Clinical trial results:
Biological standarization of allergic extracts of wild grasses: Phleum pratense, Lolium perenne, Poa pratensis y Dactylis glomerata and its mixture to determinate their biological activity, the In House Reference Preparation, measures in Histamine unit equivalents (HEP) in sensitized patients

Summary

EudraCT number	2019-002644-24
Trial protocol	ES
Global end of trial date	18 February 2021
Results information	
Result version number	v1 (current)
This version publication date	26 December 2024
First version publication date	26 December 2024
Summary attachment (see zip file)	Biological standarization of wild grasses (ct_result_EN_FINAL.pdf)

Trial information

Trial identification	
Sponsor protocol code	DIA-STA-11-01-19
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Diater S.A.
Sponsor organisation address	Avda Gregorio Peces Barba, nº 2, Leganés - Madrid, Spain, 28024
Public contact	Medical Department, DIATER, Laboratorio de Diagnóstico y Aplicaciones Terapéuticas, S.A., 34 9149660131419, departamento.medico@diater.com
Scientific contact	Medical Department, DIATER, Laboratorio de Diagnóstico y Aplicaciones Terapéuticas, S.A., 34 9149660131419, departamento.medico@diater.com
Sponsor organisation name	Diater S.A.
Sponsor organisation address	Avda Gregorio Peces Barba, nº 2, Leganés - Madrid, Spain, 28024
Public contact	M. Munoz, M. Munoz, m.munoz@diater.com
Scientific contact	M. Munoz, M. Munoz, 34 914966013, m.munoz@diater.com

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	14 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate in vivo the concentration of the allergenic extracts of wild grass pollen individually: Phleum pratense, Lolium perenne, Poa pratensis and Dactylis glomerata and their mixture that provoked a papule of a size equivalent to that produced by a solution of Histamine dihydrochloride at 10 mg/ml. And standardize the allergenic extracts in biological units.

Protection of trial subjects:

Each potential subject was adequately informed of the aims, method, anticipated benefits and potential hazards of the study and the discomfort that it might entail. All of them were informed that they were free to participate in the study and stop their participation at any time. Participants had the opportunity to make all kind of questions about the study, and every subject confirmed his or her participation by filling in and signing the informed consent form. Written informed consent was obtained from each subjects prior to the performance of any study-specific procedures

Background therapy:

NA

Evidence for comparator:

-

Actual start date of recruitment	06 October 2020
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	31
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period (from the date of the first site ready to recruit to the date for the last patient entered into the study): October 2020 to February 2021. FPFV: 6 October 2020; LPLV: 18 February 2021
31 patients were enrolled.

Pre-assignment

Screening details:

The patients were allocated to the the following arm:

EXPERIMENTAL GROUP:
31 patients who had been diagnosed positive for any of the allergens of the study by SPT Specific IgE positive received the allergenic extracts of wild grass pollen individually: Phleum pratense, Lolium perenne, Poa pratensis and Dactylis glomerata and their mixture.

Period 1

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

Blinding implementation details:

NA

Arms

Arm title	Treatment arm

Arm description:

Patients who had been diagnosed positive for any of the allergens of the study by SPT Specific IgE positive

Arm type	Experimental
Investigational medicinal product name	Phleum pratense, Lolium perenne, Poa pratensis y Dactylis glomerata and its mixture
Investigational medicinal product code	V04CL
Other name	NA
Pharmaceutical forms	Solution for skin-prick test
Routes of administration	Cutaneous use

Dosage and administration details:

The test consisted the direct application of the four concentrations of the experimental allergenic extract (10 mg/ml; 1 mg/ml, 0.1 mg/ml and 0.01 mg/ml), together with the prick mixture of grasses (10 mg/ml, 1 mg/ml, 0.1 mg/ml and 0.01 mg/ml), the positive control of Histamine and the negative control of saline solution each allergen upon the skin and the performance of a Prick test

Number of subjects in period 1	Treatment arm
Started	31
Completed	31

Baseline characteristics

End points

End points reporting groups

Reporting group title	Treatment arm
Reporting group description:	
Patients who had been diagnosed positive for any of the allergens of the study by SPT Specific IgE positive	
Subject analysis set title	PP population
Subject analysis set type	Per protocol
Subject analysis set description:	

Reporting group values	ITT Population	PP population
Number of subjects [1]	31	
Phleum pratense	31	26
Lolium perenne	31	21
Poa pratensis	31	26
Dactylis glomerata	31	27
Mixture of wild grasses	31	26

Primary: To evaluate in vivo the concentration of allergic extracts of wild grasses individually and its mixture

End point title	To evaluate in vivo the concentration of allergic extracts of wild grasses individually and its mixture

End point description:

The Biological standarization consisted the direct application of the four concentrations of the experimental allergenic extracts (10 mg/ml; 1 mg/ml, 0.1 mg/ml and 0.01 mg/ml), together with the prick mixture of grasses (10 mg/ml, 1 mg/ml, 0.1 mg/ml and 0.01 mg/ml), the positive control of histamine and the negative control of saline solution upon the skin and the performance of a Prick test. Where the Prick test gave a positive response, the areas of erythema and papules, were measured (mm2).
The skin tests were used to obtain the optimum allergen extract concentrations that provoked a response with the same wheal area to that obtained with the positive control solution of histamine dihydrochloride 10 mg/mL reaction.

End point type	Primary

End point timeframe:

The primary variable was the area of papule (mm2) produced on the skin after application of the extracts

End point values	Treatment arm	PP population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	26		
Units: mm2				
geometric mean (confidence interval 95%)	0.85 (0 to 1)	0.85 (0 to 1)		

Statistical analyses

Statistical analysis title	Outcome

Statistical analysis description:

Statistical analysis description: Validated and protected Microsoft Excel specifically designed for these

analyses

Comparison groups	Treatment arm v PP population
Number of subjects included in analysis	52
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	> 95 [2]
Method	linear regression analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1
Variability estimate	Standard deviation
Dispersion value	0

Notes:

[1] - The geometric mean of the areas of the papules (mm2) of each patient was calculated for each of the dilution series of each extract, as well as that of the positive control solution of histamine dihydrochloride 10 mg/mL. For each subject, a linear regression analysis was performed using the least squares method.

[2] - NA

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From enrollment to 1 week after completion of the skin tests. The administration of a prick test is a very safe technique with few adverse events in the literature	
Adverse event reporting additional description:	
NA	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	3

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

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: The administration of a prick test is a very safe technique with few adverse events in the literature

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

None reported