Clinical trial results:
A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Study of Fostamatinib Disodium in the Treatment of Persistent/Chronic Immune Thrombocytopenic Purpura

Summary

EudraCT number	2013-005452-15
Trial protocol	GB IT HU NL DK
Global end of trial date	21 April 2016

Results information

Result version number	v1 (current)
This version publication date	08 April 2021
First version publication date	08 April 2021

Trial information

Trial identification

Sponsor protocol code	C-935788-047

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02076399
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigel Pharmaceuticals, Inc.
Sponsor organisation address	1180 Veterans Blvd , South San Francisco, CA, United States, 94080
Public contact	Clinical trials, Rigel Pharmaceuticals, Inc., +1 650-624-1100, clinicaltrials@rigel.com
Scientific contact	Clinical trials, Rigel Pharmaceuticals, Inc., +1 650-624-1100, clinicaltrials@rigel.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	03 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 April 2016
Global end of trial reached?	Yes
Global end of trial date	21 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to establish the efficacy of fostamatinib as compared with placebo in achieving a stable platelet response in subjects with persistent/chronic ITP.

Protection of trial subjects:

The study was conducted in accordance with Good Clinical Practice (GCP) and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator:

Placebo OFC tablets were provided to match the appearance of fostamatinib 100 mg and 150 mg OFC tablets. Tablets were administered orally bid using the same escalation scheme as fostamatinib tablets over the course of 24 weeks.

Actual start date of recruitment	14 July 2014
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	Netherlands: 1
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Australia: 13
Worldwide total number of subjects	76
EEA total number of subjects	13

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	50
From 65 to 84 years	22
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Approximately 75 subjects were planned to be enrolled at multiple sites. Seventy-six subjects were enrolled, and all enrolled subjects were included in the efficacy and safety analyses.

76 patients were enrolled from July 2014 to April 2016.

Pre-assignment

Screening details:

A total of 117 subjects were screened, 41 subjects failed screening (primarily they did not meet inclusion criteria or did meet one or more exclusion criterion), and the remaining 76 subjects were randomized; 51 to the fostamatinib group and 25 to the placebo group (ITT population). One subject (1.3% overall) was lost to follow-up.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Fostamatinib Recipient

Arm description:

Fostamatinib (100 mg PO bid or 150 mg PO bid)

Arm type	Experimental
Investigational medicinal product name	Fostamatinib Disodium
Investigational medicinal product code	R935788
Other name	R788, Fostamatinib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects begin with Fostamatinib Disodium tablet 100 mg PO bid and increase to 150 mg big after week 4 based on platelet count and tolerability.

Arm title	Placebo Recipient

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablet PO bid (morning and evening) over the course of 24 weeks

Number of subjects in period 1	Fostamatinib Recipient	Placebo Recipient
Started	51	25
Completed	12	1
Not completed	39	24
Physician decision	1	-
Subject decision	1	-
AE meeting study specific discontinuation criteria	4	1
Subject uncooperative or noncompliant	1	-
Lost to follow-up	1	-
other adverse event	3	1
Lack of efficacy	28	22

Baseline characteristics

Reporting groups	
Reporting group title	Fostamatinib Recipient
Reporting group description:	
Fostamatinib (100 mg PO bid or 150 mg PO bid)	
Reporting group title	Placebo Recipient
Reporting group description:	
Placebo	

Reporting group values	Fostamatinib Recipient	Placebo Recipient	Total
Number of subjects	51	25	76
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	57.3	53.2	
standard deviation	± 17.7	± 16	-
Gender categorical			
Units: Subjects			
Female	30	17	47
Male	21	8	29
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	3	1	4
Not Hispanic or Latino	48	24	72
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	4
White	44	21	65
More than one race	0	0	0
Unknown or Not Reported	2	0	2

End points

End points reporting groups	
Reporting group title	Fostamatinib Recipient
Reporting group description:	
Fostamatinib (100 mg PO bid or 150 mg PO bid)	
Reporting group title	Placebo Recipient
Reporting group description:	
Placebo	

Primary: Number of Participants With Stable Platelet Response (Count of ≥50,000/µL on at Least 4 of the Last 6 Scheduled Visits Between Weeks 14 and 24)	
End point title	Number of Participants With Stable Platelet Response (Count of ≥50,000/µL on at Least 4 of the Last 6 Scheduled Visits Between Weeks 14 and 24)
End point description:	
A stable platelet response by Week 24 defined as a platelet count of at least 50,000/µL on at least 4 of the last 6 scheduled visits between Weeks 14 and 24.	
End point type	Primary
End point timeframe:	
From Week 14 to Week 24	

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	25		
Units: no. of participants	9	0		

Statistical analyses

Statistical analysis title	Analysis for primary endpoint
Comparison groups	Fostamatinib Recipient v Placebo Recipient
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0261
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	17.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.2
upper limit	28.1

Secondary: Number of Participants With Platelet Count ≥ 50,000/µL at Week 12

End point title	Number of Participants With Platelet Count ≥ 50,000/µL at Week 12
End point description: Platelet Count ≥ 50,000/µL at Week 12	
End point type	Secondary
End point timeframe: Week 12	

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	25		
Units: no.of participants	11	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Platelet Count ≥ 50,000/µL at Week 24

End point title	Number of Participants With Platelet Count ≥ 50,000/µL at Week 24
End point description: Platelet Count ≥ 50,000/µL at Week 24	
End point type	Secondary
End point timeframe: Week 24	

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	25		
Units: no. of participants	8	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet Count ≥ 30,000/µL and ≥ 20,000/µL Above Baseline in Subjects With Baseline Platelet Count of <15,000/µL at Week 24.

End point title	Platelet Count ≥ 30,000/µL and ≥ 20,000/µL Above Baseline in Subjects With Baseline Platelet Count of <15,000/µL at Week 24.

End point description:

Number of subjects with baseline platelet count <15,000/µL who showed platelet count increase to ≥30,000/µL and ≥20,000/µL from baseline count at Week 24.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: no. of participants	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean of the ITP Bleeding Score (IBLS)

End point title	Mean of the ITP Bleeding Score (IBLS)

End point description:

The ITP Bleeding Scale (IBLS) is an immune thrombocytopenic purpura (ITP)-specific bleeding score used to analyze the correlation of clinical and laboratory platelet variables with bleeding. The IBLS comprises of 11 grades from 0 (none) to 2 (marked bleeding) by history over the previous week or by exam; 2 being worse. These 11 grades include: skin by physical exam, oral by physical exam, skin by history, oral by history, epistaxis, gastrointestinal, urinary, gynecological, pulmonary, intracranial hemorrhage, and subconjunctival hemorrhage. After each grade is scored, the mean value for all 11 grades is calculated (lowest score being 0 and highest score being 2) for each subject visit. LOCF method was used to impute any missing data.

The mean of the IBLS scores across visits during the 24-week treatment period was summarized by treatment group using descriptive statistics. A 2-sided, 2-sample t-test was used to test for a difference in means between treatments for this endpoint.

End point type	Secondary

End point timeframe:

Assessed over the 24-week study period

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	25		
Units: scores on a scale				
arithmetic mean (standard deviation)	0.13 (± 0.12)	0.14 (± 0.10)		

Statistical analyses

Statistical analysis title	Analysis for mean of the ITP bleeding score (IBLS)
Comparison groups	Fostamatinib Recipient v Placebo Recipient
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6642 [1]
Method	t-test, 2-sided
Parameter estimate	Risk difference (RD)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0

Notes:

[1] - P-value from a two-sided two-sample t-test, testing for a difference in means between fostamatinib and placebo.

Secondary: Mean of World Health Organization (WHO) Bleeding Scale

End point title	Mean of World Health Organization (WHO) Bleeding Scale

End point description:

The World Health Organization (WHO) bleeding scale is a standardized grading scale created to measure the severity of bleeding. The scale is a clinical investigator-assessed five-point scale with a score range starting at the lowest 0=No bleeding, 1 = Petechiae, 2=Mild blood loss, 3=Gross blood loss, to the worse 4=Debilitating blood loss. The WHO bleeding scale is scored by history over the previous-week or by exam. After each grade is scored, the mean value is calculated (lowest score being 0 [no bleeding] to the highest score being 4 [debilitating blood loss]) for each visit. LOCF method was used to impute any missing data.

The mean of the WHO bleeding scale across visits during the 24-week treatment period was summarized by treatment group using descriptive statistics. A 2-sided, 2-sample t-test was used to test for a difference in means between treatments for this endpoint.

End point type	Secondary

End point timeframe:

Assessed over the 24-week study period

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	25		
Units: scores on a scale				
arithmetic mean (standard deviation)	0.61 (± 0.66)	0.46 (± 0.56)		

Statistical analyses

Statistical analysis title	Analysis for mean of WHO Bleeding Scale
Comparison groups	Placebo Recipient v Fostamatinib Recipient
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3365 [2]
Method	t-test, 2-sided
Parameter estimate	Risk difference (RD)
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.5

Notes:

[2] - P-value from a two-sided two-sample t-test, testing for a difference in means between fostamatinib and placebo.

Secondary: Platelet Count ≥ 30,000/µL and ≥ 20,000/µL Above Baseline in Subjects With Baseline Platelet Count of <15,000/µL at Week 12

End point title	Platelet Count ≥ 30,000/µL and ≥ 20,000/µL Above Baseline in Subjects With Baseline Platelet Count of <15,000/µL at Week 12

End point description:

Number of subjects with baseline platelet count <15,000/µL who showed platelet count increase to ≥30,000/µL and ≥20,000/µL from baseline count at Week 12.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Fostamatinib Recipient	Placebo Recipient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: no. of participants	4	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 Weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Fostamatinib Recipient
Reporting group description: -	
Reporting group title	Placebo Recipient

Reporting group description: -

Serious adverse events	Fostamatinib Recipient	Placebo Recipient	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 51 (15.69%)	5 / 25 (20.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 51 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune Thrombocytopenic Purpura			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal tear			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 51 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Fostamatinib Recipient	Placebo Recipient	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 51 (96.08%)	19 / 25 (76.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 51 (17.65%)	0 / 25 (0.00%)	
occurrences (all)	11	0	
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 51 (15.69%)	0 / 25 (0.00%)	
occurrences (all)	10	0	
Blood pressure increased			
subjects affected / exposed	3 / 51 (5.88%)	1 / 25 (4.00%)	
occurrences (all)	3	1	

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 51 (5.88%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 51 (25.49%)	1 / 25 (4.00%)	
occurrences (all)	16	1	
Rash			
subjects affected / exposed	4 / 51 (7.84%)	0 / 25 (0.00%)	
occurrences (all)	5	0	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 51 (13.73%)	6 / 25 (24.00%)	
occurrences (all)	8	7	
Dizziness			
subjects affected / exposed	9 / 51 (17.65%)	4 / 25 (16.00%)	
occurrences (all)	10	6	
Dysgeusia			
subjects affected / exposed	4 / 51 (7.84%)	0 / 25 (0.00%)	
occurrences (all)	5	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 51 (3.92%)	2 / 25 (8.00%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 51 (11.76%)	1 / 25 (4.00%)	
occurrences (all)	8	2	
Pyrexia			
subjects affected / exposed	2 / 51 (3.92%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Chest pain			
subjects affected / exposed	4 / 51 (7.84%)	1 / 25 (4.00%)	
occurrences (all)	4	1	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	21 / 51 (41.18%)	4 / 25 (16.00%)	
occurrences (all)	35	5	
Nausea			
subjects affected / exposed	15 / 51 (29.41%)	1 / 25 (4.00%)	
occurrences (all)	17	2	
Constipation			
subjects affected / exposed	3 / 51 (5.88%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Abdominal pain			
subjects affected / exposed	3 / 51 (5.88%)	0 / 25 (0.00%)	
occurrences (all)	5	0	
Flatulence			
subjects affected / exposed	3 / 51 (5.88%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	2 / 51 (3.92%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Rectal haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	9 / 51 (17.65%)	4 / 25 (16.00%)	
occurrences (all)	15	7	
Dyspnoea			
subjects affected / exposed	3 / 51 (5.88%)	3 / 25 (12.00%)	
occurrences (all)	3	5	
Oropharyngeal pain			
subjects affected / exposed	1 / 51 (1.96%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 51 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 8	1 / 25 (4.00%) 1	
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4	0 / 25 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2014	Notable changes made between Version 1.0 (16Dec2013) and Version 2.0 (08Apr2014) of the protocol were as follows: • Inclusion criterion #2 has been revised to clarify the amount of time a subject who is participating in the study must have had a diagnosis of ITP prior to being randomized. • Exclusion criterion #6 has been revised and #7 has been added in an effort to exclude only subjects at significant risk of deep vein thrombosis (DVT). Thus, the timeframe has been shortened to thrombosis within the 6 months prior to randomization and, for subjects who have a more distant history of DVT, results of a D-dimer test must be within the normal range as a measure of low risk for DVT recurrence. • Exclusion criterion #8 has been revised to specify that the IBLS score cannot be greater than 2 at any of the 11 sites evaluated. • D-dimer testing has been added to Screening Visit A (V1). D-dimer test should be performed at the local lab and is only required for subjects who have a history of DVT greater than 6 months prior to randomization. • An ECG has been added to the Visit 15 assessment for subjects going onto the extension study. • To assure that subjects sign an ICF prior to any study related procedures, text was added to clarify that subjects who require a washout period greater than 30 days should sign the ICF at a prescreening visit prior to beginning washout. • When Visit 2 and Visit 3 occur on the same day, following clarification added: Visit 3 SF-36 assessment will be administered after Visit 2 assessments are complete. • Section 7.4.2: subjects who have a dose reduction due to adverse events may be allowed to have their dose reescalated after the adverse event has resolved following consultation with the Medical Monitor (if clinical benefit of study drug is shown). • Measurement of IgD and IgE levels has been removed from the protocol. • The D-dimer test was added to the list of laboratory tests that will be performed during the study.
21 November 2014	Notable changes made between Version 2.0 (08Apr2014) and Version 3.0 (21Nov2014) of the protocol were as follows: • Inclusion criterion #4 was revised to clarify a typical treatment regimen for ITP (Master protocol and 3 country-specific protocols). • Exclusion criterion #18 was added to exclude subjects who had major surgery within 28 days prior to randomization. • Prior ITP treatments were defined as including therapies granted market authorization, and examples of typical prior ITP treatments were provided. Washout requirements were revised to clarify that subjects must discontinue all therapeutic agents other than those allowed as concomitant ITP therapy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported