Clinical trial results:
A randomised, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of PQ Grass in subjects with seasonal allergic rhinitis and/or rhinoconjunctivitis induced by grass pollen exposure

Summary

EudraCT number	2019-001517-16
Trial protocol	DE HU CZ AT PL
Global end of trial date	01 November 2023

Results information

Result version number	v1 (current)
This version publication date	16 November 2024
First version publication date	16 November 2024

Trial information

Trial identification

Sponsor protocol code	PQGrass306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05540717
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergy Therapeutics (UK) Ltd.
Sponsor organisation address	Dominion Way, Worthing BN14 8SA, West Sussex, United Kingdom,
Public contact	Clinical Research Management, Bencard Allergie GmbH, pqgrass306@allergytherapeutics.com
Scientific contact	Clinical Research Management, Bencard Allergie GmbH, pqgrass306@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	15 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2023
Global end of trial reached?	Yes
Global end of trial date	01 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy: To evaluate the efficacy of PQ Grass 27600 SU in subjects with grass pollen induced SAR and/or rhinoconjunctivitis based on symptoms and medications.
Safety: To evaluate the safety and tolerability of PQ Grass in subjects with grass pollen induced SAR and/or rhinoconjunctivitis.

Protection of trial subjects:

The risk of anaphylaxis was mitigated by carefully selecting sites with trained personnel and specific equipment to manage anaphylaxis, by excluding high-risk participants and by providing specific instructions to participants in order to minimise the risk.
An independent Adjudication Committee was installed to evaluate any important safety information.
A Trial Oversight Committee with regular meetings was installed to oversee the safety of the participants during the conduct of the study.
Participants were monitored from the time of ICF signature throughout the study for the detection of exacerbations of pre-existing allergy symptoms.
The use of placebo was mitigated by providing subjects with relief medication during the grass pollen season and by extensive safety monitoring.

Background therapy:

Participants were provided relief medication including oral and ocular antihistamine, and nasal and oral coricosteroids.

Evidence for comparator: -

Actual start date of recruitment	22 August 2022
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	Poland: 153
Country: Number of subjects enrolled	Austria: 25
Country: Number of subjects enrolled	Czechia: 67
Country: Number of subjects enrolled	Germany: 242
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	555
EEA total number of subjects	488

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)	555
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The clinical trial was conducted at 89 sites (65 in Europe and 24 in the United States) and overall, 555 subjects were randomised and included in the FAS and the SAF. There was a near equal assignment of subjects to PQ Grass and placebo. One subject randomised to placebo received PQ Grass therefore, 279 subjects were treated with PQ Grass.

Pre-assignment

Screening details:

Male or female aged 18 to 65 years with a positive history of moderate to severe seasonal allergic rhinoconjunctivitis ascribed to grass pollen exposure requiring treatment for at least two consecutive seasons prior to study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PQ Grass 27600 SU

Arm description:

6 pre-seasonal injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU

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

Dosage and administration details:

6 injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU

Arm title	Placebo

Arm description:

6 pre-seasonal injections of placebo

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

Dosage and administration details:

6 doses of placebo

Number of subjects in period 1	PQ Grass 27600 SU	Placebo
Started	278	277
Completed	278	277

Period 2	
Period 2 title	Period 2 (randomisation and treatment)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms	
Are arms mutually exclusive?	Yes
Arm title	PQ Grass 27600 SU

Arm description:

6 pre-seasonal injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU

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

Dosage and administration details:

6 injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU

Arm title	Placebo

Arm description:

6 pre-seasonal injections of placebo

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

Dosage and administration details:

6 injections of placebo

Number of subjects in period 2	PQ Grass 27600 SU	Placebo
Started	278	277
Completed	250	257
Not completed	28	20
Consent withdrawn by subject	6	4
Adverse event, non-fatal	4	5
Sponsor request	2	3
Study terminated by sponsor	3	3
other, unknown	12	4
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	PQ Grass 27600 SU
Reporting group description:	
6 pre-seasonal injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU	
Reporting group title	Placebo
Reporting group description:	
6 pre-seasonal injections of placebo	

Reporting group values	PQ Grass 27600 SU	Placebo	Total
Number of subjects	278	277	555
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)	278	277	555
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	32.8	34.8	
standard deviation	± 10.02	± 10.34	-
Gender categorical			
Units: Subjects			
Female	123	126	249
Male	155	151	306
Race			
Units: Subjects			
White	268	265	533
Black or African American	4	5	9
Asian	3	3	6
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	1	1
Other	3	3	6
Ethnicity			
Units: Subjects			
Hispanic or Latino	4	2	6
Not Hispanic or Latino	274	275	549
Alcohol consumption			
Units: Subjects			
Never	56	59	115

Currently - Daily	3	6	9
Currently - Weekly	30	29	59
Currently - Monthly	29	26	55
Currently - Occasionally	144	146	290
Previously - Daily	1	0	1
Previously - Weekly	1	1	2
Previously - Monthly	8	7	15
Previously - Occasonally	6	3	9
Smoking habit Units: Subjects			
Never	209	204	413
Currently - Daily	25	24	49
Currently - Weekly	3	2	5
Currently - Monthly	0	1	1
Currently - Occasionally	9	16	25
Previously - Daily	16	20	36
Previously - Weekly	1	2	3
Previously - Monthly	1	1	2
Previously - Occasionally	14	7	21
BMI Units: kg/m2			
arithmetic mean	26.45	26.32	
standard deviation	± 5.874	± 5.018	-
Height Units: centimetres			
arithmetic mean	174.1	173.8	
standard deviation	± 9.70	± 9.72	-
Weight Units: Kilograms			
arithmetic mean	80.44	79.69	
standard deviation	± 19.546	± 17.327	-
grass-specific IgE values Units: kUA/L			
arithmetic mean	28.5	27.2	
standard deviation	± 32.4617	± 30.7472	-

End points

End points reporting groups

Reporting group title	PQ Grass 27600 SU
Reporting group description:	
6 pre-seasonal injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU	
Reporting group title	Placebo
Reporting group description:	
6 pre-seasonal injections of placebo	
Reporting group title	PQ Grass 27600 SU
Reporting group description:	
6 pre-seasonal injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU	
Reporting group title	Placebo
Reporting group description:	
6 pre-seasonal injections of placebo	

Primary: Combined symptom and medication score Averaged Over Peak GPS

End point title	Combined symptom and medication score Averaged Over Peak GPS
End point description:	
The combined symptom and medication score was calculated as an average score during the Grass pollen season (GPS).	
End point type	Primary
End point timeframe:	
The combined symptom and medication score was was recorded during the peak GPS. The peak GPS timeframe was dependent on each geographical region with an average of approximately 3-4 weeks	

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278[1]	277[2]		
Units: score on a scale				
least squares mean (confidence interval 95%)	1.07 (0.84 to 1.30)	1.34 (1.12 to 1.57)		

Notes:

[1] - The analysis of CSMS is reported on the full analysis set. See justification

[2] - The analysis of CSMS is reported on the full analysis set, see justification

Statistical analyses

Statistical analysis title	Comparison of CSMS averaged over the peak GPS
Comparison groups	PQ Grass 27600 SU v Placebo

Number of subjects included in analysis	555
Analysis specification	Post-hoc
Analysis type	superiority[3]
P-value	= 0.00048
Method	Mixed models analysis
Parameter estimate	relative difference (%)
Point estimate	-20.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31
upper limit	-9.49

Notes:

[3] - Linear mixed model using treatment group as fixed effect and pooled geographical region as random effect

Secondary: CSMS averaged over the entire (or truncated) GPS

End point title	CSMS averaged over the entire (or truncated) GPS

End point description:

End point type	Secondary

End point timeframe:

The CSMS was recorded during the entire GPS. The entire GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 13-14 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	266		
Units: score on a scale				
arithmetic mean (standard deviation)	0.99 (± 0.786)	1.23 (± 0.965)		

Statistical analyses

Statistical analysis title	Comparison of CSMS averaged over the entire GPS
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	533
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.00032
Method	Mixed models analysis
Parameter estimate	relative difference (%)
Point estimate	-20.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.13
upper limit	-10.27

Notes:

[4] - Linear mixed model using treatment group as fixed effect and pooled geographical region as random effect

Secondary: dSS component of the CSMS averaged over the peak GPS

End point title	dSS component of the CSMS averaged over the peak GPS

End point description:

End point type	Secondary

End point timeframe:

The dSS component of the CSMS was recorded during the peak GPS. The peak GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 3-4 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	266		
Units: score on a scale				
arithmetic mean (standard deviation)	0.82 (± 0.589)	0.95 (± 0.640)		

Statistical analyses

Statistical analysis title	Comparison of dSS of CSMS on peak GPS
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.00223
Method	Mixed models analysis
Parameter estimate	relative difference (%)
Point estimate	-16.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.27
upper limit	-6.44

Notes:

[5] - Linear mixed model using treatment group as fixed effect and pooled geographical region as random effect

Secondary: dSS component of the CSMS averaged over the entire GPS

End point title	dSS component of the CSMS averaged over the entire GPS

End point description:

End point type	Secondary

End point timeframe:

The dSS component of the CSMS was recorded during the entire GPS. The peak GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 13-14 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	266		
Units: score on a scale				
arithmetic mean (standard deviation)	0.65 (± 0.478)	0.78 (± 0.564)		

Statistical analyses

Statistical analysis title	Comparison of dSS of CSMS on entire GPS
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	533
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.00076
Method	Mixed models analysis
Parameter estimate	relative difference (%)
Point estimate	-16.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.66
upper limit	-7.5

Notes:

[6] - Linear mixed model using treatment group as fixed effect and pooled geographical region as random effect

Secondary: dMS component of the CSMS averaged over the peak GPS

End point title	dMS component of the CSMS averaged over the peak GPS

End point description:

End point type	Secondary

End point timeframe:

The dMS component of the CSMS was recorded during the peak GPS. The peak GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 3-4 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	266		
Units: score on a scale				
arithmetic mean (standard deviation)	0.47 (± 0.554)	0.59 (± 0.589)		

Statistical analyses

Statistical analysis title	Comparison of dMS of CSMS on peak GPS
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.0008
Method	Mixed models analysis
Parameter estimate	relative difference (%)
Point estimate	-26.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.15
upper limit	-11.94

Notes:

[7] - Linear mixed model using treatment group as fixed effect and pooled geographical region as random effect

Secondary: dMS component of the CSMS averaged over the entire GPS

End point title	dMS component of the CSMS averaged over the entire GPS

End point description:

End point type	Secondary

End point timeframe:

The dMS component of the CSMS was recorded during the entire GPS. The peak GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 13-14 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	266		
Units: score on a scale				
arithmetic mean (standard deviation)	0.33 (± 0.393)	0.46 (± 0.485)		

Statistical analyses

Statistical analysis title	Comparison of dMS of CSMS on entire GPS
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	533
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.00031
Method	Mixed models analysis
Parameter estimate	relative difference (%)
Point estimate	-26.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.49
upper limit	-12.72

Notes:

[8] - Linear mixed model using treatment group as fixed effect and pooled geographical region as random effect.

Secondary: Number of well days during peak GPS

End point title	Number of well days during peak GPS

End point description:

End point type	Secondary

End point timeframe:

The number of well days was recorded during the peak GPS. The peak GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 3-4 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	266		
Units: day				
median (standard deviation)	6.6 (± 8.16)	5.5 (± 7.11)		

Statistical analyses

Statistical analysis title	Probability of well days during peak GPS
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.10846 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.254

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.951
upper limit	1.652

Notes:

[9] - GEE model for binary response with treatment as fixed effect, pooled geographical region and grass pollen count per day as covariates, and assuming a within-subject working correlation.

Secondary: RQLQ(S) measured within the peak GPS

End point title	RQLQ(S) measured within the peak GPS

End point description:

End point type	Secondary

End point timeframe:

Rhinoconjunctivitis Quality of Life Questionnaire with standardised activities (RQLQ) was recorded during the peak GPS. The peak GPS depends on the pollen counts, which differs across geographical regions, but usually lasts approximately 3-4 weeks.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	171		
Units: score on a scale				
least squares mean (standard error)	1.26 (± 0.160)	1.77 (± 0.160)		

Statistical analyses

Statistical analysis title	Comparison of average total RQLQ
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	340
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.00009
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.25

Notes:

[10] - Linear mixed model using treatment group as fixed effect, Baseline total RQLQ score as covariate and pooled geographical region as random effect

Secondary: Serum grass specific IgG4 at Baseline and Visit 7

End point title	Serum grass specific IgG4 at Baseline and Visit 7

End point description:

End point type	Secondary

End point timeframe:

Measurement of grass-specific IgG4 was performed at baseline and visit 7.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	243		
Units: mg/L				
median (standard deviation)	4.516 (± 6.0466)	0.627 (± 1.0170)		

Statistical analyses

Statistical analysis title	Change of serum grass-specific IgG4 levels
Comparison groups	PQ Grass 27600 SU v Placebo
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.00001
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	3.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.28
upper limit	4.7

Notes:

[11] - Linear mixed model using treatment group as fixed effect, Baseline serum grass-specific IgG4 [mg/L] as a covariate and pooled geographical region as random effect

Secondary: Frequency, severity and relationship of AEs to treatment

End point title	Frequency, severity and relationship of AEs to treatment

End point description:

End point type	Secondary

End point timeframe:

Adverse events were reported from baseline to the last follow-up visit.

End point values	PQ Grass 27600 SU	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278[12]	277[13]		
Units: subjects				
Any AE	232	163		
Any AESI	0	0		
Any serious AE	6	4		
AE leading to premature treatment discontinuation	4	5		
AE leading to premature study discontinuation	1	3		
AE definitively related to treatment	144	53		
AE probably related to treatment	34	23		
AE possibly related to treatment	34	31		
AE unlikely related to treatment	1	4		
AE not related to treatment	19	43		

Notes:

[12] - The AEs are reported on the number of subjects receiving the active treatment (n=279)

[13] - The number of AEs are reported on the subjects receiving placebo (n=276)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reporting was performed throughout the study, which had an overall duration of 387 days.

Adverse event reporting additional description:

One subject randomised to placebo received PQ Grass throughout the trial, consequently 279 subjects were treated with PQ Grass and 276 subjects with placebo; results are based on treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	PQ Grass 27600 SU

Reporting group description:

injections of active treatment (900, 2700, 6000, 6000, 6000 and 6000 SU sequentially) to achieve a cumulative nominal dose of 27600 SU

Reporting group title	Placebo

Reporting group description:

6 injections of placebo

Serious adverse events	PQ Grass 27600 SU	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 279 (2.15%)	8 / 276 (2.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 279 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Rhythm idioventricular			

subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (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			
Dizziness			
subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 279 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			

subjects affected / exposed	1 / 279 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 279 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PQ Grass 27600 SU	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 279 (81.00%)	155 / 276 (56.16%)	
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 279 (9.32%)	20 / 276 (7.25%)	
occurrences (all)	64	38	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	183 / 279 (65.59%)	28 / 276 (10.14%)	
occurrences (all)	755	62	
Injection site swelling			
subjects affected / exposed	161 / 279 (57.71%)	43 / 276 (15.58%)	
occurrences (all)	607	80	
Injection site pain			
subjects affected / exposed	123 / 279 (44.09%)	65 / 276 (23.55%)	
occurrences (all)	307	151	
Injection site pruritus			
subjects affected / exposed	133 / 279 (47.67%)	24 / 276 (8.70%)	
occurrences (all)	433	32	
Injection site warmth			
subjects affected / exposed	19 / 279 (6.81%)	5 / 276 (1.81%)	
occurrences (all)	47	11	
Injection site urticaria			

subjects affected / exposed	16 / 279 (5.73%)	1 / 276 (0.36%)	
occurrences (all)	38	2	
Eye disorders			
Eye pruritus			
subjects affected / exposed	23 / 279 (8.24%)	23 / 276 (8.33%)	
occurrences (all)	45	44	
Lacrimation increased			
subjects affected / exposed	14 / 279 (5.02%)	10 / 276 (3.62%)	
occurrences (all)	17	24	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	35 / 279 (12.54%)	25 / 276 (9.06%)	
occurrences (all)	55	91	
Sneezing			
subjects affected / exposed	34 / 279 (12.19%)	27 / 276 (9.78%)	
occurrences (all)	55	69	
Nasal congestion			
subjects affected / exposed	21 / 279 (7.53%)	26 / 276 (9.42%)	
occurrences (all)	40	78	
Nasal pruritus			
subjects affected / exposed	16 / 279 (5.73%)	23 / 276 (8.33%)	
occurrences (all)	36	60	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	28 / 279 (10.04%)	22 / 276 (7.97%)	
occurrences (all)	31	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2022	Version 3.0_Global was created to harmonize the protocol so that all the updates included in the different versions of the protocol (as stipulated in the tables below) that are currently in use in the different regions can be in one global version. Furthermore, additional updates were made to the Version 3.0_Global clinical trial protocol as indicated in the table below. Administrative edits were also made as needed all through the document.
20 June 2023	Version 4.0_Global was created to incorporate an interim analysis in the ongoing clinical trial and to provide the option of a second season (Year 2) for the clinical trial if needed as it was not possible to recruit the initially planned number of subjects within one year (Year 1). The amendment includes a description of the changes if a second season will become part of the trial, and it describes the process for an interim analysis that is planned to be performed based on Year 1 data. Administrative edits were also made as needed all through the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported