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 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 Units: years			
arithmetic mean	43.1		
standard deviation	± 14.98	-	
Gender categorical 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.
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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 subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 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