Clinical trial results:
An open trial to assess the tolerability of AVANZ® Cupressus immunotherapy

Summary

EudraCT number	2013-004720-11
Trial protocol	ES
Global end of trial date	11 January 2016

Results information

Result version number	v1 (current)
This version publication date	20 July 2016
First version publication date	20 July 2016

Trial information

Trial identification

Sponsor protocol code	AV-X-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02069535
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ALK-Abelló S.A.
Sponsor organisation address	Miguel Fleta, 19, Madrid, Spain, 28037
Public contact	clinicaltrials@alk.net, ALK-Abelló S.A., 0034 913276127, clinicaltrials@alk.net
Scientific contact	clinicaltrials@alk.net, ALK-Abelló S.A., 0034 913276127, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 May 2015
Global end of trial reached?	Yes
Global end of trial date	11 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the tolerability of the up-dosing phase of AVANZ® Cupressus arizonica.

Protection of trial subjects:

Safety surveillance, use of symptomatic medication allowed. Telephone contact within 48h after IMP administration

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2014
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	Spain: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	0
Adults (18-64 years)	52
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited inSpain

Pre-assignment

Screening details:

The trial population comprises adults suffering from allergic rhinoconjunctivitis with or without asthma due to sensitisation to Cupressus arizonica pollen.

Period 1

Period 1 title	Visit 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ACTIVE TREATMENT

Arm description:

AVANZ Cupressus arizonica, updosing treatment (5step) 1 maintenance dose

Arm type	Experimental
Investigational medicinal product name	AVANZ Cupressus arizonica
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Weekly administration dose during up-dosing phase until reach the administration dose of 15000SQ+.

Number of subjects in period 1	ACTIVE TREATMENT
Started	52
Completed	50
Not completed	2
Adverse event, non-fatal	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Visit 1
Reporting group description: -	

Reporting group values	Visit 1	Total	
Number of subjects	52	52	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	52	52	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	31	31	
Male	21	21	

Subject analysis sets	
Subject analysis set title	VISIT 1
Subject analysis set type	Full analysis
Subject analysis set description: Subjects treated	
Subject analysis set title	Visit 6
Subject analysis set type	Per protocol
Subject analysis set description: Subjects who completed the clinical trial visits. Visit 6	

Reporting group values	VISIT 1	Visit 6	
Number of subjects	52	50	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	52	50	

From 65-84 years	0	0	
85 years and over	0	0	

Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	ACTIVE TREATMENT
Reporting group description:	
AVANZ Cupressus arizonica, updosing treatment (5step) 1 maintenance dose	
Subject analysis set title	VISIT 1
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects treated	
Subject analysis set title	Visit 6
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects who completed the clinical trial visits. Visit 6	

Primary: Frequency of subjects with adverse drug reaction

End point title	Frequency of subjects with adverse drug reaction[1]
End point description:	

End point type	Primary
End point timeframe:	
6 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical analysis provided for Frequency of Subjects with Adverse event Drug Reaction

End point values	ACTIVE TREATMENT			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Frequency				
number (confidence interval 95%)				
Mild	76.9 (63.2 to 87.5)			
Moderate	11.5 (4.4 to 23.4)			
Severe	1.9 (0 to 10.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of subjects with systemic reaction

End point title	Frequency of subjects with systemic reaction
End point description:	

End point type	Secondary

End point timeframe:
6 weeks

End point values	ACTIVE TREATMENT			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Frequency				
arithmetic mean (confidence interval 95%)	9.6 (3.2 to 21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in IgG4 for Cupressus arizonica

End point title	Change in IgG4 for Cupressus arizonica

End point description:

End point type	Secondary

End point timeframe:
6 weeks

End point values	VISIT 1	Visit 6		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: mA/L				
median (standard deviation)	0.03 (± 0.08)	0.19 (± 0.83)		

Statistical analyses

Statistical analysis title	Change in IgG4 Cupressus arizonica

Statistical analysis description:
Increase in IgG4 Cupressus arizonica

Comparison groups	Visit 6 v VISIT 1

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.01
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.56
Variability estimate	Standard deviation

Secondary: Change in IgE for Cupressus arizonica

End point title	Change in IgE for Cupressus arizonica
End point description:	
End point type	Secondary
End point timeframe:	
6 weeks	

End point values	VISIT 1	Visit 6		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: ku/L				
median (standard deviation)	8.13 (± 17.85)	25.16 (± 30.98)		

Statistical analyses

Statistical analysis title	Increase in IgE Cupressus arizonica
Comparison groups	VISIT 1 v Visit 6
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	19.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	13.24
upper limit	25.18
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 weeks	
Adverse event reporting additional description:	
From the first trial related activity after the subject signed the informed consent until the follow up telephone contact	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 52 (76.92%)		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	15		
General disorders and administration site conditions			
Injection site pruritus			
subjects affected / exposed	14 / 52 (26.92%)		
occurrences (all)	25		
Injection site reaction			
subjects affected / exposed	31 / 52 (59.62%)		
occurrences (all)	62		

Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all)	 3 / 52 (5.77%) 4		
Respiratory, thoracic and mediastinal disorders Rhinitis allergic subjects affected / exposed occurrences (all)	 5 / 52 (9.62%) 7		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Pruritus generalised subjects affected / exposed occurrences (all)	 4 / 52 (7.69%) 4 3 / 52 (5.77%) 3		

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