



Clinical trial results:

A Phase III, Multicenter, Open-label, Randomized, Two-Period, Crossover Bioequivalence Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Gammaplex® 10 and Gammaplex® 5% in Primary Immunodeficiency Diseases

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-002290-21 |
| Trial protocol | GB HU |
| Global end of trial date | 13 April 2016 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 22 April 2017 |
| First version publication date | 22 April 2017 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | GMX07 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01963143 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bio Products Laboratory Limited |
| Sponsor organisation address | Dagger Lane, Elstree, United Kingdom, WD6 3BX |
| Public contact | Head of Medical Affairs, Bio Products Laboratory Limited, 44 2089572200, medinfo@bpl.co.uk |
| Scientific contact | Head of Medical Affairs, Bio Products Laboratory Limited, 44 2089572200, medinfo@bpl.co.uk |

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 April 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 11 January 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 April 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the bioequivalence of Gammaplex® 10 (Gammaplex® [10%] 10 g in 100 mL) intravenous immunoglobulin (IGIV) and Gammaplex® 5% (Gammaplex® [5%] 5 g in 100 mL) IGIV with respect to area under the curve within a 28-day dosing interval (AUC0-28) in a cohort of adult subjects.

Protection of trial subjects:

The number of PK samples was the minimum number required to provide an evaluable PK profile.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 06 January 2014 |
| 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 | United Kingdom: 3 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | United States: 44 |
| Worldwide total number of subjects | 48 |
| EEA total number of subjects | 4 |

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) | 9 |
| Adolescents (12-17 years) | 8 |
| Adults (18-64 years) | 31 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects underwent screening assessments within 30 days before first dose of Gammaplex 5% or Gammaplex 10%

Period 1

| | |
|------------------------------|-------------------------------|
| Period 1 title | All subjects (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Gammaplex 5% & Gammaplex 10% on a 21-day treatment schedule |

Arm description:

Adult subjects aged 16+ years

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Gammaplex 5% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All subjects were to receive a dose of 300 to 800 mg/kg/infusion. Subjects were to receive the same dose as per their prior IGIV.

Infusions were administered on either a 21-day or 28-day treatment schedule, depending on the subject's cycle of infusions during prior IGIV treatment. Subjects were randomised to receive either 5 infusions of Gammaplex 5% followed by 5 infusions of Gammaplex 10%, or 5 infusions of Gammaplex 10% followed by 5 infusions of Gammaplex 5%.

| | |
|--|-----------------------|
| Investigational medicinal product name | Gammaplex 10% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All subjects were to receive a dose of 300 to 800 mg/kg/infusion. Subjects were to receive the same dose as per their prior IGIV.

Infusions were administered on either a 21-day or 28-day treatment schedule, depending on the subject's cycle of infusions during prior IGIV treatment. Subjects were randomised to receive either 5 infusions of Gammaplex 5% followed by 5 infusions of Gammaplex 10%, or 5 infusions of Gammaplex 10% followed by 5 infusions of Gammaplex 5%.

| | |
|------------------|---|
| Arm title | Gammaplex 5% & Gammaplex 10% on a 28-day treatment schedule |
|------------------|---|

Arm description:

Adult subjects aged 16+ years

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------------------|
| Investigational medicinal product name | Gammaplex 5% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All subjects were to receive a dose of 300 to 800 mg/kg/infusion. Subjects were to receive the same dose as per their prior IGIV.

Infusions were administered on either a 21-day or 28-day treatment schedule, depending on the subject's cycle of infusions during prior IGIV treatment. Subjects were randomised to receive either 5 infusions of Gammaplex 5% followed by 5 infusions of Gammaplex 10%, or 5 infusions of Gammaplex 10% followed by 5 infusions of Gammaplex 5%.

| | |
|--|-----------------------|
| Investigational medicinal product name | Gammaplex 10% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All subjects were to receive a dose of 300 to 800 mg/kg/infusion. Subjects were to receive the same dose as per their prior IGIV.

Infusions were administered on either a 21-day or 28-day treatment schedule, depending on the subject's cycle of infusions during prior IGIV treatment. Subjects were randomised to receive either 5 infusions of Gammaplex 5% followed by 5 infusions of Gammaplex 10%, or 5 infusions of Gammaplex 10% followed by 5 infusions of Gammaplex 5%.

| | |
|------------------|--|
| Arm title | Gammaplex 10% on a 21 or 28 day treatment schedule |
|------------------|--|

Arm description:

Paediatric subjects aged <16 years

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Gammaplex 10% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All subjects were to receive a dose of 300 to 800 mg/kg/infusion. Subjects were to receive the same dose as per their prior IGIV.

Infusions were administered on either a 21-day or 28-day treatment schedule, depending on the subject's cycle of infusions during prior IGIV treatment.

| Number of subjects in period 1 | Gammaplex 5% & Gammaplex 10% on a 21-day treatment schedule | Gammaplex 5% & Gammaplex 10% on a 28-day treatment schedule | Gammaplex 10% on a 21 or 28 day treatment schedule |
|---------------------------------------|---|---|--|
| Started | 14 | 19 | 15 |
| Completed | 14 | 18 | 14 |
| Not completed | 0 | 1 | 1 |
| Consent withdrawn by subject | - | 1 | - |
| Physician decision | - | - | 1 |

Baseline characteristics

Reporting groups

| | |
|------------------------------------|---|
| Reporting group title | Gammaflex 5% & Gammaflex 10% on a 21-day treatment schedule |
| Reporting group description: | |
| Adult subjects aged 16+ years | |
| Reporting group title | Gammaflex 5% & Gammaflex 10% on a 28-day treatment schedule |
| Reporting group description: | |
| Adult subjects aged 16+ years | |
| Reporting group title | Gammaflex 10% on a 21 or 28 day treatment schedule |
| Reporting group description: | |
| Paediatric subjects aged <16 years | |

| Reporting group values | Gammaflex 5% & Gammaflex 10% on a 21-day treatment schedule | Gammaflex 5% & Gammaflex 10% on a 28-day treatment schedule | Gammaflex 10% on a 21 or 28 day treatment schedule |
|--|---|---|--|
| Number of subjects | 14 | 19 | 15 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 9 |
| Adolescents (12-17 years) | 1 | 1 | 6 |
| Adults (18-64 years) | 13 | 18 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 12 | 9 | 7 |
| Male | 2 | 10 | 8 |

| Reporting group values | Total | | |
|--|-------|--|--|
| Number of subjects | 48 | | |
| 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) | 9 | | |
| Adolescents (12-17 years) | 8 | | |
| Adults (18-64 years) | 31 | | |
| From 65-84 years | 0 | | |

| | | | |
|-------------------|---|--|--|
| 85 years and over | 0 | | |
|-------------------|---|--|--|

| | | | |
|--------------------|----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 28 | | |
| Male | 20 | | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Gammaplex 5% & Gammaplex 10% on a 21-day treatment schedule |
| Reporting group description: Adult subjects aged 16+ years | |
| Reporting group title | Gammaplex 5% & Gammaplex 10% on a 28-day treatment schedule |
| Reporting group description: Adult subjects aged 16+ years | |
| Reporting group title | Gammaplex 10% on a 21 or 28 day treatment schedule |
| Reporting group description: Paediatric subjects aged <16 years | |

Primary: Area under the curve within a 28-day dosing interval (absolute values)

| | |
|--|--|
| End point title | Area under the curve within a 28-day dosing interval (absolute values) ^{[1][2]} |
| End point description: Absolute AUC(0-t) | |
| End point type | Primary |
| End point timeframe: After a minimum of 5 infusions of Gammaplex 5% and a minimum of 5 infusions of Gammaplex 10% | |

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: Statistical analysis was not performed. This secondary analysis comprised a bioequivalence assessment on the PK parameters.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The primary endpoint was based on the bioequivalence of Gammaplex 10% and Gammaplex 5% at the 28 day dosing interval only.

| | | | | |
|---|---|--|--|--|
| End point values | Gammaplex 5% & Gammaplex 10% on a 28-day treatment schedule | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 16 | | | |
| Units: ratio Gammaplex 10%/Gammaplex 5% | | | | |
| number (confidence interval 90%) | 1.01 (0.98 to 1.03) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Area under the curve within a 28-day dosing interval (baseline-adjusted values)

| | |
|--|---|
| End point title | Area under the curve within a 28-day dosing interval (baseline-adjusted values) ^{[3][4]} |
| End point description: Baseline-adjusted AUC(0-t) | |
| End point type | Primary |

End point timeframe:

After a minimum of 5 infusions of Gammaplex 5% and a minimum of 5 infusions of Gammaplex 10%

Notes:

[3] - 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: Statistical analysis was not performed. The primary analysis comprised a bioequivalence assessment on the PK parameters.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The primary endpoint was based on the bioequivalence of Gammaplex 10% and Gammaplex 5% at the 28 day dosing interval only.

| | | | | |
|---|---|--|--|--|
| End point values | Gammaplex 5% & Gammaplex 10% on a 28-day treatment schedule | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 16 | | | |
| Units: ratio Gammaplex 10%/Gammaplex 5% | | | | |
| number (confidence interval 90%) | 1.07 (0.93 to 1.23) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve within a 21-day dosing interval (absolute values)

| | |
|-----------------|---|
| End point title | Area under the curve within a 21-day dosing interval (absolute values) ^[5] |
|-----------------|---|

End point description:

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

End point timeframe:

After a minimum of 5 infusions of Gammaplex 5% and a minimum of 5 infusions of Gammaplex 10%

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This secondary endpoint was based on the bioequivalence of Gammaplex 10% and Gammaplex 5% at the 21 day dosing interval only.

| | | | | |
|---|---|--|--|--|
| End point values | Gammaflex 5% & Gammaflex 10% on a 21-day treatment schedule | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ratio Gammaflex 10%/Gammaflex 5% | | | | |
| number (confidence interval 90%) | 0.99 (0.95 to 1.02) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve within a 21-day dosing interval (baseline-adjusted values)

| | |
|-----------------|--|
| End point title | Area under the curve within a 21-day dosing interval (baseline-adjusted values) ^[6] |
|-----------------|--|

End point description:

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

End point timeframe:

After a minimum of 5 infusions of Gammaflex 5% and a minimum of 5 infusions of Gammaflex 10%

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This secondary endpoint was based on the bioequivalence of Gammaflex 10% and Gammaflex 5% at the 21 day dosing interval only.

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Gammaflex 5% & Gammaflex 10% on a 21-day treatment schedule | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ratio | | | | |
| number (confidence interval 90%) | 1.1 (0.96 to 1.26) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: IgG trough levels for 28-day dosing interval

| | |
|-----------------|---|
| End point title | IgG trough levels for 28-day dosing interval ^[7] |
|-----------------|---|

End point description:

| | | | | |
|--|---|--|--|--|
| End point type | Secondary | | | |
| End point timeframe: | | | | |
| After a minimum of 5 infusions of Gammaplex 5% and a minimum of 5 infusions of Gammaplex 10% | | | | |
| Notes: | | | | |
| [7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This secondary endpoint was based on the bioequivalence of Gammaplex 10% and Gammaplex 5% at the 28 day dosing interval only. | | | | |
| End point values | Gammaplex 5% & Gammaplex 10% on a 28-day treatment schedule | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 16 | | | |
| Units: ratio Gammaplex 10%/Gammaplex 5% | | | | |
| number (confidence interval 90%) | 0.98 (0.94 to 1.02) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: IgG trough levels for 21-day dosing interval

| | | | | |
|--|---|--|--|--|
| End point title | IgG trough levels for 21-day dosing interval ^[8] | | | |
| End point description: | | | | |
| | | | | |
| End point type | Secondary | | | |
| End point timeframe: | | | | |
| After a minimum of 5 infusions of Gammaplex 5% and a minimum of 5 infusions of Gammaplex 10% | | | | |
| Notes: | | | | |
| [8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This secondary endpoint was based on the bioequivalence of Gammaplex 10% and Gammaplex 5% at the 28 day dosing interval only. | | | | |
| End point values | Gammaplex 5% & Gammaplex 10% on a 21-day treatment schedule | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ratio Gammaplex 10%/Gammaplex 5% | | | | |
| number (confidence interval 90%) | 0.95 (0.92 to 0.99) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signature of informed consent until 28 days following the last dose of Gammaplex 5% or Gammaplex 10%

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | Gammaplex 5% - all subjects |
|-----------------------|-----------------------------|

Reporting group description: -

| | |
|-----------------------|------------------------------|
| Reporting group title | Gammaplex 10% - all subjects |
|-----------------------|------------------------------|

Reporting group description: -

| Serious adverse events | Gammaplex 5% - all subjects | Gammaplex 10% - all subjects | |
|---|-----------------------------|------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 1 / 47 (2.13%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| neuroendocrine tumour | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 47 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 47 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| IIIrd nerve paralysis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 47 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 47 (2.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Gammaplex 5% - all subjects | Gammaplex 10% - all subjects | |
|---|------------------------------------|-------------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 23 / 33 (69.70%) | 44 / 47 (93.62%) | |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 47 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | 11 / 47 (23.40%) | |
| occurrences (all) | 16 | 28 | |
| Migraine | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 3 / 47 (6.38%) | |
| occurrences (all) | 4 | 4 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 47 (2.13%) | |
| occurrences (all) | 7 | 5 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 3 / 47 (6.38%) | |
| occurrences (all) | 0 | 3 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 2 / 47 (4.26%) | |
| occurrences (all) | 2 | 2 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 47 (2.13%) | |
| occurrences (all) | 3 | 1 | |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|-----------------|-----------------|--|
| disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 4 / 47 (8.51%) | |
| occurrences (all) | 2 | 4 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 2 / 47 (4.26%) | |
| occurrences (all) | 3 | 2 | |
| Rales | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 47 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 5 / 47 (10.64%) | |
| occurrences (all) | 0 | 6 | |
| Dermatitis | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 47 (2.13%) | |
| occurrences (all) | 3 | 1 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 47 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 3 / 47 (6.38%) | |
| occurrences (all) | 2 | 4 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 8 / 47 (17.02%) | |
| occurrences (all) | 2 | 8 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 5 / 47 (10.64%) | |
| occurrences (all) | 2 | 7 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 33 (12.12%) | 4 / 47 (8.51%) | |
| occurrences (all) | 5 | 5 | |
| Acute sinusitis | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 5 / 33 (15.15%) | 3 / 47 (6.38%) | |
| occurrences (all) | 6 | 3 | |
| Chronic sinusitis | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 4 / 47 (8.51%) | |
| occurrences (all) | 2 | 4 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 7 / 47 (14.89%) | |
| occurrences (all) | 1 | 7 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 6 / 47 (12.77%) | |
| occurrences (all) | 0 | 6 | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 47 (0.00%) | |
| occurrences (all) | 3 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 21 May 2014 | Investigational New Drug number added Abbreviations updated Exclusion criterion 18: clarified fructose intolerance Exclusion criteria 13 and 14: defined 'chronic' added recommended frequency of monitoring vital signs PK sample collection windows expanded to allow for subject compliance guidance provided for recording medical history defined who could record TEE monitoring added that results of a chest x-ray or CT scan could be used at Screening instead of only chest x-ray clarified dosing calculation formula removed reference to Table 6, Appendix I (Summary of Investigator and Sponsor Reporting Responsibilities) DMC first meeting date modified correction of DMC abbreviation Table 6 (Schedule of Study Visit Assessments): footnote d amended to include CT scan Table 7 (Schedule of Pharmacokinetic Assessments): PK sample collection windows expanded to allow for subject compliance |
| 09 October 2014 | Added text to allow for additional infusions if subjects have dosing/scheduling issues and are not at steady state prior to the scheduled PK sampling Added text to mention the role of the Home Health Agency in PK sampling Removed the requirement for the infusion bag to be made of polyvinyl chloride |
| 16 July 2015 | Added measles antibody testing to the list of specific antibody tests (to be performed on the last available reserve blood sample taken after each treatment period) Updated Sponsor contact details |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28316003>