



Clinical trial results:

CLINICAL PHASE III STUDY TO EVALUATE THE PHARMACOKINETICS, EFFICACY, TOLERABILITY AND SAFETY OF SUBCUTANEOUS HUMAN IMMUNOGLOBULIN (OCTANORM 16.5%) IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISEASES

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-003877-87 |
| Trial protocol | CZ HU PL SK |
| Global end of trial date | 09 June 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 07 April 2021 |
| First version publication date | 07 April 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | SCGAM-01 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01888484 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Octapharma Pharmazeutika Produktionsges.m.b.H. |
| Sponsor organisation address | Oberlaaer Strasse 235, Vienna, Austria, 1100 |
| Public contact | clinical.department@octapharma.com, Octapharma Pharmazeutika Prod.Ges.m.b.H, +43 1610320 , clinical.department@octapharma.com |
| Scientific contact | clinical.department@octapharma.com, Octapharma Pharmazeutika Prod.Ges.m.b.H, +43 1610320, clinical.department@octapharma.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 | 04 December 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 June 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The first primary objective of the study is to assess the efficacy of octanorm in preventing serious bacterial infections compared with historical control data.
The second primary objective is to evaluate the pharmacokinetic characteristics of octanorm and to compare the area under the curve (AUC) with that of IVIG.

Protection of trial subjects:

This trial was conducted in accordance to the principles of ICH- GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki and national regulatory requirements. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product.
Study safety was assessed such as monitoring of AEs and SAEs, monitoring of local injection site reactions, concomitant medication, physical examination, vital signs and safety lab parameters.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 27 May 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Poland: 11 |
| Country: Number of subjects enrolled | Slovakia: 5 |
| Country: Number of subjects enrolled | Czechia: 11 |
| Country: Number of subjects enrolled | Hungary: 3 |
| Country: Number of subjects enrolled | United States: 32 |
| Country: Number of subjects enrolled | Canada: 3 |
| Country: Number of subjects enrolled | Russian Federation: 10 |
| Worldwide total number of subjects | 75 |
| EEA total number of subjects | 30 |

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) | 26 |
| Adolescents (12-17 years) | 12 |
| Adults (18-64 years) | 35 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with documented diagnosis primary immunodeficiency diseases as defined by the European Society for Immunodeficiencies (ESID) and Pan-American Group for Immunodeficiency and requiring immunoglobulin replacement therapy due to hypogammaglobulinaemia or agammaglobulinaemia were screened according to predefined in- and exclusion criteria.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|----------|
| Arm title | Octanorm |
|-----------|----------|

Arm description:

Octanorm 16.5%, human normal immunoglobulin for weekly (± 2 days) subcutaneous (SC) administration.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Octanorm 16.5% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Octanorm, a human normal immunoglobulin, had to be administered subcutaneously every week (± 2 days). A minimum time of 4 days had to be kept in between two single SC infusions.

| Number of subjects in period 1 | Octanorm |
|--------------------------------|----------|
| Started | 75 |
| Completed | 68 |
| Not completed | 7 |
| patient's non-compliance | 1 |
| Withdrawal by subject | 6 |

Baseline characteristics

Reporting groups

Reporting group title

Overall Trial

Reporting group description: -

| Reporting group values | Overall Trial | Total | |
|---|------------------|-------|--|
| Number of subjects | 75 | 75 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean full range (min-max) | 27.81 2 to 72 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 36 | 36 | |
| Male | 39 | 39 | |

End points

End points reporting groups

| | |
|--|-------------------------|
| Reporting group title | Octanorm |
| Reporting group description: Octanorm 16.5%, human normal immunoglobulin for weekly (± 2 days) subcutaneous (SC) administration. | |
| Subject analysis set title | Full analysis set (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The FAS is defined according to the intention-to-treat principle and consists of all patients of the Safety Analysis Set who satisfy all major eligibility criteria and for whom any postbaseline data are available; it is the set of eligible patients with treatment effects measured. | |
| Subject analysis set title | Per Protocol (PP) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The per-protocol (PP) set consists of all patients of the FAS excluding those with major protocol violations which may have an impact on the analysis of the primary efficacy endpoint. This is the set of patients who participated in the study as intended and for whom the primary efficacy endpoint can be evaluated as planned. | |
| Subject analysis set title | PK Set |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Patients who had a full PK profile after the last administration of the previously used IVIG product before he was switched to octanorm (PKIV), a full PK profile at the end of the wash-in/wash-out phase (PKSC1) and a final PK profile after 28 administrations of octanorm (at steady state) to assess the bioavailability of total IgG with respect to the two administration methods (PKSC2). | |

Primary: Primary Efficacy Endpoint: Rate of Serious Bacterial Infections per person-year on treatment.

| | |
|---|--|
| End point title | Primary Efficacy Endpoint: Rate of Serious Bacterial Infections per person-year on treatment. ^[1] |
| End point description: The primary efficacy endpoint is the rate of SBI (defined as bacteremia/sepsis, bacterial meningitis, osteomyelitis/septic arthritis, bacterial pneumonia, and visceral abscess) per person-year on treatment. No SBIs were observed during the study. For this reason, it was not possible to calculate a CI using the originally planned compound Poisson process model. In the alternative analysis of CIs based on the standard Poisson distribution, overall the upper limit of the 2- sided 98% CI was 0.065 in the primary observation period and 0.054 in the total treatment period in both the FAS and PP analysis set. | |
| End point type | Primary |
| End point timeframe: Baseline to end of the study. (Every 4 weeks until the final evaluation at week 65) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

| End point values | Full analysis set (FAS) | Per Protocol (PP) | | |
|-----------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 75 | 75 | | |
| Units: Rate of SBI | | | | |
| number (not applicable) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Primary Pharmacokinetic Endpoint: AUC_T at Steady-State Conditions

| | |
|-----------------|--|
| End point title | Primary Pharmacokinetic Endpoint: AUC _T at Steady-State Conditions ^[2] |
|-----------------|--|

End point description:

The AUC_T (i.e., AUC from time 0 (start of the infusion) to the end of the nominal dosing period, standardised to 1 week) at PKSC2 (steady-state conditions) In several cases, AUC_T could not be calculated due to very flat time-concentration profiles.

Geometric mean was 2166.13 h*g/L.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

AUC from time 0 (start of the infusion) to the end of the nominal dosing period. Measured at Week 12 and Week 28.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

| End point values | PK Set | | | |
|--|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 24 | | | |
| Units: AUC _T of IgG (h*g/L) | | | | |
| arithmetic mean (standard deviation) | 2232.61 (± 585.842) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total number (rate) of infections per person-year

| | |
|-----------------|---|
| End point title | Total number (rate) of infections per person-year |
|-----------------|---|

End point description:

The annual rate of all infections of any kind or seriousness.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to end of the study, up to 65 weeks

| End point values | Full analysis set (FAS) | | | |
|-----------------------------|-------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 75 | | | |
| Units: Rate | | | | |
| number (not applicable) | | | | |
| Rate of other infections | 3.414 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Non-serious Infections

| | |
|------------------------|------------------------|
| End point title | Non-serious Infections |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 65 weeks | |

| End point values | Full analysis set (FAS) | | | |
|---------------------------------------|-------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 75 | | | |
| Units: infections | | | | |
| number (not applicable) | | | | |
| Ear infections | 8 | | | |
| Eye infections | 3 | | | |
| Infections of the GI tract | 25 | | | |
| Infections of the genitourinary tract | 24 | | | |
| Upper respiratory tract infections | 179 | | | |
| Lower respiratory tract infections | 32 | | | |
| Infections of the skin | 6 | | | |
| Infections not (elsewhere) classified | 16 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Total IgG and IgG Subclasses

| | |
|--------------------------------------|--------------------------------------|
| End point title | Cmax of Total IgG and IgG Subclasses |
| End point description: | |
| Cmax of Total IgG and IgG Subclasses | |
| End point type | Secondary |

End point timeframe:

Up to 28 days

| End point values | PK Set | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: g/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| IgG Total Cmax | 13.47 (± 3.655) | | | |
| IgG1 Cmax | 8.56 (± 1.858) | | | |
| IgG2 Cmax | 3.88 (± 1.532) | | | |
| IgG3 Cmax | 0.32 (± 0.127) | | | |
| IgG4 Cmax | 0.40 (± 0.567) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of Total IgG and IgG Subclasses

| | |
|------------------------|--------------------------------------|
| End point title | Tmax of Total IgG and IgG Subclasses |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 28 days | |

| End point values | PK Set | | | |
|--|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: hours | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| Tmax Total IgG | 49.62 (0.8 to 98.3) | | | |
| Tmax IgG1 | 50.50 (1.5 to 167.7) | | | |
| Tmax IgG2 | 72.20 (0.5 to 167.7) | | | |
| Tmax IgG3 | 49.62 (1.8 to 98.1) | | | |
| Tmax IgG4 | 47.50 (0.6 to 167.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Total IgG and IgG Subclasses

| | |
|-----------------|-------------------------------------|
| End point title | AUC of Total IgG and IgG Subclasses |
|-----------------|-------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 28 days

| End point values | PK Set | | | |
|--|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 25 | | | |
| Units: h*g/L | | | | |
| number (not applicable) | | | | |
| IgG Total AUC Number Patients Analyzed | 24 | | | |
| IgG Total AUC Mean | 2232.61 | | | |
| IgG Total AUC SD | 585.842 | | | |
| IgG1 AUC Number Patients Analyzed | 22 | | | |
| IgG1 AUC Mean | 1424.69 | | | |
| IgG1 AUC SD | 298.776 | | | |
| IgG2 AUC Number Patients Analyzed | 23 | | | |
| IgG2 AUC Mean | 659.57 | | | |
| IgG2 AUC SD | 262.295 | | | |
| IgG3 AUC Number Patients Analyzed | 25 | | | |
| IgG3 AUC Mean | 48.65 | | | |
| IgG3 AUC SD | 18.455 | | | |
| IgG4 AUC Number Patients Analyzed | 25 | | | |
| IgG4 AUC Mean | 71.40 | | | |
| IgG4 AUC SD | 102.578 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Levels of Serum IgG

| | |
|-----------------|----------------------------|
| End point title | Trough Levels of Serum IgG |
|-----------------|----------------------------|

| | |
|--|-----------|
| End point description: | |
| Trough levels of serum IgG, IgG1, IgG2, IgG3, IgG4 at PK 7 days after 28th infusion of octanorm. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 65 weeks | |

| End point values | PK Set | | | |
|---------------------------------------|------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: g/L | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Total IgG | 11.85 (10.00 to 13.70) | | | |
| IgG1 | 7.51 (6.58 to 9.00) | | | |
| IgG2 | 3.12 (2.69 to 3.85) | | | |
| IgG3 | 0.27 (0.20 to 0.34) | | | |
| IgG4 | 0.15 (0.11 to 0.32) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: IVIG to Octanorm DCF (Based on the Area Under the Concentration-time Curve [AUC_T])

| | |
|--|---|
| End point title | IVIG to Octanorm DCF (Based on the Area Under the Concentration-time Curve [AUC _T]) |
| End point description: | |
| IVIG to octanorm Dose Conversion Factor (based on the area under the concentration-time curve [AUC _T]) - Regression Model without Restriction. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 29 weeks | |

| End point values | PK Set | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | 1.278 (± 0.9401) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the whole study from Visit 1 up to Visit 22 (Termination visit)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Safety Population (SAF) |
|-----------------------|-------------------------|

Reporting group description: -

| Serious adverse events | Safety Population (SAF) | | |
|---|-------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 75 (12.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Grand mal convulsion | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Asperger's disorder | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute odontogenic jaw osteomyelitis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumocystis jirovecii infection | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus bronchiolitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tracheitis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Safety Population (SAF) | | |
|---|-------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 61 / 75 (81.33%) | | |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 9 / 75 (12.00%) | | |
| occurrences (all) | 10 | | |
| Excoriation | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | | |
| occurrences (all) | 6 | | |
| Fall | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | | |
| occurrences (all) | 4 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | | |
| occurrences (all) | 14 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 11 / 75 (14.67%) | | |
| occurrences (all) | 14 | | |
| Infusion site erythema | | | |
| subjects affected / exposed | 7 / 75 (9.33%) | | |
| occurrences (all) | 12 | | |
| Infusion site reaction | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 10 | | |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 4 / 75 (5.33%) 5 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 11 / 75 (14.67%) 18 6 / 75 (8.00%) 8 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all) | 12 / 75 (16.00%) 22 7 / 75 (9.33%) 7 6 / 75 (8.00%) 8 | | |
| Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 4 / 75 (5.33%) 6 | | |
| Renal and urinary disorders Dysuria | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | | |
| Muscle spasms | | | |
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed occurrences (all) | 21 / 75 (28.00%) 33 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed occurrences (all) | 17 / 75 (22.67%) 37 | | |
| Sinusitis | | | |
| subjects affected / exposed occurrences (all) | 15 / 75 (20.00%) 25 | | |
| Rhinitis | | | |
| subjects affected / exposed occurrences (all) | 11 / 75 (14.67%) 17 | | |
| Bronchitis | | | |
| subjects affected / exposed occurrences (all) | 7 / 75 (9.33%) 14 | | |
| Urinary tract infection | | | |
| subjects affected / exposed occurrences (all) | 6 / 75 (8.00%) 11 | | |
| Acute sinusitis | | | |
| subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 13 | | |
| Rhinovirus infection | | | |
| subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 7 | | |
| Influenza | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 5 / 75 (6.67%) | | |
| occurrences (all) | 5 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | | |
| occurrences (all) | 6 | | |
| Laryngitis | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | | |
| occurrences (all) | 5 | | |
| Otitis media | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | | |
| occurrences (all) | 5 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 16 September 2015 | Protocol Version 7: incorporates the change of the maximal number of patients in the age group ≥ 16 years: amended from 28 to a maximum of 39. In the PK substudy, the number of enrolled patients was changed from 24 to maximum of 34 patients. Exclusion criterion no. 3 was amended allowing the upper level of the BMI to be <40 (previously BMI ≤ 30). The method of subcutaneous administration for adult patients was amended: increase of maximal volume to 40 mL per site, and the total flow rate of max. 100mL per hour together for all sites after the 40th s.c. administration. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported