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 (Cmax, tmax, t1/2el, 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 (Cmax, tmax, t1/2el, AUC for serum concentration of IgG and IgG subclasses 1 to 4) and maintenance of IgG trough levels ≥5–6 g/L.
PART B:
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Primary: Serum IgG concentration (Cmax)

End point title	Serum IgG concentration (Cmax)[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

No statistical analyses for this end point

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

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.

None

Notes: