

**Clinical trial results:**

A phase IIIB trial investigating 3-year treatment efficacy, tolerability and safety of Grazax in children aged 5-18 years with grass pollen induced rhinoconjunctivitis with/without controlled asthma (three consecutive pollen seasons treatment)

Summary

EudraCT number	2009-014923-22
Trial protocol	IT
Global end of trial date	31 December 2014

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	26 July 2015

Trial information**Trial identification**

Sponsor protocol code	GT-23
-----------------------	-------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ALK-Abellò S.p.A
Sponsor organisation address	Via Settembrini, 29, LAINATE, Italy, 20020
Public contact	Global Clinical Development, ALK, 45 45747576, ClinicalTrials@alk.net
Scientific contact	Global Clinical Development, ALK, 45 45747576, ClinicalTrials@alk.net

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	31 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2014
Global end of trial reached?	Yes
Global end of trial date	31 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the 3 years efficacy, tolerability, safety of specific immunotherapy with Grazax compared to placebo on the top of rescue allergic symptomatic drugs in children with grass pollen induced rhinoconjunctivitis with or without controlled or partly controlled asthma.

Protection of trial subjects:

Rescue medication allowed, safety monitoring

Background therapy:

As required by the underlying clinical conditions (allergic rhinitis with or without allergic asthma)

Evidence for comparator:

N/A. Placebo comparator

Actual start date of recruitment	03 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 68
Worldwide total number of subjects	68
EEA total number of subjects	68

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)	48
Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Children were recruited in 11 different sites in Italy. The patients were recruited either prior to the 2010 grass pollen season or prior to the 2011 grass pollen season.

Period 1

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

Blinding implementation details:

Placebo and active treatment were identical in colour, taste and appearance

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Sublingual use

Dosage and administration details:

One tablet per day; the tablet should be taken from the blister unit with dry fingers, and placed under the tongue, where it will disperse.

Swallowing should be avoided for about 1 minute. Food and beverage should not be taken for the following 5 minutes.

Arm title	Grazax
Arm description:	
Active treatment	
Arm type	Experimental
Investigational medicinal product name	Grazax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Sublingual use

Dosage and administration details:

One tablet per day; the tablet should be taken from the blister unit with dry fingers, and placed under the tongue, where it will disperse.

Swallowing should be avoided for about 1 minute. Food and beverage should not be taken for the following 5 minutes.

Number of subjects in period 1	Placebo	Grazax
Started	35	33
Completed	26	27
Not completed	9	6
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	1
Never received IMP	2	-
Amendment not approved by local EC	2	2
Lost to follow-up	1	-
history of anaphylaxis	1	-
Lack of efficacy	1	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Grazax
Reporting group description:	
Active treatment	

Reporting group values	Placebo	Grazax	Total
Number of subjects	35	33	68
Age categorical			
Units: Subjects			
Children (2-11 years)	25	23	48
Adolescents (12-17 years)	10	10	20
Age continuous			
Units: years			
arithmetic mean	9.6	9.7	
standard deviation	± 3.5	± 3.4	-
Gender categorical			
Units: Subjects			
Female	11	9	20
Male	24	24	48

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Grazax
Reporting group description: Active treatment	

Primary: IMP-related AEs

End point title	IMP-related AEs ^[1]
End point description: Adverse events with possible causal relationship to IMP	
End point type	Primary
End point timeframe: From randomisation to end of trial	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: GT-23 was changed to a safety and tolerability trial for two reasons: 1) after the first two years of recruitment, the sample size was underpowered to make any statistical analysis of endpoints originally chosen; 2) patients were recruited and studied in each site in different pollen seasons (2010, 2011, and 2012; or 2011, 2012, and 2013), thus exposing them to different pollen counts. Thus not formal statistical analyses was carried out and the primary endpoint was merely descriptive.

End point values	Placebo	Grazax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: events	2	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Severe AE

End point title	Severe AE
End point description: Adverse events assessed as severe	
End point type	Secondary
End point timeframe: From randomisation to end of trial	

End point values	Placebo	Grazax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: events	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Global evaluation

End point title	Global evaluation
End point description:	In subjects opinion, 'much better' season than before treatment
End point type	Secondary
End point timeframe:	3rd treatment year/grass pollen season

End point values	Placebo	Grazax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26 ^[2]	27 ^[3]		
Units: percent of subjects				
number (not applicable)	3.8	25.9		

Notes:

[2] - All subjects continuing in year 3

[3] - All subjects continuing in year 3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from randomisation to end of trial (March 2010 to June 2014)

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.0
--------------------	------

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Reporting group title	Grazax
-----------------------	--------

Reporting group description: -

Serious adverse events	Placebo	Grazax	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	1 / 33 (3.03%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 35 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Grazax	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 35 (2.86%)	5 / 33 (15.15%)	
Gastrointestinal disorders			
Lip pruritus			
subjects affected / exposed	0 / 35 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	3	
Respiratory, thoracic and mediastinal disorders			
Throat irritation			

subjects affected / exposed	1 / 35 (2.86%)	3 / 33 (9.09%)	
occurrences (all)	1	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2012	Changed with amendment-1 from phase IIIB efficacy study to safety study for 2 reasons: firstly, after the first two years of recruitment, the sample size was underpowered to make any statistical analysis of endpoints originally chosen; secondly, patients were recruited and studied in each Centre in different pollen seasons (2010, 2011, and 2012; or 2011, 2012, and 2013), thus exposing them to different pollen counts.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA

Notes: