



Clinical trial results:

An open, prospective trial investigating pharmacokinetics and safety (Part A) of the human normal immunoglobulin for intravenous infusion (IVIG) BT090 and tolerability and safety of escalating infusion rates (Part B) in patients with primary immunodeficiency disease (PID)

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2010-019249-25 |
| Trial protocol | DE HU |
| Global end of trial date | 12 January 2012 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 15 September 2021 |
| First version publication date | 15 September 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----|
| Sponsor protocol code | 981 |
|-----------------------|-----|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Biotest AG |
| Sponsor organisation address | Landsteinerstr. 5, Dreieich, Germany, 63303 |
| Public contact | Corporate Clinical Research and Development, Biotest AG, andrea.wartenberg-demand@biotest.com, Biotest AG, +49 6103801492, 981@biotest.de |
| Scientific contact | Corporate Clinical Research and Development, Biotest AG, andrea.wartenberg-demand@biotest.com, Biotest AG, +49 6103801492, 981@biotest.de |

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 | 15 September 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 January 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 January 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Investigation of pharmacokinetics (Part A) and tolerability of BT090 at escalating infusion rates (Part B)

Protection of trial subjects:

none

Background therapy:

none

Evidence for comparator:

not applicable

| | |
|---|------------------|
| Actual start date of recruitment | 15 November 2010 |
| 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 | Poland: 5 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Hungary: 16 |
| Worldwide total number of subjects | 30 |
| EEA total number of subjects | 30 |

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) | 2 |
| Adolescents (12-17 years) | 5 |
| Adults (18-64 years) | 23 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Recruitment period from 15-Nov-2010 (first patient in) until 12-Jan-2012 (last patient out)

Pre-assignment

Screening details:

none

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 30 |
| Number of subjects completed | 30 |

Period 1

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

Arms

| | |
|-----------|------------|
| Arm title | Part A + B |
|-----------|------------|

Arm description:

PART A:

Pharmacokinetics at 3rd infusion in week 6 or 8 (C_{max}, t_{max}, t_{1/2el}, AUC for serum concentration of IgG and IgG subclasses 1 to 4) and maintenance of IgG trough levels ≥5–6 g/L.

PART B:

Tolerability and safety of escalating infusion rates for determination of a maximum tolerated rate. Tolerability was expressed as percentage of total patients being treated at the specified infusion rates on the basis of data received from the 5th and 6th infusions.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Human normal Immunoglobulin for intravenous use |
| Investigational medicinal product code | BT090 |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

In the present trial, the planned monthly dose of BT090 is 200–800 mg/kg BW (2–8 mL/kg BW) administered as intravenous infusions in 3 or 4-week intervals for a treatment period of about 6 months. The dose and dosage intervals must be consistent with pre-trial standard IVIG treatment and are only to be changed if medically indicated.

The infusion rates will be increased from 0.3 to 1.4 to 2.0 mL/kg/h for each infusion in each patient at initially 30-minute intervals.

| Number of subjects in period 1 | Part A + B |
|--|------------|
| Started | 30 |
| Completed | 24 |
| Not completed | 6 |
| Less than 2 samples between end of infusion and Da | 1 |
| Less than 2 samples between Day 7 and Day 21/28 | 1 |
| At least one outlier in PK profile | 1 |
| PK dose of less than 200 mg/kg | 3 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|--------------------------|
| Reporting group title | Overall (overall period) |
| Reporting group description: - | |

| Reporting group values | Overall (overall period) | Total | |
|---------------------------------------|--------------------------|-------|--|
| Number of subjects | 30 | 30 | |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 2 | 2 | |
| Adolescents (12-17 years) | 5 | 5 | |
| Adults (18-64 years) | 23 | 23 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous Units: years | | | |
| arithmetic mean | 33.7 | | |
| standard deviation | ± 16.85 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 9 | 9 | |
| Male | 21 | 21 | |

Subject analysis sets

| | |
|--|--------------------|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All patients who received at least one dose of trial medication (full analysis set). | |
| Subject analysis set title | PK Analysis Set |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All patients of the safety set with sufficient data for analysis of pharmacokinetic (PK) parameters. | |
| Subject analysis set title | PP Set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: All patients of the safety set without any major protocol violations. Patients with major protocol deviations or incomplete documentation of relevant data or premature termination of the treatment due to reasons that were definitely not related to trial medication will be excluded from the per-protocol analysis. | |

| Reporting group values | Safety Set | PK Analysis Set | PP Set |
|------------------------------------|------------|-----------------|--------|
| Number of subjects | 30 | 24 | 18 |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 2 | 1 | 1 |
| Adolescents (12-17 years) | 5 | 2 | 2 |
| Adults (18-64 years) | 23 | 21 | 15 |

| | | | |
|-------------------|---|---|---|
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |

| | | | |
|--------------------|---------|---------|--------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 33.7 | 37 | 35.2 |
| standard deviation | ± 16.85 | ± 16.05 | ± 16.8 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 9 | 8 | 5 |
| Male | 21 | 16 | 13 |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Part A + B |
| Reporting group description: | |
| PART A: Pharmacokinetics at 3rd infusion in week 6 or 8 (C _{max} , t _{max} , t _{1/2el} , AUC for serum concentration of IgG and IgG subclasses 1 to 4) and maintenance of IgG trough levels ≥5–6 g/L. | |
| PART B: Tolerability and safety of escalating infusion rates for determination of a maximum tolerated rate. Tolerability was expressed as percentage of total patients being treated at the specified infusion rates on the basis of data received from the 5th and 6th infusions. | |
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All patients who received at least one dose of trial medication (full analysis set). | |
| Subject analysis set title | PK Analysis Set |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All patients of the safety set with sufficient data for analysis of pharmacokinetic (PK) parameters. | |
| Subject analysis set title | PP Set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| All patients of the safety set without any major protocol violations. Patients with major protocol deviations or incomplete documentation of relevant data or premature termination of the treatment due to reasons that were definitely not related to trial medication will be excluded from the per-protocol analysis. | |

Primary: Serum IgG concentration (C_{max})

| | |
|---|--|
| End point title | Serum IgG concentration (C _{max}) ^[1] |
| End point description: | |
| Standard Pharmacokinetic Parameter: the maximum observed serum IgG concentration | |
| End point type | Primary |
| End point timeframe: | |
| At the 3rd infusion (week 6 or 8) standard pharmacokinetic parameters will be determined. | |

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: Variables were descriptively summarised. No formal statistical tests were planned or performed.

| End point values | Part A + B | PK Analysis Set | | |
|-------------------------------|------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 24 | 24 | | |
| Units: milligram(s)/dL | | | | |
| median (full range (min-max)) | 177 (130 to 217) | 177 (130 to 217) | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Recording of AEs commences at the time when the patient is enrolled into the trial (date of signature of the informed consent) until the end of trial visit has been performed.

Adverse event reporting additional description:

not applicable

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 13.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Safety Set |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events | Safety Set | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Dental caries | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendiceal abscess | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| 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 | Safety Set | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 30 (90.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 4 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 8 / 30 (26.67%) | | |
| occurrences (all) | 11 | | |
| General disorders and administration site conditions | | | |
| Discomfort | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 6 | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | | |
| occurrences (all) | 4 | | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|---|--|--|
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 3 1 / 30 (3.33%) 2 | | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 4 | | |
| Skin and subcutaneous tissue disorders Blister subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 2 | | |
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 4 4 / 30 (13.33%) 5 1 / 30 (3.33%) 2 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis | 5 / 30 (16.67%) 5 2 / 30 (6.67%) 2 | | |

| | | | |
|-----------------------------------|------------------|--|--|
| subjects affected / exposed | 11 / 30 (36.67%) | | |
| occurrences (all) | 12 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 2 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 3 | | |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 5 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 06 April 2011 | SA4 (Protocol Amendment 1) /Prot. Version 2.0: Adaptation of Inclusion criteria/ Section 11.4 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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| None |
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Notes: