Clinical trial results:
Safety and tolerability of shortened up-dosing with Alutard SQ

Summary

EudraCT number	2017-000971-97
Trial protocol	DE ES
Global end of trial date	22 May 2018

Results information

Result version number	v1 (current)
This version publication date	08 December 2018
First version publication date	08 December 2018

Trial information

Trial identification

Sponsor protocol code	AL-X-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ALK-Abelló A/S
Sponsor organisation address	Bøge Allé 1, Hørsholm, Denmark, 2970
Public contact	Global Pharmacovigilance and Clinical Development, ALK-Abelló A/S, 0045 45747576, clinicaltrials@alk.net
Scientific contact	Global Pharmacovigilance and Clinical Development, ALK-Abelló A/S, 0045 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2018
Global end of trial reached?	Yes
Global end of trial date	22 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the trial is to evaluate the safety and tolerability of a 7-injection up-dosing schedule with Alutard SQ 6-grasses and rye, birch and house dust mite mix compared with the 11-injection up-dosing schedule established for pollen allergens.

Protection of trial subjects:

Safety surveillance and access to rescue medication

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	Germany: 290
Worldwide total number of subjects	341
EEA total number of subjects	341

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)	89
Adults (18-64 years)	252
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subject were recruited from 20 sites in Germany and 7 in Spain

Pre-assignment

Screening details:

Main selection criteria:
Documented clinically relevant history of moderate-to-severe grass pollen, birch pollen or HDM-induced rhinoconjunctivitis with or without controlled asthma despite having received treatment with symptom-relieving medication during the previous 2 grass or birch pollen seasons or 2 years

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Grass-11

Arm description:

Alutard SQ 6 grasses and rye, 11 updosing steps

Arm type	Active comparator
Investigational medicinal product name	Alutard SQ 6 grasses and rye
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

11 updosing steps

Arm title	Grass-7

Arm description:

Alutard SQ 6 grasses and rye, 7 updosing steps

Arm type	Experimental
Investigational medicinal product name	Alutard SQ 6 grasses and rye
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

7 updosing steps

Arm title	Tree-7

Arm description:

Alutard SQ birch, 7 updosing steps

Arm type	Experimental

Investigational medicinal product name	Alutard SQ birch
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
7 updosing steps

Arm title	HDM-7

Arm description:
Alutard SQ house dust mite mix, 7 updosing steps

Arm type	Experimental
Investigational medicinal product name	Alutard SQ HDM mix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
7 updosing steps

Number of subjects in period 1	Grass-11	Grass-7	Tree-7
Started	85	86	87
Completed	79	73	85
Not completed	6	13	2
Consent withdrawn by subject	1	1	-
Reason not given	3	2	1
Adverse event, non-fatal	2	9	-
Lost to follow-up	-	1	1

Number of subjects in period 1	HDM-7
Started	83
Completed	78
Not completed	5
Consent withdrawn by subject	-
Reason not given	2
Adverse event, non-fatal	3
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Grass-11
Reporting group description:	
Alutard SQ 6 grasses and rye, 11 updosing steps	
Reporting group title	Grass-7
Reporting group description:	
Alutard SQ 6 grasses and rye, 7 updosing steps	
Reporting group title	Tree-7
Reporting group description:	
Alutard SQ birch, 7 updosing steps	
Reporting group title	HDM-7
Reporting group description:	
Alutard SQ house dust mite mix, 7 updosing steps	

Reporting group values	Grass-11	Grass-7	Tree-7
Number of subjects	85	86	87
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	22	23	21
Adults (18-64 years)	63	63	66
From 65-84 years	0	0	0
85 years and over	0	0	0
Age	0	0	0
Gender categorical Units: Subjects			
Female	42	44	44
Male	43	42	43

Reporting group values	HDM-7	Total	
Number of subjects	83	341	
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)	23	89	
Adults (18-64 years)	60	252	

From 65-84 years	0	0	
85 years and over	0	0	
Age	0	0	
Gender categorical Units: Subjects			
Female	43	173	
Male	40	168	

End points

End points reporting groups

Reporting group title	Grass-11
Reporting group description: Alutard SQ 6 grasses and rye, 11 updosing steps	
Reporting group title	Grass-7
Reporting group description: Alutard SQ 6 grasses and rye, 7 updosing steps	
Reporting group title	Tree-7
Reporting group description: Alutard SQ birch, 7 updosing steps	
Reporting group title	HDM-7
Reporting group description: Alutard SQ house dust mite mix, 7 updosing steps	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description: All subjects included	

Primary: All treatment-related adverse events

End point title	All treatment-related adverse events[1]
End point description:	
End point type	Primary
End point timeframe: Entire 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: This was a safety trial with no formal statistical analysis planned. Only descriptive analyses were planned for the primary endpoint.

End point values	Grass-11	Grass-7	Tree-7	HDM-7
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	85[2]	87	83
Units: events	711	561	444	446

Notes:

[2] - 1 subject not treated

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire trial (only treatment emergent adverse events)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Grass-11
Reporting group description:	
Alutard SQ 6 grasses and rye, 11 updosing steps	
Reporting group title	Grass-7
Reporting group description:	
Alutard SQ 6 grasses and rye, 7 updosing steps	
Reporting group title	Tree-7
Reporting group description:	
Alutard SQ birch, 7 updosing steps	
Reporting group title	HDM-7
Reporting group description:	
Alutard SQ house dust mite mix, 7 updosing steps	

Serious adverse events	Grass-11	Grass-7	Tree-7
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 85 (4.71%)	2 / 85 (2.35%)	0 / 87 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	2 / 85 (2.35%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic shock			

subjects affected / exposed	1 / 85 (1.18%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 85 (1.18%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	HDM-7		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 83 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaphylactic shock			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Grass-11	Grass-7	Tree-7
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 85 (85.88%)	79 / 85 (92.94%)	75 / 87 (86.21%)
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 85 (14.12%)	16 / 85 (18.82%)	15 / 87 (17.24%)
occurrences (all)	22	31	26
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	42 / 85 (49.41%)	35 / 85 (41.18%)	41 / 87 (47.13%)
occurrences (all)	188	127	113
Injection site oedema			
subjects affected / exposed	2 / 85 (2.35%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences (all)	2	1	0
Injection site pain			
subjects affected / exposed	13 / 85 (15.29%)	8 / 85 (9.41%)	7 / 87 (8.05%)
occurrences (all)	16	12	8
Injection site pruritus			
subjects affected / exposed	39 / 85 (45.88%)	43 / 85 (50.59%)	41 / 87 (47.13%)
occurrences (all)	178	132	118
Injection site swelling			
subjects affected / exposed	49 / 85 (57.65%)	49 / 85 (57.65%)	41 / 87 (47.13%)
occurrences (all)	238	165	129
Injection site warmth			
subjects affected / exposed	7 / 85 (8.24%)	4 / 85 (4.71%)	3 / 87 (3.45%)
occurrences (all)	25	17	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 85 (2.35%)	6 / 85 (7.06%)	2 / 87 (2.30%)
occurrences (all)	2	6	2
Nasal congestion			
subjects affected / exposed	3 / 85 (3.53%)	5 / 85 (5.88%)	5 / 87 (5.75%)
occurrences (all)	3	5	7
Oropharyngeal pain			
subjects affected / exposed	5 / 85 (5.88%)	7 / 85 (8.24%)	4 / 87 (4.60%)
occurrences (all)	6	7	5

Throat irritation			
subjects affected / exposed	1 / 85 (1.18%)	2 / 85 (2.35%)	5 / 87 (5.75%)
occurrences (all)	1	2	20
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 85 (1.18%)	5 / 85 (5.88%)	0 / 87 (0.00%)
occurrences (all)	1	5	0
Pruritus			
subjects affected / exposed	1 / 85 (1.18%)	5 / 85 (5.88%)	5 / 87 (5.75%)
occurrences (all)	1	9	5
Urticaria			
subjects affected / exposed	6 / 85 (7.06%)	9 / 85 (10.59%)	1 / 87 (1.15%)
occurrences (all)	11	12	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 85 (17.65%)	15 / 85 (17.65%)	13 / 87 (14.94%)
occurrences (all)	20	18	17
Respiratory tract infection			
subjects affected / exposed	5 / 85 (5.88%)	4 / 85 (4.71%)	0 / 87 (0.00%)
occurrences (all)	6	5	0
Rhinitis			
subjects affected / exposed	2 / 85 (2.35%)	7 / 85 (8.24%)	4 / 87 (4.60%)
occurrences (all)	2	9	4

Non-serious adverse events	HDM-7		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 83 (89.16%)		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 83 (20.48%)		
occurrences (all)	28		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	45 / 83 (54.22%)		
occurrences (all)	111		
Injection site oedema			

subjects affected / exposed	6 / 83 (7.23%)		
occurrences (all)	7		
Injection site pain			
subjects affected / exposed	12 / 83 (14.46%)		
occurrences (all)	19		
Injection site pruritus			
subjects affected / exposed	48 / 83 (57.83%)		
occurrences (all)	129		
Injection site swelling			
subjects affected / exposed	49 / 83 (59.04%)		
occurrences (all)	142		
Injection site warmth			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	3 / 83 (3.61%)		
occurrences (all)	6		
Throat irritation			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	3		
Urticaria			

subjects affected / exposed occurrences (all)	1 / 83 (1.20%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Respiratory tract infection subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all)	 13 / 83 (15.66%) 15 5 / 83 (6.02%) 6 4 / 83 (4.82%) 5		

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