# Clinical trial results:
# PROSPECTIVE, OPEN-LABEL, NON-CONTROLLED, MULTICENTER, PHASE III CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF OCTAGAM 10% IN PRIMARY IMMUNE THROMBOCYTOPENIA

## Summary

| | |
|---|---|
| EudraCT number | 2012-000796-16 |
| Trial protocol | DE CZ BG PL |
| Global end of trial date | 28 March 2013 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 20 July 2016 |
| First version publication date | 20 July 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | GAMr-30 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| 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 m.b. H., clinical.department@octapharma.com |
| Scientific contact | Clinical Research Department, Octapharma Pharmazeutika Produktionsgesellschaft m.b. H., 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 | 25 October 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 March 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 March 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary efficacy measure was the platelet count and the increase in platelets to – and the maintenance of – specific thresholds. Number and percentage of patients with response, complete response, no response and loss of response as well as time to response and duration of response are presented.

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 safety factors associated with the investigational medicinal product. Safety was assessed by the evaluation of AEs, monitoring of vital signs (blood pressure, heart rate, temperature and respiratory rate), physical examinations (to detect relevant somatic or neurological diseases and with attention to signs and symptomes consistent with a thromboembolic event), laboratory parameters and haematology parameters.

Background therapy:

NA

Evidence for comparator:

NA

| | |
|---|---|
| Actual start date of recruitment | 30 August 2012 |
| 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: 8 |
| Country: Number of subjects enrolled | Bulgaria: 8 |
| Country: Number of subjects enrolled | Czech Republic: 9 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Romania: 7 |
| Worldwide total number of subjects | 33 |
| EEA total number of subjects | 33 |

Notes:

| Subjects enrolled per age group | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 32 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

33 patients were enrolled - 13 centres recruited patients for the analysis in Poland, Germany, Czech Republik, Bulgaria and Romania.

### Pre-assignment

Screening details:

For the study design chosen, randomisation was not applicable. Patients with confirmed diagnosis of chronic primary ITP (threshold PC less than 100x10^9/L) of at least 12 months, older than 18 years of age, complying to all inclusion criteria and no exclusion criterion were enrolled into this study after having given their written IC.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | OCTAGAM 10% |

Arm description:

investigation of efficacy and safety of Intravenous immunoglobulin (IVIG) in patients suffering from primary immune thrombocytopenia (ITP)
A daily dose of 1 g/kg was administered for 2 consecutive days (Day 1 and Day 2), for a total of 2 g/kg.
The initial infusion rate of 0.01 mL/kg/min (60 mg/kg/h) was chosen for safety reasons.
The infusion rate was to be increased gradually to a maximum of 0.12 mL/kg/min (720 mg/kg/h) only if tolerated by the patient.
The patients received IVIG using an infusion pump for precise infusion rates.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Octagam 10% |
| Investigational medicinal product code | GAMr-30 |
| Other name | Octagam 10% |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Daily dose of 1 g/kg given for two consecutive days, for a total of 2 g/kg.
The initial infusion rate of 0.01 mL/kg/min (60 mg/kg/h) has been chosen for safety reasons. The infusion rate was increased gradually to a maximum of 0.12 mL/kg/min (720 mg/kg/h), only if tolerated by the patient. The patients received IVIG using an infusion pump for precise infusion rates.

| **Number of subjects in period 1** | OCTAGAM 10% |
|---|---|
| Started | 33 |
| Completed | 29 |
| Not completed | 4 |
| Physician decision | 1 |
| Adverse event, non-fatal | 3 |

## Baseline characteristics

### Reporting groups

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

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 33 | 33 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 32 | 32 | |
| From 65-84 years | 1 | 1 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 43.1 | | |
| standard deviation | ± 14.98 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 21 | 21 | |
| Male | 12 | 12 | |

### Subject analysis sets

| Subject analysis set title | Treated (Safety Set) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

set of all patients exposed to treatment

| Subject analysis set title | Full Analysis Set (FAS) |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

consists of all patients of the safety set who satisfied all major eligibility criteria and for whom at least one post-baseline  measurement of platelet concentration data is available.

| Subject analysis set title | Per-Protocol Set (PP) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

The PP set consists of all patients of the FA set excluding those who showed major protocol violations which may have an impact on the evaluation of the primary endpoint. This is the set of patients who participated in the study as intended and are available for the primary efficacy evaluation.

| **Reporting group values** | Treated (Safety Set) | Full Analysis Set (FAS) | Per-Protocol Set (PP) |
|---|---|---|---|
| Number of subjects | 33 | 29 | 28 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | 32 | 28 | 27 |
| From 65-84 years | 1 | 1 | 1 |
| 85 years and over | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 21 | | |
| Male | 12 | | |

## End points

### End points reporting groups

| Reporting group title | OCTAGAM 10% |
|---|---|

Reporting group description:

investigation of efficacy and safety of Intravenous immunoglobulin (IVIG) in patients suffering from primary immune thrombocytopenia (ITP)
A daily dose of 1 g/kg was administered for 2 consecutive days (Day 1 and Day 2), for a total of 2 g/kg.
The initial infusion rate of 0.01 mL/kg/min (60 mg/kg/h) was chosen for safety reasons.
The infusion rate was to be increased gradually to a maximum of 0.12 mL/kg/min (720 mg/kg/h) only if tolerated by the patient.
The patients received IVIG using an infusion pump for precise infusion rates.

| Subject analysis set title | Treated (Safety Set) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

set of all patients exposed to treatment

| Subject analysis set title | Full Analysis Set (FAS) |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

consists of all patients of the safety set who satisfied all major eligibility criteria and for whom at least one post-baseline measurement of platelet concentration data is available.

| Subject analysis set title | Per-Protocol Set (PP) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

The PP set consists of all patients of the FA set excluding those who showed major protocol violations which may have an impact on the evaluation of the primary endpoint. This is the set of patients who participated in the study as intended and are available for the primary efficacy evaluation.

### Primary: Clinical response

| End point title | Clinical response[1] |
|---|---|

End point description:

Efficacy Endpoint:
The primary efficacy measure was the platelet count and the increase in platelets to – and the maintenance of – specific thresholds. Number and percentage of patients with response, complete response, no response and loss of response. The exact definitions of response, complete response and no response were taken from the applicable CHMP Guideline.

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

End point timeframe:

The entire study duration for an individual patient was approximately 3–4 weeks. All patients received 1 g/kg/day Octagam 10% by intravenous infusion for 2 consecutive days.

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: Derived PK parameter; no statistical analysis or comparison performed (single-arm study)

| End point values | Full Analysis Set (FAS) | Per-Protocol Set (PP) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 29 | 28 | | |
| Units: number of patients | | | | |
| Response (R) | 23 | 21 | | |
| Complete Response (CR) | 15 | 14 | | |
| Non-Response | 7 | 7 | | |
| Loss of Response | 11 | 11 | | |

| | | | | |
|---|---|---|---|---|
| Loss of Complete Response | 11 | 11 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Time to response

| End point title | Time to response[2] |
|---|---|

End point description:

the time to response and duration of response are presented descriptively to facilitate the comparison of the study results to data from the literature.

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

End point timeframe:

The entire study duration for an individual patient was approximately 3–4 weeks. All patients received 1 g/kg/day Octagam 10% by intravenous infusion for 2 consecutive days.

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: Derived PK parameter; no statistical analysis or comparison performed (single-arm study)

| End point values | Full Analysis Set (FAS) | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 29 | | | |
| Units: days | | | | |
| 1 day | 17 | | | |
| 2 days | 5 | | | |
| 3 days | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Duration of response

| End point title | Duration of response[3] |
|---|---|

End point description:

Duration of response was measured from the achievement of complete response or response to loss of complete response or response.

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

End point timeframe:

The entire study duration for an individual patient was approximately 3–4 weeks. All patients received 1 g/kg/day Octagam 10% by intravenous infusion for 2 consecutive days.

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: Derived PK parameter; no statistical analysis or comparison performed (single-arm study)

| End point values | Full Analysis Set (FAS) | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 23 | | | |
| Units: number of days | | | | |
| 7 days | 1 | | | |
| 10 days | 3 | | | |
| 13 days | 2 | | | |
| 15 days | 1 | | | |
| 16 days | 1 | | | |
| 18 days | 3 | | | |
| 19 days | 3 | | | |
| 20 days | 9 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

24 hours SAE reporting adverse events

Adverse event reporting additional description:

The condition of the patient was monitored throughout the study. At each visit, whether scheduled or unscheduled, AEs were elicited using a standard non-leading question.
All AEs/SAEs that occured after singing the informed consent but before the first administration of the IMP, were considered “baseline” or “non-treatment-emergent”.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | all patients exposed to treatment (safety set) |

Reporting group description: -

| Serious adverse events | all patients exposed to treatment (safety set) | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| aseptic meningitis | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | all patients exposed to treatment (safety set) | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 33 (72.73%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 33 (39.39%) | | |
| occurrences (all) | 18 | | |
| Blood and lymphatic system disorders | | | |
| Autoimmune thrombocytopenia | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | | |
| occurrences (all) | 5 | | |
| Idiopathic thrombocytopenic purpura | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | | |
| occurrences (all) | 3 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | | |
| occurrences (all) | 8 | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | | |
| occurrences (all) | 3 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | | |
| occurrences (all) | 3 | | |
| Vometing | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Meningitis aseptic<br>subjects affected / exposed<br>occurrences (all) | 2 / 33 (6.06%)<br>2 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported