Clinical trial results:
Non-interventional Study in Allergic Patients Suffering from Grass Pollen Induced Rhinitis/Rhinoconjunctivitis with or without Asthma. Retrospective Assessment of the Efficacy of a Perennial Specific Immunotherapy on the Allergy Symptoms / Disease Activity during the Pollen Season

Summary

EudraCT number	2013-004920-12
Trial protocol	CZ
Global end of trial date	17 June 2014

Results information

Result version number	v1 (current)
This version publication date	02 January 2020
First version publication date	02 January 2020
Summary attachment (see zip file)	PRO-2013_Lay Men Summary (PRO-2013_lay man summary_1.0.pdf) PRO-2013_Summary (PRO-2013_summary_1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	PRO-2013

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LETI Pharma GmbH
Sponsor organisation address	Stockumer Str., 28, Witten, Germany, 58453
Public contact	Medical Department, LETI Pharma GmbH, 0049 2302202860, info@leti.de
Scientific contact	Medical Department, LETI Pharma GmbH, 0049 2302202860, info@leti.de

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	02 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

· Patient Reported Outcome (PRO) of 5-6 months of pre-seasonal therapy with Depigoid Phleum by means of the Symptom and Rescue Medication Score (SMS).
· PRO of 5-6 months of pre-seasonal therapy with Depigoid Phleum by means of the VAS for disease activity.
· PRO of 5-6 months of pre-seasonal therapy with Depigoid Phleum on the allergy symptoms during the grass pollen season 2013 by means of the symptom score (SS)
· PRO of 5-6 months of pre-seasonal therapy with Depigoid Phleum on the intake of rescue medication during the grass pollen season 2013 by means of the rescue medication score (RMS)
· PRO of 5-6 months of pre-seasonal therapy with Depigoid Phleum during the grass pollen season 2013 by means of global assessment.

Protection of trial subjects:

Prior to participation in this NIS, each patient was informed by the physician on the purpose and extent of the documentation the patient provided by completing the questionnaire. No data provided by the patient in the questionnaire was forwarded to the sponsor without prior written informed consent by the patient. The consent was also necessary for possible verification of the identity of the patient though his patient clinic file (Source Data Verification, EUguideline 95/46/EC and – if applicable - national regulations on data protection). The informed consent procedure and date had to be documented in the patients' clinic files.

Background therapy:

No background therapy as it was a NIS – questionnaire to collect retrospective data only.

Evidence for comparator:

no comparators

Actual start date of recruitment	01 October 2013
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	Germany: 3
Country: Number of subjects enrolled	Czech Republic: 101
Country: Number of subjects enrolled	Poland: 80
Worldwide total number of subjects	184
EEA total number of subjects	184

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)	181
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients who have been treated during the period October 2012 until April 2013 with one of the 4 concentrations of Depigoid Phleum (100, 1000, 5000 and 10000 DPP/ml) were contacted and asked if they were willing to complete a questionnaire about their personal assessment of their grass pollen allergy during the pollen season 2013.

Pre-assignment

Screening details:

Patients who have been treated during the period October 2012 until April 2013 with one of the 4 concentrations of Depigoid Phleum (100, 1000, 5000 and 10000 DPP/ml) were contacted and asked if they were willing to complete a questionnaire about their personalassessment of their grass pollen allergy during the pollen season 2013.

Period 1

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

Blinding implementation details:

not blinded, retrospective questionnaire, Non-interventional

Arms

Are arms mutually exclusive?	Yes
Arm title	Depigoid Phleum 100 DDP/mL

Arm description:

Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 100 DPP/ml.

Arm type	Placebo
Investigational medicinal product name	Depigoid Phleum 100 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Route of administration not applicable

Dosage and administration details:

no treatment

Arm title	Depigoid Phleum 1000 DPP/ml

Arm description:

Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 1000 DPP/ml.

Arm type	Active comparator
Investigational medicinal product name	Depigoid Phleum 1000 DPP/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Route of administration not applicable

Dosage and administration details:

no treatment

Arm title	Depigoid Phleum 5000 DPP/ml

Arm description:

Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 5000 DPP/ml.

Arm type	Active comparator
Investigational medicinal product name	Depigoid Phleum 5000 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Route of administration not applicable

Dosage and administration details:

no administration

Arm title	Depigoid Phleum 10000 DPP/mL

Arm description:

Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 10000 DPP/ml.

Arm type	Active comparator
Investigational medicinal product name	Depigoid Phleum 10000 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Route of administration not applicable

Dosage and administration details:

no treatment

Number of subjects in period 1	Depigoid Phleum 100 DDP/mL	Depigoid Phleum 1000 DPP/ml	Depigoid Phleum 5000 DPP/ml
Started	47	48	49
Completed	47	48	49

Number of subjects in period 1	Depigoid Phleum 10000 DPP/mL
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	data collection

Reporting group description: -

Reporting group values	data collection	Total	
Number of subjects	184	184	
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)	181	181	
From 65-84 years	3	3	
85 years and over	0	0	
Adults	0	0	
Age continuous Units: years			
arithmetic mean	34.02		
standard deviation	± 0	-	
Gender categorical Units: Subjects			
Female	89	89	
Male	95	95	

End points

End points reporting groups

Reporting group title	Depigoid Phleum 100 DDP/mL
Reporting group description:	
Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 100 DPP/ml.	
Reporting group title	Depigoid Phleum 1000 DPP/ml
Reporting group description:	
Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 1000 DPP/ml.	
Reporting group title	Depigoid Phleum 5000 DPP/ml
Reporting group description:	
Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 5000 DPP/ml.	
Reporting group title	Depigoid Phleum 10000 DPP/mL
Reporting group description:	
Patients who have been treated during the period October 2012 until April 2013 with Depigoid Phleum 10000 DPP/ml.	

Primary: #1 Symptom and medication score

End point title	#1 Symptom and medication score
End point description:	
The SMS was defined as the sum of the SS and the RMS.	
End point type	Primary
End point timeframe:	
retrospective data collection OCT-DEC 2013	

End point values	Depigoid Phleum 100 DDP/mL	Depigoid Phleum 1000 DPP/ml	Depigoid Phleum 5000 DPP/ml	Depigoid Phleum 10000 DPP/mL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	48	49	40
Units: score				
arithmetic mean (standard deviation)	11.9 (± 6.71)	9.8 (± 6.13)	11.1 (± 6.77)	10.1 (± 5.96)

Statistical analyses

Statistical analysis title	SMS
Comparison groups	Depigoid Phleum 100 DDP/mL v Depigoid Phleum 1000 DPP/ml v Depigoid Phleum 5000 DPP/ml v Depigoid Phleum 10000 DPP/mL

Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4211
Method	Kruskal-wallis

Primary: #2 Symptom Score (SS)

End point title	#2 Symptom Score (SS)

End point description:

The SS was the sum score of all symptoms as documented in the Likert scale (none (0) – mild (1) – moderate (2) – severe (3)).

End point type	Primary

End point timeframe:

retrospective data collection OCT-DEC 2013

End point values	Depigoid Phleum 100 DDP/mL	Depigoid Phleum 1000 DPP/ml	Depigoid Phleum 5000 DPP/ml	Depigoid Phleum 10000 DPP/mL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	48	49	40
Units: percentage				
arithmetic mean (standard deviation)	7.2 (± 3.10)	6.3 (± 3.62)	7.2 (± 4.13)	6.3 (± 3.32)

Statistical analyses

Statistical analysis title	SS
Comparison groups	Depigoid Phleum 100 DDP/mL v Depigoid Phleum 1000 DPP/ml v Depigoid Phleum 5000 DPP/ml v Depigoid Phleum 10000 DPP/mL
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3218
Method	Kruskal-wallis

Primary: #3 Rescue Medication Score

End point title	#3 Rescue Medication Score

End point description:

The RMS was defined as the sum score of documented allergy (rescue) medications taken.

End point type	Primary

End point timeframe:

retrospective data collection OCT-DEC 2013

End point values	Depigoid Phleum 100 DDP/mL	Depigoid Phleum 1000 DPP/ml	Depigoid Phleum 5000 DPP/ml	Depigoid Phleum 10000 DPP/mL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	48	49	40
Units: comparison				
arithmetic mean (standard deviation)	3.2 (± 2.87)	2.0 (± 2.22)	2.7 (± 2.33)	2.9 (± 2.58)

Statistical analyses

Statistical analysis title	RMS
Statistical analysis description: Rescue Medication Score	
Comparison groups	Depigoid Phleum 100 DDP/mL v Depigoid Phleum 1000 DPP/ml v Depigoid Phleum 5000 DPP/ml v Depigoid Phleum 10000 DPP/mL
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.1512
Method	Kruskal-wallis
Parameter estimate	Median difference (final values)

Notes:

[1] - The RMS regarding rhinitis/ rhinoconjunctivitis and lung symptoms was lowest for the 1000 DPP/ml group with a median score of 1.5 and a mean score of 2.0.
The difference compared to the 100 DPP/ml group was statistically significant with p = 0.0387.
The highest score was found for the 100 DPP/ml group with median 2.0 and mean 3.2.
Also for the 10000 DPP/ml group, high values were found (median: 3.0; mean: 2.9).

Primary: # 4 VAS for disease acitvity

End point title	# 4 VAS for disease acitvity
End point description: change of disease activity	
End point type	Primary
End point timeframe: retrospective data collection OCT-DEC 2013	

End point values	Depigoid Phleum 100 DDP/mL	Depigoid Phleum 1000 DPP/ml	Depigoid Phleum 5000 DPP/ml	Depigoid Phleum 10000 DPP/mL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	48	49	40
Units: cm				
arithmetic mean (standard deviation)	-3.1 (± 2.18)	-4.1 (± 2.59)	-3.1 (± 2.25)	-4.2 (± 2.05)

Statistical analyses

Statistical analysis title	VAS
Comparison groups	Depigoid Phleum 100 DDP/mL v Depigoid Phleum 1000 DPP/ml v Depigoid Phleum 5000 DPP/ml v Depigoid Phleum 10000 DPP/mL
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.0209
Method	Kruskal-wallis
Parameter estimate	Mean difference (final values)

Notes:

[2] - comparison

Primary: #5 global assessment

End point title	#5 global assessment
End point description:	
patients rated efficacy of therapy as "positive"	
End point type	Primary
End point timeframe:	
retrospective data collection OCT-DEC 2013	

End point values	Depigoid Phleum 100 DDP/mL	Depigoid Phleum 1000 DPP/ml	Depigoid Phleum 5000 DPP/ml	Depigoid Phleum 10000 DPP/mL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	48	49	40
Units: impression				
number (not applicable)	25	30	28	28

Statistical analyses

Statistical analysis title	global assessment of disease

Statistical analysis description:

A further endpoint of this NIS was the patients' global assessment of the efficacy of the pre-seasonal immunotheraypy. Therefore, patients were asked to rate their overall impression as either "excellent", "good", (which was classified as "positive" assessment) or as "moderate", "poor" or "unacceptable" (classified as "negative").

Comparison groups	Depigoid Phleum 100 DDP/mL v Depigoid Phleum 1000 DPP/ml v Depigoid Phleum 5000 DPP/ml v Depigoid Phleum 10000 DPP/mL

Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 53.2
Method	Kruskal-wallis

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: retrospective questionnaire - no AE reporting (was done within dose finding trial)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	na

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: As this was a NIS - retrospective data collection - no adverse reactions were recorded.

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