Clinical trial results:
A 12 week, multi-center, randomized, double-blind, placebo-controlled phase III study to evaluate the efficacy and safety of omalizumab in adult and adolescent patients with inadequately controlled severe Japanese cedar pollinosis despite the current recommended therapies Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd. com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2017-002154-36
Trial protocol	Outside EU/EEA
Global end of trial date	20 October 2018

Results information

Result version number	v1 (current)
This version publication date	24 April 2019
First version publication date	24 April 2019

Trial information

Trial identification

Sponsor protocol code	CIGE025F1301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03369704
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, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of omalizumab compared with placebo.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2017
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: 337
Worldwide total number of subjects	337
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	28
Adults (18-64 years)	289
From 65 to 84 years	20

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 22 centers in Kanto-area of Japan.

Pre-assignment

Screening details:

337 patients were randomized

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Omalizumab

Arm description:

Omalizumab administered subcutaneously for 12 weeks

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

Dosage and administration details:

Dose (75 to 600 mg) and dosing frequency (every 2 or 4 weeks) of the study drug were determined by serum total IgE level (IU/mL) and body weight (kg), measured during the screening epoch.

Arm title	Placebo

Arm description:

Placebo administered subcutaneously for 12 weeks

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

Dosage and administration details:

Matching placebo was supplied in an open-label manner and in a 5mL glass vial.

Number of subjects in period 1	Omalizumab	Placebo
Started	162	175
Completed	158	172
Not completed	4	3
technical problems	1	-
Adverse event, non-fatal	2	-
Lost to follow-up	-	1
Protocol deviation	1	-
Lack of efficacy	-	2

Period 2	
Period 2 title	Follow-up epoch
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms	
Are arms mutually exclusive?	No
Arm title	Omalizumab

Arm description:

Omalizumab administered subcutaneously for 12 weeks

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

Dosage and administration details:

Dose (75 to 600 mg) and dosing frequency (every 2 or 4 weeks) of the study drug were determined by serum total IgE level (IU/mL) and body weight (kg), measured during the screening epoch.

Arm title	Placebo

Arm description:

Placebo administered subcutaneously for 12 weeks

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

Dosage and administration details:

Matching placebo was supplied in an open-label manner and in a 5mL glass vial.

Number of subjects in period 2	Omalizumab	Placebo
Started	161	174
Completed	160	174
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Omalizumab
Reporting group description:	
Omalizumab administered subcutaneously for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo administered subcutaneously for 12 weeks	

Reporting group values	Omalizumab	Placebo	Total
Number of subjects	162	175	337
Age, Customized Units: Subjects			
< 15 years	4	6	10
15 <=, < 65 years	149	158	307
>= 65 years	9	11	20
Age continuous Units: years			
arithmetic mean	42.3	41.0	
standard deviation	± 14.31	± 15.43	-
Sex: Female, Male Units: Subjects			
Female	99	97	196
Male	63	78	141
Race/Ethnicity, Customized Units: Subjects			
Asians	162	175	337

End points

End points reporting groups

Reporting group title	Omalizumab
Reporting group description: Omalizumab administered subcutaneously for 12 weeks	
Reporting group title	Placebo
Reporting group description: Placebo administered subcutaneously for 12 weeks	
Reporting group title	Omalizumab
Reporting group description: Omalizumab administered subcutaneously for 12 weeks	
Reporting group title	Placebo
Reporting group description: Placebo administered subcutaneously for 12 weeks	

Primary: Mean nasal symptom score

End point title	Mean nasal symptom score
End point description: Nasal symptoms (sneezing, rhinorrhea and nasal congestion) were recorded by the patient everyday in their e-Diary, on a scale of 0 (none) to 4 (intense/severe). Nasal symptom score (0-12 point) consisted of score for severity of sneezing (0-4 point), rhinorrhea (0-4 point) and nasal congestion (0-4 point). Severe symptom period: The three weeks where the cumulative value of the mean daily nasal symptom score is the maximum. The three weeks must also meet one of the following criteria: 2) ≥ 70% of the period with concomitant use of fluticasone propionate is included in this three weeks. 2) ≥ 70% of this three weeks includes the period with concomitant use of fluticasone propionate. If not, severe symptom period was extended at a minimum to meet one of the criteria above.	
End point type	Primary
End point timeframe: Severe symptom period	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: score				
least squares mean (standard error)	3.66 (± 0.151)	4.69 (± 0.144)		

Statistical analyses

Statistical analysis title	Nasal symptom score
Comparison groups	Omalizumab v Placebo

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [1]
Method	ANCOVA
Parameter estimate	Least Square Mean
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.44
upper limit	-0.62
Variability estimate	Standard error of the mean
Dispersion value	0.209

Notes:

[1] - H0: Omalizumab is not different to placebo with respect to mean nasal symptom score over the severe symptom period. H1: Omalizumab is different to placebo with respect to mean nasal symptom score over the severe symptom period.

Secondary: Mean ocular symptom score and mean nasal ocular symptom score

End point title	Mean ocular symptom score and mean nasal ocular symptom score

End point description:

Ocular symptoms (itchy and watery eye) were recorded by the patient everyday in their e-Diary, on a scale of 0 (none) to 4 (intense/severe). Ocular symptom score (0-8 point) consisted of score for severity of itchy eye (0-4 point) and watery eye (0-4 point). Nasal ocular symptom score consisted of nasal symptom score and ocular symptom score.

End point type	Secondary

End point timeframe:

Severe symptom period

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: Score				
least squares mean (standard error)				
Mean ocular symptom score	2.45 (± 0.115)	3.32 (± 0.110)		
Mean nasal ocular symptom score	6.11 (± 0.240)	8.01 (± 0.228)		

Statistical analyses

Statistical analysis title	Nasal Ocular Symptom
Comparison groups	Omalizumab v Placebo

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-1.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.55
upper limit	-1.24
Variability estimate	Standard error of the mean
Dispersion value	0.331

Statistical analysis title	Ocular symptom
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	-0.55
Variability estimate	Standard error of the mean
Dispersion value	0.159

Secondary: Mean nasal symptom medication score, mean ocular symptom medication score, and mean nasal ocular symptom medication score

End point title	Mean nasal symptom medication score, mean ocular symptom medication score, and mean nasal ocular symptom medication score

End point description:

Medication scores were given for fluticasone propionate (nasal, 2 point), fexofenadine hydrochloride (oral, 1 point), tramazoline hydrochloride (nasal, 1 point), and levocabastine hydrochloride (ocular, 1 point). Symptom medication score consisted of severe symptom period.

End point type	Secondary

End point timeframe:

Severe symptom period

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: score				
least squares mean (standard error)				
Mean nasal symptom medication score	6.19 (± 0.166)	7.29 (± 0.158)		
Mean ocular symptom medication score	3.91 (± 0.137)	4.86 (± 0.130)		
Mean nasal ocular symptom medication score	9.10 (± 0.271)	11.15 (± 0.259)		

Statistical analyses

Statistical analysis title	Nasal symptom medication score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	-0.64
Variability estimate	Standard error of the mean
Dispersion value	0.229

Statistical analysis title	Ocular symptom medication score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.32
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.189

Statistical analysis title	Nasal ocular symptom medication score
Comparison groups	Omalizumab v Placebo

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.78
upper limit	-1.31
Variability estimate	Standard error of the mean
Dispersion value	0.375

Secondary: Mean score for severity of sneezing, rhinorrhea and nasal congestion

End point title	Mean score for severity of sneezing, rhinorrhea and nasal congestion

End point description:

Symptoms of sneezing, rhinorrhea and nasal congestion were evaluated on a scale of 0 (none) to 4 (intense/severe).

End point type	Secondary

End point timeframe:

Severe symptom period

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: score				
least squares mean (standard error)				
Mean sneezing score	1.15 (± 0.053)	1.56 (± 0.050)		
Mean rhinorrhea score	1.46 (± 0.063)	1.79 (± 0.060)		
Mean nasal congestion score	1.05 (± 0.058)	1.34 (± 0.056)		

Statistical analyses

Statistical analysis title	Sneezing score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.26
Variability estimate	Standard error of the mean
Dispersion value	0.073

Statistical analysis title	Rhinorrhea score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.088

Statistical analysis title	Nasal congestion score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.081

Secondary: Mean score for severity of itchy and watery eye	
End point title	Mean score for severity of itchy and watery eye
End point description:	
Symptoms of itchy and watery eye were evaluated on a scale of 0 (none) to 4 (intense/severe).	
End point type	Secondary

End point timeframe:
Severe symptom period

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: score				
least squares mean (standard error)				
Mean itchy eye score	1.47 (± 0.061)	1.94 (± 0.058)		
Mean watery eye score	0.98 (± 0.063)	1.38 (± 0.060)		

Statistical analyses

Statistical analysis title	Itchy eye score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.084

Statistical analysis title	Watery eye score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	0.087

Secondary: Mean score for impairment of daily activities

End point title	Mean score for impairment of daily activities
End point description:	
Impairment of daily activities were evaluated on a scale of 0 (none) to 4 (intense/severe).	
End point type	Secondary
End point timeframe:	
Severe symptom period	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: score				
least squares mean (standard error)	1.09 (± 0.052)	1.43 (± 0.050)		

Statistical analyses

Statistical analysis title	Score for impairment of daily activities
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.072

Secondary: Number of symptom free days

End point title	Number of symptom free days
End point description:	
Nasal symptom free days (days with all nasal symptoms are not more than mild in severity) during the severe symptom period. Ocular symptom free days (days with all ocular symptoms are not more than mild in severity) during the severe symptom period.	
End point type	Secondary
End point timeframe:	
Severe symptom period	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: days				
Nasal symptom free days	15	10		
Ocular symptom free days	12	6		

Statistical analyses

Statistical analysis title	Nasal symptom free days
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	5
Variability estimate	Standard error of the mean
Dispersion value	1.02

Statistical analysis title	Ocular symptom free days
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	6.5
Variability estimate	Standard error of the mean
Dispersion value	1.15

Secondary: Rescue medication free days

End point title	Rescue medication free days
End point description: Number of days with no rescue medication (tramazoline hydrochloride, levocabastine hydrochloride)	
End point type	Secondary
End point timeframe: Severe symptom period	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: days				
number (not applicable)				
Nasal rescue medication free days	27.0	23.5		
Ocular rescue medication free days	16.0	11.0		
Nasal ocular rescue medication free days	12.5	9.0		

Statistical analyses

Statistical analysis title	Nasal rescue medication score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.011
Method	van Elteren test
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.5
Variability estimate	Standard error of the mean
Dispersion value	0.89

Statistical analysis title	Ocular rescue medication free days
Comparison groups	Omalizumab v Placebo

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.074
Method	van Elteren test
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4.8
Variability estimate	Standard error of the mean
Dispersion value	1.21

Statistical analysis title	Nasal ocular rescue medication free days
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.098
Method	van Elteren test
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4
Variability estimate	Standard error of the mean
Dispersion value	1.02

Secondary: Number of rescue medication used	
End point title	Number of rescue medication used
End point description: Amount number of rescue medication used (a total number of times used).	
End point type	Secondary
End point timeframe: Severe symptom period	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: Number of times used				
number (not applicable)				
Number of rescue nasal medication used	1.0	6.0		
Number of ocular rescue medication used	18.5	28.5		

Statistical analyses

Statistical analysis title	Nasal rescue medication used
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006
Method	van Elteren test
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	1.15

Statistical analysis title	Ocular rescue medication used
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012
Method	van Elteren test
Parameter estimate	Hodges-Lehmann Estimate
Point estimate	-7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	2.81

Secondary: Japanese Rhinoconjunctivitis Quality of Life Questionnaire (JRQLQ, No1) score

End point title	Japanese Rhinoconjunctivitis Quality of Life Questionnaire (JRQLQ, No1) score

End point description:

Nasal and eye symptoms (JRQLQ I) included 6 categories: Runny nose, Sneezing, Nasal congestion, Itchy nose, itchy eyes and watery eyes, on a 5-point scale of 0 to 4 (no symptoms to very severe symptoms). JRQLQ I score was a mean of these 6 categories. JRQLQ II included 17 items on a 5-point scale, 0 to 4 (no significant problem to very greatly). JRQLQ II scores was a mean of these 17 items. Overall face scale (JRQLQ III) evaluated overall symptoms, condition and feelings on a 5-point scale from 0 to 4 (fine to crying). Evaluation visit was defined as follows independently for each evaluation item and for each patient: 1) If there was a single visit during the severe symptom period, the visit was the evaluation visit. 2) If there were ≥ 2 visits during the severe symptom period and a) if Visit 105 was one of them, Visit 105 was the evaluation visit; b) if Visit 105 was outside the period, the closest visit to Visit 105 during the period was the evaluation visit.

End point type	Secondary

End point timeframe:

Evaluation Visit

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	175		
Units: Score				
least squares mean (standard error)				
Nasal and eye symptoms (JRQLQ I)	1.27 (± 0.062)	1.76 (± 0.059)		
Mean score of QoL-related questionnaire (JRQLQ II)	0.70 (± 0.067)	1.20 (± 0.064)		
Overall face scale (JRQLQ III)	1.6 (± 0.08)	2.2 (± 0.07)		

Statistical analyses

Statistical analysis title	JRQLQ I
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.33
Variability estimate	Standard error of the mean
Dispersion value	0.086

Statistical analysis title	JRQLQ II
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.33
Variability estimate	Standard error of the mean
Dispersion value	0.093

Statistical analysis title	JRQLQ III
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.1

Secondary: Number of Participants with Anti-omalizumab antibodes	
End point title	Number of Participants with Anti-omalizumab antibodes
End point description:	
Number of participants with antibodies against the Fab and Fc region of omalizumab in serum.	
End point type	Secondary
End point timeframe:	
Prior to first dosing (Day 1), At follow-up investigation which were conducted 20/22 weeks after 12 week-treatment epoch	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	175		
Units: participants				
Anti-Fab-(pre-dose)	0	0		
Anti-Fab (post dose)	0	0		
Anti-Fc-(pre-dose)	1	2		
Anti-Fc-(post-dose)	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum trough omalizumab concentration

End point title	Serum trough omalizumab concentration[2]

End point description:

Blood samples were collected Prior to first dosing (Day 1), at Day 29, Day 57, Day 85 and follow-up investigation which were conducted 20/22 weeks after 12 week-treatment epoch

End point type	Secondary

End point timeframe:

Prior to first dosing (Day 1), at Day 29, Day 57, Day 85 and 24 weeks after last dose

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: descriptive statistics.

End point values	Omalizumab			
Subject group type	Reporting group			
Number of subjects analysed	161			
Units: µg/mL				
arithmetic mean (standard deviation)				
Day 1 (pre-dose)	0 (± 0)			
Day 29 (N=159)	42.6 (± 34.8)			
Day 57 (N=158)	54.1 (± 42.3)			
Day 85 (N=161)	66.3 (± 49.0)			
Day 225/239 (N=160)	0.928 (± 1.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Free IgE and total IgE

End point title	Free IgE and total IgE

End point description:

Blood samples were collected Prior to first dosing (Day 1), at Day 29, Day 57, Day 85 and follow-up investigation were conducted 20/22 weeks after 12 week-treatment epoch

End point type	Secondary

End point timeframe:

Day 1, at Day 29, Day 57, Day 85 and 24 weeks after last dose

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	175		
Units: ng/mL				
arithmetic mean (standard deviation)				
Free IgE (Day 1 predose)	999 (± 999)	999 (± 999)		
Free IgE (Day 29)	21.3 (± 9.8)	999 (± 999)		
Free IgE (Day 57)	20.8 (± 10.1)	999 (± 999)		
Free IgE (Day 85)	18.6 (± 11.9)	999 (± 999)		
Free IgE (Day 225/239)	999 (± 999)	999 (± 999)		
Total IgE (Day 1 pre-dose)	524 (± 531)	570 (± 641)		
Total IgE (Day 29)	2040 (± 1620)	558 (± 608)		
Total IgE (Day 57)	2160 (± 1660)	640 (± 721)		
Total IgE (Day 85)	1960 (± 1480)	673 (± 775)		
Total IgE (Day 225/239)	702 (± 639)	669 (± 783)		

Statistical analyses

No statistical analyses for this end point

Secondary: Completely nasal symptom free patients

End point title	Completely nasal symptom free patients

End point description:

Completely nasal symptom free patients is the number of patients who were nasal symptom free (all nasal symptoms were not more than mild in severity) on all non-missing days and had nasal symptom scores for at least 26 days during the 30 days of severe symptom period.

End point type	Secondary

End point timeframe:

Severe symptom period

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: Patients	13	4		

Statistical analyses

Statistical analysis title	Completely nasal symptom free patients
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.005
Method	logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	3.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	9.75

Secondary: Rescue medication score

End point title	Rescue medication score
End point description:	
Rescue medication scores were given for tramazoline hydrochloride (nasal, 1 point) and levocabastine hydrochloride (ocular, 1 point).	
End point type	Secondary
End point timeframe:	
Severe symptom period	

End point values	Omalizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	174		
Units: score				
least squares mean (standard error)				
Nasal rescue medication score	0.20 (± 0.024)	0.28 (± 0.023)		
Ocular rescue medication score	0.46 (± 0.029)	0.54 (± 0.027)		
Nasal ocular rescue medication score	0.66 (± 0.045)	0.82 (± 0.043)		

Statistical analyses

Statistical analysis title	Nasal rescue medication score
Comparison groups	Omalizumab v Placebo

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.033

Statistical analysis title	Ocular rescue medication score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.04

Statistical analysis title	Nasal ocular rescue medication score
Comparison groups	Omalizumab v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	ANCOVA
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.063

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected after providing written informed consent for participation in the study until the end of the treatment epoch. Serious Adverse Events were collected until 30 days after the end of the treatment epoch.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	IGE025

Reporting group description:

Eligible patients randomized to this arm received omalizumab subcutaneously for 12 weeks

Reporting group title	Placebo

Reporting group description:

Placebo administered subcutaneously for 12 weeks

Serious adverse events	IGE025	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 161 (0.62%)	0 / 175 (0.00%)	
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)			
Testicular neoplasm			
subjects affected / exposed	1 / 161 (0.62%)	0 / 175 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	IGE025	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 161 (16.15%)	21 / 175 (12.00%)	
Infections and infestations			
Influenza			
subjects affected / exposed	4 / 161 (2.48%)	8 / 175 (4.57%)	
occurrences (all)	4	8	
Nasopharyngitis			

subjects affected / exposed	15 / 161 (9.32%)	8 / 175 (4.57%)	
occurrences (all)	15	9	
Pharyngitis			
subjects affected / exposed	7 / 161 (4.35%)	5 / 175 (2.86%)	
occurrences (all)	7	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported