



## Clinical trial results:

**A double blind placebo controlled randomised trial to study the effects of birch pollen specific immunotherapy (BP-SIT) on the symptoms of the oral allergy syndrome in adult patients.**

### Summary

EudraCT number	2011-004078-26
Trial protocol	GB
Global end of trial date	03 March 2017

### Results information

Result version number	v1 (current)
This version publication date	05 January 2020
First version publication date	05 January 2020
Summary attachment (see zip file)	OAS Findings Summary (OAS End of study summary signed.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	10/143/FRE
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#### Additional study identifiers

ISRCTN number	ISRCTN01027357
ClinicalTrials.gov id (NCT number)	NCT01431859
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Brighton and Sussex University Hospitals Trust
Sponsor organisation address	Royal Sussex County Hospital Eastern Road, Brighton, United Kingdom, BN2 5BE
Public contact	Mr Scott Harfield, Brighton and Sussex University Hospitals Trust, 044 01273 696955, Scott.Harfield@bsuh.nhs.uk
Scientific contact	Mr Scott Harfield, Brighton and Sussex University Hospitals Trust, 044 01273 696955, Scott.Harfield@bsuh.nhs.uk

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	06 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 March 2017
Global end of trial reached?	Yes
Global end of trial date	03 March 2017
Was the trial ended prematurely?	Yes

Notes:

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**General information about the trial**

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Main objective of the trial:

Does immunotherapy (the process of giving small but increasing doses of birch pollen as injections under the skin) improve symptoms of mouth and throat itch, irritation and swelling on eating apples in patients with oral allergy syndrome?

Protection of trial subjects:

Patients were given full advice and information through the participation information sheet before being asked if they wished to participate in the study and once involved they were asked at each visit whether they wished to continue and were free to withdraw from the study. After treatment the patients were monitored to ensure they were in no distress and all was well before being told that they were free to return home. They were given the contact numbers of the research staff in case they had any queries and also the contact details of the Patient Advice and Liaison Service

Background therapy:

None

Evidence for comparator:

This was a placebo controlled trial. A placebo solution was supplied as a comparator. The placebo preparation used is the verum solution without any added allergen substance, also termed Allergovit diluent.

Actual start date of recruitment	06 August 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	United Kingdom: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

Notes:

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**Subjects enrolled per age group**

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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)	32
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 32 patients were randomised and contributed data. They were recruited at two sites in the UK: Royal Sussex County Hospital, Brighton and Homerton Hospital London between 2012 and 2017

### Pre-assignment

Screening details:

143 patients were screened in Brighton and 16 at Homerton. The lower number at Homerton being due to them having a database which allowed them to pre-identify potential patients.

### Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The active food challenges provided to the patients consisted of a base containing yogurt, orange juice, apple juice, processed apple sauce and oatflakes, to which aliquots of freshly shredded apple are added. Each meal was prepared by an investigator 5 minutes before administration and handed to the supervising clinician who remains unaware of the content. Placebo meals are identical but contain no fresh apple. The vaccines and placebo were prepared by the same manufacturer

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Treatment

Arm description:

The treatment arm received a modified birch allergen vaccine (Allergovit) in which the allergenic proteins have been treated with aldehydes to reduce their potential for side-effects, while retaining their ability to be recognised by T-cells (the principal immunological target for SIT). This type of vaccine is in widespread use in Europe.

Arm type	Active comparator
Investigational medicinal product name	Allergovit
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

This consisted of a 7 week course of subcutaneous injections.

Strength = 1,000 TU/ml, Dosage in ml 0.1, 0.2, 0.4, 0.8. Strength = 10,000 TU/ml  
Dosage in ml 0.15, 0.3, 0.6

<b>Arm title</b>	Placebo
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Arm description:

The placebo preparation used was the verum solution without any added allergen substance, also termed Allergovit diluent.

Arm type	Placebo
Investigational medicinal product name	Allergovit
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

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Dosage and administration details:

This consisted of a 7 week course of subcutaneous injections.

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Dosage in ml 0.15, 0.3, 0.6

<b>Number of subjects in period 1</b>	Treatment	Placebo
Started	17	15
Completed	12	11
Not completed	5	4
Lost to follow-up	5	4

## Baseline characteristics

### Reporting groups

Reporting group title

Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	32	32	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Mean age			
Units: years			
arithmetic mean	39.4		
standard deviation	± 11.4	-	
Gender categorical			
Units: Subjects			
Female	25	25	
Male	7	7	

## End points

### End points reporting groups

Reporting group title	Treatment
Reporting group description: The treatment arm received a modified birch allergen vaccine (Allergovit) in which the allergenic proteins have been treated with aldehydes to reduce their potential for side-effects, while retaining their ability to be recognised by T-cells (the principal immunological target for SIT). This type of vaccine is in widespread use in Europe.	
Reporting group title	Placebo
Reporting group description: The placebo preparation used was the verum solution without any added allergen substance, also termed Allergovit diluent.	

### Primary: Double Blind Placebo Controlled Food Challenge

End point title	Double Blind Placebo Controlled Food Challenge <sup>[1]</sup>
End point description: The change in level was calculated for year 1 and year 2 as Year 1 or 2 - Year 0. A negative change indicates a higher threshold at Year 0 and therefore a worse outcome at year1/2. A positive change indicates a higher threshold at Year 1 or 2 and therefore a positive outcome.	
End point type	Primary
End point timeframe: Year 1 and year 2	
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: See attached documents for results	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	7		
Units: Concentration of apple	25	41		

Attachments (see zip file)	OAS analysis 1.0 signed.pdf
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### Statistical analyses

No statistical analyses for this end point

### Secondary: Skin test sensitivity

End point title	Skin test sensitivity
End point description:	
End point type	Secondary
End point timeframe: Two years	

<b>End point values</b>	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: Diameter of reaction in mm				
arithmetic mean (standard deviation)	0.31 (± 3.31)	0.14 (± 2.58)		

### Statistical analyses

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No statistical analyses for this end point



## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

For the duration of the study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Frequency threshold for reporting non-serious adverse events: 1 %

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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: See attached document for list of AEs there were no SAEs

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2011	1. The protocol has been amended to more accurately reflect the contra-indications contained within the SmPC. 2. Further information about the manufacture and control of placebo is included 3. A copy of the manufacturer's authorisation for the placebo is included. 4. The "Allergovit diluent" is now specified as being the same as the placebo product in the protocol.
08 October 2012	1. GP Practices to search their databases for hay fever sufferers and invite them to take part in the study by sending them the GP Invitation Letter (Version 1.2, dated 13/08/2012). 2. The protocol was amended so that people with autoimmune diseases who are not on immunosuppressive drugs (e.g. Coeliac disease) could be included. 3. Diary card approved.
09 October 2012	The addition of PIC sites.
24 January 2013	Addition of an open apple challenge at the end of the double blind placebo controlled food challenges.
06 June 2013	Homerton Hospital becoming an additional site for the study.
10 June 2013	Amendment to the protocol, patient information sheet and advert to be more generic, and less BSUH specific in order for the study to become multi-centred. Also the addition of an invitation letter to those patients who are interested in research.
23 September 2013	The protocol was updated to allow appropriately qualified and trained nurses to give the IMP injection, as well as a doctor.
28 October 2013	To amend the recruitment procedure so that delegated nurses can consent patients (but eligibility will still be confirmed by a doctor). No documentation is affected in this amendment.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported