / 40 (2.50%)
occurrences (all)	2	1	1

Pharyngotonsillitis			
subjects affected / exposed	2 / 16 (12.50%)	1 / 17 (5.88%)	3 / 40 (7.50%)
occurrences (all)	2	1	3
Rhinopharyngitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Sore throat			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	4 / 40 (10.00%)
occurrences (all)	0	0	4
Tonsillitis - acute			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
flu-like symptoms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	5 / 40 (12.50%)
occurrences (all)	0	0	5

Non-serious adverse events	Adult Patients: Budesonide and Formoterol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 39 (53.85%)		
Injury, poisoning and procedural complications			
Pruritus - injection site reaction			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Sea food allergy			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Head trauma			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		

Headache			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Lipothymia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Adynamia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Fever			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Eye disorders			

Burning in the eye subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Conjunctivitis - bacterial subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Pruritus - ocular subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Abdominal pain -localized subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Colitis subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Constipation subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Epigastric pain - food-related subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Gastroenteritis - acute subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Nausea			

subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Pyelonephritis - acute			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Allergic asthma			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Asthma exacerbation			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
CRUP syndrome			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Cough - dry			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Cough - with sputum			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Dyspnea			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Flu illness			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Nasal congestion			

subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Nasal obstruction			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Nose bleeding			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Odinofagia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Otorhinolaryngological examination			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Rhinitis - acute			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Rhinitis - allergic			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Rhinorrhea			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Rhinosinusitis			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Runny nose			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		
Sneezing			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Sore throat			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Sputum			

subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Sputum increase subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Skin and subcutaneous tissue disorders Pruritus - allergic subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Endocrine disorders Increased hunger subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Musculoskeletal and connective tissue disorders Hands tremor subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Lower Limb cramp subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3		
Muscle cramp subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Muscle pain - localized subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Myalgia subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Pain - leg subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Pain - localized subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Tremor			

subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Infections and infestations			
Diarrhea - Acute			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
External Otitis			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Flu - common			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Influenza virus infection			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Pharyngitis - Acute			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Pharyngitis - bacterial			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Pharyngotonsillitis			
subjects affected / exposed	7 / 39 (17.95%)		
occurrences (all)	7		
Rhinopharyngitis			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Sore throat			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		

Tonsillitis - acute			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
flu-like symptoms			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2013	Updated with dose determination chart for appropriate omalizumab dose assignment for every 4 weeks and 2 weeks. The spirometry with a β_2 reversibility test should be performed at the beginning of the study (Visit -1) as part of the asthma diagnosis and also at the final visit (Visit 20). Updated Schedule of evaluations. Additional laboratory evaluations for Hemogram and Allergens. Other administrative changes.
29 March 2014	Inclusion criteria. Change in dosage of budesonide and formoterol (mg to μ g). Other administrative changes
29 August 2014	Novartis will provide Omalizumab (Xolair), Budesonide (Miflonide, Pulmicort or generic drugs equivalent to Budesonide) and Formoterol (Foradil or generic drug equivalent to Formoterol). Other administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
06 August 2015	A premature termination of clinical trial was done by the Sponsor for reasons unrelated to efficacy and/or drug safety. The main rationale behind premature termination was due to identified errors in data management handling after an internal audit by the sponsor performed by third party; validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning and decommissioning requirements were assessed according to ICH GCP E6 with significant findings.	-

Notes:

Limitations and caveats

None reported