Clinical trial results:
EXTEND (Eltrombopag eXTENded Dosing Study): An extension study of eltrombopag olamine (SB-497115-GR) in adults, with idiopathic thrombocytopenic purpura (ITP), previously enrolled in an eltrombopag study.

Summary

EudraCT number	2006-000471-14
Trial protocol	SI SE DE ES IE NL GR FR SK GB CZ DK IT FI AT
Global end of trial date	06 July 2015

Results information

Result version number	v1 (current)
This version publication date	22 July 2016
First version publication date	22 July 2016

Trial information

Trial identification

Sponsor protocol code	TRA105325

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00351468
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	06 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2015
Global end of trial reached?	Yes
Global end of trial date	06 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to describe the long-term safety and tolerability of oral eltrombopag treatment of subjects with ITP with or without concomitant ITP medication

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Rescue medication, defined as the addition of new therapies intended to raise the platelet count, including medications, platelet transfusions, splenectomy or the increase of the dose of any concomitant ITP medications was allowed at any time the investigator deemed it necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	China: 10
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Hong Kong: 19
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	New Zealand: 9

Country: Number of subjects enrolled	Pakistan: 4
Country: Number of subjects enrolled	Peru: 11
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 29
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	Tunisia: 22
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 62
Country: Number of subjects enrolled	Vietnam: 3
Worldwide total number of subjects	302
EEA total number of subjects	104

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	252
From 65 to 84 years	49
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were previously enrolled in a study of eltrombopag: TRA100773A, TRA100773B, TRA102537/RAISE, or TRA108057/REPEAT. Eligibility of consenting subjects was assessed during the screening period of up to
28 days prior to Day 1 of treatment.

Period 1

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

Arms

Arm title	Eltrombopag

Arm description:

Open-label eltrombopag was supplied in 25 or 50 mg tablets. All subjects started at 50mg once daily and dose was increased or decreased based on platelet count (target range 50-200Gi/L). Alternate days and interruption of dosing was permitted to maintain target range of platelet count. Doses could range from 25 to 75mg. Subjects could remain on treatment up to 2 years.

Arm type	Experimental
Investigational medicinal product name	Eltrombopag
Investigational medicinal product code	SB-497115
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Dosing started at 50 mg daily and could be adjusted by the investigator from 25mg to 75 or less than daily depending on platelet counts

Number of subjects in period 1	Eltrombopag
Started	302
Subjects from TRA100773A	51 [1]
Subjects from TRA100773B	61 [2]
Subjects from TRA102537 Raise	146
Subjects from TRA108057 Repeat	43 [3]
Completed	135
Not completed	167
Consent withdrawn by subject	39
Adverse event, non-fatal	42
Non-compliance	8
Various -follow up w clinical team	39

Lost to follow-up	4
Lack of efficacy	32
Protocol deviation	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All subjects enrolled in this trial were previously enrolled in one of three eltrombopag trials. Milestones were created to provide number of participants from each of the three trials.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All subjects enrolled in this trial were previously enrolled in one of three eltrombopag trials. Milestones were created to provide number of participants from each of the three trials.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All subjects enrolled in this trial were previously enrolled in one of three eltrombopag trials. Milestones were created to provide number of participants from each of the three trials.

Baseline characteristics

Reporting groups	
Reporting group title	Eltrombopag
Reporting group description:	
Open-label eltrombopag was supplied in 25 or 50 mg tablets. All subjects started at 50mg once daily and dose was increased or decreased based on platelet count (target range 50-200Gi/L). Alternate days and interruption of dosing was permitted to maintain target range of platelet count. Doses could range from 25 to 75mg. Subjects could remain on treatment up to 2 years.	

Reporting group values	Eltrombopag	Total	
Number of subjects	302	302	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	252	252	
From 65-84 years	49	49	
85 years and over	1	1	
Age Continuous Units: Years			
arithmetic mean	48.9		
standard deviation	± 15.61	-	
Gender, Male/Female Units: Participants			
Female	201	201	
Male	101	101	
Concomitant ITP Medication at Baseline Units: Subjects			
Yes	101	101	
No	201	201	
Splenectomy Status at Baseline Units: Subjects			
Yes	115	115	
No	187	187	
Baseline Platelet Count Units: Subjects			
<30 Gi/L	211	211	
30 - 50 Gi/L	52	52	
> 50 Gi/L	39	39	

End points

End points reporting groups

Reporting group title	Eltrombopag

Reporting group description:

Open-label eltrombopag was supplied in 25 or 50 mg tablets. All subjects started at 50mg once daily and dose was increased or decreased based on platelet count (target range 50-200Gi/L). Alternate days and interruption of dosing was permitted to maintain target range of platelet count. Doses could range from 25 to 75mg. Subjects could remain on treatment up to 2 years.

Primary: Safety and tolerability parameters including, clinicallaboratory tests, ocular examinations, and frequency ofall adverse events

End point title	Safety and tolerability parameters including, clinicallaboratory tests, ocular examinations, and frequency ofall adverse events[1]

End point description:

See Safety Section

End point type	Primary

End point timeframe:

through study completion estimated to be approximately 5 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This was an open-label study and hence no formal statistical hypothesis tests were done.

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Incidences of Adverse Events	302			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Achieving Maximum Platelet Counts Greater Than or Equal to 30 Gi/L or 50 Gi/L in the Absence of Rescue Medication

End point title	Subjects Achieving Maximum Platelet Counts Greater Than or Equal to 30 Gi/L or 50 Gi/L in the Absence of Rescue Medication

End point description:

Subjects who achieved maximum platelet count at least once during treatment. All platelet counts after an on-study splenectomy are not classed as responses. Platelet counts within 7 days after a platelet transfusion are not classed as responses. Platelet counts while taking an increased ITP medication or within 6 weeks after the end of an increased ITP medication are not classed as responses.

End point type	Secondary

End point timeframe:

Baseline up to 2 years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
Baseline Platelet counts >= 30 Gi/L,	91			
Baseline Platelet counts >= 50 Gi/L,	42			
Maximum Platelet Count >= 30 Gi/L	276			
Maximum Platelet Count >= 50 Gi/L	259			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subjects Achieving Platelet Count Levels by Week, in the Absence of Rescue Medication

End point title	Summary of Subjects Achieving Platelet Count Levels by Week, in the Absence of Rescue Medication

End point description:

If a subject has more than 1 platelet count result within a week, the lowest value observed is used to determine response. All platelet counts after an on-study splenectomy are not classed as responses. Platelet counts within 7 days after a platelet transfusion are not classed as responses. Platelet counts while taking an increased ITP medication or within 6 weeks after the end of an increased ITP medication are not classed as responses.

End point type	Secondary

End point timeframe:

Baseline up to Year 7/Week 364

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
Baseline Platelet counts >= 30 Gi/L, n=302	91			
Baseline Platelet counts >= 50 Gi/L, n=302	42			
Week 1 Platelet Count >= 30 Gi/L n=293	172			
Week 1 Platelet Count >= 50 Gi/L n=293	127			
Week 2 Platelet Count >= 30 Gi/L n=288	199			
Week 2 Platelet Count >= 50 Gi/L n=288	165			
Week 3 Platelet Count >= 30 Gi/L n=275	192			

Week 3 Platelet Count >= 50 Gi/L n=275	159			
Week 4 Platelet Count >= 30 Gi/L n=275	192			
Week 4 Platelet Count >= 50 Gi/L n=275	149			
Week 5 Platelet Count >= 30 Gi/L n=274	197			
Week 5 Platelet Count >= 50 Gi/L n=274	159			
Week 6 Platelet Count >= 30 Gi/L n=276	203			
Week 6 Platelet Count >= 50 Gi/L n=276	169			
Week 12 Platelet Count >= 30 Gi/L n=197	147			
Week 12 Platelet Count >= 50 Gi/L n=197	120			
Month 6/Week 26 Platelet Count >= 30 Gi/L n=130	93			
Month 6/Week 26 Platelet Count >= 50 Gi/L n=130	82			
Year 1/Week 52 Platelet Count >= 30 Gi/L n=83	62			
Year 1/Week 52 Platelet Count >= 50 Gi/L n=83	50			
Year 1.5/Week 78 Platelet Count >= 30 Gi/L n=63	47			
Year 1.5/Week78 Platelet Count >= 50 Gi/L n=63	41			
Year 2/Week 104 Platelet Count >= 30 Gi/L n=59	46			
Year 2/Week 104 Platelet Count >= 50 Gi/L n=59	42			
Year 2.5/Week 130 Platelet Count >= 30 Gi/L n=42	32			
Year 2.5/Week 130 Platelet Count >= 50 Gi/L n=42	28			
Year 3/Week 156 Platelet Count >= 30 Gi/L n=27	22			
Year 3/Week 156 Platelet Count >= 50 Gi/L n=27	19			
Year 3.5/Week 182 Platelet Count >= 30 Gi/L n=23	19			
Year 3.5/Week 182 Platelet Count >= 50 Gi/L n=23	17			
Year 4/Week 208 Platelet Count >= 30 Gi/L n=17	12			
Year 4/Week 208 Platelet Count >= 50 Gi/L n=17	11			
Year 4.5/Week 234 Platelet Count >= 30 Gi/L n=15	13			
Year 4.5/Week 234 Platelet Count >= 50 Gi/L n=15	12			
Year 5/Week 260 Platelet Count >= 30 Gi/L n=9	6			
Year 5/Week 260 Platelet Count >= 50 Gi/L n=9	6			
Year 5.5/Week 286 Platelet Count >= 30 Gi/L n=9	7			
Year 5.5/Week 286 Platelet Count >= 50 Gi/L n=9	7			

Year 6/Week 312 Platelet Count >= 30 Gi/L n=9	7			
Year 6/Week 312 Platelet Count >= 50 Gi/L n=9	7			
Year 6.5/Week 338 Platelet Count >= 30 Gi/L n=5	3			
Year 6.5/Week 338 Platelet Count >= 50 Gi/L n=5	3			
Year 7/Week 364 Platelet Count >= 30 Gi/L n=3	3			
Year 7/Week 364 Platelet Count >= 50 Gi/L n=3	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who responded to eltrombopag in a previous study and who respond to retreatment with a rise in platelet count to either ≥ 50,000/µL or ≥30,000/µL

End point title	Number of subjects who responded to eltrombopag in a previous study and who respond to retreatment with a rise in platelet count to either ≥ 50,000/µL or ≥30,000/µL

End point description:

- Responder in TRA100773: Platelet count 50 Gi/L and 2 x baseline (BL)at last on-treatment assessment. Responders in EXTEND: Platelet count 50 Gi/L and 2 x baseline (BL), 50 Gi/L, and 30 Gi/L at any time. - Responder in RAISE: Platelet count 50GI/L and 2 x baseline at Week 6 assessment. Responders in EXTEND: Platelet count 50 Gi/L and 2 x baseline, 50 Gi/L, and 30 Gi/L at any time. - Responder in REPEAT: Platelet count 50GI/L and 2 x baseline (BL) at Week 6 assessment in Cycle 1. Responders in EXTEND: Platelet count 50 Gi/L and 2 x baseline (BL), 50 Gi/L, and 30 Gi/L at any time.

End point type	Secondary

End point timeframe:

Baseline up to 2 years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
TRA100773 Responders >= 50 Gi/L in EXTEND, n=51	49			
TRA100773 >=50 Gi/L and 2 x BL in EXTEND, n=51	47			
TRA100773 Responders >= 30 Gi/L in EXTEND, n=51	49			
RAISE Responders >= 50 Gi/L in EXTEND, n=59	54			
RAISE >= 50 Gi/L and 2 x BL in EXTEND, n=59	53			
RAISE Responders >= 30 Gi/L in EXTEND, n=51	55			
REPEAT Responders >= 50 Gi/L in EXTEND, n=36	33			

REPEAT>= 50 Gi/L and 2 x BL in EXTEND, n=36	33			
REPEAT Responders >= 30 Gi/L in EXTEND, n=36	35			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with reduction and/or sparing of concomitant ITP therapies, while maintaining a platelet count ≥ 50,000/mL.

End point title	Number of participants with reduction and/or sparing of concomitant ITP therapies, while maintaining a platelet count ≥ 50,000/mL.

End point description:

Sustain reduct =Sustained reduction[1] Denominator is number of subjects taking an ITP medication at baseline. [2] Denominator is number of subjects with a sustained reduction. Note: Sustained reduction defined as reduction from baseline in dose and/or frequency which is maintained for at least 4 weeks. Excludes sustained reductions started more than 1 day after last dose.

End point type	Secondary

End point timeframe:

For at least 2 years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
ITP medication at baseline	101			
Sustain reduct or stopping at least 1 ITP med [1]	71			
Permanently stopping at least 1 ITP med [1]	53			
Sustained reduction[1]	70			
Maximum sustained reduction ≥ 24 weeks[2]	66			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who required Rescue Therapy during treatment with eltrombopag.

End point title	Number of subjects who required Rescue Therapy during treatment with eltrombopag.

End point description:

Rescue treatment is defined as a composite of: new ITP medication, increased dose of a concomitant ITP medication, platelet transfusion, and splenectomy. Subjects may have received more than 1 type of rescue therapy

End point type	Secondary
End point timeframe: Baseline up to 2 years	

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
New ITP medication, n=103	82			
Increase in dose of ITP med from baseline, n=103	27			
Platelet transfusion, n=103	21			
Splenectomy, n=103	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum ITP Bleeding Score at any time during the study during all stages.

End point title	Maximum ITP Bleeding Score at any time during the study during all stages.
End point description: The ITP bleeding score is a tool which has been designed specifically to assess the bruising and bleeding in patients with ITP across body sites, ranging from mild to severe. The WHO Grades were dichotomized into the following categories: Grade 0: No bleeding Grade 1 to 4: Any bleeding Grade 0 to 1: No clinically significant bleeding Grade 2 to 4: Clinically significant bleeding	
End point type	Secondary
End point timeframe: Baseline up to 2 years	

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
Epistaxis n=300 Grade 0	204			
Epistaxis n=300 Grade 1	65			
Epistaxis n=300 Grade 2	31			
Gastrointestinal n=300 Grade 0	264			
Gastrointestinal n=300 Grade 1	26			
Gastrointestinal n=300 Grade 2	10			
Genitourinary n=300 Grade 0	262			
Genitourinary n=300 Grade 1	29			
Genitourinary n=300 Grade 2	9			
Gynecologic n=108 Grade 0	68			

Gynecologic n=108 Grade 1	15			
Gynecologic n=108 Grade 2	25			
Intracerebral hemorrhage n=300 Grade 0	297			
Intracerebral hemorrhage n=300 Grade 1	3			
Intracerebral hemorrhage n=300 Grade 2	0			
Ocular n=300 Grade 0	258			
Ocular n=300 Grade 1	37			
Ocular n=300 Grade 2	5			
Oral n=300 Grade 0	191			
Oral n=300 Grade 1	81			
Oral n=300 Grade 2	28			
Pulmonary n=300 Grade 0	287			
Pulmonary n=300 Grade 1	13			
Pulmonary n=300 Grade 2	0			
Skin, ecchymosis n=300 Grade 0	74			
Skin, ecchymosis n=300 Grade 1	159			
Skin, ecchymosis n=300 Grade 2	67			
Skin, petechiae n=300 Grade 0	142			
Skin, petechiae n=300 Grade 1	126			
Skin, petechiae n=300 Grade 2	32			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Post-Baseline Change in SF-36v2 Questionnaire Score Compared with Baseline - All Patients

End point title	Best Post-Baseline Change in SF-36v2 Questionnaire Score Compared with Baseline - All Patients

End point description:

The SF-36v2 assessment tool was used to obtain information about subjects' general health status and health-related quality of life. The tool was to be completed by each subject prior to any other intervention, including physician interaction, at the baseline visit, prior to completion of a Stage, and upon withdrawal or completion of the study. Until a formal assessment of minimal clinically important differences (MCID) is performed, changes from baseline of more than 0.5 standard deviations are suggested as clinically meaningful,Scores were transformed to a 0-100 point scale, with higher scores representing more positive answers Scores were normalized to have a mean of 50 and SD of 10 to allow for comparison with outcomes from other chronic diseases Recall period is the past week prior to administration.

End point type	Secondary

End point timeframe:

Baseline, transitioning between stages, withdrawal/completion of study up to two years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Points on a scale				
arithmetic mean (confidence interval 95%)				
SF-36v2 Physical function (n=273	12 (9.6 to 14.5)			
SF-36v2 Physical role (n=273)	14.2 (11.5 to 16.9)			
SF-36v2 Bodily pain (n=273)	14.5 (11.6 to 17.4)			
SF-36v2 General health (n=273)	11.1 (9 to 13.1)			
SF-36v2 Vitality (n=290)	13.9 (11.6 to 16.3)			
SF-36v2 Social function (n=290)	12.6 (10.2 to 15.1)			
SF-36v2 Emotional role (n=290)	11.4 (8.7 to 14)			
SF-36v2 Mental health (n=290)	11.3 (9.4 to 13.3)			
SF-36v2 Physical component summary (n=273)	5.3 (4.5 to 6.2)			
SF-36v2 Mental component summary (n=290)	5.8 (4.6 to 6.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Post-Baseline Change in the short form of the Motivation and Energy Scale (MEI-SF) compared with Baseline - All Patients

End point title	Best Post-Baseline Change in the short form of the Motivation and Energy Scale (MEI-SF) compared with Baseline - All Patients

End point description:

The MEI-SF (18 questions) was used to measure the reductions in mental energy, physical energy, and social motivation, either as symptoms of chronic ITP or as a side effect of pharmacotherapy. Minimal clinically important differences are estimated as 0.5 standard deviations or 7.5 points. All items use either a 7-level (0 to 6) or 5-level (0 to 4) response scale; items with a 5-level response scale were rescaled to 7-levels, and items were reverse-scored as necessary such that higher scores represent higher HRQoL Total score ranges from 0 to 108 points. Recall period is past week prior to administration. n=292

End point type	Secondary

End point timeframe:

Baseline, transitioning between stages, withdrawal/completion of study up to two years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Points on a scale				
arithmetic mean (confidence interval 95%)	11.2 (9.1 to 13.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Post-Baseline Change in the FACIT-Fatigue 13 Item Subscale Score Baseline, prior to completion of a Stage, and upon withdrawal or at completion of the study - All Patients

End point title	Best Post-Baseline Change in the FACIT-Fatigue 13 Item Subscale Score Baseline, prior to completion of a Stage, and upon withdrawal or at completion of the study - All Patients

End point description:

The FACIT-Fatigue consists of 13 questions in which patients rate the frequency (0-4) of symptoms of fatigue, in terms of tiredness, weakness, and fatigue Items were reverse-scored as necessary such that higher scores represent higher HRQoL Total score ranges from 0 to 52.Using anchor-based estimates, the minimally important difference in this subscale is 3.0 points. Recall period is past week prior to administration

End point type	Secondary

End point timeframe:

Baseline, prior to completion of a Stage, and upon withdrawal or at completion of the study up to 2 years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Points on a scale				
arithmetic mean (confidence interval 95%)	6.9 (5.7 to 8.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Post-Baseline Change in the FACT-TH6 (Baseline, prior to completion of a Stage, and upon withdrawal or at completion of the study) - All Patients

End point title	Best Post-Baseline Change in the FACT-TH6 (Baseline, prior to completion of a Stage, and upon withdrawal or at completion of the study) - All Patients

End point description:

The FACT-TH6 consists of 6 questions in which patients rate (0-4) their general degree of worry related

to bleeding and bruising, and resulting activity impairment and frustration. Although the six items do not constitute a formal domain or subscale of the FACTTh assessment tool, these items had been identified by focus groups of patients with chronic ITP as important indicators of their HRQoL. Items were reverse-scored as necessary such that higher scores represent higher HRQoL. Total scores ranged from 0 to 24. Recall period is not specified. n=288

End point type	Secondary

End point timeframe:

Baseline, transitioning between stages, withdrawal/completion of study up to two years

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Points on a scale				
arithmetic mean (confidence interval 95%)	4 (3.4 to 4.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment + 1 Day: start date was between the first dose of investigational product and up to the day after the last dose . Post-therapy: start date was more than 1 day after the last dose and up to 30 days after last dose of investigational product

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Eltrombopag, Treatment + 1 day

Reporting group description:

Eltrombopag, Treatment + 1 day

Reporting group title	Eltrombopag, gt 1 to 30 Days Post-Therapy

Reporting group description:

Eltrombopag, gt 1 to 30 Days Post-Therapy

Serious adverse events	Eltrombopag, Treatment + 1 day	Eltrombopag, gt 1 to 30 Days Post-Therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	96 / 302 (31.79%)	10 / 302 (3.31%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
B-cell unclassifiable lymphoma low grade			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arteriovenous fistula			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			

subjects affected / exposed	4 / 302 (1.32%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haematoma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Local swelling			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device pain			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (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			
Asthma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	4 / 302 (1.32%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 302 (0.66%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary infarction			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	5 / 302 (1.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 302 (1.32%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	4 / 302 (1.32%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	3 / 302 (0.99%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract traumatic			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eye injury			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Spinal cord injury			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 302 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic neuropathy			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (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	5 / 302 (1.66%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bone marrow oedema			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 302 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic cyst			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (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	2 / 302 (0.66%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	16 / 302 (5.30%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	8 / 17	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract subcapsular			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroidal neovascularisation			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 302 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenitis haemorrhagic			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival bleeding			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis acute			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder pain			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Calculus urinary			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus nephritis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	2 / 302 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	8 / 302 (2.65%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	2 / 8	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 302 (0.99%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wound infection			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar state			
subjects affected / exposed	1 / 302 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Eltrombopag, Treatment + 1 day	Eltrombopag, gt 1 to 30 Days Post-Therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	253 / 302 (83.77%)	28 / 302 (9.27%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	23 / 302 (7.62%)	0 / 302 (0.00%)	
occurrences (all)	36	0	
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 302 (6.95%)	0 / 302 (0.00%)	
occurrences (all)	37	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 302 (7.28%)	1 / 302 (0.33%)	
occurrences (all)	26	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	26 / 302 (8.61%)	0 / 302 (0.00%)	
occurrences (all)	34	0	
Headache			
subjects affected / exposed	86 / 302 (28.48%)	3 / 302 (0.99%)	
occurrences (all)	178	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	26 / 302 (8.61%)	1 / 302 (0.33%)	
occurrences (all)	62	1	

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	50 / 302 (16.56%)	4 / 302 (1.32%)	
occurrences (all)	73	4	
Influenza like illness			
subjects affected / exposed	25 / 302 (8.28%)	1 / 302 (0.33%)	
occurrences (all)	37	1	
Pyrexia			
subjects affected / exposed	27 / 302 (8.94%)	2 / 302 (0.66%)	
occurrences (all)	36	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	18 / 302 (5.96%)	0 / 302 (0.00%)	
occurrences (all)	34	0	
Abdominal pain upper			
subjects affected / exposed	18 / 302 (5.96%)	1 / 302 (0.33%)	
occurrences (all)	23	1	
Constipation			
subjects affected / exposed	26 / 302 (8.61%)	2 / 302 (0.66%)	
occurrences (all)	33	2	
Diarrhoea			
subjects affected / exposed	46 / 302 (15.23%)	3 / 302 (0.99%)	
occurrences (all)	78	3	
Nausea			
subjects affected / exposed	34 / 302 (11.26%)	1 / 302 (0.33%)	
occurrences (all)	65	1	
Vomiting			
subjects affected / exposed	19 / 302 (6.29%)	2 / 302 (0.66%)	
occurrences (all)	23	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	32 / 302 (10.60%)	0 / 302 (0.00%)	
occurrences (all)	51	0	
Epistaxis			
subjects affected / exposed	23 / 302 (7.62%)	2 / 302 (0.66%)	
occurrences (all)	51	3	

Oropharyngeal pain			
subjects affected / exposed	27 / 302 (8.94%)	1 / 302 (0.33%)	
occurrences (all)	45	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	17 / 302 (5.63%)	1 / 302 (0.33%)	
occurrences (all)	22	1	
Rash			
subjects affected / exposed	25 / 302 (8.28%)	0 / 302 (0.00%)	
occurrences (all)	48	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	27 / 302 (8.94%)	2 / 302 (0.66%)	
occurrences (all)	33	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	45 / 302 (14.90%)	0 / 302 (0.00%)	
occurrences (all)	83	0	
Back pain			
subjects affected / exposed	39 / 302 (12.91%)	0 / 302 (0.00%)	
occurrences (all)	63	0	
Pain in extremity			
subjects affected / exposed	28 / 302 (9.27%)	0 / 302 (0.00%)	
occurrences (all)	43	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	25 / 302 (8.28%)	0 / 302 (0.00%)	
occurrences (all)	34	0	
Cystitis			
subjects affected / exposed	16 / 302 (5.30%)	0 / 302 (0.00%)	
occurrences (all)	24	0	
Influenza			
subjects affected / exposed	29 / 302 (9.60%)	0 / 302 (0.00%)	
occurrences (all)	36	0	
Nasopharyngitis			

subjects affected / exposed	74 / 302 (24.50%)	2 / 302 (0.66%)	
occurrences (all)	156	2	
Pharyngitis			
subjects affected / exposed	21 / 302 (6.95%)	0 / 302 (0.00%)	
occurrences (all)	28	0	
Sinusitis			
subjects affected / exposed	20 / 302 (6.62%)	1 / 302 (0.33%)	
occurrences (all)	36	1	
Upper respiratory tract infection			
subjects affected / exposed	69 / 302 (22.85%)	5 / 302 (1.66%)	
occurrences (all)	135	5	
Urinary tract infection			
subjects affected / exposed	32 / 302 (10.60%)	2 / 302 (0.66%)	
occurrences (all)	63	2	
Viral infection			
subjects affected / exposed	23 / 302 (7.62%)	0 / 302 (0.00%)	
occurrences (all)	35	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2007	Modification of eligibility criteria for clarity and to meet regulatory feedback. Addition of a secondary endpoint to evaluate retreatment with eltrombopag based on regulatory input. Addition of Liver Chemistry stopping criteria. Addition of platelet count assessment after treatment interruption. Modification of lifestyle wording concerning precautions to direct sunlight and/or UV exposure. Revision of prohibited medications based on new data.
10 September 2007	Addition of enhanced monitoring for the potential presence of renal toxicity. Inclusion of Tunisian study population regulatory requirements. Addition of bone marrow biopsy for subjects who were dosed with eltrombopag for longer than one year in this study.
16 January 2009	Requirement for regular bone marrow biopsies (including after 12 and 24 months of treatment), addition of central bone marrow morphology review, and addition of bone marrow biopsy stopping criteria. Requirement of a single ocular exam for subjects who were bilaterally pseudophakic or aphakic. Inclusion of Pharmacogenetic (PGx) sample collection. Modification of the requirements to change between stages of study. Update to the estimate of the number of subjects to be enrolled. Modification of the requirement for transitioning subjects to commercially available medication. Dietary and cation-containing product restrictions were updated to be consistent with current guidelines.
11 June 2009	A country-specific amendment for the UK to include a definitive date for the end of the study, as required by the UK regulatory authority.
13 April 2010	Inclusion of thrombophilia risk factor testing, and permitted continuation of subjects following a thrombotic event based upon Investigator assessment of individual risk-benefit assessment. Reduction in the frequency of required investigator/ GlaxoSmithKline (GSK) medical monitor contact, physical exams, ECGs, ocular exams, anti-platelet antibody testing, proteomic sample collection, pharmacokinetic (PK) sampling, renal assessments, and visit frequency. Follow-up requirements for subjects continuing on commercial eltrombopag were reduced. Removal of specific tests within clinical chemistry panel. Removal of ITP Bleeding Score assessment. Removal of phototoxicity precaution statement based on results of photoirritancy study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported