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

Summary

EudraCT number	2013-001728-20
Trial protocol	ES
Global end of trial date	31 October 2014

Results information

Result version number	v1 (current)
This version publication date	21 July 2016
First version publication date	21 July 2016

Trial information

Trial identification

Sponsor protocol code	AV-X-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02065856
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	Departamento Médico, ALK-Abelló S. A., +34 913276127NA, clinicaltrials@alk.net
Scientific contact	Departamento Médico, ALK-Abelló S. A., +34 913276127NA, 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	05 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2014
Global end of trial reached?	Yes
Global end of trial date	31 October 2014
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® Salsola kali. The frequency of patients with investigational medicinal product (IMP)-related adverse events (AEs) will be the primary endpoint.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 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: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	51
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in Spain

Pre-assignment

Screening details:

The subjects eligible for the trial were adults with a clinical history of Salsola kali pollen induced allergic rhinoconjunctivitis with or without asthma at least one year prior to trial entry, a positive skin prick test (SPT) to Salsola kali pollen, and a positive specific IgE against Salsola kali pollen (≥ IgE class 2; ≥0.70 KU/L).

Period 1

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

Blinding implementation details:

Trial is one arm only

Arms

Arm title	ACTIVE TREATMENT

Arm description:

AVANZ Salsola kali, updosing treament (5 step) and 1 maintenance dose.

Arm type	Experimental
Investigational medicinal product name	AVANZ Salsola kali
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 15000 SQ+.

Number of subjects in period 1	ACTIVE TREATMENT
Started	51
Completed	51

Baseline characteristics

Reporting groups

Reporting group title	Visit 1

Reporting group description: -

Reporting group values	Visit 1	Total	
Number of subjects	51	51	
Age categorical			
The trial population included had a mean age of 36 years.			
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)	51	51	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	36		
standard deviation	± 10.7	-	
Gender categorical			
Overall the trial population included 27 (52.9%) women and 24 (47.1%) men			
Units: Subjects			
Female	27	27	
Male	24	24	

Subject analysis sets

Subject analysis set title	AVANZ Salsola
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 performed visit 6

Reporting group values	AVANZ Salsola	Visit 6	
Number of subjects	51	50	
Age categorical			
The trial population included had a mean age of 36 years.			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	51		
Age continuous Units: years arithmetic mean standard deviation	±	±	
Gender categorical			
Overall the trial population included 27 (52.9%) women and 24 (47.1%) men			
Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	ACTIVE TREATMENT
Reporting group description: AVANZ Salsola kali, updosing treament (5 step) and 1 maintenance dose.	
Subject analysis set title	AVANZ Salsola
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 performed visit 6	

Primary: Frequency of Subject with adverse drug reaction

End point title	Frequency of Subject with adverse drug reaction[1]
End point description: Frequency of patients with adverse drug reactions, local or systemic	
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 provide fro Frequency of Subjects with Adverse Drug Reactions

End point values	AVANZ Salsola			
Subject group type	Subject analysis set			
Number of subjects analysed	51			
Units: Frequency				
number (confidence interval 95%)				
Mild	68.6 (54.1 to 80.9)			
Moderate	7.8 (2.2 to 18.9)			
Severe	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of subjects with systemic reactions

End point title	Frequency of subjects with systemic reactions
End point description: Frequency of patients with systemic reactions, based on EAACI classification: Grade I(mild systemic reaction) to IV(anaphylactic shoc)	
End point type	Secondary

End point timeframe: 6 weeks

End point values	AVANZ Salsola			
Subject group type	Subject analysis set			
Number of subjects analysed	51			
Units: Frequency				
number (confidence interval 95%)	13.7 (5.7 to 26.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in IgG4 for Salsola kali

End point title	Change in IgG4 for Salsola kali
End point description: Increase in IgG4 for Salsola kali from baseline to final	
End point type	Secondary
End point timeframe: 6 weeks	

End point values	AVANZ Salsola	Visit 6		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: mga/L				
median (standard deviation)	0.02 (± 0.18)	0.19 (± 0.62)		

Statistical analyses

Statistical analysis title	Student-t Test
Statistical analysis description: Increase in IgG4 Salsola kali	
Comparison groups	AVANZ Salsola v Visit 6
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.005
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.4
Variability estimate	Standard deviation

Secondary: Change in IgE for Salsola kali

End point title	Change in IgE for Salsola kali
End point description:	
End point type	Secondary
End point timeframe:	
Visit 1 to visit 6	

End point values	AVANZ Salsola	Visit 6		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: ku/L				
median (standard deviation)	5.32 (± 10.92)	11.49 (± 18.03)		

Statistical analyses

Statistical analysis title	Increase in IgE Salsola kali
Comparison groups	AVANZ Salsola 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	8.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.49
upper limit	12.4
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 6 weeks

Adverse event reporting additional description:

From the first trial related activity after the subject signed the informed consent and 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 trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Colitis ulcerative	Additional description: Ulcerative colitis moderate outbreak		
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 51 (90.20%)		
Nervous system disorders			
Headache	Additional description: Headache and Dizziness		
subjects affected / exposed	18 / 51 (35.29%)		
occurrences (all)	33		
General disorders and administration site conditions			

Injection site reaction	Additional description: Injection Site pruritus and Injection site swelling		
subjects affected / exposed	41 / 51 (80.39%)		
occurrences (all)	84		
Eye disorders			
eye pruritus			
subjects affected / exposed	10 / 51 (19.61%)		
occurrences (all)	11		
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic	Additional description: Cough and Sneezing		
subjects affected / exposed	20 / 51 (39.22%)		
occurrences (all)	28		

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