Clinical trial results:
CLINICAL STUDY TO EVALUATE THE EFFICACY, PHARMACOKINETICS AND SAFETY OF IMMUNOGLOBULIN INTRAVENOUS (HUMAN) 10% (NEWGAM) IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISEASES

Summary

EudraCT number	2009-011434-10
Trial protocol	DE Outside EU/EEA
Global end of trial date	07 June 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-01

Additional study identifiers

ISRCTN number	ISRCTN05425999
ClinicalTrials.gov id (NCT number)	NCT01012323
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 and Development, Octapharma Pharmazeutika Produktionsgesellschaft mbH, 43 1610320,
Scientific contact	Clinical Research and Development, Octapharma Pharmazeutika Produktionsgesellschaft mbH, 43 1610320,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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:

Results analysis stage

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	07 June 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the efficacy of NewGam in preventing serious bacterial infections compared to historical control data.

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. Throughout the study safety was assessed, such as occurrence of AEs, lab values, vital signs and physical examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2010
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: 11
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	51
EEA total number of subjects	13

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)	13
Adolescents (12-17 years)	13
Adults (18-64 years)	24

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The patients were to be recruited into three age strata (at least 2 years and less than 12 years, at least 12 years and less than 16 years of age, and at least 16 years and no greater than 75 years) and- depending on the patient's pre-study infusion interval- on two treatment schedules (3-week or 4 week IVIG schedule)

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:

Participants received NewGam 200-800 mg/kg body weight intravenously every 3 weeks (17 infusions) or 4 weeks (13 infusions) for 1 year.

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:

200 to 800 mg/kg body weight every 21 (+/-3) days or 28 (+/-3) days, with individual doses and intervals being dependent on the patient's previous IVIG dose and interval before entry into the study

Number of subjects in period 1	NewGam
Started	51
Completed	50
Not completed	1
Physician decision	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial
Reporting group description:	
All patients exposed to treatment	

Reporting group values	overall trial	Total	
Number of subjects	51	51	
Age categorical Units: Subjects			
Children (2-11 years)	13	13	
Adolescents (12-15 years)	12	12	
Adults (16-75 years)	26	26	
Age continuous Units: years			
arithmetic mean	26.8		
full range (min-max)	2 to 65	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	33	33	

End points

End points reporting groups

Reporting group title	NewGam

Reporting group description:

Participants received NewGam 200-800 mg/kg body weight intravenously every 3 weeks (17 infusions) or 4 weeks (13 infusions) for 1 year.

Primary: rate of serious bacterial infections per person-year

End point title	rate of serious bacterial infections per person-year[1]

End point description:

The number of serious bacterial infections per person-year of treatment was calculated by the following formula: Total number of serious bacterial infections / patient-years on NewGam treatment. Serious bacterial infections were defined as bacteraemia/sepsis, bacterial meningitis, osteomyelitis/septic arthritis, bacterial pneumonia, and visceral abscess.

End point type	Primary

End point timeframe:

Baseline to end of the study (up to 12 months)

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 primary endpoint (rate of serious bacterial infections per person-year) is presented as point estimates of the rate along with a 99% confidence interval (CI).
The rate of serious bacterial infections per year was calculated by the following formula: r = Total number of serious bacterial infections/Patient years on NewGam treatment

End point values	NewGam			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Baseline to end of the study (up to 12m)				
number (confidence interval 99%)	0.08 (0.0127 to 0.5033)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The condition of the patient was monitored throughout the whole study (baseline up to completion/termination of the study)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Safety Set

Reporting group description:

all patients who received at least part of one treatment with NewGam.

Serious adverse events	Safety Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 51 (9.80%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Septoplasty			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			

subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 51 (1.96%)		
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	Safety Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 51 (88.24%)		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 51 (27.45%)		
occurrences (all)	36		
Migraine			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 51 (19.61%)		
occurrences (all)	12		
Pain			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Pyrexia			

subjects affected / exposed occurrences (all)	11 / 51 (21.57%) 14		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	 3 / 51 (5.88%) 4		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 3 / 51 (5.88%) 3 6 / 51 (11.76%) 7 4 / 51 (7.84%) 7 3 / 51 (5.88%) 4 7 / 51 (13.73%) 11 7 / 51 (13.73%) 7		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 7 / 51 (13.73%) 8 3 / 51 (5.88%) 3 5 / 51 (9.80%) 6		
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	9		
Myalgia			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Pain in extremity			
subjects affected / exposed	6 / 51 (11.76%)		
occurrences (all)	8		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Bronchitis			
subjects affected / exposed	8 / 51 (15.69%)		
occurrences (all)	10		
Gastroenteritis			
subjects affected / exposed	8 / 51 (15.69%)		
occurrences (all)	9		
Gastroenteritis viral			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	6 / 51 (11.76%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	13 / 51 (25.49%)		
occurrences (all)	19		
Oral herpes			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	4		
Otitis media			

subjects affected / exposed	7 / 51 (13.73%)		
occurrences (all)	10		
Pharyngitis			
subjects affected / exposed	6 / 51 (11.76%)		
occurrences (all)	11		
Pharyngitis streptococcal			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	7		
Sinusitis			
subjects affected / exposed	13 / 51 (25.49%)		
occurrences (all)	23		
Upper respiratory tract infection			
subjects affected / exposed	15 / 51 (29.41%)		
occurrences (all)	21		
Viral infection			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	4		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2010	Amendment 4: • The recruitment period was prolonged and the number of sites was increased. • Patients less than 16 years of age with a history of diabetes mellitus type II were allowed to enter the study. • Flu vaccination including H1N1 strain during the study was allowed. • Measles was to be reported as an SAE. • Only AEs classified as at least possibly related to the study drug (ADRs) to be assessed as to their expectedness by the sponsor in accordance with current Octapharma drug safety procedures • Following the adoption of a new CHMP guideline on the clinical investigation of IVIG (EMA/CHMP/BPWP/94033/2007 rev 2) , interim analysis after 6 months of treatment in 15 patients was deleted without any consequence for the study.
16 February 2012	Amendment 5: • The planned clinical end was delayed by one quarter. • A clarification was added that patients were to be evaluated in the age group assigned at the time when they had signed the informed consent • Secondary endpoints and safety evaluation were updated upon request of the Paediatric Committee (PDCO). • A clarification was added that discrepancies between diary entries and eCRF entries were to be explained by investigator in source records. • Information was added that therapeutic efficacy parameters were to be evaluated per person-year on treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported