Clinical trial results:
An open-label, prospective, multicenter study to investigate the specificity of in vivo antibody binding to red blood cells in subjects with chronic immune thrombocytopenic purpura (ITP) treated with IgPro10 (Privigen®) who have shown signs of hemolysis.

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-000263-27
Trial protocol	PL BG
Global end of trial date	17 September 2014

Results information

Result version number	v1 (current)
This version publication date	24 July 2016
First version publication date	24 July 2016

Trial information

Trial identification

Sponsor protocol code	IgPro10_4001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01390649
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring GmbH
Sponsor organisation address	Emil-von-Behring-Strasse 76, Marburg, Germany, 35041
Public contact	Clinical Trial Disclosure Manager, CSL Behring, clinicaltrials@cslbehring.com
Scientific contact	Clinical Trial Disclosure Manager, CSL Behring, clinicaltrials@cslbehring.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	19 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study was requested as a post-marketing commitment study by the United States Food and Drug Administration (FDA). The primary objective was to investigate the specificity of in vivo antibody binding to red blood cells in 10 subjects with chronic Immune thrombocytopenic purpura (ITP) who showed signs of hemolysis and who experienced clinically significant intravascular hemolytic reactions following treatment with Privigen.
The study was designed to explore potential mechanisms of hemolysis by analysis of the specificity of the antibodies possibly involved.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines, applicable international and national regulatory requirements, and standard operating procedures for clinical research and development at CSL Behring.
The study protocol and all amendments were approved by the Independent Ethics Committee(s) / Institutional Review Board(s) of the participating centers. Before undergoing screening procedures for possible enrollment into the study, subjects were informed, in an understandable form, about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study. The investigator may have ceased study treatment and withdrawn the subject, or the subject may have withdrawn himself from participation in the study at any time. If a subject was withdrawn from the study or further participation was declined, the subject continued to have access to medical care and will be treated according to routine medical practice, but will no longer receive the investigational medicinal product.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	02 November 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	Bulgaria: 7
Country: Number of subjects enrolled	Romania: 31
Country: Number of subjects enrolled	Serbia: 19
Worldwide total number of subjects	57
EEA total number of subjects	38

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)	55
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening occurred within 6 days before treatment with IgPro10 (Privigen). Subjects who met all of the inclusion criteria and none of the exclusion criteria could be enrolled into the study. Of 58 eligible subjects, 1 withdrew consent before treatment and 57 subjects were treated with Privigen.

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	IgPro10

Arm description:

Subjects treated with IgPro10

Arm type	Experimental
Investigational medicinal product name	Privigen®
Investigational medicinal product code	IgPro10
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IgPro10 was administered by IV infusion either as a single dose of 1 g/kg bw on 1 day or 2 doses of 1 g/kg bw on 2 days (2 g/kg bw total dose) dependent on the response to the first IgPro10 dose.

Number of subjects in period 1	IgPro10
Started	57
Completed	56
Not completed	1
Physician decision	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
All subjects who received at least 1 IgPro10 infusion.	

Reporting group values	Overall Trial	Total	
Number of subjects	57	57	
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)	55	55	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	43.5		
standard deviation	± 13.1	-	
Gender categorical Units: Subjects			
Female	37	37	
Male	20	20	

End points

End points reporting groups

Reporting group title	IgPro10

Reporting group description:

Subjects treated with IgPro10

Primary: Set of Antibodies Most Frequently Bound to Red Blood Cells (RBCs) in Subjects Experiencing Clinically Significant Intravascular Hemolysis

End point title	Set of Antibodies Most Frequently Bound to Red Blood Cells (RBCs) in Subjects Experiencing Clinically Significant Intravascular Hemolysis[1]

End point description:

The occurrence of clinically significant intravascular hemolysis was determined by an independent Adjudication Committee. No subject experienced clinically significant intravascular hemolysis; therefore, the primary safety endpoint could not be analyzed.

End point type	Primary

End point timeframe:

Within 3 days of infusion

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: No subject experienced clinically significant intravascular hemolysis; therefore, the primary safety endpoint could not be analyzed.

End point values	IgPro10			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Antibodies to erythrocytes				

Notes:

[2] - No subject experienced clinically significant intravascular hemolysis; therefore, no analysis made.

Statistical analyses

No statistical analyses for this end point

Secondary: Responder Rate

End point title	Responder Rate

End point description:

The responder rate is the percentage of subjects who have a platelet response (defined as a platelet count increase at least once to ≥ 50 x 10^9/L after the first IgPro10 administration).

End point type	Secondary

End point timeframe:

Within 6 days after the first infusion

End point values	IgPro10			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Percent of subjects				
number (confidence interval 95%)	74 (61 to 83)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: For the duration of individual subject participation in the study, up to approximately 35 days.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	IgPro10
Reporting group description: IgPro10 was administered by IV infusion either as a single dose of 1 g/kg bw on 1 day or 2 doses of 1 g/kg bw on 2 days (2 g/kg bw total dose) dependent on the response to the first IgPro10 dose.	

Serious adverse events	IgPro10		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 57 (1.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Immune Thrombocytopenic Purpura			
subjects affected / exposed	1 / 57 (1.75%)		
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	IgPro10		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 57 (33.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 57 (29.82%)		
occurrences (all)	23		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed occurrences (all)	3 / 57 (5.26%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 April 2012	The main changes to the protocol in this amendment were as follows: - Update of efficacy endpoints towards new EMA guideline from 2010: EMA/CHMP/BPWP/94033/2007 rev. 2 from 22 Jul 2010. Guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg). - Updates to revise wording on risks for hemolysis. - Deletion of certain exclusion criteria. - Changes in permitted concomitant medications. - Allowance of re-screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
17 September 2014	By September 2014, no case of clinically significant intravascular hemolysis was found, and the Food and Drug Administration (FDA) agreed to halt the study and analyze all hemolysis-relevant endpoints using FDA criteria for hemolysis in addition to analyses planned in the protocol. The study was not restarted.	-

Notes:

Limitations and caveats

None reported