Clinical trial results:
A Randomised, Double-Blind, Parallel Group, Multicentre Study to Assess the Efficacy and Safety of Four Concentrations of Depigoid® Phleum versus Placebo in Patients with Allergic Rhinitis and/or Rhinoconjunctivitis with or without Intermittent Asthma

Summary

EudraCT number	2014-004732-19
Trial protocol	DE PL ES
Global end of trial date	13 May 2016

Results information

Result version number	v1 (current)
This version publication date	10 May 2018
First version publication date	10 May 2018

Trial information

Trial identification

Sponsor protocol code	6043-PG-PSC-206

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, +49 2302 20286 0, info@leti.de
Scientific contact	Medical Department, LETI Pharma GmbH, +49 2302 20286 0, 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	13 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2016
Global end of trial reached?	Yes
Global end of trial date	13 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assessment of the effective dose range and the optimum dose of Depigoid® Phleum (vs. placebo) administered subcutaneously in adult patients with allergic rhinitis and/or rhinoconjunctivitis with or without intermittent asthma. Efficacy parameters will be assessed in an Environmental Challenge Chamber (ECC).

Protection of trial subjects:

Depigoid® Phleum pratense has been extensively used over the last years at both lower concentrations proposed in this study. It is estimated that more than 105,000 patients have been exposed to Depigoid® Phleum pratense or a mixture of grasses from 2000 until March 2016. More than 53,000 vials with the 100 DPP/mL concentration and more than 300,000 vials with the 1000 DPP/mL concentration have been sold in this period.
Globally assessed, available results indicate that doses up to 10,000 DPP/mL of Depigoid®Phleum pratense do not bear an inappropriately high risk for patients included in the study.
Stopping rules were implemented in this study in order to reduce the risk to participating patients. Patients who suffered from a systemic reaction ≥ Grade 2 or a severe local reaction or have a lung function test (LFT) result of ≤ 80% of predicted value (for forced expiratory volume in the first second [FEV1]) after the administration of the investigational medicinal product (IMP) during the build-up phase were withdrawn. Patients who suffered from repeated systemic reactions ≥ Grade 2 or severe local reactions or had LFT results of ≤ 80% of predicted value prior to administration of the IMP during the maintenance phase were withdrawn at the discretion of the investigator. In general, the occurrence of systemic reactions Grade 3 or 4, or LFT results ≤ 80% of predicted value prior to administration of the IMP at 2 study visits, at any time during the course of the study, elicited the patient's termination of administration of IMP and withdrawal.
To summarise, the benefits of this study outweighed the potential risks, provided that these rules were implemented and study patients were monitored properly.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2015
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: 61
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	Germany: 116
Worldwide total number of subjects	217
EEA total number of subjects	217

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)	217
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	584[1]
Number of subjects completed	217

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 363
Reason: Number of subjects	Protocol deviation: 1
Reason: Number of subjects	Consent withdrawn by subject: 2
Reason: Number of subjects	lost to follow up: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 584 patients were enrolled into the trial, of these 217 were randomized. 363 patients were screen failures, 1 protocol-deviation, 2 withdrawal of informed consent and 2 lost to follow-up.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1

Arm description:

Depigoid Phleum 1000 DPP/mL

Arm type	Experimental
Investigational medicinal product name	Depigoid Phleum 1000 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Depigoid® Phleum (depigmented and glutaraldehyde polymerised grass pollen allergenic extract adsorbed to aluminium hydroxide [DPP])

Arm title	Arm 2

Arm description:

Depigoid Phleum 3000 DPP/mL

Arm type	Experimental

Investigational medicinal product name	Depigoid Phleum 3000 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A total of 0.5 mL/day of 1 of 4 concentrations of Depigoid® Phleum (1000 DPP/mL, 3000 DPP/mL, 5000 DPP/mL or 8000 DPP/mL) or matching placebo. Administered on 6 days, at 4-week intervals during the treatment period (from Week 0 to Week 20)

Arm title	Arm 3

Arm description:

Depigoid Phleum 5000 DPP/mL

Arm type	Experimental
Investigational medicinal product name	Depigoid Phleum 5000 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A total of 0.5 mL/day of 1 of 4 concentrations of Depigoid® Phleum (1000 DPP/mL, 3000 DPP/mL, 5000 DPP/mL or 8000 DPP/mL) or matching placebo. Administered on 6 days, at 4-week intervals during the treatment period (from Week 0 to Week 20)

Arm title	Arm 4

Arm description:

Depigoid Phleum 8000 DPP/mL

Arm type	Experimental
Investigational medicinal product name	Depigoid Phleum 8000 DPP/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A total of 0.5 mL/day of 1 of 4 concentrations of Depigoid® Phleum (1000 DPP/mL, 3000 DPP/mL, 5000 DPP/mL or 8000 DPP/mL) or matching placebo. Administered on 6 days, at 4-week intervals during the treatment period (from Week 0 to Week 20)

Arm title	Placebo

Arm description:

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:

A total of 0.5 mL/day of 1 of 4 concentrations of Depigoid® Phleum (1000 DPP/mL, 3000 DPP/mL, 5000 DPP/mL or 8000 DPP/mL) or matching placebo. Administered on 6 days, at 4-week intervals during the treatment period (from Week 0 to Week 20)

Number of subjects in period 1	Arm 1	Arm 2	Arm 3
Started	40	44	42
Completed	34	39	36
Not completed	6	5	6
Consent withdrawn by subject	2	-	1
Adverse event, non-fatal	2	4	5
accidentially unblinded	1	-	-
Protocol deviation	1	1	-

Number of subjects in period 1	Arm 4	Placebo
Started	47	44
Completed	43	41
Not completed	4	3
Consent withdrawn by subject	-	2
Adverse event, non-fatal	4	1
accidentially unblinded	-	-
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1
Reporting group description:	
Depigoid Phleum 1000 DPP/mL	
Reporting group title	Arm 2
Reporting group description:	
Depigoid Phleum 3000 DPP/mL	
Reporting group title	Arm 3
Reporting group description:	
Depigoid Phleum 5000 DPP/mL	
Reporting group title	Arm 4
Reporting group description:	
Depigoid Phleum 8000 DPP/mL	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Reporting group values	Arm 1	Arm 2	Arm 3
Number of subjects	40	44	42
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			
Age continuous Units: years			
arithmetic mean	35.08	33.16	33.90
standard deviation	± 12.14	± 13.25	± 10.83
Gender categorical Units: Subjects			
Female	15	17	23
Male	25	27	19
Race Units: Subjects			
Caucasian	36	41	40
Other	4	3	2
Smoking habit Units: Subjects			
current smoker	6	8	4

former smoker	4	7	4
never	30	29	34
Alkohol consumption Units: Subjects			
daily	1	0	0
never or occasionally	39	44	42
Perception of disease activity during grass pollen season 2015 Units: Subjects			
moderate	21	27	21
severe	19	17	21
Height Units: cm			
arithmetic mean	35.08	33.16	33.90
standard deviation	± 12.14	± 13.25	± 10.83
Weight Units: kg			
arithmetic mean	80.20	72.73	71.07
standard deviation	± 16.31	± 18.19	± 13.90
BMI			
Body Mass Index			
Units: kg/m2			
arithmetic mean	25.95	24.48	23.92
standard deviation	± 5.42	± 4.39	± 3.74
Age at diagnosis Units: years			
arithmetic mean	13.23	10.32	11.64
standard deviation	± 12.03	± 10.18	± 12.21

Reporting group values	Arm 4	Placebo	Total
Number of subjects	47	44	217
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	32.15	33.20	
standard deviation	± 11.87	± 9.34	-
Gender categorical Units: Subjects			
Female	19	22	96
Male	28	22	121

Race Units: Subjects			
Caucasian	46	44	207
Other	1	0	10
Smoking habit Units: Subjects			
current smoker	5	6	29
former smoker	7	3	25
never	35	35	163
Alkohol consumption Units: Subjects			
daily	0	0	1
never or occasionally	47	44	216
Perception of disease activity during grass pollen season 2015 Units: Subjects			
moderate	24	29	122
severe	23	15	95
Height Units: cm			
arithmetic mean	32.15	33.20	
standard deviation	± 11.87	± 9.34	-
Weight Units: kg			
arithmetic mean	75.36	74.75	
standard deviation	± 13.39	± 17.37	-
BMI			
Body Mass Index			
Units: kg/m2			
arithmetic mean	25.03	24.26	
standard deviation	± 3.50	± 4.30	-
Age at diagnosis Units: years			
arithmetic mean	12.87	15.09	
standard deviation	± 11.69	± 13.30	-

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) population will include all randomised patients who received the IMP at least once and present both baseline and final primary efficacy assessments.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) population consists of all patients who entered the study without major violation of study entry criteria and who completed the study without major protocol violations or terminated the study prematurely due to an AE that was related to the IMP or due to lack of efficacy.

Reporting group values	FAS	PP	
Number of subjects	193	189	
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			
Age continuous Units: years			
arithmetic mean	33.06	32.98	
standard deviation	± 11.20	± 11.27	
Gender categorical Units: Subjects			
Female	79	77	
Male	144	112	
Race Units: Subjects			
Caucasian	184	180	
Other	9	9	
Smoking habit Units: Subjects			
current smoker	26	26	
former smoker	23	23	
never	144	140	
Alkohol consumption Units: Subjects			
daily	1	1	
never or occasionally	192	188	
Perception of disease activity during grass pollen season 2015 Units: Subjects			
moderate	109	106	
severe	84	83	
Height Units: cm			
arithmetic mean	173.90	173.92	
standard deviation	± 9.51	± 9.60	
Weight Units: kg			
arithmetic mean	75.38	75.26	
standard deviation	± 16.27	± 16.32	
BMI			
Body Mass Index			
Units: kg/m2			

arithmetic mean	24.80	24.75	
standard deviation	± 4.37	± 4.37	
Age at diagnosis			
Units: years			
arithmetic mean	12.63	11.93	
standard deviation	± 11.92	± 11.15	

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description: Depigoid Phleum 1000 DPP/mL	
Reporting group title	Arm 2
Reporting group description: Depigoid Phleum 3000 DPP/mL	
Reporting group title	Arm 3
Reporting group description: Depigoid Phleum 5000 DPP/mL	
Reporting group title	Arm 4
Reporting group description: Depigoid Phleum 8000 DPP/mL	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: The full analysis set (FAS) population will include all randomised patients who received the IMP at least once and present both baseline and final primary efficacy assessments.	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description: The per-protocol (PP) population consists of all patients who entered the study without major violation of study entry criteria and who completed the study without major protocol violations or terminated the study prematurely due to an AE that was related to the IMP or due to lack of efficacy.	

Primary: TNSS

End point title	TNSS
End point description: The reduction of the TNSS assessed after provocation in an ECC in patients with grass pollen induced allergic rhinitis at baseline and after treatment for up to 20 weeks with 4 different doses of Depigoid® Phleum vs. placebo. The results from the End of Study visit (Visit E1) will be compared to those at baseline (Visit S3).	
End point type	Primary
End point timeframe: Visit E1 - Visit S3	

End point values	Arm 1	Arm 2	Arm 3	Arm 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	39	36	43
Units: TNSS				
arithmetic mean (standard deviation)	-0.85 (± 1.78)	-1.36 (± 1.55)	-1.14 (± 1.91)	-1.84 (± 1.91)

End point values	Placebo	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	41	193		
Units: TNSS				
arithmetic mean (standard deviation)	-1.08 (± 1.74)	-1.28 (± 1.80)		

Statistical analyses

Statistical analysis title	Mean TNSS difference from Visit S3 to Visit E1
Statistical analysis description:	
Mean TNSS difference from Visit S3 to Visit E1 - Full Analysis Set Population	
Comparison groups	Arm 1 v Arm 2 v Arm 3 v Arm 4 v Placebo v FAS
Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2796
Method	Rank-ANCOVA

Primary: TNSS

End point title	TNSS
End point description:	
End point type	Primary
End point timeframe:	
Visit E1 - Visit S3	

End point values	Arm 1	Arm 2	Arm 3	Arm 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	39	35	41
Units: TNSS				
arithmetic mean (standard deviation)	-0.85 (± 1.78)	-1.36 (± 1.55)	-1.12 (± 1.94)	-1.76 (± 1.88)

End point values	Placebo	PP		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	40	189		
Units: TNSS				
arithmetic mean (standard deviation)	-1.12 (± 1.75)	-1.26 (± 1.79)		

Statistical analyses

Statistical analysis title	Mean TNSS difference from Visit S3 to Visit E1
Statistical analysis description: Mean TNSS difference from Visit S3 to Visit E1 - Per Protocol Population	
Comparison groups	Arm 1 v Arm 2 v Arm 3 v Arm 4 v Placebo v PP
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3959
Method	Rank-Ancova

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 217,5 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	Arm 1
Reporting group description: Depigoid Phleum 1000 DPP/mL	
Reporting group title	Arm 2
Reporting group description: Depigoid Phleum 3000 DPP/mL	
Reporting group title	Arm 3
Reporting group description: Depigoid Phleum 5000 DPP/mL	
Reporting group title	Arm 4
Reporting group description: Depigoid Phleum 8000 DPP/mL	
Reporting group title	Arm 5
Reporting group description: Placebo	

Serious adverse events	Arm 1	Arm 2	Arm 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	1 / 44 (2.27%)	3 / 42 (7.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 40 (0.00%)	1 / 44 (2.27%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 40 (0.00%)	0 / 44 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Tension headache			
subjects affected / exposed	0 / 40 (0.00%)	0 / 44 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 44 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 40 (0.00%)	0 / 44 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm 4	Arm 5	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)	0 / 44 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 47 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Tension headache			
subjects affected / exposed	0 / 47 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Amyloidosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 47 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Arm 1	Arm 2	Arm 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)	41 / 44 (93.18%)	37 / 42 (88.10%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 40 (7.50%)	4 / 44 (9.09%)	1 / 42 (2.38%)
occurrences (all)	3	4	1
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	38 / 40 (95.00%)	37 / 44 (84.09%)	35 / 42 (83.33%)
occurrences (all)	157	171	162
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	15 / 40 (37.50%)	17 / 44 (38.64%)	19 / 42 (45.24%)
occurrences (all)	34	45	55
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 40 (5.00%)	0 / 44 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 40 (25.00%)	7 / 44 (15.91%)	8 / 42 (19.05%)
occurrences (all)	10	9	10
Tonsillitis bacterial			

subjects affected / exposed	0 / 40 (0.00%)	0 / 44 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)	2 / 44 (4.55%)	1 / 42 (2.38%)
occurrences (all)	2	3	1

Non-serious adverse events	Arm 4	Arm 5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 47 (97.87%)	37 / 44 (84.09%)	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 47 (8.51%)	1 / 44 (2.27%)	
occurrences (all)	4	1	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	42 / 47 (89.36%)	35 / 44 (79.55%)	
occurrences (all)	228	157	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	24 / 47 (51.06%)	19 / 44 (43.18%)	
occurrences (all)	59	34	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 47 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 47 (6.38%)	7 / 44 (15.91%)	
occurrences (all)	3	7	
Tonsillitis bacterial			
subjects affected / exposed	3 / 47 (6.38%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 44 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2015	Protocol Version 3.0 1. The first PEF measurement should be scheduled 30 minutes after initiation of exposure session on visits S3 and E1, as asthmatic patients are enrolled in the present trial 2. A final check (vital signs, PEF) should be performed before discharge of patients from Fraunhofer unit in order to guarantee patient's well-being before return journey 3. Risk minimizing procedures in relation to the ECC session should be more restrictive to ensure that patients would be withdrawn earlier from test session if PEF values decreased.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported