



Clinical trial results: A Dose Response Evaluation of SLIToneULTRA HDM Mix Immunotherapy Summary

EudraCT number	2012-002177-62
Trial protocol	ES
Global end of trial date	04 September 2013

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	SU-M-01
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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 Clinical Development, ALK-Abelló A/S, +45 45747576, ClinicalTrials@alk.net
Scientific contact	Global Clinical Development, ALK-Abelló A/S, +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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 September 2013
Global end of trial reached?	Yes
Global end of trial date	04 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the dose-response relationship with regards to change in immunological parameters and safety for SLIToneULTRA house dust mite (HDM) mix in adult subjects with moderate to severe HDM allergic rhinitis.

Protection of trial subjects:

Safety surveillance, use of symptomatic medications allowed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2012
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: 91
Country: Number of subjects enrolled	France: 128
Worldwide total number of subjects	219
EEA total number of subjects	219

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)	218
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in France and Spain

Pre-assignment

Screening details:

The subjects eligible for the trial were adults with HDM allergic rhinitis. The clinical history was consistent with moderate to severe persistent HDM allergic rhinitis with or without asthma, with allergic rhinitis symptoms despite having received symptomatic treatment of at least one year prior to trial entry.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	50 SRU

Arm description:

No updosing

Maintenance: 50 SRU/day

Arm type	Active comparator
Investigational medicinal product name	SLIToneULTRA HDM mix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Sublingual use

Dosage and administration details:

The solution was to be administered once daily. The solution was to be placed under the tongue (sublingual) and kept there for 2 minutes before swallowing. Eating and drinking was to be avoided for the next 5 minutes.

Arm title	150 SRU
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Arm description:

Updosing for 5 days: 50 SRU/day

Maintenance for the rest of the trial: 150 SRU/day

Arm type	Active comparator
Investigational medicinal product name	SLIToneULTRA HDM mix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Sublingual use

Dosage and administration details:

The solution was to be administered once daily. The solution was to be placed under the tongue (sublingual) and kept there for 2 minutes before swallowing. Eating and drinking was to be avoided for the next 5 minutes.

Arm title	300 SRU
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Arm description:

Updosing: 50 SRU/day for 5 days, then 150 SRU/day for 5 days

Maintenance for the rest of the trial: 300 SRU/day

Arm type	Active comparator
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Investigational medicinal product name	SLIToneULTRA HDM mix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Sublingual use

Dosage and administration details:

The solution was to be administered once daily. The solution was to be placed under the tongue (sublingual) and kept there for 2 minutes before swallowing. Eating and drinking was to be avoided for the next 5 minutes.

Number of subjects in period 1	50 SRU	150 SRU	300 SRU
Started	73	73	73
Completed	67	65	64
Not completed	6	8	9
Consent withdrawn by subject	1	-	-
Lost to follow-up	3	-	-
Adverse event, non-fatal	2	3	5
Pregnancy	-	1	-
Lost to follow-up	-	2	2
Other causes, not specified	-	2	-
Protocol deviation	-	-	2

Baseline characteristics

Reporting groups

Reporting group title	50 SRU
Reporting group description:	
No updosing	
Maintenance: 50 SRU/day	
Reporting group title	150 SRU
Reporting group description:	
Updosing for 5 days: 50 SRU/day	
Maintenance for the rest of the trial: 150 SRU/day	
Reporting group title	300 SRU
Reporting group description:	
Updosing: 50 SRU/day for 5 days, then 150 SRU/day for 5 days	
Maintenance for the rest of the trial: 300 SRU/day	

Reporting group values	50 SRU	150 SRU	300 SRU
Number of subjects	73	73	73
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)	0	0	0
Adults (18-64 years)	73	73	72
From 65-84 years	0	0	1
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	32	32	32
standard deviation	± 10	± 9	± 10
Gender categorical			
Units: Subjects			
Female	41	39	38
Male	32	34	35

Reporting group values	Total		
Number of subjects	219		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	218		
From 65-84 years	1		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	118		
Male	101		

End points

End points reporting groups

Reporting group title	50 SRU
Reporting group description: No updosing Maintenance: 50 SRU/day	
Reporting group title	150 SRU
Reporting group description: Updosing for 5 days: 50 SRU/day Maintenance for the rest of the trial: 150 SRU/day	
Reporting group title	300 SRU
Reporting group description: Updosing: 50 SRU/day for 5 days, then 150 SRU/day for 5 days Maintenance for the rest of the trial: 300 SRU/day	

Primary: Change in IgE-blocking factor for Dermatophagoides pteronyssinus

End point title	Change in IgE-blocking factor for Dermatophagoides pteronyssinus
End point description: Change in IgE-blocking factor for Dermatophagoides pteronyssinus from baseline to end-of-trial using Last Observation Carried Forward (LOCF) for missing data	
End point type	Primary
End point timeframe: Baseline to visit 4 (6 months)	

End point values	50 SRU	150 SRU	300 SRU	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73 ^[1]	70 ^[2]	72 ^[3]	
Units: kU/l				
arithmetic mean (standard deviation)	0.09 (± 0.15)	0.14 (± 0.19)	0.17 (± 0.17)	

Notes:

[1] - All subjects with valid samples

[2] - All subjects with valid samples

[3] - All subjects with valid samples

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description: Changes in IgE-blocking factor were assessed using Analysis of Covariance (ANCOVA) including group as factor and baseline IgE-blocking testing the hypothesis of no difference between doses with respect to IgE-blocking factor	
Comparison groups	50 SRU v 150 SRU v 300 SRU

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	= 0.0152 ^[5]
Method	ANCOVA

Notes:

[4] - Test for overall difference between groups

[5] - Significant overall difference between doses

Statistical analysis title	Primary analysis
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Statistical analysis description:

Pairwise comparison of 50 SRU and 300 SRU

Comparison groups	50 SRU v 300 SRU
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0075 ^[6]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.06999

Confidence interval

level	95 %
sides	2-sided
lower limit	-0.1211
upper limit	-0.01886
Variability estimate	Standard deviation

Notes:

[6] - Significantly superior change in 300 SRU versus 50 SRU

Statistical analysis title	Primary analysis
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Statistical analysis description:

Pairwise comparison of 150 SRU and 300 SRU

Comparison groups	300 SRU v 150 SRU
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0602 ^[7]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.04951

Confidence interval

level	95 %
sides	2-sided
lower limit	-0.1012
upper limit	0.0021
Variability estimate	Standard deviation

Notes:

[7] - Not statistically significantly difference between 300 SRU and 150 SRU

Statistical analysis title	Primary analysis
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Statistical analysis description:

Pairwise comparison of 50 SRU and 150 SRU

Comparison groups	150 SRU v 50 SRU
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4342 ^[8]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.02048
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0702
upper limit	0.03105
Variability estimate	Standard deviation

Notes:

[8] - Not statistically significantly difference between 50 SRU and 150 SRU

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 6 months

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	50 SRU
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Reporting group description:

No up dosing

Maintenance: 50 SRU/day

Reporting group title	150 SRU
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Reporting group description:

Up dosing for 5 days: 50 SRU/day

Maintenance for the rest of the trial: 150 SRU/day

Reporting group title	300 SRU
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Reporting group description:

Up dosing: 50 SRU/day for 5 days, then 150 SRU/day for 5 days

Maintenance for the rest of the trial: 300 SRU/day

Serious adverse events	50 SRU	150 SRU	300 SRU
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 73 (1.37%)	1 / 73 (1.37%)	0 / 73 (0.00%)
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)			
Uterine leiomyoma			
subjects affected / exposed	1 / 73 (1.37%)	0 / 73 (0.00%)	0 / 73 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 73 (0.00%)	1 / 73 (1.37%)	0 / 73 (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	50 SRU	150 SRU	300 SRU
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 73 (49.32%)	36 / 73 (49.32%)	41 / 73 (56.16%)
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	4 / 73 (5.48%)	1 / 73 (1.37%)	1 / 73 (1.37%)
occurrences (all)	4	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 73 (2.74%)	4 / 73 (5.48%)	4 / 73 (5.48%)
occurrences (all)	4	9	5
Gastrointestinal disorders			
Oral pruritus			
subjects affected / exposed	10 / 73 (13.70%)	11 / 73 (15.07%)	17 / 73 (23.29%)
occurrences (all)	12	12	18
Tongue pruritus			
subjects affected / exposed	6 / 73 (8.22%)	3 / 73 (4.11%)	5 / 73 (6.85%)
occurrences (all)	6	3	5
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	4 / 73 (5.48%)	7 / 73 (9.59%)	5 / 73 (6.85%)
occurrences (all)	4	9	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

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

NA

Notes: