



Clinical trial results:

An open label, prospective, randomized, multicenter study investigating clinical efficacy and safety of the human normal immunoglobulin for intravenous administration BT595 in patients with chronic primary immune thrombocytopenia (ITP)

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-003653-17 |
| Trial protocol | DE HU ES CZ BG |
| Global end of trial date | 21 December 2018 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 27 August 2021 |
| First version publication date | 27 August 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----|
| Sponsor protocol code | 992 |
|-----------------------|-----|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02859909 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Biotest AG |
| Sponsor organisation address | Landsteinerstr. 5, Dreieich, Germany, 63303 |
| Public contact | Dr. med. Andrea Wartenberg-Demand, Biotest AG, +49 61038010, andrea.wartenberg-demand@biotest.com |
| Scientific contact | Dr. med. Andrea Wartenberg-Demand, Biotest AG, +49 61038010, andrea.wartenberg-demand@biotest.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-002092-PIP01-16 |
| 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 | 21 November 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 December 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 December 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to assess the efficacy and safety of BT595 in adult subjects with chronic ITP. The primary objective of the study is to determine the rate of subjects with a response. A response is defined as a platelet count of $\geq 30 \times 10^9/L$ and at least a 2 fold increase of the baseline count, confirmed on at least 2 separate occasions at least 7 days apart, and the absence of bleeding.

Protection of trial subjects:

To monitor the safety data from adult subjects and to provide advice and recommendations on the enrollment a DSMB consisting of independent experts has been implemented.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 31 August 2016 |
| 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 | Spain: 1 |
| Country: Number of subjects enrolled | Bulgaria: 5 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Hungary: 14 |
| Country: Number of subjects enrolled | Serbia: 13 |
| Worldwide total number of subjects | 34 |
| 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) | 27 |
| From 65 to 84 years | 7 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Date of first enrollment 09-Jan-2017, first IMP administration 17-Jan-2017, date of last subject completed 21-Dec-2018

Pre-assignment

Screening details:

Diagnosis of chronic ITP, male or female, age 18 through 75 (inclusive), mean screening platelet count of $<30 \times 10^9/L$ from 3 qualifying platelet counts and no individual platelet count above $35 \times 10^9/L$, high risk of bleeding

Period 1

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

Arms

| | |
|-----------|-------------------|
| Arm title | Full Analysis Set |
|-----------|-------------------|

Arm description:

Subjects were treated with a total of 2 g/kg body weight (bw) administered as intravenous infusion for 2 or 5 consecutive days, i.e. subjects were treated for 2 consecutive days with 1 g/kg bw per day or for 5 consecutive days with 0.4 g/kg bw per day.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | IgG Next Generation |
| Investigational medicinal product code | BT595 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

2 g/kg body weight (bw) administered as intravenous infusion for 2 or 5 consecutive days.

| Number of subjects in period 1 | Full Analysis Set |
|--------------------------------|-------------------|
| Started | 34 |
| Completed | 33 |
| Not completed | 1 |
| Consent withdrawn by subject | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Full Analysis Set |
|-----------------------|-------------------|

Reporting group description:

Subjects were treated with a total of 2 g/kg body weight (bw) administered as intravenous infusion for 2 or 5 consecutive days, i.e. subjects were treated for 2 consecutive days with 1 g/kg bw per day or for 5 consecutive days with 0.4 g/kg bw per day.

| Reporting group values | Full Analysis Set | Total | |
|------------------------|-------------------|-------|--|
| Number of subjects | 34 | 34 | |
| Age categorical | | | |
| Adult 18-75 years | | | |
| Units: Subjects | | | |
| Age 18-75 | 34 | 34 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 20 | 20 | |
| Male | 14 | 14 | |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | Full Analysis Set |
| Reporting group description: Subjects were treated with a total of 2 g/kg body weight (bw) administered as intravenous infusion for 2 or 5 consecutive days, i.e. subjects were treated for 2 consecutive days with 1 g/kg bw per day or for 5 consecutive days with 0.4 g/kg bw per day. | |
| Subject analysis set title | Full Analysis set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Full analysis and safety analysis set is identical and includes all subjects who received ≥ 1 dose of BT595. | |

Primary: Rate of subjects with Response

| | |
|--|--------------------------------|
| End point title | Rate of subjects with Response |
| End point description: Rate of subjects with R: defined as subjects with a platelet count of $\geq 30 \times 10^9/L$ and at least a 2-fold increase of the baseline count, confirmed on at least 2 separate occasions at least 7 days apart, and the absence of bleeding. | |
| End point type | Primary |
| End point timeframe: Rate of subjects with R: defined as subjects with a platelet count of $\geq 30 \times 10^9/L$ and at least a 2-fold increase of the baseline count, confirmed on at least 2 separate occasions at least 7 days apart, and the absence of bleeding. | |

| End point values | Full Analysis Set | Full Analysis set | | |
|-----------------------------|-------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 34 | 34 | | |
| Units: numbers | 1 | 1 | | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | Primary Analysis rate of response |
| Comparison groups | Full Analysis Set v Full Analysis set |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| Parameter estimate | Response Rate |
| Point estimate | 52.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 35.1 |
| upper limit | 70.2 |

Notes:

[1] - The primary endpoint will be analyzed using the 2-sided 95% CI for response rate, which will be calculated for each treatment schedule and overall using exact binomial distribution.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Observation period, Visit 1-13, until day 36

Adverse event reporting additional description:

On site visit

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Full Analysis Set |
|-----------------------|-------------------|

Reporting group description:

Full Analysis Set and Safety Analysis Set are identical and include all subjects who received ≥ 1 dose of BT595.

| Serious adverse events | Full Analysis Set | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Full Analysis Set | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 34 (79.41%) | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |
| Haematoma | | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chest discomfort subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 | | |
| Reproductive system and breast disorders Menorrhagia subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 | | |
| Investigations Coombs direct test positive subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all) Red blood cell sedimentation rate increased | 4 / 34 (11.76%) 4 4 / 34 (11.76%) 5 | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 2 / 34 (5.88%) | | |
| occurrences (all) | 2 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Subcutaneous haematoma | | | |
| subjects affected / exposed | 4 / 34 (11.76%) | | |
| occurrences (all) | 4 | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 7 / 34 (20.59%) | | |
| occurrences (all) | 9 | | |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | | |
| occurrences (all) | 3 | | |
| Intravascular haemolysis | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | | |
| occurrences (all) | 2 | | |
| Immune thrombocytopenic purpura | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|---|--|--|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | | |
| Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | | |
| Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | | |
| Gastrointestinal disorders Gingival bleeding subjects affected / exposed occurrences (all) Angina bullosa haemorrhagica subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 5 / 34 (14.71%) 5 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 | | |
| Skin and subcutaneous tissue disorders Petechiae subjects affected / exposed occurrences (all) Ecchymosis subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Blood blister subjects affected / exposed occurrences (all) | 8 / 34 (23.53%) 11 4 / 34 (11.76%) 5 3 / 34 (8.82%) 3 1 / 34 (2.94%) 1 | | |

| | | | |
|--|---|--|--|
| Skin reaction subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 2 | | |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Gastrointestinal viral infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported