



## Clinical trial results:

### A Multicenter Study of Long-Term Clinical Outcomes of Immune Globulin Subcutaneous (Human) (SCIG) IgPro20 in Subjects with Primary Immunodeficiency

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2014-003409-13 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 22 July 2014   |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 13 July 2016     |
| First version publication date | 18 February 2015 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | IgPro20_3006 |
|-----------------------|--------------|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | CSL Behring K.K.  |
| Sponsor organisation address | KDX Toyosu Grandsquare, 1-7-12 Shinonome, Koto-ku, Tokyo, Japan, 135-0062   |
| Public contact               | Trial Registration Co-ordinator, CSL Behring, clinicaltrials@cslbehring.com |
| Scientific contact           | Trial Registration Co-ordinator, CSL Behring, clinicaltrials@cslbehring.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? | Yes |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 07 October 2014 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 22 July 2014    |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To assess the long-term efficacy, tolerability, and safety of IgPro20 in subjects with primary immunodeficiency (PID) as an extension to the preceding follow-up study ZLB07\_001CR.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Ministry of Health, Labor, and Welfare (Japan, MHLW) Notification #28 (Good Clinical Practice [GCP], 27 March 1997), YakuShokuShinsaHatsu Notification #1001001 (01 October 2010), and the Declaration of Helsinki (version of 2008). The study was also carried out in keeping with requirements set forth in the Pharmaceutical Affairs Law 14-3 and 80-2. In addition, this study was conducted in accordance with the International Conference on Harmonisation (ICH) GCP guidelines, and Standard Operating Procedures (SOPs) for clinical research and development at CSL Behring and the clinical research organizations involved. The study protocol and all amendments were approved by an Independent Ethics Committee(s) (IECs) / Institutional Review Board(s) (IRBs). Before undergoing screening procedures for possible enrollment into the study, subjects were informed, in an understandable form, about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 12 October 2011 |
| 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 | Japan: 22 |
| Worldwide total number of subjects   | 22        |
| EEA total number of subjects         | 0         |

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)     | 5  |
| Adolescents (12-17 years) | 5  |
| Adults (18-64 years)      | 12 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This multicenter study enrolled subjects at 9 study centers in Japan who had participated in the preceding follow-up study ZLB07\_001CR (CT.gov identifier: NCT01458171).

### Pre-assignment

Screening details:

Only subjects participating in the preceding follow-up study ZLB07\_001CR were eligible. Enrolment visit of this study was on same day as completion visit of the preceding follow-up study ZLB07\_001CR.

### Period 1

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

### Arms

|           |         |
|-----------|---------|
| Arm title | IgPro20 |
|-----------|---------|

Arm description:

IgPro20 is a 20% (weight per volume [w/v]) liquid formulation of human immunoglobulin for subcutaneous (SC) use.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Hizentra®   |
| Investigational medicinal product code |   |
| Other name                             | Human Normal Immunoglobulin, Immune globulin subcutaneous (Human) |
| Pharmaceutical forms                   | Solution for injection  |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

IgPro20 is a 20% (weight per volume [w/v]) liquid formulation of human immunoglobulin for subcutaneous (SC) use.

| Number of subjects in period 1 | IgPro20 |
|--------------------------------|---------|
| Started                        | 22      |
| Completed                      | 19      |
| Not completed                  | 3       |
| Consent withdrawn by subject   | 1       |
| Adverse event, non-fatal       | 1       |
| Pregnancy                      | 1       |

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Overall |
|-----------------------|---------|

Reporting group description: -

| Reporting group values                                | Overall | Total |  |
|---|---------|-------|--|
| Number of subjects                                    | 22      | 22    |  |
| Age categorical                                       |         |       |  |
| Units: Subjects                                       |         |       |  |
| In utero  | 0       | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0       | 0     |  |
| Newborns (0-27 days)                                  | 0       | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0       | 0     |  |
| Children (2-11 years)                                 | 5       | 5     |  |
| Adolescents (12-17 years)                             | 5       | 5     |  |
| Adults (18-64 years)                                  | 12      | 12    |  |
| From 65-84 years                                      | 0       | 0     |  |
| 85 years and over                                     | 0       | 0     |  |
| Age continuous  |         |       |  |
| Units: years  |         |       |  |
| arithmetic mean                                       | 21.6    |       |  |
| standard deviation                                    | ± 13.98 | -     |  |
| Gender categorical                                    |         |       |  |
| Units: Subjects                                       |         |       |  |
| Female  | 9       | 9     |  |
| Male  | 13      | 13    |  |

## End points

### End points reporting groups

|  |                         |
|--|-------------------------|
| Reporting group title  | IgPro20                 |
| Reporting group description:<br>IgPro20 is a 20% (weight per volume [w/v]) liquid formulation of human immunoglobulin for subcutaneous (SC) use.   |                         |
| Subject analysis set title   | FAS (Full analysis set) |
| Subject analysis set type  | Full analysis           |
| Subject analysis set description:<br>The FAS comprised all subjects receiving at least 1 IgPro20 infusion.   |                         |
| Subject analysis set title   | PPS (Per protocol set)  |
| Subject analysis set type  | Per protocol            |
| Subject analysis set description:<br>The PPS population comprised all subjects with the disease under study who a) received uniformly repeated IgPro20 infusions at weeks intervals and b) who had at least 1 documented total serum IgG trough level. |                         |

### Primary: Annualized rate of infection episodes (serious and non-serious)

|   |   |
|---|---|
| End point title   | Annualized rate of infection episodes (serious and non- |
| End point description:<br>The annualized rate of infection episodes (serious and non-serious) was based on the total number of infection episodes and the total number of subject study days for all subjects in the FAS and the PPS and adjusted to 365 days.                                  |   |
| End point type  | Primary   |
| End point timeframe:<br>Up to 36 months   |   |
| Notes:<br>[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.<br>Justification: Variables were descriptively summarised. No formal statistical tests were planned or performed. |   |

| End point values                   | FAS (Full analysis set) | PPS (Per protocol set) |  |  |
|------------------------------------|-------------------------|------------------------|--|--|
| Subject group type                 | Subject analysis set    | Subject analysis set   |  |  |
| Number of subjects analysed        | 22                      | 17                     |  |  |
| Units: infections per subject year |                         |                        |  |  |
| number (not applicable)            | 2.42                    | 1.91                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with newly developing or worsening adverse events (AEs)

|  |  |
|--|--|
| End point title  | Number of subjects with newly developing or worsening adverse events (AEs) |
| End point description:<br>Number of subjects with newly developing or worsening AEs, overall and classified (i) by severity (mild, moderate, severe) and (ii) by causal relationship to study medication (at least possibly related [i.e., |  |

possibly related, probably related, or related])).

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 36 months      |           |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | IgPro20         |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 22              |  |  |  |
| Units: subjects             |                 |  |  |  |
| All AEs                     | 22              |  |  |  |
| Mild AEs                    | 22              |  |  |  |
| Moderate AEs                | 4               |  |  |  |
| Severe AEs                  | 2               |  |  |  |
| At least possibly related   | 13              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with newly developing or worsening adverse events (AEs)

|   |  |
|---|--|
| End point title   | Percentage of subjects with newly developing or worsening adverse events (AEs) |
| End point description:  |  |
| Percentage of subjects with newly developing or worsening AEs, overall and classified (i) by severity (mild, moderate, severe) and (ii) by causal relationship to study medication (at least possibly related [i.e., possibly related, probably related, or related])). |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Up to 36 months   |  |

|                               |                 |  |  |  |
|-------------------------------|-----------------|--|--|--|
| <b>End point values</b>       | IgPro20         |  |  |  |
| Subject group type            | Reporting group |  |  |  |
| Number of subjects analysed   | 22              |  |  |  |
| Units: Percentage of subjects |                 |  |  |  |
| number (not applicable)       |                 |  |  |  |
| All AEs                       | 100             |  |  |  |
| Mild AEs                      | 100             |  |  |  |
| Moderate AEs                  | 18.2            |  |  |  |
| Severe AEs                    | 9.1             |  |  |  |
| At least possibly related     | 59.1            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Rate of AEs per infusion

|                 |                          |
|-----------------|--------------------------|
| End point title | Rate of AEs per infusion |
|-----------------|--------------------------|

End point description:

Rate of adverse events per infusion, overall and classified (i) by severity (mild, moderate, severe) and (ii) by causal relationship to study medication (not related or unlikely related; at least possibly related [i.e., possibly related, probably related, or related]).

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

End point timeframe:

Up to 36 months

| End point values                | IgPro20         |  |  |  |
|---------------------------------|-----------------|--|--|--|
| Subject group type              | Reporting group |  |  |  |
| Number of subjects analysed     | 22              |  |  |  |
| Units: AE rate per infusion     |                 |  |  |  |
| number (not applicable)         |                 |  |  |  |
| All AEs                         | 0.248           |  |  |  |
| Mild AEs                        | 0.244           |  |  |  |
| Moderate AEs                    | 0.003           |  |  |  |
| Severe AEs                      | 0.001           |  |  |  |
| Not related or unlikely related | 0.098           |  |  |  |
| At least possibly related       | 0.15            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Annualized rate of clinically documented serious bacterial infections (SBIs)

|                 |  |
|-----------------|--|
| End point title | Annualized rate of clinically documented serious bacterial infections (SBIs) |
|-----------------|--|

End point description:

SBIs are defined as bacterial pneumonia, bacteremia and septicemia, osteomyelitis/septic arthritis, bacterial meningitis, or visceral abscess. The annualized rate was based on the total number of SBIs and the total number of subject study days for all subjects in the FAS (N=22) and PPS (N=17) and adjusted to 365 days.

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



End point timeframe:

Up to 36 months

| End point values             | FAS (Full analysis set) | PPS (Per protocol set) |  |  |
|------------------------------|-------------------------|------------------------|--|--|
| Subject group type           | Subject analysis set    | Subject analysis set   |  |  |
| Number of subjects analysed  | 22                      | 17                     |  |  |
| Units: SBIs per subject year |                         |                        |  |  |
| number (not applicable)      | 0                       | 0                      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Annualized rate of days out of work/school/kindergarten/day care or unable to perform normal daily activities due to infections

|                 |   |
|-----------------|---|
| End point title | Annualized rate of days out of work/school/kindergarten/day care or unable to perform normal daily activities due to infections |
|-----------------|---|

End point description:

The annualized rate was based on the total number of days out of work/school/kindergarten/day care or unable to perform normal daily activities due to infections and the total number of subject study days for all subjects in the FAS and PPS and adjusted to 365 days.

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

End point timeframe:

Up to 36 months

| End point values               | FAS (Full analysis set) | PPS (Per protocol set) |  |  |
|--------------------------------|-------------------------|------------------------|--|--|
| Subject group type             | Subject analysis set    | Subject analysis set   |  |  |
| Number of subjects analysed    | 22                      | 17                     |  |  |
| Units: Annualized rate of days |                         |                        |  |  |
| number (not applicable)        | 3.24                    | 3.26                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Annualized rate of days of hospitalization due to infections

|                 |  |
|-----------------|--|
| End point title | Annualized rate of days of hospitalization due to infections |
|-----------------|--|

End point description:

The annualized rate was based on the total number of days hospitalized and the total number of subject study days for all subjects in the FAS and PPS and adjusted to 365 days.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 36 months      |           |

| End point values                            | FAS (Full analysis set) | PPS (Per protocol set) |  |  |
|---|-------------------------|------------------------|--|--|
| Subject group type                          | Subject analysis set    | Subject analysis set   |  |  |
| Number of subjects analysed                 | 22                      | 17                     |  |  |
| Units: Annualized rate of days hospitalized |                         |                        |  |  |
| number (not applicable)                     | 0.27                    | 0.34                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of use of antibiotics for infection prophylaxis and treatment

|   |  |
|---|--|
| End point title   | Duration of use of antibiotics for infection prophylaxis and treatment |
| End point description:  |  |
| The annualized rate was based on the total number of days treated with antibiotics and the total number of subject study days for all subjects in the FAS and PPS and adjusted to 365 days. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Up to 36 months   |  |

| End point values                       | FAS (Full analysis set) | PPS (Per protocol set) |  |  |
|--|-------------------------|------------------------|--|--|
| Subject group type                     | Subject analysis set    | Subject analysis set   |  |  |
| Number of subjects analysed            | 22                      | 17                     |  |  |
| Units: Annualized rate of days treated |                         |                        |  |  |
| number (not applicable)                | 170.1                   | 199.42                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Median serum IgG concentration

|                        |                                |
|------------------------|--------------------------------|
| End point title        | Median serum IgG concentration |
| End point description: |                                |
| End point type         |                                |
| Secondary              |                                |

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End point timeframe:

Up to 36 months

---

| <b>End point values</b>       | FAS (Full analysis set) | PPS (Per protocol set) |  |  |
|-------------------------------|-------------------------|------------------------|--|--|
| Subject group type            | Subject analysis set    | Subject analysis set   |  |  |
| Number of subjects analysed   | 22                      | 17                     |  |  |
| Units: g/L                    |                         |                        |  |  |
| median (full range (min-max)) | 8.32 (5.64 to 11.08)    | 8.13 (5.64 to 11.08)   |  |  |

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

For the duration of the study, that is, up to 36 months per subject.

Adverse event reporting additional description:

Only AEs starting at or after the first study drug infusion are included. A total of 2660 infusions of IgPro20 were administered to 22 subjects.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | IgPro20 |
|-----------------------|---------|

Reporting group description:

IgPro20 is a 20% (weight per volume [w/v]) liquid formulation of human immunoglobulin for subcutaneous (SC) use.

| Serious adverse events                            | IgPro20        |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 2 / 22 (9.09%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |
| Respiratory, thoracic and mediastinal disorders   |                |  |  |
| Asthma  |                |  |  |
| subjects affected / exposed                       | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all   | 1 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Infections and infestations                       |                |  |  |
| Bronchitis bacterial                              |                |  |  |
| subjects affected / exposed                       | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Meningitis aseptic                                |                |  |  |
| subjects affected / exposed                       | 1 / 22 (4.55%) |  |  |
| 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 %

| <b>Non-serious adverse events</b>                     | IgPro20          |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 21 / 22 (95.45%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Contusion   |                  |  |  |
| subjects affected / exposed                           | 3 / 22 (13.64%)  |  |  |
| occurrences (all)                                     | 7                |  |  |
| Arthropod bite  |                  |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Nervous system disorders                              |                  |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 8 / 22 (36.36%)  |  |  |
| occurrences (all)                                     | 14               |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Injection site pain                                   |                  |  |  |
| subjects affected / exposed                           | 5 / 22 (22.73%)  |  |  |
| occurrences (all)                                     | 150              |  |  |
| Injection site haematoma                              |                  |  |  |
| subjects affected / exposed                           | 3 / 22 (13.64%)  |  |  |
| occurrences (all)                                     | 3                |  |  |
| Infusion site pain                                    |                  |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)   |  |  |
| occurrences (all)                                     | 108              |  |  |
| Injection site haemorrhage                            |                  |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Gastrointestinal disorders                            |                  |  |  |
| Diarrhoea   |                  |  |  |
| subjects affected / exposed                           | 4 / 22 (18.18%)  |  |  |
| occurrences (all)                                     | 8                |  |  |
| Abdominal pain  |                  |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)   |  |  |
| occurrences (all)                                     | 6                |  |  |

|  |  |  |  |
|--|--|--|--|
| Constipation<br>subjects affected / exposed<br>occurrences (all)   | 2 / 22 (9.09%)<br>2  |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 2 / 22 (9.09%)<br>2  |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 2 / 22 (9.09%)<br>2  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Rhinitis allergic<br>subjects affected / exposed<br>occurrences (all)<br><br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Epistaxis<br>subjects affected / exposed<br>occurrences (all) | 5 / 22 (22.73%)<br>7<br><br>4 / 22 (18.18%)<br>6<br><br>3 / 22 (13.64%)<br>9 |  |  |
| Skin and subcutaneous tissue disorders<br>Eczema<br>subjects affected / exposed<br>occurrences (all)<br><br>Acne<br>subjects affected / exposed<br>occurrences (all)<br><br>Pruritus<br>subjects affected / exposed<br>occurrences (all)                       | 5 / 22 (22.73%)<br>9<br><br>2 / 22 (9.09%)<br>2<br><br>2 / 22 (9.09%)<br>2   |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)  | 4 / 22 (18.18%)<br>6   |  |  |
| Infections and infestations<br>Upper respiratory tract infection   |  |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 8 / 22 (36.36%) |  |  |
| occurrences (all)           | 14              |  |  |
| Influenza                   |                 |  |  |
| subjects affected / exposed | 6 / 22 (27.27%) |  |  |
| occurrences (all)           | 6               |  |  |
| Gastroenteritis             |                 |  |  |
| subjects affected / exposed | 5 / 22 (22.73%) |  |  |
| occurrences (all)           | 5               |  |  |
| Acute sinusitis             |                 |  |  |
| subjects affected / exposed | 3 / 22 (13.64%) |  |  |
| occurrences (all)           | 8               |  |  |
| Conjunctivitis infective    |                 |  |  |
| subjects affected / exposed | 3 / 22 (13.64%) |  |  |
| occurrences (all)           | 3               |  |  |
| Otitis media                |                 |  |  |
| subjects affected / exposed | 3 / 22 (13.64%) |  |  |
| occurrences (all)           | 3               |  |  |
| Pharyngitis                 |                 |  |  |
| subjects affected / exposed | 3 / 22 (13.64%) |  |  |
| occurrences (all)           | 3               |  |  |
| Sinusitis                   |                 |  |  |
| subjects affected / exposed | 3 / 22 (13.64%) |  |  |
| occurrences (all)           | 3               |  |  |
| Bronchitis                  |                 |  |  |
| subjects affected / exposed | 2 / 22 (9.09%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Cystitis                    |                 |  |  |
| subjects affected / exposed | 2 / 22 (9.09%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Dermatitis infected         |                 |  |  |
| subjects affected / exposed | 2 / 22 (9.09%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Impetigo                    |                 |  |  |
| subjects affected / exposed | 2 / 22 (9.09%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Nasopharyngitis             |                 |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 11 / 22 (50.00%) |  |  |
| occurrences (all)           | 44               |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date        | Amendment   |
|-------------|---|
| 22 May 2013 | There was 1 amendment to the original study protocol that was implemented during the study. The main changes were:<br>1. Change in regulatory status of the study from "phase 3 study" to "post-marketing approval study" after approval of IgPro20 in Japan, in compliance with Japanese regulations.<br>2. Extension of expected maximum study duration from "30" to "36" months, until availability of IgPro20 on the market in Japan. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported