Clinical trial results:
A randomized, 20 week, double-blind, placebo-controlled, parallel-group, multiple-dose, multicenter study to assess the efficacy and safety of Omalizumab in combination with Depigoid, versus Depigoid only, in adult and adolescent patients with seasonal allergic asthma and comorbid seasonal allergic rhinoconjunctivitis

Summary

EudraCT number	2005-003860-47
Trial protocol	DE
Global end of trial date	05 September 2008

Results information

Result version number	v1 (current)
This version publication date	04 June 2016
First version publication date	04 June 2016

Trial information

Trial identification

Sponsor protocol code	CIGE025ADE03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00396409
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111 ,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111 ,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 September 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to demonstrate that grass/rye pollen extract in combination with omalizumab has superior efficacy compared to grass/rye pollen extract monotherapy, for daily symptom load averaged over the pollen season in adult and adolescent subjects, sensitized against grass pollen allergens with seasonal allergic asthma and comorbidity with seasonal allergic rhinoconjunctivitis.

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 local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial. For symptoms of inter-current bronchospasm subjects were allowed to take short acting β-2 agonist (SABA) (salbutamol sulfate) as initial rescue medication. If the initial SABA did not result in symptom control , escalation co-medication was provided by the study physician. Escalation medication for treatment of seasonal asthma included low-dose inhaled corticosteroid (ICS) (budesonide) 200 microgram (mcg) once daily (o.d.) dose was provided, if no symptom control was achieved medium-dose inhaled corticosteroid (budesonide) 200 mcg twice daily (bid) dose was provided and if this dose was also insufficient to control asthma symptoms, oral corticosteroid (prednisone) 50 milligram (mg) was provided. If no symptom control was achieved after this step, patients had to be discontinued from the study. In this case, the responsible study physician needs to specifically optimize the patient's individual treatment regimen, considering combination treatment with long acting beta agonists and inhaled corticosteroids.
For symptoms of grass pollen allergic rhino-conjunctivitis subjects were allowed to take systemic antihistamine (levocetirizine dihydrochloride) 5 mg as initial rescue medication. If initial systemic antihistamine was insufficient , escalated co-medication was provided by the study physician. Escalation medication for treatment of seasonal rhino-conjunctivitis included a nasal steroid (mometasone) 50 mcg , if no symptom control was achieved , the next step was an oral corticosteroid (prednisone) 50 mg .
The investigator provided follow-up medical care for all subjects who prematurely withdrew from study or referred them for appropriate ongoing care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2006
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	Germany: 140
Worldwide total number of subjects	140
EEA total number of subjects	140

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)	1
Adolescents (12-17 years)	27
Adults (18-64 years)	112
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 20 centres in Germany.

Pre-assignment

Screening details:

A total of 201 subjects were screened, of which 140 subjects were enrolled in core study. From 130 subjects who completed core period, 128 subjects entered extension period -2007. Out of 128 patients , 114 entered in extension period - 2008.

Period 1

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

Blinding implementation details:

Randomization data were kept strictly confidential and the identity of treatments were concealed by the use of identical study drugs. Unblinding was allowed from time of randomization to database lock, except in the case of subject emergencies and at the conclusion of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Core: Grass/Rye Pollen extract + Omalizumab

Arm description:

Subjects received omalizumab and grass/rye pollen extract in core study. Omalizumab (75 mg-375 mg) was administered through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Grass/Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 Depigmented Polymerised Particle (DPP)/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.

Arm type	Experimental
Investigational medicinal product name	Grass/Rye pollen extract
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Grass/rye pollen extract solution (0.5 ml) was administered weekly via s.c. route every 4 weeks. Grass/rye pollen extract solution consists depigmented and glutaraldehyde polymerised allergenic extract of 50% grass / 50% rye pollen adsorbed onto aluminum hydroxide.

Investigational medicinal product name	Omalizumab
Investigational medicinal product code	IGE025
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab (75-375 mg) individualized dose was administered weekly via s.c. after reconstitution with 1.4 ml Sterile Water for Injection for 2-4 weeks.

Arm title	Core: Grass/ Rye Pollen extract + Placebo

Arm description:

Subjects received placebo and Grass/ Rye Pollen Extract in core study. Placebo matched to omalizumab (75-375 mg) was administered weekly via s.c. route for 2-4 weeks. Grass/ Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 DPP/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.

Arm type	Experimental
Investigational medicinal product name	Grass/Rye pollen extract
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pollen extract solution (0.5 ml) was administered weekly via s.c. route every 4 weeks. Pollen extract solution consists depigmented and glutaraldehyde polymerised allergenic extract of 50% grass / 50% rye pollen adsorbed onto aluminum hydroxide.

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

Dosage and administration details:

Placebo matched to omalizumab (75 - 375 mg) was administered weekly via s.c. route for 2-4 weeks.

Number of subjects in period 1	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo
Started	70	70
Completed	65	65
Not completed	5	5
Consent withdrawn by subject	4	1
Adverse event, non-fatal	-	1
Administrative problems	1	-
Lost to follow-up	-	3

Period 2

Period 2 title	Period 2 (Extension Period - 2007)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The extension period was open label, hence no blinding was performed.

Arms

Are arms mutually exclusive?	Yes

Arm title	Pollen extract (Core and Extension- 2007) + Omalizumab (Core)

Arm description:

Subjects who received omalizumab and grass/rye pollen extract in the core, received only open label pollen extract in the extension study during grass pollen season year 2007 . Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2007.

Arm type	Experimental
Investigational medicinal product name	Grass/Rye pollen extract
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Grass/Rye pollen extract solution (0.5 ml) was administered weekly via s.c. route every 4 weeks. Grass/Rye pollen extract solution consisted of depigmented and glutaraldehyde polymerized allergenic extract of 50% grass / 50% rye pollen adsorbed onto aluminum hydroxide

Arm title	Pollen extract (Core and Extension - 2007) + Placebo (Core)

Arm description:

Subjects who received placebo and grass/rye pollen extract in core, received only grass/rye pollen extract in extension study during grass pollen season year 2007. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2007.

Arm type	Experimental
Investigational medicinal product name	Grass/rye pollen extract
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Grass/rye pollen extract solution (0.5 ml) was administered weekly via s.c. route every 4 weeks. Grass/rye pollen extract solution consists depigmented and glutaraldehyde polymerised allergenic extract of 50% grass / 50% rye pollen adsorbed onto aluminum hydroxide.

Number of subjects in period 2[1]	Pollen extract (Core and Extension- 2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Started	65	63
Completed	62	57
Not completed	3	6
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	1
Lost to follow-up	2	3
Lack of efficacy	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Some patients who completed the core did not continue to extension.

Period 3

Period 3 title	Period 3 (Extension Period- 2008)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The extension period was open label, hence no blinding was performed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pollen extract (Core and Extension-2008) + Omalizumab (Core)

Arm description:

Subjects who received omalizumab and grass/rye pollen extract in the core, received only open label pollen extract in the extension study during grass pollen season year 2008. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2008.

Arm type	Experimental
Investigational medicinal product name	Grass/rye pollen extract
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Grass/rye pollen extract solution (0.5 ml) was administered weekly via s.c. route every 4 weeks. Grass/rye pollen extract solution consists depigmented and glutaraldehyde polymerised allergenic extract of 50% grass / 50% rye pollen adsorbed onto aluminum hydroxide.

Arm title	Pollen extract (Core and Extension - 2008) + Placebo (Core)

Arm description:

Subjects who received placebo and grass/rye pollen extract in core, received only pollen extract in extension study during grass pollen season year 2008. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2008.

Arm type	Experimental
Investigational medicinal product name	Grass/rye pollen extract
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Grass/rye pollen extract solution (0.5 ml) was administered weekly via s.c. route every 4 weeks. Grass/rye pollen extract solution consists depigmented and glutaraldehyde polymerised allergenic extract of 50% grass / 50% rye pollen adsorbed onto aluminum hydroxide.

Number of subjects in period 3[2]	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)
Started	59	55
Completed	52	53
Not completed	7	2
Consent withdrawn by subject	3	1

Lost to follow-up	3	1
Protocol deviation	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Some patients who completed the core did not continue to extension.

Baseline characteristics

Reporting groups	
Reporting group title	Core: Grass/Rye Pollen extract + Omalizumab
Reporting group description:	
Subjects received omalizumab and grass/rye pollen extract in core study. Omalizumab (75 mg-375 mg) was administered through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Grass/Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 Depigmented Polymerised Particle (DPP)/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.	
Reporting group title	Core: Grass/ Rye Pollen extract + Placebo
Reporting group description:	
Subjects received placebo and Grass/ Rye Pollen Extract in core study. Placebo matched to omalizumab (75-375 mg) was administered weekly via s.c. route for 2-4 weeks. Grass/ Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 DPP/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.	

Reporting group values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Total
Number of subjects	70	70	140
Age categorical Units: Subjects			
Children (2-11 years)	1	0	1
Adolescents (12-17 years)	13	14	27
Adults (18-64 years)	56	56	112
Age continuous Units: years			
arithmetic mean	28.2	30.4	
standard deviation	± 10.23	± 10.61	-
Gender categorical Units: Subjects			
Female	31	30	61
Male	39	40	79

End points

End points reporting groups

Reporting group title	Core: Grass/Rye Pollen extract + Omalizumab

Reporting group description:

Subjects received omalizumab and grass/rye pollen extract in core study. Omalizumab (75 mg-375 mg) was administered through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Grass/Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 Depigmented Polymerised Particle (DPP)/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.

Reporting group title	Core: Grass/ Rye Pollen extract + Placebo

Reporting group description:

Subjects received placebo and Grass/ Rye Pollen Extract in core study. Placebo matched to omalizumab (75-375 mg) was administered weekly via s.c. route for 2-4 weeks. Grass/ Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 DPP/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.

Reporting group title	Pollen extract (Core and Extension- 2007) + Omalizumab (Core)

Reporting group description:

Subjects who received omalizumab and grass/rye pollen extract in the core, received only open label pollen extract in the extension study during grass pollen season year 2007 . Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2007.

Reporting group title	Pollen extract (Core and Extension - 2007) + Placebo (Core)

Reporting group description:

Subjects who received placebo and grass/rye pollen extract in core, received only grass/rye pollen extract in extension study during grass pollen season year 2007. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2007.

Reporting group title	Pollen extract (Core and Extension-2008) + Omalizumab (Core)

Reporting group description:

Subjects who received omalizumab and grass/rye pollen extract in the core, received only open label pollen extract in the extension study during grass pollen season year 2008. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2008.

Reporting group title	Pollen extract (Core and Extension - 2008) + Placebo (Core)

Reporting group description:

Subjects who received placebo and grass/rye pollen extract in core, received only pollen extract in extension study during grass pollen season year 2008. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2008.

Primary: Mean daily symptom load based on subjects assessed daily symptom

End point title	Mean daily symptom load based on subjects assessed daily symptom

End point description:

Symptom load is sum of mean daily symptom severity score plus mean daily rescue/escalation medication score combined for asthma and rhinoconjunctivitis. Overall symptom severity score was derived from subject diaries for various allergy symptoms. Subjects rated the symptoms on a 4-point scale: from 0 to 3 for "no", "mild", "moderate" and "severe" symptoms respectively. The rescue medication score is defined as mean of daily rescue medications scores during pollen season. Patients recorded daily usage of their rescue/escalation medication in patient diary. The point values assigned to usage of each individual medication on each day. A lower score indicated an improvement in the allergic condition. The analysis was on intent to treat (ITT) population defined as all subjects randomized receiving at least one dose of study drug and had at least one assessment of symptom load in their diaries. The missing values were imputed using last observation carried forward (LOCF).

End point type	Primary

End point timeframe:
Week 1 up to Week 18 (Core period), Week 4 up to Week 104 (Extension period)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension- 2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	65	65	63
Units: Units on a scale				
arithmetic mean (standard deviation)	0.77 (± 0.79)	0.94 (± 0.69)	1.25 (± 0.99)	1.1 (± 0.99)

End point values	Pollen extract (Core and Extension- 2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	55		
Units: Units on a scale				
arithmetic mean (standard deviation)	1.32 (± 1.74)	0.97 (± 1.02)		

Statistical analyses

Statistical analysis title	Core Study : Treatment diference between arms
Comparison groups	Core: Grass/Rye Pollen extract + Omalizumab v Core: Grass/ Rye Pollen extract + Placebo
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.10689
Method	ANOVA
Parameter estimate	Least square mean difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.05

Statistical analysis title	Extension - 2007: Treatment diference between arms

Comparison groups	Pollen extract (Core and Extension- 2007) + Omalizumab (Core) v Pollen extract (Core and Extension - 2007) + Placebo (Core)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36888
Method	ANOVA
Parameter estimate	Least square mean difference
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.54

Statistical analysis title	Extension - 2008: Treatment diference between arms
Comparison groups	Pollen extract (Core and Extension-2008) + Omalizumab (Core) v Pollen extract (Core and Extension - 2008) + Placebo (Core)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43873
Method	ANOVA
Parameter estimate	Least square mean difference
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.86

Secondary: Mean daily symptom severity score for rhinoconjunctivitis and asthma

End point title	Mean daily symptom severity score for rhinoconjunctivitis and asthma

End point description:

The overall symptom severity score of asthma/rhinoconjunctivits was derived from subject diaries for difficulty in breathing, difficulty in breathing on exercise, cough, tightness of chest, nocturnal awakening, sneezing, itchy nose, runny nose, stuffy nose, red eyes, watery eyes and itchy eyes. Subjects rated the symptoms on a 4-point scale: 0 – no symptoms, 1: mild symptoms, 2: moderate symptoms, 3: severe symptoms. A lower score indicated an improvement in the allergic condition. The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects assessed for severity score during the study for each arm, respectively. The missing values were imputed using LOCF method.

End point type	Secondary

End point timeframe:

Week 1 up to Week 18 (Core period), Week 4 up to Week 104 (Extension period)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	65	65	63
Units: Units on a scale				
arithmetic mean (standard deviation)	0.39 (± 0.36)	0.57 (± 0.47)	0.55 (± 0.4)	0.55 (± 0.38)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	55		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.54 (± 0.42)	0.5 (± 0.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall daily rescue medication score for relief from rhinoconjunctivitis and asthma symptoms

End point title	Overall daily rescue medication score for relief from rhinoconjunctivitis and asthma symptoms

End point description:

The rescue medication score was defined as mean score of daily rescue medication utilized for relief from asthma/ rhinoconjuctivitis during the pollen season. The improvement in symptoms post administration of any rescue medication were rated by subjects from 1 point to 6 point based on usage of medication, SABA: 1 point per accentuation, H1-blocking agent: 1 point per tablet, ICS (200 mcg): 3 points per capsule, Nasal steroid: 3 points per accentuation and Oral corticosteroids (50 mg): 6 points per tablet. The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects assessed for rescue medication score during the study for each arm, respectively. The missing values were imputed using LOCF method.

End point type	Secondary

End point timeframe:

Week 1 up to Week 18 (Core period), Week 4 up to Week 104 (Extension period)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	65	65	63
Units: Units on a scale				
arithmetic mean (standard deviation)	0.38 (± 0.55)	0.37 (± 0.43)	0.7 (± 0.8)	0.55 (± 0.8)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	55		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.78 (± 1.6)	0.47 (± 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma symptom control based on Asthma Control Questionnaire (ACQ) overall score

End point title	Asthma symptom control based on Asthma Control Questionnaire (ACQ) overall score

End point description:

Asthma Control Questionnaire (ACQ), has 7 questions, each with a 7 point scale (0 – good control, 6 –poor control). The average score was calculated as the total of all 7 questions divided by 7 (or the number of questions that were answered at the time point as long as there are at least 4 questions answered). Lower score indicated improvement in symptoms. The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects who had evaluable ACQ data in the corresponding time points during study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 after core period (End of extension - 2007), Week 104 after core period (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension- 2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	64	56
Units: Score on a scale				
arithmetic mean (standard deviation)	1.73 (± 0.75)	2.02 (± 0.94)	1.87 (± 0.74)	1.96 (± 0.91)

End point values	Pollen extract (Core and Extension- 2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Score on a scale				
arithmetic mean (standard deviation)	1.82 (± 0.71)	1.95 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma symptom control based on Asthma Quality of Life Questionnaire (AQLQ) overall score

End point title	Asthma symptom control based on Asthma Quality of Life Questionnaire (AQLQ) overall score

End point description:

Asthma Quality of Life Questionnaire (AQLQ) was 32 item questionnaire defined in 4 domains (symptoms, activity limitation, emotional function and environmental exposure). Each question was answered on a 7 point scale (1–totally limited/problems all the time to 7–not at all limited/no problems). The overall AQLQ score was the mean of all 32 responses (overall score of 1 = severely impaired, overall score of 7 = not impaired at all). Higher score indicated improvement. The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects who had evaluable AQLQ data in the corresponding time points during study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 after core period (End of extension- 2007), Week 104 after core period (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	62	56
Units: Units on a scale				
arithmetic mean (standard deviation)	6.32 (± 0.72)	6.03 (± 1.01)	6.18 (± 0.82)	6.07 (± 0.98)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Units on a scale				
arithmetic mean (standard deviation)	6.22 (± 0.77)	6.21 (± 0.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma symptom control based on Rhino-conjunctivitis Quality of Life Questionnaire (RQLQ) overall score

End point title	Asthma symptom control based on Rhino-conjunctivitis Quality of Life Questionnaire (RQLQ) overall score

End point description:

Rhinoconjunctivitis quality of life questionnaire (RQLQ) was 28-item disease-specific questionnaire defined in 7 domains (activities, sleep, common complaints, practical problems, nasal symptoms, ocular symptoms, and emotions). Each question was answered on a 7 point scale. The overall RQLQ score was the mean of all 28 responses (1–low to 7–high). Higher values represented worse quality of life. The analysis was performed in ITT population. Here "Number of subjects analysed" signifies the subjects with evaluable data for RQLQ during the study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 after core period (End of extension - 2007), Week 104 after core period (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	62	56
Units: Units on a scale				
arithmetic mean (standard deviation)	1.91 (± 0.89)	2.16 (± 0.96)	2.09 (± 0.96)	2.06 (± 0.96)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Units on a scale				
arithmetic mean (standard deviation)	2.05 (± 0.99)	1.98 (± 0.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with change from baseline in AQLQ and RQLQ score at Week 18 (Core period)

End point title	Percentage of subjects with change from baseline in AQLQ and RQLQ score at Week 18 (Core period)

End point description:

The AQLQ and RQLQ clinical differences were categorized as important, moderate, or meaningful improvement; no clinical change; meaningful, moderate, or important impairment. Clinically important differences was scored between any two assessments determined by the authors of the AQLQ and RQLQ. Changes in scores of 0.5 to 1.0 were considered clinically meaningful; 1.0 to 1.5 as moderate and > 1.5 as marked clinically important differences for any individual domain or for the overall summary score. Baseline = Core Screening period i.e. Day -14 to Day -1. The analysis was performed in ITT population. Here "Number of subjects analysed" signifies the subjects who had evaluable data in AQLQ and RQLQ for the core study for each arm, respectively.The missing values were not imputed.

End point type	Secondary

End point timeframe:

Baseline to Week 18 (End of core period)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	65		
Units: Percentage of subjects				
number (not applicable)				
AQLQ improvement	23.9	16.9		
AQLQ no clinical change	55.2	60		
AQLQ impairment	19.4	23.1		
RQLQ improvement	19.4	16.9		
RQLQ no clinical change	52.2	38.5		
RQLQ impairment	26.9	44.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with change from baseline in AQLQ and RQLQ at Week 52 and Week 104 (Extension period)

End point title	Percentage of subjects with change from baseline in AQLQ and RQLQ at Week 52 and Week 104 (Extension period)

End point description:

The AQLQ and RQLQ clinical differences were categorized as important, moderate, or meaningful improvement; no clinical change; meaningful, moderate, or important impairment. Clinically important differences was scored between any two assessments determined by the authors of the AQLQ and RQLQ. Changes in scores of 0.5 to 1.0 were considered clinically meaningful; 1.0 to 1.5 as moderate and > 1.5 as marked clinically important differences for any individual domain or for the overall summary score. Baseline = Core Screening period i.e. Day -14 to Day -1. The analysis was performed in ITT population. Here "Number of subjects analysed" signifies the subjects who had evaluable data in AQLQ and RQLQ for the extension study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Baseline to Week 52 after core period (End of extension- 2007), Week 104 after core period (End of extension-2008)

End point values	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	56	56	54
Units: Percentage of subjects				
number (not applicable)				
AQLQ: important improvement	4.6	7.9	3.4	7.3
AQLQ: moderate improvement	10.8	1.6	5.1	3.6
AQLQ: meaningful improvement	10.8	9.5	10.2	7.3
AQLQ: no clinical change	50.8	36.5	61	50.9

AQLQ: meaningful impairment	7.7	17.5	3.4	16.4
AQLQ: moderate impairment	1.5	4.8	5.1	7.3
AQLQ: important impairment	9.2	11.1	6.8	5.5
RQLQ: important improvement	6.2	4.8	3.4	5.5
RQLQ: moderate improvement	6.2	4.8	3.4	3.6
RQLQ: meaningful improvement	7.7	6.3	11.9	12.7
RQLQ: no clinical change	44.6	41.3	44.1	40
RQLQ: meaningful impairment	10.8	15.9	15.3	21.8
RQLQ: moderate impairment	12.3	7.1	10.2	5.5
RQLQ: important impairment	7.7	7.1	6.8	9.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects by investigator's Global Evaluation of Treatment Effectiveness (GETE) categories at Week 18, Week 52 and Week 104

End point title	Percentage of subjects by investigator's Global Evaluation of Treatment Effectiveness (GETE) categories at Week 18, Week 52 and Week 104

End point description:

Subjects were assessed by investigator based on GETE, a five point scale that evaluated change in asthma control/symptoms (1: excellent for complete control of asthma, 2: good for marked improvement of asthma, 3: moderate for discernible, but limited improvement of asthma, 4: poor for no appreciable change, and 5: worsening for asthma). The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects with evaluable data for GETE assessment during the study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 after core period (End of extension - 2007), Week 104 after core period (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	65	63	56
Units: Percentage of subjects				
number (not applicable)				
Excellent	29.69	12.31	10.77	9.52
Good	45.31	24.62	64.62	47.62
Moderate	18.75	49.23	16.92	19.05
Poor	6.25	13.85	3.08	12.7
Worsening	0	0	1.54	0
Missing	0	0	3.08	11.11

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	54		
Units: Percentage of subjects				
number (not applicable)				
Excellent	18.64	14.55		
Good	49.15	30.91		
Moderate	18.64	43.64		
Poor	6.78	9.09		
Worsening	0	0		
Missing	6.78	1.82		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects by subject's Global Evaluation of Treatment Effectiveness (GETE) categories at Week 18, Week 52 and Week 104

End point title	Percentage of subjects by subject's Global Evaluation of Treatment Effectiveness (GETE) categories at Week 18, Week 52 and Week 104

End point description:

Subjects were assessed by subject/caregiver based on GETE, a five point scale that evaluated change in asthma control/symptoms (1: excellent for complete control of asthma, 2: good for marked improvement of asthma, 3: moderate for discernible, but limited improvement of asthma, 4: poor for no appreciable change, and 5: worsening for asthma). The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects with evaluable data for GETE assessment during the study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 after core period (End of extension - 2007), Week 104 after core period (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	65	59	55
Units: Percentage of subjects				
number (not applicable)				

Excellent	27.69	9.23	18.46	6.35
Good	50.77	36.92	41.54	46.03
Moderate	20	40	18.46	15.87
Poor	1.54	13.85	10.77	19.05
Worsening	0	0	1.54	0
Missing	0	0	9.23	12.7

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	53		
Units: Percentage of subjects				
number (not applicable)				
Excellent	13.56	5.45		
Good	45.76	43.64		
Moderate	25.42	36.36		
Poor	6.78	9.09		
Worsening	1.69	1.82		
Missing	6.78	3.64		

Statistical analyses

No statistical analyses for this end point

Secondary: Work Productivity and Activity Impairment questionnaire specific to allergic asthma (WPAI-AA) scores

End point title	Work Productivity and Activity Impairment questionnaire specific to allergic asthma (WPAI-AA) scores

End point description:

Work Productivity and Activity Impairment-Allergic Asthma (WPAI-AA) questionnaire, covers 6 questions relating to hours missed from work and work productivity in the previous 7 days. The 6 items and 5 additional derived scores was summarized for each time point. The scale ranged from minimum value as 0 to the maximum value of 1. A negative change indicated improvement. The analysis was performed in the ITT population. Here "Number of subjects analysed" signifies the subjects assessed for WPAI-AA during the study for each arm, respectively. The 'n' in each category signifies those subjects evaluable for this measure at specified time points for each group respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 after core period (End of extension - 2007), Week 104 after core period (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	65	65	63
Units: Units on a scale				
arithmetic mean (standard deviation)				
Work time missed (n= 29,39,35,35,33,30)	0.05 (± 0.2)	0.03 (± 0.16)	0 (± 0.01)	0.01 (± 0.04)
Impairment while working (n= 30,38,35,35,34,30)	0.11 (± 0.16)	0.11 (± 0.18)	0.17 (± 0.2)	0.09 (± 0.16)
Overall work impairment (n= 28,38,35,35,33,29)	0.13 (± 0.19)	0.11 (± 0.18)	0.17 (± 0.2)	0.1 (± 0.17)
Activity impairment (n= 64,64,62,54,54,53)	0.14 (± 0.15)	0.19 (± 0.21)	0.14 (± 0.15)	0.16 (± 0.22)
Time of missed activities (n= 17,17,20,9,15,7)	0.07 (± 0.24)	0.01 (± 0.04)	0 (± 0)	0.01 (± 0.02)
Impaired school activities (n= 17,17,20,9,15,7)	0.09 (± 0.17)	0.14 (± 0.24)	0.04 (± 0.08)	0.11 (± 0.18)
Overall activities impaired (n= 17,17,20,9,15,7)	0.08 (± 0.25)	0.02 (± 0.07)	0 (± 0)	0.01 (± 0.03)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	55		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Work time missed (n= 29,39,35,35,33,30)	0 (± 0.01)	0.04 (± 0.18)		
Impairment while working (n= 30,38,35,35,34,30)	0.11 (± 0.13)	0.1 (± 0.16)		
Overall work impairment (n= 28,38,35,35,33,29)	0.11 (± 0.14)	0.1 (± 0.16)		
Activity impairment (n= 64,64,62,54,54,53)	0.16 (± 0.18)	0.15 (± 0.19)		
Time of missed activities (n= 17,17,20,9,15,7)	0 (± 0)	0 (± 0)		
Impaired school activities (n= 17,17,20,9,15,7)	0.05 (± 0.06)	0.14 (± 0.3)		
Overall activities impaired (n= 17,17,20,9,15,7)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Forced Expiratory Volume in One Second (FEV1%)

End point title	Percentage of Forced Expiratory Volume in One Second (FEV1%)

End point description:

Forced Expiratory Volume in One Second (FEV1) was defined as the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, was measured during grass pollen season before each injection of pollen extract. FEV 1 more than or equal to (≥) 70% was ensured prior to administration of pollen extract. Percentage of Forced Expiratory Volume in One Second (FEV1 %) is calculated for each patietn as FEV1(%) = [FEV (best test) * 100]/ Predicted FEV1
At least three maneuvers are performed at each sampling time point. The FEV1 "best test" curve is defined as the spirogram that gives the largest FEV1. The analysis was performed in ITT population. Here "Number of subjects analysed" signifies the subjects assessed for FEV1 during the study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

Week 18 (End of core period), Week 52 (End of extension - 2007), Week 104 (End of extension - 2008)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	64	55
Units: Millilitre(s)				
arithmetic mean (standard deviation)	3751.4 (± 782.63)	3601.5 (± 827.22)	3831.4 (± 753.75)	3644.5 (± 723.49)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Millilitre(s)				
arithmetic mean (standard deviation)	3814.3 (± 721.04)	3574.3 (± 691.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Expiratory Flow (PEF)

End point title	Peak Expiratory Flow (PEF)

End point description:

The Peak Expiratory Flow (PEF) was measured during grass pollen season before each injection of pollen extract, through spirometry testing. The PEF was assessed using a Mini Peak Flow Meter provided to

subjects within 15 minutes of awakening in the morning, prior to any rescue medication use. The analysis was performed in ITT population. Here "Number of subjects analysed" signifies the subjects with evaluable data for PEF during the study for each arm, respectively. The missing values were not imputed.

End point type	Secondary

End point timeframe:

7 days after Week 16 (Day 113) (Core period), 7 days after Week 48 after core period (Extension - 2007), 7 days after Week 100 after core period (Extension - 2007)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab (Core)	Pollen extract (Core and Extension - 2007) + Placebo (Core)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	62	56	54
Units: Litre(s)/minute				
arithmetic mean (standard deviation)	461 (± 121.57)	438.6 (± 114.73)	465.6 (± 111.5)	441 (± 111.8)

End point values	Pollen extract (Core and Extension-2008) + Omalizumab (Core)	Pollen extract (Core and Extension - 2008) + Placebo (Core)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: Litre(s)/minute				
arithmetic mean (standard deviation)	463.9 (± 113.2)	446.1 (± 116.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with local reactions to specific immunotherapy during core study

End point title	Number of subjects with local reactions to specific immunotherapy during core study

End point description:

Local reactions defined according to the size, itching and pain, for size of swelling the largest diameter was evaluated. Local reactions were graded as, mild (< 5 cm), moderate (> 5–10 cm) and severe (> 10 cm). The analysis was performed in Safety (SAF) population, defined as all subjects who received at least one dose of study drug. Here, "Number of subjects analysed" signifies subjects with evaluable data for local reactions for each arm, respectively.

End point type	Secondary

End point timeframe:

Day 1 (Start of treatment), Week 18 (End of core period)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	68		
Units: Number of subjects	8	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with systemic reactions to specific imunotherapy during core period (1 hour after last injection)

End point title	Number of subjects with systemic reactions to specific imunotherapy during core period (1 hour after last injection)

End point description:

Patients were evaluated for allergic symptoms and unwanted effects in terms of adverse events, and the intensity based on the grades as per German Society for Allergology and Immunology (DGAI) criteria: Grade 1 Mild: General skin redness, urticaria, pruritus (palmar and plantar), rhino-conjunctivitis, unspecific symptoms like headache, restlessness ; Grade 2 Moderate: Circulation disturbances like changes in blood pressure or heart rate, mild dyspnea or mild bronchial obstruction, tenesmus, anxiety; Grade 3 Severe: Shock (severe hypotension, paleness), severe bronchial obstruction, unconsciousness, urge incontinence; Grade 4 Anaphylaxis; Heart or circulatory failure. The severity was judged using visual analogue scale (VAS) from 0 = none to 10 = very severe. The analysis was performed in the SAF population. Here, "Number of subjects analysed" signifies subjects with evaluable data for systemic reactions for each arm, respectively.

End point type	Secondary

End point timeframe:

Day 1 (Start of treatment), Week 18 (End of core period)

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	68		
Units: Number of subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in bronchial hyperreactivity (PC20) at Week 12, Week 18

End point title	Change from baseline in bronchial hyperreactivity (PC20) at Week 12, Week 18

End point description:

Airway inflammation was assessed by bronchial hyperreactivity (PC20) test defined as a provocative concentration of omalizumab producing a 20 % fall in FEV1 from baseline. Baseline = Core Screening period i.e. Day -14 to Day -1. The analysis was performed in the SAF population. Here "Number of subjects analysed" signifies the subjects assessed for bronchial hyperreactivity during core study for each arm, respectively. The 'n' signifies those subjects evaluable data for this measure for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Day 85), Week 18 (Day 127) of core period

End point values	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	8		
Units: Milligram(s)/millilitre				
arithmetic mean (standard deviation)				
Day 85 (n= 6, 7)	2 (± 14.82)	-2.9 (± 6.73)		
Day 127 (n= 6, 6)	-4.1 (± 6.09)	-1.8 (± 6.36)		

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 are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Core: Grass/Rye Pollen extract + Omalizumab

Reporting group description:

Subjects received omalizumab and grass/rye pollen extract in core study. Omalizumab (75 mg-375 mg) was administered through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Grass/Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 Depigmented Polymerised Particle (DPP)/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.

Reporting group title	Core: Grass/ Rye Pollen extract + Placebo

Reporting group description:

Subjects received placebo and Grass/ Rye Pollen Extract in core study. Placebo matched to omalizumab (75-375 mg) was administered weekly via s.c. route for 2-4 weeks. Grass/ Rye Pollen Extract (0.5 ml) was administered via s.c. route 100 DPP/ml in core every 4 weeks. The total duration core treatment period was 18 weeks.

Reporting group title	Pollen extract (Core and Extension- 2007) + Omalizumab

Reporting group description:

Subjects who received omalizumab and grass/rye pollen extract in the core, received only open label pollen extract in the extension study during grass pollen season year 2007 . Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2007.

Reporting group title	Pollen extract (Core and Extension - 2007) + Placebo (Core)

Reporting group description:

Subjects who received placebo and grass/rye pollen extract in core, received only grass/rye pollen extract in extension study during grass pollen season year 2007. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2007.

Reporting group title	Pollen extract (Core and Extension-2008) + Omalizumab

Reporting group description:

Subjects who received omalizumab and grass/rye pollen extract in the core, received only open label pollen extract in the extension study during grass pollen season year 2008. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2008.

Reporting group title	Pollen extract (Core and Extension - 2008) + Placebo (Core)

Reporting group description:

Subjects who received placebo and grass/rye pollen extract in core, received only pollen extract in extension study during grass pollen season year 2008. Grass/rye pollen extract (0.5 ml) was administered via s.c. route every 4 weeks during this extension period of year 2008.

Serious adverse events	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	2 / 65 (3.08%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 65 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperventilation			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hypoglycaemia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pollen extract (Core and Extension - 2007) + Placebo (Core)	Pollen extract (Core and Extension-2008) + Omalizumab	Pollen extract (Core and Extension - 2008) + Placebo (Core)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 63 (3.17%)	5 / 59 (8.47%)	1 / 55 (1.82%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	1 / 63 (1.59%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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
Radius fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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
Cardiac disorders			

Pericardial effusion			
subjects affected / exposed	1 / 63 (1.59%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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			
Nausea			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperventilation			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	1 / 63 (1.59%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	0 / 55 (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

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

Non-serious adverse events	Core: Grass/Rye Pollen extract + Omalizumab	Core: Grass/ Rye Pollen extract + Placebo	Pollen extract (Core and Extension-2007) + Omalizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 70 (32.86%)	30 / 70 (42.86%)	36 / 65 (55.38%)
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 70 (5.71%)	7 / 70 (10.00%)	2 / 65 (3.08%)
occurrences (all)	5	12	5
General disorders and administration site conditions			
Application site reaction			
subjects affected / exposed	2 / 70 (2.86%)	4 / 70 (5.71%)	0 / 65 (0.00%)
occurrences (all)	3	5	0
Injection site reaction			
subjects affected / exposed	1 / 70 (1.43%)	1 / 70 (1.43%)	11 / 65 (16.92%)
occurrences (all)	4	1	42
Local reaction			
subjects affected / exposed	7 / 70 (10.00%)	12 / 70 (17.14%)	0 / 65 (0.00%)
occurrences (all)	8	19	0
Pyrexia			

subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	3 / 65 (4.62%)
occurrences (all)	0	0	3
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 70 (1.43%)	1 / 70 (1.43%)	2 / 65 (3.08%)
occurrences (all)	1	1	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	4 / 65 (6.15%)
occurrences (all)	0	0	5
Cough			
subjects affected / exposed	0 / 70 (0.00%)	5 / 70 (7.14%)	5 / 65 (7.69%)
occurrences (all)	0	6	5
Rhinitis allergic			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	4 / 65 (6.15%)
occurrences (all)	0	1	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	6 / 65 (9.23%)
occurrences (all)	1	0	9
Gastroenteritis			
subjects affected / exposed	1 / 70 (1.43%)	1 / 70 (1.43%)	2 / 65 (3.08%)
occurrences (all)	1	1	3
Nasopharyngitis			
subjects affected / exposed	8 / 70 (11.43%)	9 / 70 (12.86%)	19 / 65 (29.23%)
occurrences (all)	8	10	32
Pharyngitis			

subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	4 / 65 (6.15%)
occurrences (all)	2	2	5
Sinusitis			
subjects affected / exposed	2 / 70 (2.86%)	3 / 70 (4.29%)	3 / 65 (4.62%)
occurrences (all)	2	3	3
Tonsillitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 65 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Pollen extract (Core and Extension - 2007) + Placebo (Core)	Pollen extract (Core and Extension-2008) + Omalizumab	Pollen extract (Core and Extension - 2008) + Placebo (Core)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 63 (53.97%)	32 / 59 (54.24%)	26 / 55 (47.27%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 63 (3.17%)	4 / 59 (6.78%)	4 / 55 (7.27%)
occurrences (all)	8	4	10
General disorders and administration site conditions			
Application site reaction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	10 / 63 (15.87%)	5 / 59 (8.47%)	8 / 55 (14.55%)
occurrences (all)	33	37	36
Local reaction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 59 (1.69%)	3 / 55 (5.45%)
occurrences (all)	0	1	3
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	2 / 63 (3.17%)	3 / 59 (5.08%)	1 / 55 (1.82%)
occurrences (all)	2	5	1
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	4 / 63 (6.35%)	0 / 59 (0.00%)	2 / 55 (3.64%)
occurrences (all)	4	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 63 (1.59%)	0 / 59 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 63 (7.94%)	0 / 59 (0.00%)	6 / 55 (10.91%)
occurrences (all)	7	0	8
Cough			
subjects affected / exposed	4 / 63 (6.35%)	6 / 59 (10.17%)	2 / 55 (3.64%)
occurrences (all)	4	6	2
Rhinitis allergic			
subjects affected / exposed	5 / 63 (7.94%)	1 / 59 (1.69%)	3 / 55 (5.45%)
occurrences (all)	5	1	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 63 (4.76%)	3 / 59 (5.08%)	5 / 55 (9.09%)
occurrences (all)	5	4	6
Gastroenteritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	4
Nasopharyngitis			
subjects affected / exposed	14 / 63 (22.22%)	19 / 59 (32.20%)	12 / 55 (21.82%)
occurrences (all)	24	27	19
Pharyngitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 59 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
Rhinitis			
subjects affected / exposed	7 / 63 (11.11%)	1 / 59 (1.69%)	2 / 55 (3.64%)
occurrences (all)	12	1	2

Sinusitis			
subjects affected / exposed	2 / 63 (3.17%)	6 / 59 (10.17%)	4 / 55 (7.27%)
occurrences (all)	3	7	5
Tonsillitis			
subjects affected / exposed	4 / 63 (6.35%)	3 / 59 (5.08%)	2 / 55 (3.64%)
occurrences (all)	5	3	2

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