



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 \geq Grade 2 or a severe local reaction or have a lung function test (LFT) result of \leq 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 \geq Grade 2 or severe local reactions or had LFT results of \leq 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 \leq 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 | Consent withdrawn by subject: 2 |
|----------------------------|---------------------------------|

| | |
|----------------------------|-----------------------|
| Reason: Number of subjects | Protocol deviation: 1 |
|----------------------------|-----------------------|

| | |
|----------------------------|---------------------|
| Reason: Number of subjects | Screen failure: 363 |
|----------------------------|---------------------|

| | |
|----------------------------|----------------------|
| 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 |
| accidentally 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 |
| accidentally 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 | |
| Alcohol 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