



Clinical trial results:

Extract allergen from Betula verrucosa. Test sensitivity and specificity of diagnostic in prick test preparation.

Summary

EudraCT number	2013-005368-24
Trial protocol	ES
Global end of trial date	30 April 2016

Results information

Result version number	v1 (current)
This version publication date	12 August 2021
First version publication date	12 August 2021
Summary attachment (see zip file)	Summary results (T502-SSP-007_summary of results.pdf)

Trial information

Trial identification

Sponsor protocol code	T502-SSP-007
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02527187
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Inmunotek
Sponsor organisation address	Punto Mobi, 5, Alcalá de Henares, Spain, 28805
Public contact	Miguel Casanovas, Inmunotek, S.L., 34 91290 89 42153, sdelpozo@inmunotek.com
Scientific contact	Miguel Casanovas, Inmunotek, S.L., 34 91290 89 42153, sdelpozo@inmunotek.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	01 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To obtain the optimal birch allergen concentration for in vivo (skin prick test) diagnosis by assessing the Sensitivity and Specificity of 4 different concentrations of the skin prick test preparation of Betula verrucosa.

Protection of trial subjects:

Although skin prick test is a safe and patients were already tested previously in the hospital, more attention was paid to the protection of trial subjects. The investigator took special care in order to check for the presence of any unwanted reaction. Patients remained in the hospital facilities (at least 30 min after test) and were instructed to report, to the investigator, any adverse event occurring after leaving the hospital.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 September 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: 201
Worldwide total number of subjects	201
EEA total number of subjects	201

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)	4
Adolescents (12-17 years)	13
Adults (18-64 years)	179
From 65 to 84 years	5

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Recruitment was performed in the north of Spain, where birch pollen is relevant. All patients were skin prick tested by the same qualified and experienced nurse, between 9AM and 11AM, before birch pollen season to avoid the allergenic stimuli, circadian variations and differences due to the site of performing the test.

Pre-assignment

Screening details:

201 patients enrolled and were eligible and received the IMP

Period 1

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

Arms

Arm title	Treatment arm
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Arm description:

All patients included will receive the IMP, some were already diagnosed as "true allergic" to birch pollen (assigned as CH+) and others were already diagnosed to be "true non-allergic" to birch pollen (assigned as CH-)

CH+ met the following criteria:

- o Clinical history of symptomatology related to the exposure to birch pollen.
- o Previous SPT positive reaction with the extract of *Betula verrucosa* in normal clinical conditions in the hospital.
- o Presence of serum specific IgE (CAP System) to the pollen of *Betula verrucosa*.
- o No immunotherapy treatment with an allergen extract of birch pollen.

CH-met the following criteria:

- o Previous skin prick test negative reaction with the extract of *Betula verrucosa* used in as diagnosis in normal clinical conditions in the hospital.
- o Absence or undetectable serum specific IgE (CAP System) to the pollen extract of *Betula verrucosa*.

Test validation:

A skin prick test reaction is positive when the mean wheal diameter is > 3 mm.

Arm type	Experimental
Investigational medicinal product name	<i>Betula verrucosa</i> 100 HEP/ml allergen extract
Investigational medicinal product code	SUB55247
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Prick test -*Betula verrucosa* at 10,25, 50 and 100 HEP/mL, positive control (histamine dihydrochloride 10mg/mL), negative control (glycerinated phenol saline solution).

Investigational medicinal product name	<i>Betula verrucosa</i> 50 HEP/ml allergen extract/T502/Cutaneous solution
Investigational medicinal product code	SUB55247
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Solution for skin-prick test;drops

Investigational medicinal product name	Betula verrucosa 25 HEP/ml allergen extract/T502/Cutaneous solution
Investigational medicinal product code	SUB55247
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use
Dosage and administration details:	
Solution for skin-prick test; drops	
Investigational medicinal product name	Betula verrucosa 10 HEP/ml allergen extract/T502/Cutaneous solution
Investigational medicinal product code	SUB55247
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use
Dosage and administration details:	
Solution for skin-prick test; drops	
Investigational medicinal product name	Histamine dihydrochloride/Cutaneous solution
Investigational medicinal product code	SUB12022MIG
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use
Dosage and administration details:	
Solution for skin-prick test; drops	
Investigational medicinal product name	Glycerinated phenol saline solution/Negative control/Cutaneous solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use
Dosage and administration details:	
Solution for skin-prick test; drops	

Number of subjects in period 1	Treatment arm
Started	201
Completed	201

Baseline characteristics

Reporting groups

Reporting group title	Treatment arm
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Reporting group description:

All patients included will receive the IMP, some were already diagnosed as "true allergic" to birch pollen (assigned as CH+) and others were already diagnosed to be "true non-allergic" to birch pollen (assigned as CH-)

CH+ met the following criteria:

- o Clinical history of symptomatology related to the exposure to birch pollen.
- o Previous SPT positive reaction with the extract of Betula verrucosa in normal clinical conditions in the hospital.
- o Presence of serum specific IgE (CAP System) to the pollen of Betula verrucosa.
- o No immunotherapy treatment with an allergen extract of birch pollen.

CH-met the following criteria:

- o Previous skin prick test negative reaction with the extract of Betula verrucosa used in as diagnosis in normal clinical conditions in the hospital.
- o Absence or undetectable serum specific IgE (CAP System) to the pollen extract of Betula verrucosa.

Test validation:

A skin prick test reaction is positive when the mean wheal diameter is > 3 mm.

Reporting group values	Treatment arm	Total	
Number of subjects	201	201	
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)	4	4	
Adolescents (12-17 years)	13	13	
Adults (18-64 years)	179	179	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	122	122	
Male	79	79	

Subject analysis sets

Subject analysis set title	Treatment arm
Subject analysis set type	Per protocol

Subject analysis set description:

A total of 201 subjects were all treated. There were no dropouts

Reporting group values	Treatment arm		
Number of subjects	201		
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)	4		
Adolescents (12-17 years)	13		
Adults (18-64 years)	179		
From 65-84 years	5		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Treatment arm
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Reporting group description:

All patients included will receive the IMP, some were already diagnosed as "true allergic" to birch pollen (assigned as CH+) and others were already diagnosed to be "true non-allergic" to birch pollen (assigned as CH-)

CH+ met the following criteria:

- o Clinical history of symptomatology related to the exposure to birch pollen.
- o Previous SPT positive reaction with the extract of Betula verrucosa in normal clinical conditions in the hospital.
- o Presence of serum specific IgE (CAP System) to the pollen of Betula verrucosa.
- o No immunotherapy treatment with an allergen extract of birch pollen.

CH-met the following criteria:

- o o Previous skin prick test negative reaction with the extract of Betula verrucosa used in as diagnosis in normal clinical conditions in the hospital.
- o Absence or undetectable serum specific IgE (CAP System) to the pollen extract of Betula verrucosa.

Test validation:

A skin prick test reaction is positive when the mean wheal diameter is > 3 mm.

Subject analysis set title	Treatment arm
Subject analysis set type	Per protocol

Subject analysis set description:

A total of 201 subjects were all treated. There were no dropouts

Primary: Sensitivity

End point title	Sensitivity ^[1]
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End point description:

It is the proportion of positives that are correctly identified by the test.

The number of patients with a positive skin prick test (X) out of all true positives (CH +; patients with the clinical diagnosis of allergy to the pollen of Betula verrucosa n=75)

2 discrete categories:

- The number of patients with a positive skin prick test (X) with the corresponding concentration (100 HEP)
- All true positives (CH +; patients with the clinical diagnosis of allergy to the pollen of Betula verrucosa n=75)

X/75

End point type	Primary
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End point timeframe:

15 minutes

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: Primary efficacy endpoints were sensitivity and sensibility, score with absolute values are available on the charts attached in this report. No comparative statistics was performed.

End point values	Treatment arm	Treatment arm		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	201	201		
Units: Rate				
number (not applicable)	201	201		

Attachments (see zip file)	Sensitivity 100 HEP/Sensitivity - 100 HEP.pdf
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Statistical analyses

No statistical analyses for this end point

Primary: Specificity

End point title	Specificity ^[2]
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End point description:

It is the proportion of negatives that are correctly identified by the test.

The number of patients with a negative skin prick test (X) out of all true negatives (CH - ; patients with the clinical diagnosis of non-allergic to the pollen of Betula verrucosa n=126)

2 discrete categories:

- The number of patients with a negative skin prick test (X) with the corresponding concentration (100 HEP)
- All true negatives(CH - ; patients with the clinical diagnosis of non-allergic to the pollen of Betula verrucosa n=126)

X/126

End point type	Primary
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End point timeframe:

15 minutes

Notes:

[2] - 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: Primary efficacy endpoints were sensitivity and sensibility, score with absolute values are available on the charts attached in this report. No comparative statistics was performed.

End point values	Treatment arm	Treatment arm		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	201	201		
Units: Score				
number (not applicable)	201	201		

Attachments (see zip file)	Specificity charts/Specificity.pdf
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From screening until 24 hours after

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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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: Not applicable because there were no adverse events.

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.

No limitations or caveats were identified in the trial
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Notes: