



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 $\geq 50 \times 10^9/L$ 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 | 3 / 57 (5.26%) | | |
| occurrences (all) | 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: <ul style="list-style-type: none">- 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