Clinical trial results:
Open multicenter clinical trial to confirm the maximum no reactive dose of allergoid of polymerized Dermatophagoides pteronyssinus, in patients with allergic rhinoconjunctivitis or mild or moderate ashtma, who are sensitive to Dermatophagoides pteronyssinus

Summary

EudraCT number	2014-004429-42
Trial protocol	ES
Global end of trial date	07 October 2015

Results information

Result version number	v1 (current)
This version publication date	26 January 2019
First version publication date	26 January 2019

Trial information

Trial identification

Sponsor protocol code	DIA-Der-02-14

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Diater Laboratorio de Diagnóstico y Aplicaciones Terapéuticas, S.A.
Sponsor organisation address	Avenida Gregorio Peces Barba, 2, Leganes / Madrid, Spain, 28918
Public contact	Medical department, Diater Laboratorio de Diagnósticos y Aplicaciones Terapéuticas, S.A., 0034 914966013, departamento.medico@diater.com
Scientific contact	Medical Department, Diater Laboratorio de Diagnósticos y Aplicaciones Terapéuticas, S.A., 0034 914966013, departamento.medico@diater.com

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	30 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 October 2015
Global end of trial reached?	Yes
Global end of trial date	07 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the maximum non- reactive dose of Polymerized Dermatophagoides pteronyssinus, administered intradermally

Protection of trial subjects:

subjects should stay under medical surveillance in the center at least 60 minutes after drug administration . Additionally subjects received a telephone call from the investigator team 24 hours later the administration to register and assess any potential late adverse event

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 May 2015
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: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

all patients recruited completed the study

Pre-assignment

Screening details:

Positive levels of IgE antibodies against Dermatophagoides pteronyssinus in the previous year to inclusión was considered valid.
Wash-out period for : Antihistamines: 7 days. Short-acting beta-2 adrenergics: 4 hours. Long-acting beta-2 adrenergics: 12 hours. Antileukotrienes: 24 hours, inhaled corticosteroids: 12 hours, chromones: 24 hours

Period 1

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

Blinding implementation details:

Given that all efficacy study endpoints are objectively measured and can not be modified by either subject or investigator , blinding was considered no necessary for this study.

Arms

Arm title	Der p pol

Arm description:

Polymerized Dermatophagoides pteronisynuss at 4 different doses: 0.001 , 0.01 , 0.1 and 1 mg/ml

Arm type	Experimental
Investigational medicinal product name	Polymerized Dermatophagoides pteronyssinus
Investigational medicinal product code	Der p pol
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

4 different concentrations (0.001, 0.01, 0.1 and 1 mcg/mL) of the IMP was administered to each single patient . Dose of each concentrarion was 0.1 ml

Number of subjects in period 1	Der p pol
Started	40
Completed	40

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	40	40	
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)	40	40	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	28.38		
standard deviation	± 7.86	-	
Gender categorical Units: Subjects			
Female	23	23	
Male	17	17	
Study disease Units: Subjects			
Rhinits and/or Rhinoconjunctivits with asthma	32	32	
Rhinitis/Rhinconjunctivitis w/ asthma not reported	8	8	

Subject analysis sets

Subject analysis set title	Per protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The statistical acceptance criteria for eligible subjects are:
* A regression line of at least 3 concentrations with a correlation coefficient > 0.85.
* A slope of the regression line > 0.1.
* Values obtained after regression within the concentration values used.

Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

all enrolled subjects receiving at least 3 out of 4 drug concentration tested

Reporting group values	Per protocol	ITT population	
Number of subjects	17	40	
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)	17	40	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	29.71	28.38	
standard deviation	± 8.53	± 7.86	
Gender categorical Units: Subjects			
Female	10	23	
Male	7	17	
Study disease Units: Subjects			
Rhinits and/or Rhinoconjunctivits with asthma	15		
Rhinitis/Rhinconjunctivitis w/ asthma not reported	2		

End points

End points reporting groups

Reporting group title	Der p pol

Reporting group description:

Polymerized Dermatophagoides pteronisynuss at 4 different doses: 0.001 , 0.01 , 0.1 and 1 mg/ml

Subject analysis set title	Per protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The statistical acceptance criteria for eligible subjects are:
* A regression line of at least 3 concentrations with a correlation coefficient > 0.85.
* A slope of the regression line > 0.1.
* Values obtained after regression within the concentration values used.

Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

all enrolled subjects receiving at least 3 out of 4 drug concentration tested

Primary: Maximum non-reactive drug concentration

End point title	Maximum non-reactive drug concentration[1]

End point description:

Maximum non-reactive drug concentration was defined as those concentration inducing a largest wheal diameter equal to 2.9 mm

End point type	Primary

End point timeframe:

Immediately after administration, and 15 minutes after. Largest wheal diameter was calculated by subtracting the initial wheal induced to the final wheal obtained. In the case of obtaining a wheal with the negative control (manitol) it was also subtracted

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: Statistical analyses as required (p-values for group comparisons) is not applicable to calculate the primary endpoint of this study. Instead, a regression line was calculated using the logarithmic values (logarithm to base 10) of the largest wheal size from the 4 IMP doses tested. The logarithmic concentration value inducing a wheal equal to 2.9 mm was calculated by interpolation. This value was thereafter converted into a non-logarithmic value to obtain the final non-reactive concentration

End point values	Per protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: mcg/mL				
arithmetic mean (standard deviation)	0.1 (± 0.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: flare of the wheal

End point title	flare of the wheal

End point description:

Erythema induced by the non-reactive concentration

End point type	Secondary

End point timeframe:

Time of administration and 15 minutes after. Largest erythema diameter was calculated by subtracting the initial wheal induced to the final value obtained . in the case of obtaining an erythema with the negative control (manitol), it was also substracted

End point values	Per protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: mm				
arithmetic mean (standard deviation)	30 (± 8.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: baseline Specific IgE antibodies to native extract

End point title	baseline Specific IgE antibodies to native extract

End point description:

serologic values

End point type	Secondary

End point timeframe:

IgE values were calculated at baseline visit

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: kU/L				
arithmetic mean (standard deviation)	32.64 (± 35.84)	28.41 (± 30.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Final Specific IgE antibodies to native extract

End point title	Final Specific IgE antibodies to native extract

End point description:

serologic values

End point type	Secondary

End point timeframe:
values measured at 30-day follow-up after single drug administration

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: kU/L				
arithmetic mean (standard deviation)	31.33 (± 35.70)	28.08 (± 30.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Specific IgG4 antibodies to native extract

End point title	Baseline Specific IgG4 antibodies to native extract

End point description:
serologic values

End point type	Secondary

End point timeframe:
baseline visit

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: mgA/L				
arithmetic mean (standard deviation)	0.64 (± 0.73)	0.57 (± 0.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Final Specific IgG4 antibodies to native extract

End point title	Final Specific IgG4 antibodies to native extract

End point description:
serologic values

End point type	Secondary

End point timeframe:
Measured at final visit (30-day follow-up)

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: mgA/L				
arithmetic mean (standard deviation)	0.65 (± 0.85)	0.56 (± 0.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Specific IgE antibodies to Der p 1

End point title	Baseline Specific IgE antibodies to Der p 1
End point description: serologic values	
End point type	Secondary
End point timeframe: Measure at baseline visit	

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: kU/L				
arithmetic mean (standard deviation)	18.1 (± 26.91)	15.17 (± 23.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Final Specific IgE antibodies to Der p 1

End point title	Final Specific IgE antibodies to Der p 1
End point description: serologic values	
End point type	Secondary
End point timeframe: Measured at final visit (30-day follow-up)	

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: kU/L				
arithmetic mean (standard deviation)	18.54 (± 28.56)	15.29 (± 24.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Specific IgG4 antibodies to Der p 1

End point title	Baseline Specific IgG4 antibodies to Der p 1
End point description: serologic values	
End point type	Secondary
End point timeframe: baseline visit	

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: mgA/L				
arithmetic mean (standard deviation)	0.17 (± 0.20)	0.14 (± 0.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Final Specific IgG4 antibodies to Der p 1

End point title	Final Specific IgG4 antibodies to Der p 1
End point description: serologic values	
End point type	Secondary
End point timeframe: final visit (30-day follow-up)	

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: mgA/L				
arithmetic mean (standard deviation)	0.17 (± 0.23)	0.13 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Specific IgE antibodies to Der p 2

End point title	Baseline Specific IgE antibodies to Der p 2

End point description:

End point type	Secondary

End point timeframe:

baseline visit before drug administration

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: kU/L				
arithmetic mean (standard deviation)	21.04 (± 28.24)	19.27 (± 25.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Final Specific IgE antibodies to Der p 2

End point title	Final Specific IgE antibodies to Der p 2

End point description:

End point type	Secondary

End point timeframe:

values measured at 30-day follow-up after single drug administration

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: kU/L				
arithmetic mean (standard deviation)	21.60 (± 29.68)	19.56 (± 25.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Specific IgG4 antibodies to Der p 2

End point title	Baseline Specific IgG4 antibodies to Der p 2

End point description:

End point type	Secondary

End point timeframe:

At baseline visit before drug administration

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: mgA/L				
arithmetic mean (standard deviation)	0.17 (± 0.23)	0.16 (± 0.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Final Specific IgG4 antibodies to Der p 2

End point title	Final Specific IgG4 antibodies to Der p 2

End point description:

End point type	Secondary

End point timeframe:

values measured at 30-day follow-up after single drug administration

End point values	Per protocol	ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	40		
Units: mgA/L				
arithmetic mean (standard deviation)	0.16 (± 0.20)	0.16 (± 0.19)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

1 month after study drug administration

Adverse event reporting additional description:

The occurrence of adverse events was to be sought by non-directive questionning of the patient at each visit including 1 phone interview 24 hours after treatment administration. Adverse events also could have been detected when they were volunteered by the patient during or between visits or through physical examination or other assessment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: this is a short- duration study , with a small number of subjects required and a single intradermal drug dose administration . Neither related (local or systemic reactions) nor unrelated adverse events were reported in this study

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