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)	EMEA-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 ≥30*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*10^9/L from 3 qualifying platelet counts and no individual platelet count above 35*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 ≥30*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 ≥30*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	
Dictionary name	MedDRA
Dictionary version	21.1

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

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