



## Clinical trial results:

**Clinical study to evaluate the safety and tolerability of immunoglobulin intravenous (human) 10% (NewGam) administered at high infusion rates to patients with primary immunodeficiency diseases (extension of study NGAM-01)**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2011-005015-82    |
| Trial protocol           | Outside EU/EEA    |
| Global end of trial date | 26 September 2012 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 30 November 2016 |
| First version publication date | 30 November 2016 |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | NGAM-05 |
|-----------------------|---------|

#### Additional study identifiers

|                                    |                |
|------------------------------------|----------------|
| ISRCTN number                      | ISRCTN11002924 |
| ClinicalTrials.gov id (NCT number) | NCT01313507    |
| WHO universal trial number (UTN)   | -              |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Octapharma AG  |
| Sponsor organisation address | Seidenstrasse 2, Lachen, Switzerland, CH-8853  |
| Public contact               | Clinical Research Department, Octapharma Pharmazeutika Produktionsgesellschaft mbH, 0043 1 61032 1202, barbara.pyringer@octapharma.com |
| Scientific contact           | Clinical Research Department, Octapharma Pharmazeutika Produktionsgesellschaft mbH, 0043 1 61032 1202, barbara.pyringer@octapharma.com |

Notes:

### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001110-PIP01-10 |
| 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:

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**Results analysis stage**

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|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 31 July 2013 |
| Is this the analysis of the primary completion data? | No           |

|                                  |                   |
|----------------------------------|-------------------|
| Global end of trial reached?     | Yes               |
| Global end of trial date         | 26 September 2012 |
| Was the trial ended prematurely? | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the safety and tolerability of NewGam when administered at infusion rates from 0.08 mL/kg/min (the maximum rate in study NGAM-01) to 0.14 mL/kg/min.

Protection of trial subjects:

This trial was conducted in accordance to the principles of GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki. 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. Throughout the study safety was assessed, such as occurrence of AEs, safety labs, vital signs and physical examinations.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 05 May 2011 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | Yes         |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 21 |
| Worldwide total number of subjects   | 21                |
| EEA total number of subjects         | 0                 |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| 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)                     | 8 |
| Adolescents (12-17 years)                 | 5 |
| Adults (18-64 years)                      | 8 |
| From 65 to 84 years                       | 0 |

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

## Subject disposition

### Recruitment

Recruitment details:

Patients were taken exclusively from the cohort of patients who had completed the study NGAM-01 and had received NewGam at the maximum infusion rate of 0.08 mL/kg/min without the need for premedication at least for the last three infusions, without restrictions as regards to age group or treatment regimen.

### Pre-assignment

Screening details:

Screening had to be performed at the follow-up visit of the NGAM-01 study.

### 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 | NewGam |
|-----------|--------|

Arm description:

Patients received 200 to 800 mg/kg body weight every 21 ( $\pm$  3) days or 28 ( $\pm$  3) days for 3 months, with individual doses and intervals being dependent on the patient's previous dosing in the NGAM-01 study. Therefore, each patient received either five infusions (at 3-week intervals) or four infusions (at 4-week intervals) of NewGam.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | NewGam, human normal immunoglobulin 10%, solvent/detergent treated solution for intravenous infusion |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for infusion  |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

The range of doses to be infused was 200 to 800 mg/kg body weight every 21 ( $\pm$  3) days or 28 ( $\pm$  3) days, with individual doses and intervals being dependent on the patient's previous dosing in the NGAM-01 study.

|                                       |        |
|---------------------------------------|--------|
| <b>Number of subjects in period 1</b> | NewGam |
| Started                               | 21     |
| Completed                             | 21     |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description:

All patients who received at least one dose of NewGam in the context of this study.

| Reporting group values      | overall trial | Total |  |
|-----------------------------|---------------|-------|--|
| Number of subjects          | 21            | 21    |  |
| Age categorical             |               |       |  |
| Units: Subjects             |               |       |  |
| Children ≥2 Years <12 Years | 8             | 8     |  |
| Adolescents ≥12 Years <16   | 3             | 3     |  |
| Adults ≥16 Years ≤75 Years  | 10            | 10    |  |
| Age continuous              |               |       |  |
| Units: years                |               |       |  |
| arithmetic mean             | 23.8          |       |  |
| standard deviation          | ± 19.78       | -     |  |
| Gender categorical          |               |       |  |
| Units: Subjects             |               |       |  |
| Female                      | 8             | 8     |  |
| Male                        | 13            | 13    |  |

## End points

### End points reporting groups

|  |        |
|--|--------|
| Reporting group title  | NewGam |
| Reporting group description:<br>Patients received 200 to 800 mg/kg body weight every 21 ( $\pm$ 3) days or 28 ( $\pm$ 3) days for 3 months, with individual doses and intervals being dependent on the patient's previous dosing in the NGAM-01 study. Therefore, each patient received either five infusions (at 3-week intervals) or four infusions (at 4-week intervals) of NewGam. |        |

### Primary: Percentage of Participants Who Experienced at Least 1 Adverse Event Causally Related to the Administration of the Study Drug

|  |   |
|--|---|
| End point title  | Percentage of Participants Who Experienced at Least 1 Adverse Event Causally Related to the Administration of the Study Drug <sup>[1]</sup> |
| End point description:<br>An adverse event was considered to be causally related to the administration of the study drug if it judged to be probably or possibly related to the study drug, as assessed by the investigator                          |   |
| End point type   | Primary   |
| End point timeframe:<br>Baseline to the end of the study   |   |
| 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: parameters were presented in descriptive statistics. |   |

| End point values              | NewGam          |  |  |  |
|-------------------------------|-----------------|--|--|--|
| Subject group type            | Reporting group |  |  |  |
| Number of subjects analysed   | 21              |  |  |  |
| Units: percentage of patients |                 |  |  |  |
| number (not applicable)       | 19              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants Who Experienced at Least 1 Adverse Event Temporally Related to the Study Drug

|  |   |
|--|---|
| End point title  | Percentage of Participants Who Experienced at Least 1 Adverse Event Temporally Related to the Study Drug <sup>[2]</sup> |
| End point description:<br>An adverse event was considered to be temporally related to the study drug if it started during an infusion or within 72 hours after the end of an infusion. |   |
| End point type   | Primary   |
| End point timeframe:<br>From Baseline to the end of the study  |   |

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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: parameters were presented in descriptive statistics.

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | NewGam          |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 21              |  |  |  |
| Units: percentage of participants |                 |  |  |  |
| number (not applicable)           | 38.1            |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs had to be reported from baseline to the end of the study.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Safety Set |
|-----------------------|------------|

Reporting group description:

The safety analysis set was the only study population that has been considered in the statistical data presentations. It is defined as all patients who received at least one dose of NewGam in the context of this study.

| Serious adverse events                            | Safety Set     |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 21 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

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

| Non-serious adverse events                            | Safety Set       |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 12 / 21 (57.14%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Contusion   |                  |  |  |
| subjects affected / exposed                           | 2 / 21 (9.52%)   |  |  |
| occurrences (all)                                     | 2                |  |  |
| Nervous system disorders                              |                  |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 2 / 21 (9.52%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| General disorders and administration site conditions  |                  |  |  |



|   |                      |  |  |
|---|----------------------|--|--|
| Chest pain<br>subjects affected / exposed<br>occurrences (all)      | 2 / 21 (9.52%)<br>2  |  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)         | 2 / 21 (9.52%)<br>2  |  |  |
| Gastrointestinal disorders  |                      |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)          | 3 / 21 (14.29%)<br>3 |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)        | 3 / 21 (14.29%)<br>3 |  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)  | 2 / 21 (9.52%)<br>2  |  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)       | 2 / 21 (9.52%)<br>2  |  |  |
| Infections and infestations   |                      |  |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)       | 4 / 21 (19.05%)<br>4 |  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>2  |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported