Clinical trial results:
A multi-centre, double-blind, randomised, placebo-controlled, parallel-group study to evaluate the efficacy and safety of Birch Modified Allergen Tyrosine adsorbed + MPL in the prevention of seasonal symptoms in subjects with allergic rhinoconjunctivitis due to birch pollen

Summary

EudraCT number	2016-002781-31
Trial protocol	DE AT SE PL
Global end of trial date	20 June 2018

Results information

Result version number	v1 (current)
This version publication date	04 April 2021
First version publication date	04 April 2021

Trial information

Trial identification

Sponsor protocol code	PQBirch301

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Allergy Therapeutics (UK) Ltd.
Sponsor organisation address	Dominion Way, Worthing, United Kingdom, BN14 8SA
Public contact	Clinical Research Management, Bencard Allergie GmbH, +49 08936811436, pqbirch301@allergytherapeutics.com
Scientific contact	Clinical Research Management, Allergy Therapeutics (UK) Ltd., +49 08936811436, pqbirch301@allergytherapeutics.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	03 September 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of PQ Birch in birch pollen-induced rhinoconjunctivitis.

Protection of trial subjects:

The conduct of this trial met all local legal and regulatory requirements. The study was conducted in accordance with the principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline E6: Good Clinical Practice (GCP). An informed consent form explaining the procedures of the study including the potential hazards was reviewed and approved by the responsible IEC/IRB before its use.

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	15 March 2017
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	Poland: 147
Country: Number of subjects enrolled	Sweden: 51
Country: Number of subjects enrolled	Austria: 51
Country: Number of subjects enrolled	Germany: 333
Worldwide total number of subjects	582
EEA total number of subjects	582

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)	582
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 58 investigational sites in four countries: Austria, Germany, Poland and Sweden.
Overall, 945 patients were screened and 582 patients were randomised and received the study medication.

Pre-assignment

Screening details:

Male or female aged 18 to 60 years with a positive history of moderate to severe seasonal allergic rhinoconjunctivitis ascribed to birch pollen exposure requiring anti-allergic treatment for symptom control for at least two consecutive seasons prior to study.

Period 1

Period 1 title	Visit 2 - 7 (Visits 1 = Screening) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The identity of study medication administered was not known by the subject, investgators or other persons directly involved in the conduct of the clinical study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

6 subcutaneous injections of Placebo given sequentially at weekly intervals

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Trained site personnel administered 6 subcutaneous injections of 1.0 mL each in eligible subjects in the outer third part of the upper arm.

Arm title	PQ Birch

Arm description:

6 subcutaneous injections of PQ Birch 900, 2400, 6000, 6000, 6000 and 6000 SU sequentially to achieve a cumulative dose of 27300 SU

Arm type	Experimental
Investigational medicinal product name	PQ Birch
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Trained site personnel administered 6 subcutaneous injections of 1.0 mL each in eligible subjects in the outer third part of the upper arm.

Number of subjects in period 1	Placebo	PQ Birch
Started	283	299
Completed	275	282
Not completed	8	17
Consent withdrawn by subject	2	6
Physician decision	-	1
N/A	1	-
Adverse event, non-fatal	1	7
Non-compliance to study drug	1	-
Failure to meet randmization criteria	1	1
Lost to follow-up	2	-
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
6 subcutaneous injections of Placebo given sequentially at weekly intervals	
Reporting group title	PQ Birch
Reporting group description:	
6 subcutaneous injections of PQ Birch 900, 2400, 6000, 6000, 6000 and 6000 SU sequentially to achieve a cumulative dose of 27300 SU	

Reporting group values	Placebo	PQ Birch	Total
Number of subjects	283	299	582
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)	283	299	582
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	37.8	36.6	
standard deviation	± 11.5	± 10.8	-
Gender categorical			
Units: Subjects			
Female	145	154	299
Male	138	145	283

Subject analysis sets	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS) consists of all patients that received at least one injection of study medication. The analysis will follow the intention-to-treat principle and will analyse patients according to the treatment group that they were randomised to, regardless of any errors in the administration of treatment.	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
The per protocol set (PPS) is a subset of the FAS and excludes all patients with major protocol violations that affect the evaluation of the primary endpoint of the study.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set will consist of all patients who received at least one injection of study medication. Patients will be analysed according to the treatment they actually received.

Reporting group values	FAS	PPS	Safety Set
Number of subjects	582	501	582
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	582	501	582
Age continuous Units: years			
arithmetic mean	37.2	37.3	37.2
standard deviation	± 11.2	± 11.0	± 11.2
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
6 subcutaneous injections of Placebo given sequentially at weekly intervals	
Reporting group title	PQ Birch
Reporting group description:	
6 subcutaneous injections of PQ Birch 900, 2400, 6000, 6000, 6000 and 6000 SU sequentially to achieve a cumulative dose of 27300 SU	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS) consists of all patients that received at least one injection of study medication. The analysis will follow the intention-to-treat principle and will analyse patients according to the treatment group that they were randomised to, regardless of any errors in the administration of treatment.	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
The per protocol set (PPS) is a subset of the FAS and excludes all patients with major protocol violations that affect the evaluation of the primary endpoint of the study.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety set will consist of all patients who received at least one injection of study medication. Patients will be analysed according to the treatment they actually received.	

Primary: N/A

End point title	N/A[1]
End point description:	
End point type	Primary
End point timeframe:	
Visit 2-7	

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: Following discussions with Paul-Ehrlich-Institute, it was agreed to invalidate the primary efficacy endpoint and all secondary efficacy endpoints related to eDiary data.

End point values	Placebo	PQ Birch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	299		
Units: NA	283	299		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency, severity and relationship of AEs

End point title	Frequency, severity and relationship of AEs

End point description:

Overall summary of frequency, severity and relationship of adverse events during study duration

End point type	Secondary

End point timeframe:

Visit 2-7

End point values	Placebo	PQ Birch	Safety Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	283	299	582	
Units: Subjects	282	300	582	

Attachments (see zip file)	Frequency, severity and relationship of AEs.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: ARCs

End point title	ARCs

End point description:

ARCs: Local and sytemic TEAE within 24 hours of injection

End point type	Secondary

End point timeframe:

Visit 2-7

End point values	Placebo	PQ Birch	Safety Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	283	299	582	
Units: Subjects	282	299	582	

Attachments (see zip file)	ARCs.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: AEs leading to premature discontinuation of treatment

End point title	AEs leading to premature discontinuation of treatment

End point description:

AEs leading to premature discontinuation of treatment

End point type	Secondary

End point timeframe:

Visit 2-7

End point values	Placebo	PQ Birch	Safety Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	283	299	582	
Units: Subjects	282	300	582	

Attachments (see zip file)	AE to premature discontinuation of treatment.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory changes

End point title	Laboratory changes

End point description:

Laboratory changes (serum chemistry, hematology, urinanalysis): changes screening - final visit

End point type	Secondary

End point timeframe:

Screening - final visit

End point values	Placebo	PQ Birch	Safety Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	283	299	582	
Units: Subjects	282	299	582	

Attachments (see zip file)	Laboratory changes.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Vital signs

End point title	Vital signs

End point description: Vital signs evaluation	
End point type	Secondary
End point timeframe: Baseline - final visit	

End point values	Placebo	PQ Birch	Safety Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	283	299	582	
Units: Subjects	282	300	582	

Attachments (see zip file)	Vital signs.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within the time period from the first injection of study medication until Visit 7.

Adverse event reporting additional description:

AEs were summarised by treatment group and primary SOC, preferred term, additionally by causality assessment and intensity
8 serious AE were reported, 4 during pre-treatment and 4 during treatment period. None of these AEs were related to the treatment. None of these serious AEs were serious adverse drug reactions.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	PQ Birch

Reporting group description:

Safety Set Evaluation data presented

Reporting group title	Placebo

Reporting group description:

Safety Set Evaluation data presented

Serious adverse events	PQ Birch	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 300 (2.00%)	2 / 282 (0.71%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Meniscus injury	Additional description: Reported in treatment period, not related to treatment, no ADR		
subjects affected / exposed	1 / 300 (0.33%)	0 / 282 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture	Additional description: Reported in treatment period, not related to treatment, no ADR		
subjects affected / exposed	1 / 300 (0.33%)	0 / 282 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture	Additional description: Reported in pre-treatment period, not related to treatment, no ADR		

subjects affected / exposed	1 / 300 (0.33%)	0 / 282 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture	Additional description: Reported in pre-treatment period, not related to treatment, no ADR		
subjects affected / exposed	1 / 300 (0.33%)	0 / 282 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Palpitations	Additional description: Reported in pre-treatment period, not related to treatment, no ADR		
subjects affected / exposed	1 / 300 (0.33%)	0 / 282 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope	Additional description: Reported in pre-treatment period, not related to treatment, no ADR		
subjects affected / exposed	0 / 300 (0.00%)	1 / 282 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre	Additional description: Reported in treatment period, not related to treatment, no ADR		
subjects affected / exposed	0 / 300 (0.00%)	1 / 282 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis	Additional description: Reported in treatment period, not related to treatment, no ADR		
subjects affected / exposed	1 / 300 (0.33%)	0 / 282 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PQ Birch	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	229 / 300 (76.33%)	140 / 282 (49.65%)	

Nervous system disorders			
Headache			
subjects affected / exposed	25 / 300 (8.33%)	14 / 282 (4.96%)	
occurrences (all)	50	23	
General disorders and administration site conditions			
Injection site swelling			
subjects affected / exposed	155 / 300 (51.67%)	50 / 282 (17.73%)	
occurrences (all)	408	89	
Injection site erythema			
subjects affected / exposed	119 / 300 (39.67%)	28 / 282 (9.93%)	
occurrences (all)	331	46	
Injection site pain			
subjects affected / exposed	89 / 300 (29.67%)	57 / 282 (20.21%)	
occurrences (all)	212	123	
Injection site pruritus			
subjects affected / exposed	94 / 300 (31.33%)	11 / 282 (3.90%)	
occurrences (all)	265	19	
Injection site warmth			
subjects affected / exposed	31 / 300 (10.33%)	5 / 282 (1.77%)	
occurrences (all)	58	7	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	84 / 300 (28.00%)	54 / 282 (19.15%)	
occurrences (all)	109	67	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 August 2017	Protocol (Version 5.0) and respective documents updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported