



Clinical trial results:

Prospective, Open-label, Non-controlled, Multicenter, Phase III Clinical Study to Evaluate the Efficacy and Safety of Immunoglobulin Intravenous (Human) 10% (NEWGAM) in Primary Immune Thrombocytopenia

Summary

EudraCT number	2009-014589-24
Trial protocol	DE CZ BG FR
Global end of trial date	22 July 2013

Results information

Result version number	v1 (current)
This version publication date	28 July 2016
First version publication date	28 July 2016

Trial information

Trial identification

Sponsor protocol code	NGAM-02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01349790
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsgesellschaft mbH
Sponsor organisation address	Oberlaaer Strasse 235 A-1100 Vienna Austria , Vienna , Austria, A-1100
Public contact	Clinical Research and Development, Octapharma Pharmazeutika Produktionsgesellschaft mbH, 0043 161032, clinical.department@octapharma.com
Scientific contact	Clinical Research and Development, Octapharma Pharmazeutika Produktionsgesellschaft mbH, 0043 161032, 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	05 March 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 July 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of NewGam in correcting the platelet count.

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 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, labvalues, vital signs and physical examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2011
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: 4
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Czech Republic: 8
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	India: 4
Worldwide total number of subjects	40
EEA total number of subjects	21

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)	38
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

40 Patients were enrolled at 20 centres, located in Germany, Czech Republic, Russia, Bulgaria, India, Poland, Romania and Ukraine.

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
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Arm description:

total dose of 2g/kg NewGam, human normal immunoglobulin 10%, for treatment in primary immune thrombocytopenia on 2 consecutive days

Arm type	Experimental
Investigational medicinal product name	NewGam, human normal immunoglobulin 10%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Infusion of 1 g/kg per day on 2 consecutive days.

Number of subjects in period 1	NewGam
Started	40
Completed	31
Not completed	9
Adverse event, serious fatal	2
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Lost to follow-up	1
Investigator decision	3

Baseline characteristics

Reporting groups

Reporting group title	overall trial
Reporting group description:	
NewGam 10%	

Reporting group values	overall trial	Total	
Number of subjects	40	40	
Age categorical			
Units: Subjects			
Adults (18-64 years)	38	38	
Age continuous			
Units: years			
arithmetic mean	36.7		
full range (min-max)	18 to 72	-	
Gender categorical			
Units: Subjects			
Female	17	17	
Male	23	23	

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

consists of all patients in the Safety Set who satisfy all major eligibility criteria and for whom at least 1 post-baseline measurement of platelet concentration data is available. This is the set of eligible patients with treatment effects measured, according to the intention-to-treat (ITT) principle.

Subject analysis set title	First Per Protocol (PP1) Set
Subject analysis set type	Per protocol

Subject analysis set description:

All patients of the FA set excluding those who had major protocol violations before the primary efficacy endpoint (Day 8) was reached and which may have had an impact on the evaluation of the primary endpoint

Reporting group values	Full Analysis Set	First Per Protocol (PP1) Set	
Number of subjects	36	33	
Age categorical			
Units: Subjects			
Adults (18-64 years)	35	32	
Age continuous			
Units: years			
arithmetic mean	36.2	36	
full range (min-max)	18 to 67	18 to 67	
Gender categorical			
Units: Subjects			
Female	17	14	
Male	19	19	

End points

End points reporting groups

Reporting group title	NewGam
Reporting group description: total dose of 2g/kg NewGam, human normal immunoglobulin 10%, for treatment in primary immune thrombocytopenia on 2 consecutive days	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: consists of all patients in the Safety Set who satisfy all major eligibility criteria and for whom at least 1 post-baseline measurement of platelet concentration data is available. This is the set of eligible patients with treatment effects measured, according to the intention-to-treat (ITT) principle.	
Subject analysis set title	First Per Protocol (PP1) Set
Subject analysis set type	Per protocol
Subject analysis set description: All patients of the FA set excluding those who had major protocol violations before the primary efficacy endpoint (Day 8) was reached and which may have had an impact on the evaluation of the primary endpoint	

Primary: Response Rate

End point title	Response Rate ^[1]
End point description: The primary endpoint of this study was the response rate, i.e., the proportion of patients with an elevation of platelet count to greater equal $50 \times 10^9/L$ within 7 days of the first infusion, i.e., by study Day 8 (at least once prior to Day 9). The evaluation of the primary objective was performed for the FA set (ITT analysis) and for the PP1 set (PP analysis).	
End point type	Primary
End point timeframe: Baseline, Day 2 to Day 8.	
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 analysis of the primary objective aimed at demonstrating that the response rate after administration of NewGam (p), defined as the proportion of patients with an elevation of platelet count to greater equal $50 \times 10^9/L$ within 7 days after the first infusion, was above a pre-defined value of 0.60. This threshold was obtained from a historical control value of $p_0=0.75$ and a region of indifference of $\delta=0.15$. The hypothesis ($H_0: p \leq p_0 - \delta$) was tested at a 1-sided significance level of $\alpha = 0.025$.	

End point values	Full Analysis Set	First Per Protocol (PP1) Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	33		
Units: Proportion in %				
number (confidence interval 95%)	80.6 (36.98 to 91.81)	81.8 (64.54 to 93.02)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE were evaluated at each visit until day 63 of the study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14
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Reporting groups

Reporting group title	All patients exposed to treatment (Safety Set)
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Reporting group description: -

Serious adverse events	All patients exposed to treatment (Safety Set)		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 40 (15.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Cerebral haematoma			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Meningitis aseptic			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Autoimmune thrombocytopenia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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	30 / 40 (75.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 40 (42.50%)		
occurrences (all)	22		
Dizziness			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	9		
Asthenia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Autoimmune thrombocytopenia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	8		
Anaemia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	7		
Idiopathic thrombocytopenic purpura			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Vomiting			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2011	Amendment #2: The inclusion criterion for age was narrowed to at least 18 years and no older than 65 years old (was 80 years) Two new exclusion criteria added: • Patients with BMI greater than or equal to 30 kg/m² • Patients with risk factors for TEE in which the risks outweigh the potential benefit of NewGam treatment Medically measurable parameters leading to an early termination of individual patients were implemented. The concomitant medications and AEs were to be monitored until Day 63 instead of until Day 22.
14 June 2012	Amendment #3: • The exclusion criterion regarding prior rituximab therapy was extended to 4 months from 3 months. • A second confirmatory assessment was included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
29 April 2013	Following discussions with the FDA, the sponsor was informed that if the submitted data provided evidence of both safety and efficacy, the FDA would review the data with 36 patients in the FA Set. Therefore, the sponsor decided to terminate the study and not enrol any further patients, and proceed with a single, final analysis using the data from the 40 enrolled patients.	-

Notes:

Limitations and caveats

None reported