Clinical trial results:
Prospective open-label single-arm study of the pharmacokinetics (PK) and safety of intravenous IgPro10 in Japanese subjects with primary immunodeficiency

Summary

EudraCT number	2016-001631-12
Trial protocol	Outside EU/EEA
Global end of trial date	26 June 2018

Results information

Result version number	v1 (current)
This version publication date	30 December 2018
First version publication date	30 December 2018

Trial information

Trial identification

Sponsor protocol code	IgPro10_3004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CSL Behring KK
Sponsor organisation address	1-7-12 Shinonome Koto-ku, Tokyo, Japan,
Public contact	Trial Registration Coordinator, CSL Behring, clinicaltrials@cslbehring.com
Scientific contact	Trial Registration Coordinator, 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	24 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the pharmacokinetics of immunoglobulin G (IgG) following intravenous IgPro10 dosing in Japanese primary immune deficiency (PID) subjects after a standard wash-in/wash-out period of 12 weeks.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines and standard operating procedures for clinical research and development at CSL Behring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 April 2017
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	Japan: 11
Worldwide total number of subjects	11
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)	8
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a prospective phase 3, open-label, single-arm study designed to assess the PK and safety of IgPro10 in Japanese subjects with PID. Male or female subjects with a diagnosis of PID and aged ≥ 6 years were enrolled into the study.

Pre-assignment

Screening details:

Enrolled subjects received 3- or 4 weekly infusions of IgPro10 based on their pre-study treatment schedule as prescribed by the treating physician.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	IgPro10 (3-weekly)

Arm description:

Ready to use 10% liquid formulation of polyvalent human IgG via intravenous infusion. Dosing expected to be between 200 to 600 mg/kg body weight per dosing cycle.

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

Dosage and administration details:

As with the subject’s previous regular intravenous immunoglobulin (IVIG) doses; expected to be between 200 to 600 mg/kg body weight per dosing cycle of 3-weekly intravenous (IV) infusions of IgPro10.

Arm title	IgPro10 (4-weekly)

Arm description:

Ready to use 10% liquid formulation of polyvalent human IgG via intravenous infusion. Dosing expected to be between 200 to 600 mg/kg body weight per dosing cycle.

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

Dosage and administration details:

As with the subject’s previous regular IVIG doses; expected to be between 200 to 600 mg/kg body weight per dosing cycle of 4-weekly IV infusions of IgPro10.

Number of subjects in period 1	IgPro10 (3-weekly)	IgPro10 (4-weekly)
Started	2	9
Completed	2	8
Not completed	0	1
To avoid the use of prohibited conmed	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	11	11	
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)	1	1	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	8	8	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	29.5		
standard deviation	± 16.95	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	8	8	

End points

End points reporting groups

Reporting group title	IgPro10 (3-weekly)
Reporting group description:	
Ready to use 10% liquid formulation of polyvalent human IgG via intravenous infusion. Dosing expected to be between 200 to 600 mg/kg body weight per dosing cycle.	
Reporting group title	IgPro10 (4-weekly)
Reporting group description:	
Ready to use 10% liquid formulation of polyvalent human IgG via intravenous infusion. Dosing expected to be between 200 to 600 mg/kg body weight per dosing cycle.	
Subject analysis set title	Pharmacokinetic Analysis Set (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects of the SAF without any major deviations related to IgPro10 administration and for whom at least 1 measureable IgG concentration was available following IgPro10 infusion.	
Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the full analysis set who received at least one dose or a partial dose of IgPro10.	

Primary: Minimum concentration (Cmin) of IgG following intravenous IgPro10 dosing (PKAS)

End point title	Minimum concentration (Cmin) of IgG following intravenous IgPro10 dosing (PKAS)[1]
End point description:	
End point type	Primary
End point timeframe:	
Before infusion on Day 85 and up to approximately 21 days (for 3 week cycle) and up to approximately 28 days (for 4 week cycle) after 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: Descriptive statistics were used for the primary endpoint.	

End point values	IgPro10 (3-weekly)	IgPro10 (4-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: g/L				
arithmetic mean (standard deviation)	10.570 (± 3.2244)	8.529 (± 3.8866)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum concentration (Cmax) of IgG following intravenous IgPro10 dosing (PKAS)

End point title	Maximum concentration (Cmax) of IgG following intravenous

	IgPro10 dosing (PKAS)[2]

End point description:

End point type	Primary

End point timeframe:

Before infusion on Day 85 and up to approximately 21 days (for 3 week cycle) and up to approximately 28 days (for 4 week cycle) after infusion

Notes:

[2] - 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: Descriptive statistics were used for the primary endpoint.

End point values	IgPro10 (3-weekly)	IgPro10 (4-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: g/L				
arithmetic mean (standard deviation)	16.610 (± 3.6911)	14.198 (± 5.5348)		

Statistical analyses

No statistical analyses for this end point

Primary: Time to reach maximum concentration (Tmax) of IgG following intravenous IgPro10 dosing (PKAS)

End point title	Time to reach maximum concentration (Tmax) of IgG following intravenous IgPro10 dosing (PKAS)[3]

End point description:

End point type	Primary

End point timeframe:

Before infusion on Day 85 and up to approximately 21 days (for 3 week cycle) and up to approximately 28 days (for 4 week cycle) after infusion

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: Descriptive statistics were used for the primary endpoint.

End point values	IgPro10 (3-weekly)	IgPro10 (4-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: Hours				
median (full range (min-max))	1.192 (0.92 to 1.47)	1.142 (0.62 to 23.37)		

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration-time curve from time zero to the last sample (AUC0-last) following intravenous IgPro10 dosing (PKAS)

End point title	Area under the concentration-time curve from time zero to the last sample (AUC0-last) following intravenous IgPro10 dosing (PKAS)[4]

End point description:

End point type	Primary

End point timeframe:

Before infusion on Day 85 and up to approximately 21 days (for 3 week cycle) and up to approximately 28 days (for 4 week cycle) after infusion

Notes:

[4] - 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: Descriptive statistics were used for the primary endpoint.

End point values	IgPro10 (3-weekly)	IgPro10 (4-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: g*h/L				
arithmetic mean (standard deviation)	5971.0220 (± 1378.2901)	6590.9626 (± 2633.1854)		

Statistical analyses

No statistical analyses for this end point

Primary: Total body clearance (CL) of IgG following intravenous IgPro10 dosing (PKAS)

End point title	Total body clearance (CL) of IgG following intravenous IgPro10 dosing (PKAS)[5]

End point description:

End point type	Primary

End point timeframe:

Before infusion on Day 85 and up to approximately 21 days (for 3 week cycle) and up to approximately 28 days (for 4 week cycle) after infusion

Notes:

[5] - 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: Descriptive statistics were used for the primary endpoint.

End point values	IgPro10 (3-weekly)	IgPro10 (4-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: mL/h				
arithmetic mean (standard deviation)	2.5278 (± 0.6455)	2.5315 (± 0.9954)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with treatment emergent adverse events (AEs)

End point title	Percentage of subjects with treatment emergent adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

Up to 4 months after first infusion of IgPro10

End point values	Safety Analysis Set (SAF)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: Percent				
number (not applicable)				
any AEs	72.7			
mild AEs	45.5			
moderate AEs	27.3			
severe AEs	0			
serious AEs	0			
causally-related AEs	9.1			
not causally-related AEs	72.7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	Safety Analysis Set

Reporting group description: -

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 11 (72.73%)		
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Skin abrasion			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
General disorders and administration site conditions			
Infusion site discomfort			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Gastrointestinal disorders			
Retained deciduous tooth			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2016	-Removal of one PK sampling period
03 July 2017	-Modifications of the virology assessment to change the tests for HIV and HCV

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported