Clinical trial results:
A two part, double-blind, randomized, placebo-controlled and open-label study to investigate the efficacy, safety and tolerability of eltrombopag, a thrombopoietin receptor agonist, in pediatric patients with previously treated chronic immune (idiopathic) thrombocytopenic purpura (ITP).

Summary

EudraCT number	2011-002184-17
Trial protocol	CZ DE ES GB PL IT
Global end of trial date	02 January 2014

Results information

Result version number	v1 (current)
This version publication date	07 March 2016
First version publication date	08 March 2015

Trial information

Trial identification

Sponsor protocol code	TRA115450

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01520909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline , +1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, +1 8664357343, GSKClinicalSupportHD@gsk.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	18 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 January 2014
Global end of trial reached?	Yes
Global end of trial date	02 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of eltrombopag, relative to placebo, in achieving platelet counts of >= 50 Gi/L, when administered to pediatric subjects with previously treated chronic ITP during the first 12 weeks of Part 1, the randomized treatment period.

Protection of trial subjects:

Liver stopping criteria – in the instance that liver tests indicate elevated levels, the criteria will advise how to monitor patients as well as study procedure interruption or discontinuation. Dosing Guidelines – guidelines are put into place to ensure, based on individual platelet response, study treatment will maintain platelet counts in a safe hemostatic range, not necessarily in the normal range.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2012
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	Argentina: 4
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	China: 2
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Thailand: 25
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	92
EEA total number of subjects	34

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)	1
Children (2-11 years)	57
Adolescents (12-17 years)	34
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pediatric participants meeting eligibility criteria were enrolled into 3 cohorts depending upon age. Cohort 1 enrolled participants who were between 12 and 17 years old, Cohort 2 enrolled participants who were between 6 and 11 years old, and Cohort 3 enrolled participants who were between 1 and 5 years old.

Pre-assignment

Screening details:

This study was comprised of a 13-week Double-Blind (DB), randomized Treatment Period (Part 1), followed by a 24-week Open-Label (OL) eltrombopag-only period (Part 2). After completion of Part 2, participants completed a 24- to 28-week Follow-up period, including an ophthalmic examination 24 weeks after the last dose of study treatment.

Period 1

Period 1 title	Part 1 (Randomized Period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1 (Randomized Period)-Placebo

Arm description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kilograms (kg) received placebo 37.5 milligrams (mg) once daily (QD), and those with a body weight >=27 kg received placebo 50 mg QD. Participants of East Asian ancestry received a starting dose of placebo 25 mg QD. Participants aged between 1 and 5 years received placebo 1.2 milligrams per kilogram (mg/kg) QD; participants of East Asian ancestry received a starting dose of placebo 0.8 milligrams per kilograms per day (mg/kg/day). Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Arm type	Placebo
Investigational medicinal product name	Placebo to match eltrombopag 12.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Placebo to match eltrombopag 25, 50, 75mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg

Investigational medicinal product name	Placebo to match eltrombopag 20mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension

Routes of administration	Oral use

Dosage and administration details:

Powder for oral suspension is combined with 9.5mL of water and drawn into a 10cc oral syringe for oral administration once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Arm title	Part 1 (Randomized Period)-Eltrombopag

Arm description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD. Participants aged between 1 and 5 years received eltrombopag 1.2 mg/kg QD; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day. Participants continued on the same dose of eltrombopag in Part 2 unless adjustments were warranted according to the dosing guidelines. Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Arm type	Active comparator
Investigational medicinal product name	Eltrombopag 12.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 25mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 50mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 75mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 20mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension

Routes of administration	Oral use

Dosage and administration details:

Powder for oral suspension is combined with 9.5mL of water and drawn into a 10cc oral syringe for oral administration once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Number of subjects in period 1	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag
Started	29	63
Completed	28	61
Not completed	1	2
Adverse event, non-fatal	1	2

Period 2

Period 2 title	Part 2 Open-Label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part 2 (Open-Label Period) - Eltrombopag

Arm description:

All participants receiving placebo in Part 1 received eltrombopag in Part 2 following starting dose guidelines for Part 1. Participants aged between 6 and 17 years with a body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD. Participants aged between 1 and 5 years received eltrombopag 1.2 mg/kg QD; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day. Participants receving eltrombopag in Part 1 continued on the same dose of eltrombopag in Part 2 unless adjustments were warranted according to the dosing guidelines. Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Eltrombopag 12.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 25mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 50mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 75mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Investigational medicinal product name	Eltrombopag 20mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Powder for oral suspension is combined with 9.5mL of water and drawn into a 10cc oral syringe for oral administration once daily at least 2 hours before and 4 hours after any product such as antacids, dairy products, or mineral supplements containing polyvalent cations. Maximum daily dose was not to exceed 75mg.

Number of subjects in period 2[1]	Part 2 (Open-Label Period) - Eltrombopag
Started	87
Completed	80
Not completed	7
Adverse event, non-fatal	4
Withdrawal by parent/guardian	1
Lack of efficacy	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Two participants completed Part 1: Randomized Period but did not endter Part 2: Open-Label Period because the participants withdrew consent.

Baseline characteristics

Reporting groups

Reporting group title	Part 1 (Randomized Period)-Placebo

Reporting group description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kilograms (kg) received placebo 37.5 milligrams (mg) once daily (QD), and those with a body weight >=27 kg received placebo 50 mg QD. Participants of East Asian ancestry received a starting dose of placebo 25 mg QD. Participants aged between 1 and 5 years received placebo 1.2 milligrams per kilogram (mg/kg) QD; participants of East Asian ancestry received a starting dose of placebo 0.8 milligrams per kilograms per day (mg/kg/day). Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Reporting group title	Part 1 (Randomized Period)-Eltrombopag

Reporting group description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD. Participants aged between 1 and 5 years received eltrombopag 1.2 mg/kg QD; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day. Participants continued on the same dose of eltrombopag in Part 2 unless adjustments were warranted according to the dosing guidelines. Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Reporting group values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag	Total
Number of subjects	29	63	92
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Infants and toddlers (28 days-23 months)			0
Newborns (0-27 days)			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	9.8	9.4	
standard deviation	± 4	± 4.43	-
Gender categorical Units: Subjects			
Female	14	30	44
Male	15	33	48
Race Units: Subjects			
African American/African Heritage	0	1	1
Central/South Asian Heritage	0	1	1
Japanese/East Asian/South East Asian Heritage	10	20	30
Arabic/North African Heritage	1	2	3
White/Caucasian/European Heritage	18	38	56

Mixed Race	0	1	1

End points

End points reporting groups

Reporting group title	Part 1 (Randomized Period)-Placebo

Reporting group description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kilograms (kg) received placebo 37.5 milligrams (mg) once daily (QD), and those with a body weight >=27 kg received placebo 50 mg QD. Participants of East Asian ancestry received a starting dose of placebo 25 mg QD. Participants aged between 1 and 5 years received placebo 1.2 milligrams per kilogram (mg/kg) QD; participants of East Asian ancestry received a starting dose of placebo 0.8 milligrams per kilograms per day (mg/kg/day). Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Reporting group title	Part 1 (Randomized Period)-Eltrombopag

Reporting group description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD. Participants aged between 1 and 5 years received eltrombopag 1.2 mg/kg QD; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day. Participants continued on the same dose of eltrombopag in Part 2 unless adjustments were warranted according to the dosing guidelines. Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Reporting group title	Part 2 (Open-Label Period) - Eltrombopag

Reporting group description:

All participants receiving placebo in Part 1 received eltrombopag in Part 2 following starting dose guidelines for Part 1. Participants aged between 6 and 17 years with a body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD. Participants aged between 1 and 5 years received eltrombopag 1.2 mg/kg QD; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day. Participants receving eltrombopag in Part 1 continued on the same dose of eltrombopag in Part 2 unless adjustments were warranted according to the dosing guidelines. Standard of care treatments were allowed during the study, and were prescribed based on the investigator's discretion.

Subject analysis set title	Eltrombopag Cohort 1 (12-17 years)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received eltrombopag in Part 1 continued on the same dose in Part 2 unless adjustments were warranted according to the dosing guidelines. Participants who received placebo in Part 1 received Eltrombopag as per age criteria as follows:body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD.

Subject analysis set title	Eltrombopag Cohort 2 (6-11 years)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received eltrombopag in Part 1 continued on the same dose in Part 2 unless adjustments were warranted according to the dosing guidelines. Participants who received placebo in Part 1 received Eltrombopag as per age criteria as follows: body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD.

Subject analysis set title	Eltrombopag Cohort 3 (1-5 years)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received eltrombopag in Part 1 continued on the same dose in Part 2 unless adjustments were warranted according to the dosing guidelines. Participants who received placebo in Part 1 received Eltrombopag 1.2 mg/kg QD and; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day.

Primary: Number of participants achieving a platelet count >=50 giga cells per liter (Gi/L) for at least 6 out of 8 weeks, between Weeks 5 and 12 of Part 1

End point title	Number of participants achieving a platelet count >=50 giga cells per liter (Gi/L) for at least 6 out of 8 weeks, between Weeks 5 and 12 of Part 1

End point description:

Participants who achieved a platelet count >=50 Gi/L for at least 6 out of 8 weeks, between Weeks 5 and 12 of Part 1, were reported.

End point type	Primary

End point timeframe:

From Week 5 up to Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[1]	63[2]		
Units: Participants	1	25		

Notes:

[1] - Intent-to-Treat (ITT) Population

[2] - Intent-to-Treat (ITT) Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The proportion of participants achieving platelet counts >=50 Gi/L for those participants receiving eltrombopag versus placebo was compared.

Comparison groups	Part 1 (Randomized Period)-Eltrombopag v Part 1 (Randomized Period)-Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	17.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.29
upper limit	140.93

Notes:

[3] - Indicated significance at the 5% (two-sided) level of significance

Secondary: Percentage of Responders

End point title	Percentage of Responders

End point description:

Percentage of participants who responded (defined as platelet count >= 50Gi/L in absence of rescue) at least once up to week 12 of Part 1 (Odds of achieving a platelet count >=50 Gi/L during the first 12

weeks of Part 1)

End point type	Secondary

End point timeframe:

From Week 1 up to Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[4]	63[5]		
Units: Percentage of Participants				
number (not applicable)				
Week 1	0	15.9		
Week 2	3.4	23.8		
Week 3	0	31.7		
Week 4	6.9	36.5		
Week 5	6.9	47.6		
Week 6	6.9	38.1		
Week 7	10.3	44.4		
Week 8	3.4	44.4		
Week 9	3.4	42.9		
Week 10	3.4	52.4		
Week 11	6.9	49.2		
Week 12	3.4	58.7		

Notes:

[4] - ITT population

[5] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Part 1 (Randomized Period)-Placebo v Part 1 (Randomized Period)-Eltrombopag
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [6]
Method	Repeated Measures model for binary data
Parameter estimate	Odds ratio (OR)
Point estimate	25.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.15
upper limit	78.73

Notes:

[6] - Repeated measures model for binary data using Generalized linear mixed model.

Secondary: Number of participants achieving a platelet count >=50 Gi/L at any time

during the first 12 weeks of Part 1

End point title	Number of participants achieving a platelet count >=50 Gi/L at any time during the first 12 weeks of Part 1

End point description:

Participants who achieved a platelet count >=50 Gi/L at any time during the first 12 weeks of Part 1 were reported.

End point type	Secondary

End point timeframe:

From Baseline up to Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[7]	63[8]		
Units: Participants	6	47		

Notes:

[7] - ITT population

[8] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving a platelet count >=50 Gi/L at any time during the first 6 weeks of Part 1

End point title	Number of participants achieving a platelet count >=50 Gi/L at any time during the first 6 weeks of Part 1

End point description:

Participants who achieved a platelet count >=50 Gi/L at any time during the first 6 weeks of Part 1 were reported.

End point type	Secondary

End point timeframe:

From Baseline up to Week 6 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[9]	63[10]		
Units: Participants	5	39		

Notes:

[9] - ITT population

[10] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Weighted mean platelet count

End point title	Weighted mean platelet count

End point description:

The weighted mean platelet count is defined as "the area under the platelet-time curve divided by the duration of the study (12 weeks)". Weighted mean platelet counts from baseline to week 12 of the randomized period was compared between placebo and eltrombopag using an analysis of covariance model (ANCOVA) adjusting for baseline platelet count and age cohort. For each subject the area between two adjacent visits with platelet counts was calculated. The area was calculated for all pairs of adjacent visits starting at Day 1 of randomized period and then the total sum of all the areas was divided by the total duration of time during the randomized period. For each subject, this method calculates an 'average' platelet count and it allows the possibility that subjects may have had different number of assessments during different times relative to baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[11]	62[12]		
Units: Gi/L				
arithmetic mean (standard deviation)				
Baseline	14.2 (± 8.01)	14 (± 8.09)		
Week 12	23.7 (± 19.56)	63.9 (± 46.68)		

Notes:

[11] - ITT Population. Only those participants with a value at Baseline and post-Baseline were analyzed

[12] - ITT Population. Only those participants with a value at Baseline and post-Baseline were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum duration for which a participant continuously maintained a platelet count of >=50 Gi/L during the first 12 weeks of Part 1

End point title	Maximum duration for which a participant continuously maintained a platelet count of >=50 Gi/L during the first 12 weeks of Part 1

End point description:

The maximum duration for which a participant continuously maintained a platelet count >=50 Gi/L was calculated and summarized for the first 12 weeks of Part 1. Participants with non-weekly assessments were assumed to have maintained a positive response for each week between two assessments that had positive responses. If a particpant achieved a positive response at an assessment and then achieved a negative response at the next assessment, then it was assumed that the participant had achieved a positive response for one day.

End point type	Secondary

End point timeframe:

From Baseline up to Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[13]	63[14]		
Units: Weeks				
arithmetic mean (standard deviation)	0.4 (± 1.5)	3.3 (± 3.13)		

Notes:

[13] - ITT population

[14] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who required a protocol-defined rescue treatment during Part 1

End point title	Number of participants who required a protocol-defined rescue treatment during Part 1

End point description:

Rescue treatment is defined as either a new immune (idiopathic) thrombocytopenic purpura (ITP) medication, an increase in the dose of a concomitant ITP medication from Baseline, a platelet transfusion, or a splenectomy.

End point type	Secondary

End point timeframe:

From Baseline up to Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[15]	63[16]		
Units: Participants				
number (not applicable)	7	12		

Notes:

[15] - ITT population

[16] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any bleeding and significant bleeding as assessed using the World Health Organization (WHO) Bleeding Scale during Part 1

End point title	Number of participants with any bleeding and significant bleeding as assessed using the World Health Organization (WHO) Bleeding Scale during Part 1

End point description:

The WHO Bleeding Scale is a measure of bleeding severity with the following grades: Grade 0=no bleeding; Grade 1=petechiae; Grade 2=mild blood loss; Grade 3=gross bleeding; Grade 4=debilitating blood loss. The WHO grades were dichotomized into the following categories: no bleeding=Grade 0; any bleeding=Grades 1 to 4; no clinically significant bleeding=Grades 0 to 1; clinically significant bleeding=Grades 2 to 4. Baseline was defined as the Day 1 assessment or the latest possible screening assessment. Only those participants that did not enroll in Part 2 were analyzed during the follow-up visits. Only those participants available at the specified time points were analyzed (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

From Baseline through Follow-up of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[17]	63[18]		
Units: Participants				
number (not applicable)				
Baseline, Any bleeding n=29,63	20	45		
Baseline, Significant bleeding n=29,63	6	16		
Week 1, Any bleeding n=29,63	19	41		
Week 1, Significant bleeding n=29,63	3	8		
Week 2, Any bleeding n=29,63	19	33		
Week 2, Significant bleeding n=29,63	6	6		
Week 3, Any bleeding n=28,62	18	32		
Week 3, Significant bleeding n=28,62	3	7		
Week 4, Any bleeding n=29, 62	20	27		
Week 4, Significant bleeding n=29, 62	4	4		
Week 5, Any bleeding n=27, 62	18	22		
Week 5, Significant bleeding n=27, 62	2	5		
Week 6, Any bleeding n=28, 62	17	24		
Week 6, Significant bleeding n=28, 62	0	5		
Week 7, Any bleeding n=28, 63	14	20		
Week 7, Significant bleeding n=28, 63	1	1		
Week 8, Any bleeding n=28, 63	17	24		
Week 8,Significant bleeding n=28, 63	1	4		
Week 9, Any bleeding n=27, 61	18	24		
Week 9, Significant bleeding n=27, 61	3	4		
Week 10, Any bleeding n=28, 62	17	20		
Week 10, Significant bleeding n=28, 62	2	4		
Week 11, Any bleeding n=28, 61	16	26		
Week 11, Significant bleeding n=28, 61	3	8		
Week 12, Any bleeding n=28, 61	16	23		
Week 12, Significant bleeding n=28, 61	2	3		
Follow-up Week 1, Any bleeding n=0,2	0	1		
Follow-up Week 1, Significant bleeding n=0,2	0	0		
Follow-up Week 2, Any bleeding n=0,2	0	1		

Follow-up Week 2, Significant bleeding n=0,2	0	0		
Follow-up Week 3, Any bleeding n=0,3	0	2		
Follow-up Week 3, Significant bleeding n=0,3	0	1		
Follow-up Week 4, Any bleeding n=0,1	0	1		
Follow-up Week 4, Significant bleeding n=0,1	0	1		
Any follow-up Week, Any bleeding n=0,3	0	2		
Any Follow-up Week, Significant bleeding n=0,3	0	1		

Notes:

[17] - ITT population

[18] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who achieved a platelet count >=50 Gi/L at any time during Part 2

End point title	Number of participants who achieved a platelet count >=50 Gi/L at any time during Part 2

End point description:

Participants who achieved a platelet count >=50 Gi/L at any time during Part 2 (up to Week 24) were reported.

End point type	Secondary

End point timeframe:

From Baseline up to Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[19]			
Units: Participants				
number (not applicable)	70			

Notes:

[19] - ITT Population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of weeks in which participants achieved a platelet count >=50 Gi/L, between Weeks 4 and 24 of Part 2

End point title	Number of weeks in which participants achieved a platelet count >=50 Gi/L, between Weeks 4 and 24 of Part 2

End point description:

Platelet response was analyzed after Week 4 for the eltrombopag-only period to allow participants who had been randomized to placebo in the Randomized Period time to escalate to their optimal dose of eltrombopag. Participants with non-weekly assessments were assumed to have maintained a positive

response for each week between two assessments that had positive responses. If the participant achieved a positive response at an assessment and then achieved a negative response at the next assessment, then it was assumed that the participant had achieved a positive response for one day.

End point type	Secondary

End point timeframe:

From Week 4 up to Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[20]			
Units: Weeks				
arithmetic mean (standard deviation)	10 (± 7.67)			

Notes:

[20] - ITT Population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum duration for which a participant continuously maintained a platelet count of >=50 Gi/L during Part 2

End point title	Maximum duration for which a participant continuously maintained a platelet count of >=50 Gi/L during Part 2

End point description:

The maximum duration for which a participant continuously maintained a platelet count of >=50 Gi/L was calculated and summarized for the 24 weeks of eltrombopag dosing (Part 2). Participants with non-weekly assessments were assumed to have maintained a positive response for each week between two assessments that had positive responses. If the participant achieved a positive response at an assessment and then achieved a negative response at the next assessment, then it was assumed that the participant had achieved a positive response for one day.

End point type	Secondary

End point timeframe:

From Baseline up to Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[21]			
Units: Weeks				
arithmetic mean (standard deviation)	8.6 (± 7.84)			

Notes:

[21] - ITT Population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who reduced or discontinued Baseline concomitant ITP medications during Part 2 without requiring subsequent rescue therapy

End point title	Number of participants who reduced or discontinued Baseline concomitant ITP medications during Part 2 without requiring subsequent rescue therapy

End point description:

Participants who discontinued or had a sustained reduction of a baseline immune (idiopathic) thrombocytopenic purpura (ITP) medication during the 24 weeks of Part 2 (Open-Label Period) and without requiring subsequent rescue therapy. For participants randomized to placebo in Part 1, Baseline is defined as Week 13 of Part 1. For participants randomized to eltrombopag in Part 1, Baseline is defined as Day 1 of Part 1. A sustained reduction was defined as a reduction for 4 weeks or more. Only those participants who entered into Part 2 (Open-label eltrombopag-only phase) and taking an ITP medication at Baseline were analyzed.

End point type	Secondary

End point timeframe:

From Baseline up to Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	15[22]			
Units: Participants				
number (not applicable)	8			

Notes:

[22] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who required a protocol-defined rescue treatment during Part 2

End point title	Number of participants who required a protocol-defined rescue treatment during Part 2

End point description:

Rescue treatment was defined as either a new immune (idiopathic) thrombocytopenic purpura (ITP) medication, an increase in the dose of a concomitant ITP medication from Baseline, a platelet transfusion, or a splenectomy.

End point type	Secondary

End point timeframe:

From Baseline up to Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[23]			
Units: Participants				
number (not applicable)	11			

Notes:

[23] - ITT Population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any bleeding and significant bleeding as assessed using the WHO Bleeding Scale during Part 2

End point title	Number of participants with any bleeding and significant bleeding as assessed using the WHO Bleeding Scale during Part 2

End point description:

The WHO Bleeding Scale is a measure of bleeding severity with the following grades: Grade 0 = no bleeding, Grade 1 = petechiae, Grade 2 = mild blood loss, Grade 3 = gross bleeding and Grade 4 = debilitating blood loss. The WHO Grades were dichotomized into the following categories: no bleeding = Grade 0; any bleeding = Grade 1 to 4; no clinically significant bleeding = Grade 0 to 1; clinically significant bleeding = Grade 2 to 4. Only those participants who entered into Part 2 open-label Eltrombopag only phase were analyzed. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

From Baseline of Part 2 through Follow-up

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[24]			
Units: Participants				
number (not applicable)				
Baseline, Any bleeding n=87	55			
Baseline, Significant bleeding n=87	17			
Week 1, Any bleeding n=86	29			
Week 1, Significant bleeding n=86	3			
Week 2, Any bleeding n=85	22			
Week 2, Significant bleeding n=85	2			
Week 3, Any bleeding n=86	20			
Week 3, Significant bleeding n=86	1			
Week 4, Any bleeding n=68	20			
Week 4, Significant bleeding n=68	4			
Week 5, Any bleeding n=61	21			
Week 5, Significant bleeding n=61	4			
Week 6, Any bleeding n=55	17			
Week 6, Significant bleeding n=55	3			

Week 7, Any bleeding n=52	14			
Week 7, Significant bleeding n=52	1			
Week 8, Any bleeding n=52	17			
Week 8, Significant bleeding n=52	4			
Week 9, Any bleeding n=45	11			
Week 9, Significant bleeding n=45	1			
Week 10, Any bleeding n=42	8			
Week 10, Significant bleeding n=42	2			
Week 11, Any bleeding n=40	12			
Week 11, Significant bleeding n=40	3			
Week 12, Any bleeding n=63	15			
Week 12, Significant bleeding n=63	5			
Week 13, Any bleeding n=30	9			
Week 13, Significant bleeding n=30	2			
Week 14, Any bleeding n=38	9			
Week 14, Significant bleeding n=38	2			
Week 15, Any bleeding n=43	10			
Week 15, Significant bleeding n=43	2			
Week 16, Any bleeding n=47	11			
Week 16, Significant bleeding n=47	4			
Week 17, Any bleeding n=37	10			
Week 17, Significant bleeding n=37	2			
Week 18, Any bleeding n=33	8			
Week 18, Significant bleeding n=33	1			
Week 19, Any bleeding n=44	15			
Week 19, Significant bleeding n=44	2			
Week 20, Any bleeding n=39	7			
Week 20, Significant bleeding n=39	2			
Week 21, Any bleeding n=41	10			
Week 21, Significant bleeding n=41	2			
Week 22, Any bleeding n=34	7			
Week 22, Significant bleeding n=34	3			
Week 23, Any bleeding n=36	15			
Week 23, Significant bleeding n=36	2			
Week 24, Any bleeding n=79	19			
Week 24, Significant bleeding n=79	5			
Follow-up Week 1, Any bleeding n=29	8			
Follow-up Week 1, Significant bleeding n=29	2			
Follow-up Week 2, Any bleeding n=37	25			
Follow-up Week 2, Significant bleeding n=37	5			
Follow-up Week 3, Any bleeding n=40	17			
Follow-up Week 3, Significant bleeding n=40	5			
Follow-up Week 4, Any bleeding n=70	23			
Follow-up Week 4, Significant bleeding n=70	3			
Any follow-up Week, Any bleeding n=77	38			
Any Follow-up Week, Significant bleeding n=77	8			

Notes:

[24] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE) during Part 1

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE) during Part 1

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose: results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, or is a congenital anomaly or birth defect. Medical or scientific judgment should be exercised in other situations.

End point type	Secondary

End point timeframe:

From Day 1 of Treatment up to Week 13 of Part 1+ 1 day

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[25]	63[26]		
Units: Participants				
number (not applicable)				
Any AE	21	51		
Any SAE	4	5		

Notes:

[25] - Safety Population: all participants who received at least one dose of the investigational product

[26] - Safety Population: all participants who received at least one dose of the investigational product

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE) during Part 2

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE) during Part 2

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose: results in death, is life threatening; requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, or is a congenital anomaly or birth defect. Medical or

scientific judgment should be exercised in other situations.

End point type	Secondary

End point timeframe:

From Day 1 of Part 2 up to Week 24 of Part 2 + 1 day

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[27]			
Units: Participants				
number (not applicable)				
Any AE	69			
Any SAE	9			

Notes:

[27] - Safety Population: all participants who received at least one dose of the investigational product

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated maximum toxicity grade for the indicated clinical chemistry parameters at any time post-Baseline (BL) during Part 1

End point title	Number of participants with the indicated maximum toxicity grade for the indicated clinical chemistry parameters at any time post-Baseline (BL) during Part 1

End point description:

Clinical chemistry parameters were summarized according to the National Cancer Institute Common Terminology Criteria for Adverse Events(NCI CTCAE), version 4.0: Grade 0(G0), none; Grade 1(G1), mild; Grade 2(G2), moderate; Grade 3(G3), severe; Grade 4(G4), life-threatening or disabling. Parameters included: aspartate amino transferase(AST), alkaline phosphatase(ALP), total bilirubin, albumin, alanine amino transferase(ALT), prothrombin international normalized ratio(PT INR), activated partial thromboplastin time(APTT), and creatinine. The BL value is defined as the value taken at Day 1 or, if missing, the latest non-missing Screening value. For serum creatinine, due to the variations in creatinine, the average of the Screening and the Day 1 values will be used as BL. The maximum post-BL toxicity grade includes any scheduled or unscheduled post-BL assessment during Part 1. Only participants available at the specified time points were analyzed(represented by n=X,X in the category titles)

End point type	Secondary

End point timeframe:

From Baseline up to Week 13 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[28]	63[29]		
Units: Participants				
number (not applicable)				

AST, G0, n=29, 63	26	50		
AST, G1, n=29, 63	3	12		
AST, G2, n=29, 63	0	1		
AST, G3, n=29, 63	0	0		
AST, G4, n=29, 63	0	0		
ALT, G0, n=29, 63	27	52		
ALT, G1, n=29, 63	2	6		
ALT, G2, n=29, 63	0	3		
ALT, G3, n=29, 63	0	2		
ALT, G4, n=29, 63	0	0		
Total Bilirubin, G0, n=29, 63	29	60		
Total Bilirubin, G1, n=29, 63	0	3		
Total Bilirubin, G2, n=29, 63	0	0		
Total Bilirubin, G3, n=29, 63	0	0		
Total Bilirubin, G4, n=29, 63	0	0		
Albumin, G0, n=29, 63	29	63		
Albumin, G1, n=29, 63	0	0		
Albumin, G2, n=29, 63	0	0		
Albumin, G3, n=29, 63	0	0		
Albumin, G4, n=29, 63	0	0		
ALP, G0, n=29, 63	28	47		
ALP, G1, n=29, 63	1	16		
ALP, G2, n=29, 63	0	0		
ALP, G3, n=29, 63	0	0		
ALP, G4, n=29, 63	0	0		
PT INR, G0, n=27, 58	26	57		
PT INR, G1, n=27, 58	1	1		
PT INR, G2, n=27, 58	0	0		
PT INR, G3, n=27, 58	0	0		
PT INR, G4, n=27, 58	0	0		
APTT, G0 n=27, 58	13	24		
APTT, G1, n=27, 58	13	32		
APTT, G2, n=27, 58	1	2		
APTT, G3, n=27, 58	0	0		
APTT, G4, n=27, 58	0	0		
Creatinine, G0, n=29, 63	22	47		
Creatinine, G1, n=29, 63	7	15		
Creatinine, G2, n=29, 63	0	1		
Creatinine, G3, n=29, 63	0	0		
Creatinine, G4, n=29, 63	0	0		

Notes:

[28] - Safety population

[29] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated maximum toxicity grade for the indicated clinical chemistry parameters at any time post-Baseline during Part 2

End point title	Number of participants with the indicated maximum toxicity grade for the indicated clinical chemistry parameters at any time post-Baseline during Part 2

End point description:

Clinical chemistry parameters were summarized according to the NCI CTCAE, version 4.0: G0, none; G1, mild; G2, moderate; G3, severe; G4, life-threatening or disabling. Parameters included: AST, ALP, total bilirubin, albumin, ALT, and creatinine. For participants randomized to Placebo in Part 1, the BL value for Part 2 is defined as the value taken at Week 13 of Part 1. For serum creatinine, the value taken at Week 13 of Part 1 will be used as BL. For participants randomized to Eltrombopag in Part 1, the BL value is defined as the value taken on Day 1 or, if missing, the latest non-missing Screening value. For serum creatinine, due to the variations in creatinine, the average of the Screening and the Day 1 values will be used as BL. For participants who do not have both a Screening and Day 1 value, the Screening or Day 1 value will be used as BL. The maximum post-BL toxicity grade includes any scheduled or unscheduled post-BL assessment.

End point type	Secondary

End point timeframe:

From Baseline (BL) of Part 2 through Follow-up

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[30]			
Units: Participants				
number (not applicable)				
AST, G0	63			
AST, G1	21			
AST, G2	1			
AST, G3	2			
AST, G4	0			
ALT, G0	67			
ALT, G1	14			
ALT, G2	3			
ALT, G3	3			
ALT, G4	0			
Total Bilirubin, G0	80			
Total Bilirubin, G1	4			
Total Bilirubin, G2	3			
Total Bilirubin, G3	0			
Total Bilirubin, G4	0			
Albumin, G0	85			
Albumin, G1	1			
Albumin, G2	1			
Albumin, G3	0			
Albumin, G4	0			
ALP, G0	67			
ALP, G1	20			
ALP, G2	0			
ALP, G3	0			
ALP, G4	0			
Creatinine, G0	72			
Creatinine, G1	14			
Creatinine, G2	1			
Creatinine, G3	0			
Creatinine, G4	0			

Notes:

[30] - Safety Population. Only participants who entered Part 2 (Open-label eltrombopag phase) were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated maximum toxicity grade for the indicated hematology parameters at any time post-Baseline during Part 1

End point title	Number of participants with the indicated maximum toxicity grade for the indicated hematology parameters at any time post-Baseline during Part 1

End point description:

Hematology parameters were summarized according to the NCI CTCAE, version 4.0: G0, none; G1, mild; G2, moderate; G3, severe; G4, life-threatening or disabling. Hematology parameters included: leukocytes, neutrophils, hemoglobin (increased), hemoglobin (anemia), lymphocytes (increased), and lymphocytes (decreased). The Baseline value is defined as the value taken at Day 1 or, if missing, the latest non-missing Screening value. The maximum post-Baseline toxicity grade includes any scheduled or unscheduled post-Baseline assessment during Part 1. Only those participants available at the specified time points were analyzed (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

From Baseline up to Week 13 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[31]	63[32]		
Units: Participants				
number (not applicable)				
Leukocytes, G0, n=29, 63	23	50		
Leukocytes, G1, n=29, 63	6	11		
Leukocytes, G2, n=29, 63	0	0		
Leukocytes, G3, n=29, 63	0	1		
Leukocytes, G4, n=29, 63	0	1		
Neutrophils G0, n=29, 63	27	52		
Neutrophils G1, n=29, 63	1	3		
Neutrophils G2, n=29, 63	0	6		
Neutrophils G3, n=29, 63	1	0		
Neutrophils G4, n=29, 63	0	2		
Hemoglobin (increased), G0, n=29, 63	26	49		
Hemoglobin (increased), G1, n=29, 63	3	12		
Hemoglobin (increased), G2, n=29, 63	0	2		
Hemoglobin (increased), G3, n=29, 63	0	0		
Hemoglobin (increased), G4, n=29, 63	0	0		
Hemoglobin (anemia), G0, n=29, 63	20	42		
Hemoglobin (anemia), G1, n=29, 63	7	17		

Hemoglobin (anemia), G2, n=29, 63	0	4		
Hemoglobin (anemia), G3, n=29, 63	2	0		
Hemoglobin (anemia), G4, n=29, 63	0	0		
Lymphocytes (increased), G0, n=29, 63	17	37		
Lymphocytes (increased), G1, n=29, 63	0	0		
Lymphocytes (increased), G2, n=29, 63	12	26		
Lymphocytes (increased), G3, n=29, 63	0	0		
Lymphocytes (increased), G4, n=29, 63	0	0		
Lymphocytes (decreased), G0, n=29, 63	25	48		
Lymphocytes (decreased), G1, n=29, 63	4	13		
Lymphocytes (decreased), G2, n=29, 63	0	1		
Lymphocytes (decreased), G3, n=29, 63	0	1		
Lymphocytes (decreased), G4, n=29, 63	0	0		

Notes:

[31] - Safety population

[32] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated maximum toxicity grade for the indicated hematology parameters at any time post-Baseline during Part 2

End point title	Number of participants with the indicated maximum toxicity grade for the indicated hematology parameters at any time post-Baseline during Part 2

End point description:

Hematology parameters were summarized according to the NCI CTCAE, version 4.0: G0, none, G1, mild; G2, moderate; G3, severe; G4, life-threatening or disabling. Hematology parameters included: leukocytes, neutrophils, hemoglobin (increased), hemoglobin (anemia), lymphocytes (increased), and lymphocytes (decreased). For participants randomized to Placebo in Part 1, the BL value for Part 2 is defined as the value taken at Week 13 of Part 1. For participants randomized to Eltrombopag in Part 1, the BL value is defined as the value taken on Day 1 or, if missing, the latest non-missing Screening value. For participants who do not have both a Screening and Day 1 value, the Screening or Day 1 value will be used as BL. The maximum post-BL toxicity grade includes any scheduled or unscheduled post-BL assessment.

End point type	Secondary

End point timeframe:

From Baseline up to Week 24 of Part 2 and Follow-up Weeks 1 to 4 (up to Study Week 41)

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[33]			
Units: Participants				
number (not applicable)				
Leukocytes, G0	59			
Leukocytes, G1	23			
Leukocytes, G2	3			
Leukocytes, G3	2			
Leukocytes, G4	0			
Neutrophils, G0	63			

Neutrophils, G1	6			
Neutrophils, G2	13			
Neutrophils, G3	2			
Neutrophils, G4	3			
Hemoglobin (increased), G0	74			
Hemoglobin (increased), G1	11			
Hemoglobin (increased), G2	2			
Hemoglobin (increased), G3	0			
Hemoglobin (increased), G4	0			
Hemoglobin (anemia), G0	48			
Hemoglobin (anemia), G1	31			
Hemoglobin (anemia), G2	7			
Hemoglobin (anemia), G3	1			
Hemoglobin (anemia), G4	0			
Lymphocytes (increased), G0	47			
Lymphocytes (increased), G1	0			
Lymphocytes (increased), G2	40			
Lymphocytes (increased), G3	0			
Lymphocytes (increased), G4	0			
Lymphocytes (decreased), G0	65			
Lymphocytes (decreased), G1	19			
Lymphocytes (decreased), G2	2			
Lymphocytes (decreased), G3	1			
Lymphocytes (decreased), G4	0			

Notes:

[33] - Safety Population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants (par) with vital sign data falling outside the reference ranges (RR) at the indicated visit during Part 1

End point title	Number of participants (par) with vital sign data falling outside the reference ranges (RR) at the indicated visit during Part 1

End point description:

Vital sign measurements were taken before blood draws and included systolic blood pressure(SBP), diastolic blood pressure(DBP), and heart rate(HR). The number of par are reported with vital sign data falling outside the standard RR: RR high(RRH) and RR low(RRL). The BL value is the value taken at Day 1 or if missing, the latest non-missing SCR value. RR for SBP or DBP (mmHg) are read: Lower Limit of Normal, Normal Range, Upper Limit of Normal. For Ages 1 to 5 years (yrs) ranges are SBP <85, 85 to 115, >115; DBP <45, 45 to70, >70. Ages 6 to 11 yrs: SBP <85, 85 to 120, >120;, DBP <50, 50 to 75, >75. Ages 12 to 17 yrs: SBP <95, 95 to 135, >135; DBP <55, 55 to 85, >85. RR for HR(bpm) are ages 1 to < 3 yrs: <90, 90 to 140, >140; ages 3 to < 5 yrs: <75, 75 to 130, >130, ages 5 to < 8yrs: <65, 65 to 115, >115; ages 8 to < 12yrs: <55, 55 to 110, >110; and ages 12 to 18 yrs: <55, 55 to 110, >110. Only par available at the specified time points were analyzed(n=X,X in the category title)

End point type	Secondary

End point timeframe:

From Screening (SCR) up to Week 13 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[34]	63[35]		
Units: Participants				
number (not applicable)				
DBP, Day 1, RRH, n=28,62	6	8		
DBP, Day 1, RRL, n=28, 62	2	5		
DBP, Week 1, RRH, n=28, 63	3	10		
DBP, Week 1, RRL, n=28, 63	0	5		
DBP, Week 2, RRH, n=29, 63	3	8		
DBP, Week 2, RRL, n=29, 63	2	6		
DBP, Week 3, RRH, n=28, 63	7	12		
DBP, Week 3, RRL, n=28, 63	2	6		
DBP, Week 4, RRH, n=29, 62	7	5		
DBP, Week 4, RRL, n=29, 62	2	9		
DBP, Week 5, RRH, n=27, 62	4	10		
DBP, Week 5, RRL, n=27, 62	2	6		
DBP, Week 6, RRH, n=28, 62	7	10		
DBP, Week 6, RRL, n=28, 62	1	8		
DBP, Week 7, RRH, n=28, 63	3	7		
DBP, Week 7, RRL, n=28, 63	2	5		
DBP, Week 8, RRH, n=28, 63	4	9		
DBP, Week 8, RRL, n=28, 63	2	8		
DBP, Week 9, RRH, n=27, 61	4	9		
DBP, Week 9, RRL, n=27, 61	2	4		
DBP, Week 10, RRH, n=28, 62	6	8		
DBP, Week 10, RRL, n=28, 62	2	7		
DBP, Week 11, RRH, n=28, 61	6	8		
DBP, Week 11, RRL, n=28, 61	3	6		
DBP, Week 12, RRH, n=28, 61	3	8		
DBP, Week 12, RRL, n=28, 61	0	6		
DBP, Week 13, RRH, n=28, 61	4	9		
DBP, Week 13, RRL, n=28, 61	3	4		
Heart Rate, Day 1, RRH, n=28, 62	0	2		
Heart Rate, Day 1, RRL, n=28, 62	0	1		
Heart Rate, Week 1, RRH, n=28, 63	0	0		
Heart Rate, Week 1, RRL, n=28, 63	0	0		
Heart Rate, Week 2, RRH, n=29, 63	2	1		
Heart Rate, Week 2, RRL, n=29, 63	0	1		
Heart Rate, Week 3, RRH, n=28, 63	1	2		
Heart Rate, Week 3, RRL, n=28, 63	0	0		
Heart Rate, Week 4, RRH, n=29, 61	0	4		
Heart Rate, Week 4, RRL, n=29, 61	0	1		
Heart Rate, Week 5, RRH, n=27, 62	1	5		
Heart Rate, Week 5, RRL, n=27, 62	1	0		
Heart Rate, Week 6, RRH, n=28,62	1	1		
Heart Rate, Week 6, RRL, n=28, 62	1	0		
Heart Rate, Week 7, RRH, n=28, 63	0	2		
Heart Rate, Week 7, RRL, n=28, 63	1	0		
Heart Rate, Week 8, RRH, n=28, 63	1	2		

Heart Rate, Week 8, RRL, n=28, 63	1	0		
Heart Rate, Week 9, RRH, n=27, 61	1	2		
Heart Rate, Week 9, RRL, n=27, 61	0	0		
Heart Rate, Week 10, RRH, n=28, 62	1	1		
Heart Rate, Week 10, RRL, n=28, 62	0	0		
Heart Rate, Week 11, RRH, n=28, 61	1	2		
Heart Rate, Week 11, RRL, n=28, 61	0	0		
Heart Rate, Week 12, RRH, n=28,61	0	2		
Heart Rate, Week 12, RRL, n=28, 61	0	0		
Heart Rate, Week 13, RRH, n=28, 61	0	3		
Heart Rate, Week 13, RRL, n=28, 61	1	0		
SBP, Day 1, RRH, n=28, 62	5	10		
SBP, Day 1, RRL, n=28, 62	3	6		
SBP, Week 1, RRH, n=28, 63	3	11		
SBP, Week 1, RRL, n=28,63	4	8		
SBP, Week 2, RRH, n=29, 63	4	7		
SBP, Week 2, RRL, n=29, 63	3	9		
SBP, Week 3, RRH, n=28, 63	3	9		
SBP, Week 3, RRL, n=28, 63	2	9		
SBP, Week 4, RRH, n=29, 62	3	10		
SBP, Week 4, RRL, n=29, 62	2	9		
SBP, Week 5, RRH, n=27, 62	5	9		
SBP, Week 5, RRL, n=27, 62	4	7		
SBP, Week 6, RRH, n=28, 62	5	7		
SBP, Week 6, RRL, n=28, 62	3	8		
SBP, Week 7, RRH, n=28, 63	5	10		
SBP, Week 7, RRL, n=28, 63	3	7		
SBP, Week 8, RRH, n=28, 63	3	14		
SBP, Week 8, RRL, n=28, 63	4	7		
SBP, Week 9, RRH, n=27, 61	4	12		
SBP, Week 9, RRL, n=27, 61	3	7		
SBP, Week 10, RRH, n=28, 62	4	11		
SBP, Week 10, RRL, n=28, 62	3	11		
SBP, Week 11, RRH, n=28, 61	6	12		
SBP, Week 11, RRL, n=28, 61	5	9		
SBP, Week 12, RRH, n=28, 61	4	11		
SBP, Week 12, RRL, n=28, 61	4	4		
SBP, Week 13, RRH, n=28, 61	6	9		
SBP, Week 13, RRL, n=28, 61	4	7		

Notes:

[34] - Safety population

[35] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants (par) with vital sign data falling outside the reference ranges (RR) at the indicated visit during Part 2

End point title	Number of participants (par) with vital sign data falling outside the reference ranges (RR) at the indicated visit during Part 2

End point description:

Vital sign measurements were taken before any blood draw and included systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate(HR). The number of par are reported with vital sign data falling outside the standard RR as RR high(RRH) and RR low(RRL) from SCR up to Week 24 of Part 2 and from Follow-up Week 1 to Week 4. RR for Blood Pressure(mmHg) are read as: Lower Limit of Normal, Normal Range, Upper Limit of Normal. For Ages 1 to 5 years (yrs) ranges are SBP <85, 85 to 115, >115; DBP <45, 45 to70, >70. Ages 6 to 11 yrs: SBP <85, 85 to 120, >120; DBP <50, 50 to 75, >75. Ages 12 to 17 yrs: SBP <95, 95 to 135, >135; DBP <55, 55 to 85, >85. RR for HR (bpm) are ages 1 to < 3 yrs: <90, 90 to 140, >140; ages 3 to < 5 yrs: <75, 75 to 130, >130, ages 5 to < 8yrs: <65, 65 to 115, >115; ages 8 to < 12yrs: <55, 55 to 110, >110; and ages 12 to 18 yrs: <55, 55 to 110, >110. Only par available at the specified time points were analyzed (represented by n=X in the category titles)

End point type	Secondary

End point timeframe:

From Week 1 up to Week 24 of Part 2 and Follow-up Week 1 to Week 4 (up to Week 41)

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[36]			
Units: Participants				
number (not applicable)				
DBP, Week 1, RRH, n=87	14			
DBP, Week 1, RRL, n=87	8			
DBP, Week 2, RRH, n=86	14			
DBP, Week 2, RRL, n=86	8			
DBP, Week 3, RRH, n=86	13			
DBP, Week 3, RRL, n=86	11			
DBP, Week 4, RRH, n=68	10			
DBP, Week 4, RRL, n=68	7			
DBP, Week 5, RRH, n=61	7			
DBP, Week 5, RRL, n=61	7			
DBP, Week 6, RRH, n=55	6			
DBP, Week 6, RRL, n=55	4			
DBP, Week 7, RRH, n=52	7			
DBP, Week 7, RRL, n=52	5			
DBP, Week 8, RRH, n=53	4			
DBP, Week 8, RRL, n=53	6			
DBP, Week 9, RRH, n=45	3			
DBP, Week 9, RRL, n=45	7			
DBP, Week 10, RRH, n=42	5			
DBP, Week 10, RRL, n=42	7			
DBP, Week 11, RRH, n=40	5			
DBP, Week 11, RRL, n=40	7			
DBP, Week 12, RRH, n=63	9			
DBP, Week 12, RRL, n=63	11			
DBP, Week 13, RRH, n=29	4			
DBP, Week 13, RRL, n=29	2			
DBP, Week 14, RRH, n=38	2			
DBP, Week 14, RRL, n=38	9			
DBP, Week 15, RRH, n=43	7			
DBP, Week 15, RRL, n=43	3			

DBP, Week 16, RRH, n=47	3			
DBP, Week 16, RRL, n=47	6			
DBP, Week 17, RRH, n=37	5			
DBP, Week 17, RRL, n=37	6			
DBP, Week 18, RRH, n=34	7			
DBP, Week 18, RRL, n=34	5			
DBP, Week 19, RRH, n=44	5			
DBP, Week 19, RRL, n=44	3			
DBP, Week 20, RRH, n=39	6			
DBP, Week 20, RRL, n=39	3			
DBP, Week 21, RRH, n=41	9			
DBP, Week 21, RRL, n=41	6			
DBP, Week 22, RRH, n=34	6			
DBP, Week 22, RRL, n=34	3			
DBP, Week 23, RRH, n=36	6			
DBP, Week 23, RRL, n=36	6			
DBP, Week 24, RRH, n=79	14			
DBP, Week 24, RRL, n=79	10			
DBP, Follow-Up Week 1, RRH, n=29	8			
DBP, Follow-Up Week 1, RRL, n=29	3			
DBP, Follow-Up Week 2, RRH, n=37	8			
DBP, Follow-Up Week 2, RRL, n=37	6			
DBP, Follow-Up Week 3, RRH, n=39	4			
DBP, Follow-Up Week 3, RRL, n=39	5			
DBP, Follow-Up Week 4, RRH, n=67	8			
DBP, Follow-Up Week 4, RRL, n=67	5			
Heart Rate, Week 1, RRH, n=87	4			
Heart Rate, Week 1, RRL, n=87	1			
Heart Rate, Week 2, RRH, n=86	3			
Heart Rate, Week 2, RRL, n=86	2			
Heart Rate, Week 3, RRH, n=86	1			
Heart Rate, Week 3, RRL, n=86	0			
Heart Rate, Week 4, RRH, n=68	2			
Heart Rate, Week 4, RRL, n=68	0			
Heart Rate, Week 5, RRH, n=61	0			
Heart Rate, Week 5, RRL, n=61	1			
Heart Rate, Week 6, RRH, n=55	1			
Heart Rate, Week 6, RRL, n=55	0			
Heart Rate, Week 7, RRH, n=52	2			
Heart Rate, Week 7, RRL, n=52	0			
Heart Rate, Week 8, RRH, n=53	2			
Heart Rate, Week 8, RRL, n=53	0			
Heart Rate, Week 9, RRH, n=45	2			
Heart Rate, Week 9, RRL, n=45	0			
Heart Rate, Week 10, RRH, n=42	1			
Heart Rate, Week 10, RRL, n=42	1			
Heart Rate, Week 11, RRH, n=40	1			
Heart Rate, Week 11, RRL, n=40	1			
Heart Rate, Week 12, RRH, n=63	1			
Heart Rate, Week 12, RRL, n=63	1			
Heart Rate, Week 13, RRH, n=29	2			
Heart Rate, Week 13, RRL, n=29	0			

Heart Rate, Week 14, RRH, n=38	2			
Heart Rate, Week 14, RRL, n=38	1			
Heart Rate, Week 15, RRH, n=43	0			
Heart Rate, Week 15, RRL, n=43	0			
Heart Rate, Week 16, RRH, n=47	2			
Heart Rate, Week 16, RRL, n=47	0			
Heart Rate, Week 17, RRH, n=37	2			
Heart Rate, Week 17, RRL, n=37	1			
Heart Rate, Week 18, RRH, n=34	0			
Heart Rate, Week 18, RRL, n=34	0			
Heart Rate, Week 19, RRH, n=44	0			
Heart Rate, Week 19, RRL, n=44	1			
Heart Rate, Week 20, RRH, n=39	2			
Heart Rate, Week 20, RRL, n=39	0			
Heart Rate, Week 21, RRH, n=41	0			
Heart Rate, Week 21, RRL, n=41	0			
Heart Rate, Week 22, RRH, n=34	2			
Heart Rate, Week 22, RRL, n=34	0			
Heart Rate, Week 23, RRH, n=36	0			
Heart Rate, Week 23, RRL, n=36	0			
Heart Rate, Week 24, RRH, n=79	1			
Heart Rate, Week 24, RRL, n=79	1			
Heart Rate, Follow-Up Week 1, RRH, n=29	1			
Heart Rate, Follow-Up Week 1, RRL, n=29	0			
Heart Rate, Follow-Up Week 2, RRH, n=37	2			
Heart Rate, Follow-Up Week 2, RRL, n=37	1			
Heart Rate, Follow-Up Week 3, RRH, n=39	2			
Heart Rate, Follow-Up Week 3, RRL, n=39	0			
Heart Rate, Follow-Up Week 4, RRH, n=67	2			
Heart Rate, Follow-Up Week 4, RRL, n=67	2			
SBP, Week 1, RRH, n=87	13			
SBP, Week 1, RRL, n=87	9			
SBP, Week 2, RRH, n=86	19			
SBP, Week 2, RRL, n=86	16			
SBP, Week 3, RRH, n=86	15			
SBP, Week 3, RRL, n=86	13			
SBP, Week 4, RRH, n=68	10			
SBP, Week 4, RRL, n=68	7			
SBP, Week 5, RRH, n=61	7			
SBP, Week 5, RRL, n=61	8			
SBP, Week 6, RRH, n=55	11			
SBP, Week 6, RRL, n=55	7			
SBP, Week 7, RRH, n=52	10			
SBP, Week 7, RRL, n=52	5			
SBP, Week 8, RRH, n=53	8			
SBP, Week 8, RRL, n=53	5			

SBP, Week 9, RRH, n=45	8			
SBP, Week 9, RRL, n=45	9			
SBP, Week 10, RRH, n=42	4			
SBP, Week 10, RRL, n=42	4			
SBP, Week 11, RRH, n=40	4			
SBP, Week 11, RRL, n=40	6			
SBP, Week 12, RRH, n=63	14			
SBP, Week 12, RRL, n=63	10			
SBP, Week 13, RRH, n=29	3			
SBP, Week 13, RRL, n=29	2			
SBP, Week 14, RRH, n=38	5			
SBP, Week 14, RRL, n=38	7			
SBP, Week 15, RRH, n=43	9			
SBP, Week 15, RRL, n=43	7			
SBP, Week 16, RRH, n=47	7			
SBP, Week 16, RRL, n=47	6			
SBP, Week 17, RRH, n=37	9			
SBP, Week 17, RRL, n=37	4			
SBP, Week 18, RRH, n=34	6			
SBP, Week 18, RRL, n=34	5			
SBP, Week 19, RRH, n=44	7			
SBP, Week 19, RRL, n=44	4			
SBP, Week 20, RRH, n=39	5			
SBP, Week 20, RRL, n=39	5			
SBP, Week 21, RRH, n=41	10			
SBP, Week 21, RRL, n=41	6			
SBP, Week 22, RRH, n=34	6			
SBP, Week 22, RRL, n=34	4			
SBP, Week 23, RRH, n=36	6			
SBP, Week 23, RRL, n=36	3			
SBP, Week 24, RRH, n=79	13			
SBP, Week 24, RRL, n=79	12			
SBP, Follow-Up Week 1, RRH, n=29	5			
SBP, Follow-Up Week 1, RRL, n=29	3			
SBP, Follow-Up Week 2, RRH, n=37	5			
SBP, Follow-Up Week 2, RRL, n=37	7			
SBP, Follow-Up Week 3, RRH, n=39	9			
SBP, Follow-Up Week 3, RRL, n=39	4			
SBP, Follow-Up Week 4, RRH, n=67	9			
SBP, Follow-Up Week 4, RRL, n=67	7			

Notes:

[36] - Safety population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with a change in visual acuity since Baseline at Week 12 of Part 1

End point title	Number of participants with a change in visual acuity since Baseline at Week 12 of Part 1

End point description:

The visual acuity assessment was performed by an ophthalmologist or an optometrist under the guidance of an ophthalmologist. Visual acuity is defined as acuteness or clearness of vision. Change in visual acuity results are presented as No (no change from Baseline), Not Clinically Significant (NCS), Improvement, and Worsening since Baseline. The Baseline value was obtained at the Screening Visit.

End point type	Secondary

End point timeframe:

Baseline and Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[37]	63[38]		
Units: Participants				
number (not applicable)				
No Change	22	47		
NCS	4	8		
Improvement	1	2		
Worsening	0	1		
Not Measured	2	5		

Notes:

[37] - Safety population

[38] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with a change in visual acuity since Baseline at Week 24 of Part 2

End point title	Number of participants with a change in visual acuity since Baseline at Week 24 of Part 2

End point description:

The visual acuity assessment was performed by an ophthalmologist or an optometrist under the guidance of an ophthalmologist. Visual acuity is defined as acuteness or clearness of vision. Change in visual acuity results are presented as No Change, NCS, Improvement, and Worsening since Baseline. The Baseline value was obtained at the Screening Visit.

End point type	Secondary

End point timeframe:

Baseline and Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[39]			
Units: Participants				
number (not applicable)				

No Change	58			
NCS	13			
Improvement	3			
Worsening	6			
Not Measured	7			

Notes:

[39] - Safety population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with a change in visual acuity since Baseline at Follow-Up Week 24

End point title	Number of participants with a change in visual acuity since Baseline at Follow-Up Week 24

End point description:

The visual acuity assessment was performed by an ophthalmologist or an optometrist under the guidance of an ophthalmologist. Visual acuity is defined as acuteness or clearness of vision. Change in visual acuity results are presented as No Change, NCS, Improvement, and Worsening since Baseline. The Baseline value was obtained at the Screening Visit.

End point type	Secondary

End point timeframe:

Baseline and Follow-Up Week 24 (Study Week 61)

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	87[40]			
Units: Participants				
number (not applicable)				
No Change	63			
NCS	12			
Improvement	9			
Worsening	2			
Not Measured	1			

Notes:

[40] - Safety population. Only participants who entered Part 2(Open-label eltrombopag phase) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worsening visual acuity due to cataracts at Week 12 of Part 1

End point title	Number of participants with worsening visual acuity due to cataracts at Week 12 of Part 1

End point description:

The visual acuity assessment was performed by an ophthalmologist or an optometrist under the guidance of an ophthalmologist. Visual acuity is defined as acuteness or clearness of vision. The number

of participants with worsening visual acuity due to cataracts at Week 12 of Part 1 are presented. Change due to cataracts is categorized as "Yes" or "No". Only those participants who had a result of 'worsening' in assessment of change of visual acuity at this timepoint were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 12 of Part 1

End point values	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[41]	1[42]		
Units: Participants				
number (not applicable)				
Yes		0		
No		1		

Notes:

[41] - Safety population

[42] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worsening visual acuity due to cataracts at Week 24 of Part 2

End point title	Number of participants with worsening visual acuity due to cataracts at Week 24 of Part 2

End point description:

The visual acuity assessment was performed by an ophthalmologist or an optometrist under the guidance of an ophthalmologist. Visual acuity is defined as acuteness or clearness of vision. The number of participants with worsening visual acuity due to cataracts at Week 24 of Part 2 are presented. Change due to cataracts is categorized as "Yes" or "No".

End point type	Secondary

End point timeframe:

Baseline and Week 24 of Part 2

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	6[43]			
Units: Participants				
number (not applicable)				
Yes	1			
No	5			

Notes:

[43] - Safety Population. Only participants who had worsening visual acuity at Week 24 were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worsening visual acuity due to cataracts at Follow-Up Week 24

End point title	Number of participants with worsening visual acuity due to cataracts at Follow-Up Week 24

End point description:

The visual acuity assessment was performed by an ophthalmologist or an optometrist under the guidance of an ophthalmologist. Visual acuity is defined as acuteness or clearness of vision. The number of participants with worsening visual acuity due to cataracts at Follow-up Week 24 are presented. Change due to cataracts is categorized as "Yes" or "No".

End point type	Secondary

End point timeframe:

Baseline and Follow-Up Week 24 (Week 61)

End point values	Part 2 (Open-Label Period) - Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	2[44]			
Units: Participants				
number (not applicable)				
Yes	0			
No	2			

Notes:

[44] - Safety population. Only those participants who had worsening visual acuity at Week 61 were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) assessments for eltrombopag for AUC (0-t)

End point title	Pharmacokinetic (PK) assessments for eltrombopag for AUC (0-t)

End point description:

Single PK samples were collected at each visit during Part 1 Weeks 2, 4, 6, 8, 10, 12 and at each weekly or monthly visit during Part 2 Weeks 1-12 (Study Weeks 13-37). The concentration data were pooled across visits to identify population PK and variability parameter estimates and covariate effects. AUC(0-t) is defined as the area under the concentration-time curve over the dosing interval. The AUC(0-t) for a 50mg dose was estimated for each cohort. From the final model, a single value of each PK parameter was estimated for each subject, and geometric mean (95% CI) values are presented for each cohort for a 50mg dose.

End point type	Secondary

End point timeframe:

Part 1 Weeks 2, 4, 6, 8, 10, 12, and Part 2 Weeks 1-12 (Study Weeks 13 - 37)

End point values	Eltrombopag Cohort 1 (12-17 years)	Eltrombopag Cohort 2 (6-11 years)	Eltrombopag Cohort 3 (1-5 years)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33[45]	38[46]	19[47]	
Units: micrograms*hour per milliliter (ug.h/mL)				
geometric mean (confidence interval 95%)	104 (86.1 to 126)	171 (147 to 200)	184 (147 to 230)	

Notes:

[45] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[46] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[47] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) assessments for eltrombopag for apparent oral clearance (CL/F) and apparent intercompartmental clearance (Q/F)

End point title	Pharmacokinetic (PK) assessments for eltrombopag for apparent oral clearance (CL/F) and apparent intercompartmental clearance (Q/F)

End point description:

Single PK samples were collected at each visit during Part 1 Weeks 2, 4, 6, 8, 10, 12 and at each weekly or monthly visit during Part 2 Weeks 1-12 (Study Weeks 13-37). The concentration data were pooled across visits to identify population PK and variability parameter estimates and covariate effects. CL/F is defined as the apparent oral clearance from plasma and Q/F is defined as apparent intercompartmental clearance. These parameters are dose independent. From the final model, a single value of each PK parameter was estimated for each subject, and geometric mean (95% CI) values are presented for each cohort.

End point type	Secondary

End point timeframe:

Part 1 Weeks 2, 4, 6, 8, 10, 12, and Part 2 Weeks 1-12 (Study Weeks 13 - 37)

End point values	Eltrombopag Cohort 1 (12-17 years)	Eltrombopag Cohort 2 (6-11 years)	Eltrombopag Cohort 3 (1-5 years)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33[48]	38[49]	19[50]	
Units: Liters per hour (L/hr)				
geometric mean (confidence interval 95%)				
CL/F	0.48 (0.4 to 0.58)	0.29 (0.25 to 0.34)	0.19 (0.15 to 0.24)	
Q/F	0.61 (0.54 to 0.68)	0.38 (0.34 to 0.42)	0.24 (0.2 to 0.28)	

Notes:

[48] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[49] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[50] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: PK assessments for eltrombopag for apparent central volume (Vc/F) and apparent peripheral volume (Vp/F)

End point title	PK assessments for eltrombopag for apparent central volume (Vc/F) and apparent peripheral volume (Vp/F)

End point description:

Single PK samples were collected at each visit during Part 1 Weeks 2, 4, 6, 8, 10, 12 and at each weekly or monthly visit during Part 2 Weeks 1-12 (Study Weeks 13-37). The concentration data were pooled across visits to identify population PK and variability parameter estimates and covariate effects. Vc/F is defined as the volume of the central (e.g. plasma) compartment and Vp/F is defined as the volume of the peripheral compartment. These parameters are dose independent. From the final model, a single value of each PK parameter was estimated for each subject, and geometric mean (95% CI) values are presented for each cohort.

End point type	Secondary

End point timeframe:

PK Population. Only those participants who provided pharmacokinetic samples were analyzed

End point values	Eltrombopag Cohort 1 (12-17 years)	Eltrombopag Cohort 2 (6-11 years)	Eltrombopag Cohort 3 (1-5 years)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33[51]	38[52]	19[53]	
Units: Liters (L)				
geometric mean (confidence interval 95%)				
Vc/F	2.46 (2.2 to 2.75)	1.57 (1.35 to 1.81)	0.9 (0.76 to 1.05)	
Vp/F	19.2 (17.7 to 20.9)	11.8 (10.9 to 12.9)	7.17 (6.58 to 7.81)	

Notes:

[51] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[52] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[53] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Population PK model point estimate for eltrombopag for absorption rate-constant (Ka)

End point title	Population PK model point estimate for eltrombopag for absorption rate-constant (Ka)

End point description:

Single PK samples were collected at each visit during Part 1 Weeks 2, 4, 6, 8, 10, 12 and at each weekly

or monthly visit during Part 2 Weeks 1-12 (Study Weeks 13-37). The concentration data were pooled across visits to identify population PK and variability parameter estimates and covariate effects. Ka is defined as the absorption rate constant. This parameter is dose independent, and the population estimate Ka is reported.

End point type	Secondary

End point timeframe:

Part 1 Weeks 2, 4, 6, 8, 10, 12, and Part 2 Weeks 1-12 (Study Weeks 13 - 37)

End point values	Eltrombopag Cohort 1 (12-17 years)	Eltrombopag Cohort 2 (6-11 years)	Eltrombopag Cohort 3 (1-5 years)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33[54]	38[55]	19[56]	
Units: Units:1/h				
number (not applicable)	0.189	0.189	0.189	

Notes:

[54] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[55] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

[56] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Assessments for Eltrombopag for Cmax

End point title	Pharmacokinetic (PK) Assessments for Eltrombopag for Cmax

End point description:

Single PK samples were collected at each visit during Part 1 Weeks 2, 4, 6, 8, 10, 12 and at each weekly or monthly
visit during Part 2 Weeks 1-12 (Study Weeks 13-37). The concentration data were pooled across visits to identify
population PK and variability parameter estimates and covariate effects. Cmax is defined as the maximum observed
concentration. The Cmax for a 50mg dose was estimated for each cohort. From the final model, a single value of each
PK parameter was estimated for each subject, and geometric mean (95% CI) values are presented for each cohort for a
50mg dose.

End point type	Secondary

End point timeframe:

Part 1 Weeks 2, 4, 6, 8, 10, 12, and Part 2 Weeks 1-12 (Study Weeks 13 - 37)

End point values	Eltrombopag Cohort 1 (12-17 years)	Eltrombopag Cohort 2 (6-11 years)	Eltrombopag Cohort 3 (1-5 years)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33[57]	38[58]	19[59]	
Units: micrograms per milliliter (ug/mL)				
geometric mean (confidence interval 95%)	6.94 (5.96 to 8.08)	11.2 (9.91 to 12.8)	12.5 (10.7 to 14.6)	

Notes:
[57] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed
[58] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed
[59] - PK Population. Only those participants who provided pharmacokinetic samples were analyzed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment adverse events (AEs) and serious adverse events (SAEs) are defined as events occuring from the start of investigational product until follow up (up to 61 weeks).

Adverse event reporting additional description:

SAEs and non-serious AEs were collected in members of the Safety Population, comprised of all participants who had received at least one dose of the investigational product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Part 1 (Randomized Period)-Placebo

Reporting group description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kilograms (kg) received placebo 37.5 milligrams (mg) once daily (QD), and those with a body weight >=27 kg received placebo 50 mg QD. Participants of East Asian ancestry received a starting dose of placebo 25 mg QD. Participants aged between 1 and 5 years received placebo 1.2 milligrams per kilogram (mg/kg) QD; participants of East Asian ancestry received a starting dose of placebo 0.8 milligrams per kilograms per day (mg/kg/day).

Reporting group title	Part 1 (Randomized Period)-Eltrombopag

Reporting group description:

In Part 1, participants aged between 6 and 17 years with a body weight <27 kg received eltrombopag 37.5 mg QD, and those with a body weight >=27 kg received eltrombopag 50 mg QD. Participants of East Asian ancestry received a starting dose of eltrombopag 25 mg QD. Participants aged between 1 and 5 years received eltrombopag 1.2 mg/kg QD; participants of East Asian ancestry received a starting dose of eltrombopag 0.8 mg/kg/day.

Reporting group title	Part 2: Eltrombopag

Reporting group description:

In Part 2, participants continued on the same dose of eltrombopag recevied in Part 1 unless adjustments were warranted according to the dosing guidelines.

Serious adverse events	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag	Part 2: Eltrombopag
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 29 (13.79%)	5 / 63 (7.94%)	9 / 87 (10.34%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase abnormal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase abnormal			

subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 29 (3.45%)	0 / 63 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 63 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic anaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 63 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rhinitis allergic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	1 / 29 (3.45%)	0 / 63 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gingivitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 63 (1.59%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haematoma infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part 1 (Randomized Period)-Placebo	Part 1 (Randomized Period)-Eltrombopag	Part 2: Eltrombopag
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 29 (37.93%)	37 / 63 (58.73%)	56 / 87 (64.37%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	4 / 63 (6.35%)	7 / 87 (8.05%)
occurrences (all)	0	4	7
Alanine aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	6 / 87 (6.90%)
occurrences (all)	0	0	6
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 29 (10.34%)	6 / 63 (9.52%)	8 / 87 (9.20%)
occurrences (all)	3	9	15
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	4 / 63 (6.35%)	9 / 87 (10.34%)
occurrences (all)	1	4	12
Influenza like illness			

subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	5 / 87 (5.75%)
occurrences (all)	0	0	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)	6 / 63 (9.52%)	7 / 87 (8.05%)
occurrences (all)	0	10	12
Vomiting			
subjects affected / exposed	3 / 29 (10.34%)	2 / 63 (3.17%)	6 / 87 (6.90%)
occurrences (all)	3	2	11
Diarrhoea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	5 / 87 (5.75%)
occurrences (all)	0	0	6
Abdominal pain upper			
subjects affected / exposed	4 / 29 (13.79%)	3 / 63 (4.76%)	0 / 87 (0.00%)
occurrences (all)	4	3	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	5 / 29 (17.24%)	8 / 63 (12.70%)	11 / 87 (12.64%)
occurrences (all)	7	23	26
Cough			
subjects affected / exposed	0 / 29 (0.00%)	7 / 63 (11.11%)	8 / 87 (9.20%)
occurrences (all)	0	8	9
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	11 / 63 (17.46%)	7 / 87 (8.05%)
occurrences (all)	2	11	8
Rhinitis			
subjects affected / exposed	2 / 29 (6.90%)	10 / 63 (15.87%)	0 / 87 (0.00%)
occurrences (all)	2	11	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	7 / 63 (11.11%)	9 / 87 (10.34%)
occurrences (all)	1	8	10
Pharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 63 (0.00%)	7 / 87 (8.05%)
occurrences (all)	0	0	7
Respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 63 (0.00%) 0	6 / 87 (6.90%) 9

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