Clinical trial results:
A Multicenter Extension Study of the Efficacy, Tolerability, and Safety of Immune Globulin Subcutaneous (Human) IgPro20 in Subjects With Primary Immunodeficiency (PID)

Summary

EudraCT number	2014-003605-15
Trial protocol	Outside EU/EEA
Global end of trial date	16 June 2010

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	IgPro20_3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00719680
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring AG
Sponsor organisation address	Wankdorfstrasse 10, Bern 22, Switzerland, 3000
Public contact	Trial Registration Co-ordinator, CSL Behring, clinicaltrials@cslbehring.com
Scientific contact	Trial Registration Co-ordinator, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 May 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 June 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine whether a long-term use of a new human immunoglobulin G with proline (IgPro) is safe and effective in the treatment of primary immunodeficiency.

Protection of trial subjects:

This study was conducted in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, the Declaration of Helsinki (version of 1996), and standard operating procedures for clinical research and development at CSL Behring and the Clinical Research Organizations (CROs) involved. Compliance with these requirements also constitutes conformity with the ethical principles of the Declaration of Helsinki. The study was conducted under a protocol reviewed and approved by an IRB; the study was conducted by scientifically and medically qualified persons; the benefits of the study were in proportion to the risks; the rights and welfare of the subjects were respected; the physicians conducting the study did not find the hazards to outweigh the potential benefits; the results reported are accurate; and each subject or subject's parent or legal guardian gave his or her written informed consent before any protocol-driven tests or evaluations were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 June 2008
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	United States: 21
Worldwide total number of subjects	21
EEA total number of subjects	0

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)	1
Adolescents (12-17 years)	1

Adults (18-64 years)	16
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This multicenter study was conducted at 4 sites in the US. The number of subjects treated at each site ranged from 2 to 9.

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	IgPro20

Arm description:

A liquid formulation of normal human IgG at a concentration of 20%. IgPro20 was administered as a subcutaneous infusion weekly or twice weekly, depending on the investigator's judgment and the subject’s preference.

Arm type	Experimental
Investigational medicinal product name	IgPro20
Investigational medicinal product code	
Other name	Human Normal Immunoglobulin for Subcutaneous Administration (IGSC), Hizentra, IgG with Proline
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IgPro20 dose is the same as in the previous pivotal study ZLB04_009CR (EudraCT Number: 2014-003607-30, NCT00419341) infused subcutaneously weekly or twice a week (in the latter case, half of a weekly dose will be used)

Number of subjects in period 1	IgPro20
Started	21
Completed	16
Not completed	5
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	IgPro20

Reporting group description:

A liquid formulation of normal human IgG at a concentration of 20%. IgPro20 was administered as a subcutaneous infusion weekly or twice weekly, depending on the investigator's judgment and the subject’s preference.

Reporting group values	IgPro20	Total	
Number of subjects	21	21	
Age categorical Units: Subjects			
>=2 to <12 years	1	1	
>=12 to < 16 years	1	1	
>=16 to < 65 years	16	16	
>=65 years	3	3	
Age continuous Units: years			
arithmetic mean	42.4		
standard deviation	± 18.53	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	6	6	

End points

End points reporting groups

Reporting group title	IgPro20

Reporting group description:

A liquid formulation of normal human IgG at a concentration of 20%. IgPro20 was administered as a subcutaneous infusion weekly or twice weekly, depending on the investigator's judgment and the subject’s preference.

Subject analysis set title	IgPro20 - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intention-to-Treat (ITT) population comprised all subjects treated with study medication during any study period.

Subject analysis set title	IgPro20 - PPE
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol Efficacy (PPE) population comprised all subjects who completed at least 48 weeks of the efficacy period that started with the first IgPro20 dose in this study.

Subject analysis set title	IgPro20 - AT
Subject analysis set type	Safety analysis

Subject analysis set description:

The all-treated (AT) safety population comprised all subjects treated with the study medication during any study period.

Primary: Annualized Rate of Serious Bacterial Infection (Intention-to-Treat Population)

End point title	Annualized Rate of Serious Bacterial Infection (Intention-to-Treat Population)[1]

End point description:

The annualized rate was based on the total number of infections and the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

Acute serious bacterial infections included pneumonia, bacteremia/septicemia, osteomyelitis/septic arthritis, bacterial meningitis, and visceral abscess.

End point type	Primary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

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: End point data analysis consisted of the estimation of the annualized rate and 99% upper confidence interval limit as per protocol; no statistical hypothesis was planned or conducted (in accordance with the US Food and Drug Administration Guidance for Industry on “Safety, efficacy, and pharmacokinetic studies to support marketing of immune globulin intravenous (human) as replacement therapy for primary humoral immunodeficiency” [June 2008]).

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[2]			
Units: infections per subject year				
number (not applicable)	0.06			

Notes:

[2] - Subject study days analyzed: 11950

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Serious Bacterial Infection (Per-Protocol Efficacy Population)

End point title	Annualized Rate of Serious Bacterial Infection (Per-Protocol Efficacy Population)

End point description:

The annualized rate was based on the total number of infections and the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

Acute serious bacterial infections included pneumonia, bacteremia/septicemia, osteomyelitis/septic arthritis, bacterial meningitis, and visceral abscess.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - PPE			
Subject group type	Subject analysis set			
Number of subjects analysed	18[3]			
Units: infections per subject year				
number (not applicable)	0.03			

Notes:

[3] - Subject study days analyzed: 11037

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Any Infection

End point title	Annualized Rate of Any Infection

End point description:

The annualized rate was based on the total number of infections and the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[4]			
Units: infections per subject year				
number (not applicable)	2.38			

Notes:

[4] - Subject study days analyzed: 11950

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Levels of Total Immunoglobulin G (IgG) Serum Concentrations

End point title	Trough Levels of Total Immunoglobulin G (IgG) Serum Concentrations

End point description:

Mean of individual median total IgG trough concentration.

End point type	Secondary

End point timeframe:

Before infusion at Weeks 1, 24, 48, 72, and 96

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: g/L				
arithmetic mean (standard deviation)	11.98 (± 3.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days Out of Work / School / Kindergarten / Day Care or Inability to Perform Normal Activities Due to Infection

End point title	Number of Days Out of Work / School / Kindergarten / Day Care or Inability to Perform Normal Activities Due to Infection

End point description:

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: days				
arithmetic mean (standard deviation)	6.67 (± 13.49)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Days Out of Work / School / Kindergarten / Day Care or Inability to Perform Normal Activities Due to Infection

End point title	Annualized Rate of Days Out of Work / School / Kindergarten / Day Care or Inability to Perform Normal Activities Due to Infection

End point description:

The annualized rate was based on the total number of days out of work / school / kindergarten / day care or inability to perform normal activities due to infection, and the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[5]			
Units: days per subject year				
number (not applicable)	4.28			

Notes:

[5] - Subject study days analyzed: 11950

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days of Hospitalization Due to Infection

End point title	Number of Days of Hospitalization Due to Infection

End point description:

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: days				
arithmetic mean (standard deviation)	0.857 (± 2.726)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Hospitalization Due to Infection

End point title	Annualized Rate of Hospitalization Due to Infection

End point description:

The annualized rate was based on the total number of days of hospitalization due to infection and the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[6]			
Units: days per subject year				
number (not applicable)	0.55			

Notes:

[6] - Subject study days analyzed: 11950

Statistical analyses

No statistical analyses for this end point

Secondary: Use of Antibiotics for Infection Prophylaxis and Treatment

End point title	Use of Antibiotics for Infection Prophylaxis and Treatment

End point description:

Annualized rate of days with antibiotics for infection prophylaxis and treatment.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[7]			
Units: days per subject year				
number (not applicable)	83.87			

Notes:

[7] - Subject exposure days analyzed: 11950

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of All AEs by Relatedness and Severity

End point title	Rate of All AEs by Relatedness and Severity

End point description:

The rate of AEs was the number of AEs over the number of infusions administered.

At least possibly related AEs included possibly related AEs, probably related AEs, and related AEs.

Mild AE: Did not interfere with routine activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[8]			
Units: AEs per infusion				
number (not applicable)				
All	0.661			
Unrelated	0.137			
At least possibly related	0.524			
Mild	0.575			
Moderate	0.076			
Severe	0.01			

Notes:

[8] - Infusions analyzed: 1735

Statistical analyses

No statistical analyses for this end point

Secondary: Relatedness and Severity of All AEs (Percentage of Total AEs)

End point title	Relatedness and Severity of All AEs (Percentage of Total AEs)

End point description:

At least possibly related AEs included possibly related AEs, probably related AEs, and related AEs.

Mild AE: Did not interfere with routine activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[9]			
Units: percentage of total AEs				
number (not applicable)				
Unrelated	20.7			
At least possibly related	79.3			
Mild	87			
Moderate	11.5			
Severe	1.5			

Notes:

[9] - AT
AEs analyzed: 1147

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any Temporally Associated Adverse Event (AE) Within 24 or 72 Hours After an Infusion

End point title	Number of Subjects With Any Temporally Associated Adverse Event (AE) Within 24 or 72 Hours After an Infusion

End point description:

AEs were considered temporally associated if they occurred between the start of infusion and within 24 or 72 hours after the end of infusion.

End point type	Secondary

End point timeframe:

Within 24 or 72 hours after each infusion

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: participants				
AEs within 24 hours	21			
AEs within 72 hours	21			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Temporally Associated AEs Within 24 or 72 Hours of an Infusion

End point title	Rate of Temporally Associated AEs Within 24 or 72 Hours of an Infusion

End point description:

The rate of AEs was the number of AEs over the number of infusions administered.

AEs were considered temporally associated if they occurred between the start of infusion and within 24 or 72 hours after the end of infusion

End point type	Secondary

End point timeframe:

Within 24 or 72 hours after each infusion

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21[10]			
Units: AEs per infusion				
number (not applicable)				
AEs within 24 hours	0.322			
AEs within 72 hours	0.575			

Notes:

[10] - Infusions analyzed: 1735

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Mild, Moderate, or Severe Local AEs

End point title	Number of Subjects Reporting Mild, Moderate, or Severe Local AEs

End point description:

In addition to the standard MedDRA System Organ Class (SOC) AE assignments, the category of 'local reactions' was defined to provide the possibility for a combined analysis of local reactions and included AEs of infusion site oedema, infusion site reaction, injection site pain, injection site rash, and injection site reaction.

Mild AE: Did not interfere with routine activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 104 weeks

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: participants				
Total	19			
Mild	16			
Moderate	3			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Changes From Baseline to the Completion Visit in Vital Signs

End point title	Number of Subjects With Clinically Significant Changes From Baseline to the Completion Visit in Vital Signs

End point description:

Vital signs included blood pressure (systolic and diastolic), heart rate, and body temperature.

End point type	Secondary

End point timeframe:

At weeks 1, 12, 24, 36, 48, 60, 72, 84, and 96

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Changes From Baseline to the Completion Visit in Routine Laboratory Parameters

End point title	Number of Subjects With Clinically Significant Changes From Baseline to the Completion Visit in Routine Laboratory Parameters

End point description:

Routine laboratory parameters included hematology, blood chemistry, and urinalysis parameters.

End point type	Secondary

End point timeframe:

At Week 1, and study completion (approximately 104 weeks)

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Changes From Baseline to the Completion Visit in Viral Safety Markers

End point title	Number of Subjects With Clinically Significant Changes From Baseline to the Completion Visit in Viral Safety Markers

End point description:

Viral safety markers included human immunodeficiency virus (HIV)-1, HIV-2, hepatitis A virus (HAV), HBV, HCV, and parvovirus B19.

End point type	Secondary

End point timeframe:

At Week 1, and study completion (approximately 104 weeks)

End point values	IgPro20 - AT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of informed consent until study completion, up to approximately 121 weeks

Adverse event reporting additional description:

The AT safety population comprised all subjects treated with the study medication during any study period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	IgPro20

Reporting group description:

A liquid formulation of normal human IgG at a concentration of 20%. IgPro20 was administered as a subcutaneous infusion weekly or twice weekly, depending on the investigator's judgment and the subject’s preference.

Serious adverse events	IgPro20		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 21 (19.05%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid cancer			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)		
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	IgPro20		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	10		
Dizziness			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	10 / 21 (47.62%)		
occurrences (all)	248		
Infusion site reaction			

subjects affected / exposed	9 / 21 (42.86%)		
occurrences (all)	614		
Fatigue			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	33		
Influenza-like illness			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	7		
Chest pain			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Abdominal pain			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Diarrhea			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	6		
Dysphagia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain subjects affected / exposed occurrences (all)	6 / 21 (28.57%) 12		
Asthma subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Cough subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 3		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 3		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 3		
Depression subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 21 (23.81%) 5		
Back pain subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 10		
Myalgia subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 21 (33.33%) 10		
Bronchitis			

subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	7		
Clostridial infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Pharyngitis streptococcal			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	6		
Viral infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	14 / 21 (66.67%)		
occurrences (all)	24		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2008	Additional safety endpoints were specified, including the total number of temporally associated AEs (i.e., AEs that began during infusion or within 24 or 72 hours after infusion) and the number of temporally associated AEs per infusion. The projected number of sites was changed from approximately 10 to approximately 5 and the projected number of subjects was changed from approximately 30 to approximately 20. The transition procedures from the preceding study ZLB04_009CR to this extension study were updated. Additional evaluation procedures in case of hemolytic and/or hepatotoxic events were specified (determination of baseline serum haptoglobin and urine hemosiderin values). This amendment was implemented after 3 subjects had received their first infusion of study medication.
16 October 2008	The trough level ratio (TLR) that was developed in response to a regulatory authority's suggestion for checking adequate dosing was introduced, together with rules for dose adjustments that were to be implemented if the TLR differed from the stipulated range (1.29 ± 15% times the latest historic IGIV Ctrough. Furthermore, a specific procedure for reporting AEs associated with infections was introduced (2 new CRF pages for reporting infections and potential SBIs). Additional details on evaluation procedures in case of hemolytic and/or hepatotoxic events were provided (repeat tests for abnormal laboratory results). This amendment was implemented after all subjects had received their first infusion of study medication.
09 September 2009	The rules for IgPro20 dose adjustments that were to be considered if the TLR differed from the stipulated range were updated. Storage and transport temperature requirements for the study medication were updated. This amendment was implemented after all subjects had received their first infusion of study medication.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24412910