Clinical trial results:
A Randomised, Double-blind, Single-centre, Controlled Trial of Low Dose Intradermal Allergen Immunotherapy in Adults with Seasonal Allergic Rhinitis

Summary

EudraCT number	2012-002193-31
Trial protocol	GB
Global end of trial date	27 August 2014

Results information

Result version number	v1 (current)
This version publication date	13 October 2018
First version publication date	13 October 2018
Summary attachment (see zip file)	STUDY REPORT (Interim study report unsigned.pdf)

Trial information

Trial identification

Sponsor protocol code	PollenLITE

Additional study identifiers

ISRCTN number	ISRCTN78413121
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Dr Stephen Till, King's College London, +44 02071880599, stephen.till@kcl.ac.uk
Scientific contact	Dr Stephen Till, King's College London, +44 02071880599, stephen.till@kcl.ac.uk
Sponsor organisation name	Guy's and St Thomas' NHS Foundation Trust
Sponsor organisation address	Great Maze Pond, London, United Kingdom, SE19RT
Public contact	Dr Stephen Till, Guy's and St Thomas' NHS Foundation Trust, +44 02071880599, stephen.till@kcl.ac.uk
Scientific contact	Dr Stephen Till, Guy's and St Thomas' NHS Foundation Trust, +44 02071880599, stephen.till@kcl.ac.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2014
Global end of trial reached?	Yes
Global end of trial date	27 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine if pre-seasonal low dose intradermal grass pollen allergen immunotherapy (either 7 or 8 two-weekly injections of 10 Biological Units (33.333 SQ-U)) reduces symptoms and requirements for anti-allergic drugs in seasonal allergic rhinitis during the 2013 grass pollen season compared to the control intervention (histamine only).

Protection of trial subjects:

Paricipants were followed-up at 4 months and randomised for follow-up at either 7, 10 or 13 months following final vaccine for open label intradermal skin tests with grass pollen (10 BU)

Background therapy:

None

Evidence for comparator: -

Actual start date of recruitment	08 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 93
Worldwide total number of subjects	93
EEA total number of subjects	93

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)	93
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Ninety-three participants allergic to grass pollen were enrolled and randomised to receive the first intradermal injection of grass pollen or histamine control between February 18 and March 1 of 2013

Pre-assignment

Screening details:

Inclusion Criteria
1) Adults aged 18 to 65 years.
2) A clinical history of grass pollen-induced allergic rhinoconjunctivitis for at least 2 years with peak symptoms in May, June, or July.
3) A clinical history of moderate-severe persistent rhinoconjunctivitis symptoms interfering with usual daily activities or with sleep.

Pre-assignment period milestones

Number of subjects started	93
Number of subjects completed	93

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ACTIVE

Arm description:

The active drug will be 1 O Biological Units (BU) (33.333 SQ-U) of Ph/eum pretense soluble grass pollen extract (Aquagen SQ Timothy, ALK Abello) contained in a 20 microlitre volume (i.e. 500 BU/ml (1666.666 SQ-U/ml)).

Arm type	Active comparator
Investigational medicinal product name	Aquagen SQ Timothy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A series of 7 intradermal active or control injections will be administered 2-weekly into the forearm between before the 2013 grass pollen season. 1 O Biological Units at each injection

Arm title	CONTROL GROUP

Arm description:

Control will be histamine only, administered at a concentration of 100 mcg/ml (histamine dose validated by Sherer et al., Clin Exp Allergy. 2007;37:39-46). To help preserve blinding, histamine concentrations·will be reduced to 30 mcg/ml for the 3rd and 4th injections, and 10 mcg/ml for 5, 6 and ?1h injections. To match the grass pollen extract dilution and preserve blinding, histamine will also be aliquoted into study vials at 60-times final working strength in 0.15 ml volumes, for further dilution with 8.85 ml of clinical grade 0.9% normal saline immediately prior to injection.

Arm type	CONTROL

Investigational medicinal product name	HISTAMINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A series of 7 intradermal active or control injections will be administered 2-weekly into the forearm between before the 2013 grass pollen season. The first injection will be administered between 18th February and 1st March 2013. We will aim to administer the 7th injection between 13th May and 24th May 2013. The injection site will again be alternated between left and right arms at each visit. lntradermal injections will be administered in a 20 microlitre volume using a 29 gauge insulin syringe (Becton Dickinson Micro-FineTM).

Number of subjects in period 1	ACTIVE	CONTROL GROUP
Started	46	47
Completed	46	46
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups

Reporting group title	Whole Group

Reporting group description: -

Reporting group values	Whole Group	Total	
Number of subjects	93	93	
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)	93	93	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	31	31	
Male	62	62	

End points

End points reporting groups

Reporting group title	ACTIVE

Reporting group description:

The active drug will be 1 O Biological Units (BU) (33.333 SQ-U) of Ph/eum pretense soluble grass pollen extract (Aquagen SQ Timothy, ALK Abello) contained in a 20 microlitre volume (i.e. 500 BU/ml (1666.666 SQ-U/ml)).

Reporting group title	CONTROL GROUP

Reporting group description:

Control will be histamine only, administered at a concentration of 100 mcg/ml (histamine dose validated by Sherer et al., Clin Exp Allergy. 2007;37:39-46). To help preserve blinding, histamine concentrations·will be reduced to 30 mcg/ml for the 3rd and 4th injections, and 10 mcg/ml for 5, 6 and ?1h injections. To match the grass pollen extract dilution and preserve blinding, histamine will also be aliquoted into study vials at 60-times final working strength in 0.15 ml volumes, for further dilution with 8.85 ml of clinical grade 0.9% normal saline immediately prior to injection.

Primary: A combined symptom and medication score during the grass pollen season period of mid May-August 2013.

End point title	A combined symptom and medication score during the grass pollen season period of mid May-August 2013.[1]

End point description:

daily combined symptom and medication scores according to treatment group over the 2013 grass pollen season

End point type	Primary

End point timeframe:

During grass pollen season between mid May-August 2013.

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 study report for full analysis

End point values	ACTIVE	CONTROL GROUP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	46		
Units: score				
number (not applicable)	46	46		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout whole trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	ACTIVE

Reporting group description:

The active drug will be 1 O Biological Units (BU) (33.333 SQ-U) of Ph/eum pretense soluble grass pollen extract (Aquagen SQ Timothy, ALK Abello) contained in a 20 microlitre volume (i.e. 500 BU/ml (1666.666 SQ-U/ml)).

Reporting group title	CONTROL GROUP

Reporting group description:

Control will be histamine only, administered at a concentration of 100 mcg/ml (histamine dose validated by Sherer et al., Clin Exp Allergy. 2007;37:39-46). To help preserve blinding, histamine concentrations·will be reduced to 30 mcg/ml for the 3rd and 4th injections, and 10 mcg/ml for 5, 6 and ?1h injections. To match the grass pollen extract dilution and preserve blinding, histamine will also be aliquoted into study vials at 60-times final working strength in 0.15 ml volumes, for further dilution with 8.85 ml of clinical grade 0.9% normal saline immediately prior to injection.

Serious adverse events	ACTIVE	CONTROL GROUP	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 46 (0.00%)	0 / 47 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	ACTIVE	CONTROL GROUP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 46 (6.52%)	6 / 47 (12.77%)	
Immune system disorders			
pruritus without wheals			
subjects affected / exposed	2 / 46 (4.35%)	6 / 47 (12.77%)	
occurrences (all)	2	6	
Erythema	Additional description: Erythema that tracked from the injection site in a lymphatic distribution (‘IgE-mediated lymphangitis’) approximately 20 minutes after each administration.		

subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 0	0 / 47 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2013	Four additional secondary endpoints have been added and the statistical analysis section has been re-worded for clarification. The changes are being made following the finalisation of the statistical analysis plan by the statistician and before the collection of primary outcome data is commenced.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27977090