Clinical trial results:
Clinical study to evaluate the efficacy, safety and kinetics of Octagam® 10% for replacement therapy in Primary Immunodeficiency Diseases (PID)

Summary

EudraCT number	2007-002611-27
Trial protocol	DE FR GB
Global end of trial date	30 September 2010

Results information

Result version number	v1 (current)
This version publication date	31 December 2016
First version publication date	31 December 2016

Trial information

Trial identification

Sponsor protocol code	GAM10-03

Additional study identifiers

ISRCTN number	ISRCTN63491981
ClinicalTrials.gov id (NCT number)	NCT00811174
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 Prod.Ges.m.b.H. , 0043 (1)61032-0,
Scientific contact	Clinical Research Department, Octapharma Pharmazeutika Prod.Ges.m.b.H. , 0043 (1)61032-0,

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	12 September 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2010
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to investigate the safety of Octagam® 10% in replacement therapy in PID and to compare the pharmacokinetic profile of Octagam® 10%with that of the previously used commercial Octagam® 5% (Pharmacokinetic sub-study).
Safety outcome parameters will be:
• Occurrence of adverse events.
• Short term tolerance parameters including vital signs (blood pressure, heart rate, temperature, respiratory rate).
• Laboratory parameters (hematology, clinical chemistry, direct Coombs'test, urinalysis) and tests for viral safety.
Pharmacokinetic outcome parameters will be the parameter Cmax, Cmin, t ½, Tmax, AUC, volume of distribution, and incremental recovery of serum total IgG; of IgG subclasses (IgG1, IgG2, IgG3, IgG4); of specific antibodies against Haemophilus influenzae, Streptococcus pneumoniae (types 4, 6B, 9V, 14, 18C, 19F, 23F), CMV, VZV, tetanus, measles; and of glucose and maltose.

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	31 March 2009
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	Poland: 2
Country: Number of subjects enrolled	Germany: 3
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	2
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was planned to be performed in patients with PID requiring antibody replacement therapy and who had received Octagam 5% replacement therapy at a steady dose and schedule for at least six infusions up to study entry

Pre-assignment

Screening details:

The study was planned to be performed in patients with PID requiring antibody replacement therapy and who had received Octagam 5% replacement therapy at a steady dose and schedule for at least six infusions up to study entry.Screening was to be performed between the end of the last pre-study infusion and the first infusion in the study

Period 1

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

Arms

Arm title	Octagam 10%

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Octagam 10% ,Human immunoglobulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Depending on the regular treatment intervals (every 3 or 4 weeks) the patient was to receive 17 or 13 infusions of Octagam 10% in the course of this study. The dose administered per kg body weight and the treatment intervals were to remain the same throughout the study, as long as trough levels of serum IgG were maintained above 5 g/L.

Number of subjects in period 1	Octagam 10%
Started	5
Completed	2
Not completed	3
Early Termination of the study	3

Baseline characteristics

Reporting groups	
Reporting group title	Enrolled Patients (Overall Study)

Reporting group description: -

Reporting group values	Enrolled Patients (Overall Study)	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
From 16-66 years	5	5	
Age continuous Units: years			
arithmetic mean	31.4		
standard deviation	± 20.8	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	5	5	

End points

End points reporting groups

Reporting group title	Octagam 10%

Reporting group description: -

Primary: Serum IgG trough levels before each administration (pre-next dose)

End point title	Serum IgG trough levels before each administration (pre-next dose)[1]

End point description:

Owing to the limited data available (only 5 patients enrolled, of whom 2 completed the study and 3 ended treatment prematurely), efficacy and PK analyses were not performed.

End point type	Primary

End point timeframe:

Screening visit until the last study visit

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: The study was terminated prematurely. Owing to the limited data available (only 5 patients enrolled, of whom 2 completed the study and 3 ended treatment prematurely), efficacy and PK analyses were not performed.

End point values	Octagam 10%			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: G/L				
number (not applicable)				

Notes:

[2] - Because of the premature termination no analyses was done

Statistical analyses

No statistical analyses for this end point

Primary: IgG-profile pharmacokinetics determined at the last but one (or last) infusion

End point title	IgG-profile pharmacokinetics determined at the last but one (or last) infusion[3]

End point description:

Owing to the limited data available (only 5 patients enrolled, of whom 2 completed the study and 3 ended treatment prematurely), efficacy and PK analyses were not performed.

End point type	Primary

End point timeframe:

From screening visit to last visit of the study

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: The study was terminated prematurely. Owing to the limited data available (only 5 patients enrolled, of whom 2 completed the study and 3 ended treatment prematurely), efficacy and PK analyses were not performed.

End point values	Octagam 10%			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: g/L				
number (not applicable)				

Notes:

[4] - Because of the premature termination no analyses was done

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed throughout the whole study from screening visit to the last visit of the study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Octagam 10%

Reporting group description: -

Serious adverse events	Octagam 10%		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Condylomata Inguinal	Additional description: surgical removal		
subjects affected / exposed	1 / 5 (20.00%)		
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 %

Non-serious adverse events	Octagam 10%		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)		
Investigations			
Urine uric acid abnormal			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		

Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Dental operation			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Wart excision			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Oropharyngeal plaque			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
pharyngolaryngeal pain			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Bronchitis chronic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Gastrointestinal infection			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Onychomycosis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Subcutaneous abscess			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2009	• Inclusion criterion of primary immunodeficiency requiring immunoglobulin replacement therapy must be associated with hypo- or agammaglobulinemia • Consistent dose to be infused is widened to 200 – 800 mg/kg BW • Update of drug safety section according to new drug safety SOP • Change of study duration • Terminology "anonymity/anonymous/anonymised" is replaced by appropriate wording

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 September 2010	The study was terminated prematurely on 30-Sep-2010 owing to temporary license suspension of Octagam 5% and 10%.	-

Notes:

Limitations and caveats

None reported