Clinical trial results:
A phase II, open-label, prospective, single-arm, study to assess ability of eltrombopag to induce sustained remission in subjects with ITP who are refractory or relapsed after first-line steroids

Summary

EudraCT number	2018-000452-18
Trial protocol	AT GR ES GB IT
Global end of trial date	03 October 2022

Results information

Result version number	v2 (current)
This version publication date	11 February 2024
First version publication date	13 October 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CETB115J2411

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03524612
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess ability of eltrombopag to induce sustained response off treatment by Month 12 in Immune Thrombocytopenia (ITP) patients who relapsed or failed to respond to first-line steroid treatment.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2018
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	Austria: 4
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Chile: 11
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Greece: 8
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Oman: 4
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Türkiye: 12
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	105
EEA total number of subjects	50

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)	78
From 65 to 84 years	24
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted in 32 investigative sites in 15 countries:1 (Austria), 3 (Brazil), 2 (Chile), 2 (France), 2 (Greece), 2 (Italy), 1 (Japan), 2 (Mexico), 1 (Oman), 2 (Russia), 7 (Spain), 1 (Switzerland), 3 (Turkey), 1 (UK), 2 (USA).

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:

Participants were treated with eltrombopag to induce sustained response off treatment to reach a target platelet count of >=100×10^9/L (CR), after 1st line steroids had failed.

Arm type	Tablet for oral use
Investigational medicinal product name	Eltrombopag
Investigational medicinal product code	
Other name	ETB115
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

12.5, 25, 50 and 75 mg tablets for oral use once daily

Number of subjects in period 1	Eltrombopag
Started	105
Completed	63
Not completed	42
Adverse event, serious fatal	3
Consent withdrawn by subject	7
Adverse event, non-fatal	10
Physician Decision (Patient non-compliant)	1
Patient Decision (Patient Changed Her Address)	1
Patient Decision (Personal Reasons)	1
Lost to follow-up	2
New therapy for study indication	6
Lack of efficacy	10
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Eltrombopag
Reporting group description:	
Participants were treated with eltrombopag to induce sustained response off treatment to reach a target platelet count of >=100×10^9/L (CR), after 1st line steroids had failed.	

Reporting group values	Eltrombopag	Total	
Number of subjects	105	105	
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)	78	78	
From 65-84 years	24	24	
85 years and over	3	3	
Age Continuous Units: Years			
arithmetic mean	48.1		
standard deviation	± 19.39	-	
Sex: Female, Male Units: Participants			
Female	64	64	
Male	41	41	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	5	
Asian	2	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	2	2	
White	95	95	
More than one race	0	0	
Unknown or Not Reported	1	1	
Time since initial diagnosis			
Time since initial diagnosis is the difference in days between the date of initial diagnosis and the date of first dose of eltrombopag.			
Units: Days			
arithmetic mean	366.37		
standard deviation	± 911.420	-	

End points

End points reporting groups

Reporting group title	Eltrombopag

Reporting group description:

Participants were treated with eltrombopag to induce sustained response off treatment to reach a target platelet count of >=100×10^9/L (CR), after 1st line steroids had failed.

Primary: Percentage of participants with sustained response off treatment (SRoT) by 12 months

End point title	Percentage of participants with sustained response off treatment (SRoT) by 12 months[1]

End point description:

Sustained response off treatment (SRoT) was defined as: reaching platelet count >= 100×10^9/L (complete response [CR]) and then maintaining platelet counts around 100×10^9/L for 2 months (no counts below 70×10^9/L), AND then tapering off the drug until treatment discontinuation while maintaining platelet count >= 30×10^9/L in the absence of bleeding (no bleeding AEs) or use of any rescue therapy until month 12.

End point type	Primary

End point timeframe:

Month 12

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: Due to EudraCT system limitations, there must be at least two comparison groups selected for statistical analysis to be entered in the EudraCT system.

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of participants				
number (confidence interval 95%)	30.5 (21.9 to 40.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of sustained response off treatment (SRoT) after treatment discontinuation for participants with sustained response off treatment

End point title	Median duration of sustained response off treatment (SRoT) after treatment discontinuation for participants with sustained response off treatment

End point description:

Sustained response off treatment (SRoT) was defined as: reaching platelet count >= 100×10^9/L (complete response [CR]) and then maintaining platelet counts around 100×10^9/L for 2 months (no counts below 70×10^9/L), AND then tapering off the drug until treatment discontinuation while maintaining platelet count >= 30×10^9/L in the absence of bleeding (no bleeding AEs) or use of any rescue therapy until month 12.

End point type	Secondary

End point timeframe:

From last dose of eltrombopag to month 12

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Weeks				
median (full range (min-max))	33.3 (4 to 51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated median duration of sustained response off treatment (SRoT) for participants with sustained response off treatment at month 12 and who enter 12 months follow-up period

End point title	Estimated median duration of sustained response off treatment (SRoT) for participants with sustained response off treatment at month 12 and who enter 12 months follow-up period

End point description:

Sustained response off treatment (SRoT) was defined as: reaching platelet count >= 100×10^9/L (complete response [CR]) and then maintaining platelet counts around 100×10^9/L for 2 months (no counts below 70×10^9/L), AND then tapering off the drug until treatment discontinuation while maintaining platelet count >= 30×10^9/L in the absence of bleeding (no bleeding AEs) or use of any rescue therapy.
Patients with SRoT until month 12 who entered follow-up and did not relapse by cut-off date/Month 24 were censored at the earliest of discontinuation date/death date/Month 24 platelet assessment date/cutoff date. Patients with SRoT until Month 12 patients who did not enter or do not yet have data in follow-up phase are censored at their Month 12 platelet assessment date.

End point type	Secondary

End point timeframe:

From last dose of eltrombopag to relapse, assessed up to month 24

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Weeks				
median (full range (min-max))	(to)			

Notes:

[2] - Not estimable due to number of patients who are censored

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated median duration of sustained response off treatment (SRot) for all patients

End point title	Estimated median duration of sustained response off treatment (SRot) for all patients

End point description:

Patients who tapered and discontinued successfully, or did not relapse/die by cutoff date /month 24 were censored at the earliest of discontinuation date/death date/month 24 platelet assessment date/cutoff date.

End point type	Secondary

End point timeframe:

From last dose of eltrombopag to month 24

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Weeks				
median (full range (min-max))	(to)			

Notes:

[3] - Not estimable due to number of patients who are censored

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with sustained response off treatment until month 24

End point title	Percentage of participants with sustained response off treatment until month 24

End point description:

Sustained response off treatment is defined as reach platelet count ≥ 100×10^9/L (complete response [CR]) and then maintain platelet counts around 100×10^9/L for 2 months (no counts below 70×10^9/L) AND then taper off the drug until treatment discontinuation while, maintain platelet count ≥ 30×10^9/L in the absence of bleeding (no bleeding AEs) or use of any rescue therapy

End point type	Secondary

End point timeframe:

Month 15, 18, 21 and 24

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Participants				
Month 15	21			
Month 18	18			
Month 21	14			
Month 24	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with early response within first month

End point title	Percentage of participants with early response within first month

End point description:

Early response is defined as reaching a platelet count >= 50×10^9/L at least once within the first month (month 1) without bleeding events and no rescue therapy.

End point type	Secondary

End point timeframe:

By 1 month

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of participants				
number (confidence interval 95%)	76.2 (66.9 to 84.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline in platelet count over time

End point title	Relative change from baseline in platelet count over time

End point description:

Relative change (%) is the absolute change divided by the platelet counts at baseline and multiplied by 100.

End point type	Secondary

End point timeframe:

Baseline, month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: Percentage of change				
arithmetic mean (standard deviation)				
3 Months	1384.29 (± 3383.702)			
6 Months	1313.10 (± 3459.616)			
9 Months	1396.68 (± 3238.680)			
12 Months	1464.95 (± 3509.964)			
15 Months	1622.19 (± 3712.156)			
18 Months	1664.90 (± 3718.191)			
21 Months	2527.20 (± 5098.612)			
24 Months	1691.68 (± 3611.977)			
end of treatment visit	1213.91 (± 2952.719)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with recovery response in case of loss of response during or after tapering of eltrombopag until month 24

End point title	Percentage of participants with recovery response in case of loss of response during or after tapering of eltrombopag until month 24

End point description:

Recovery response is defined as platelet count >=30×10^9/L after eltrombopag is re-introduced, in case of loss of response (< 30×10^9/L and/or bleeding event) without bleeding events and no rescue therapy.

End point type	Secondary

End point timeframe:

Up to month 24

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of participants				
number (confidence interval 95%)				
Participants with loss of response	11.4 (6.0 to 19.1)			
Participants with recovery response	6.7 (2.7 to 13.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who maintain platelet counts level within 12 months and every 3 months until month 24

End point title	Percentage of participants who maintain platelet counts level within 12 months and every 3 months until month 24

End point description:

Platelet counts level is defined as having platelet counts >=30×10^9/L without bleeding events and no rescue therapy.

End point type	Secondary

End point timeframe:

From first time of reaching the level to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of participants				
number (confidence interval 95%)				
Mnt PLT lvl f/1st time of reach. that lvl to mo 3	49.5 (39.6 to 59.5)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 6	38.1 (28.8 to 48.1)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 9	28.6 (20.2 to 38.2)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 12	28.6 (20.2 to 38.2)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 15	20.0 (12.8 to 28.9)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 18	17.1 (10.5 to 25.7)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 21	13.3 (7.5 to 21.4)			
Mnt PLT lvl f/1st time of reach. that lvl to mo 24	14.3 (8.2 to 22.5)			
Mnt PLT lvl f/1st time of reach. that lvl to EOT	31.4 (22.7 to 41.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) questionaire

End point title	Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) questionaire

End point description:

The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue©) is a 13- item questionnaire that assesses self-reported fatigue and its impact upon daily activities over the past 7 days. FACIT-fatigue is scored using a 4-point Likert scale. Items are scored as follows: 4 = Not At All; 3 = A Little Bit; 2 = Somewhat; 1 = Quite A Bit; 0 = Very Much, EXCEPT items #7 and #8 which are reversed scored. Score range from 0-52. A score of less than 30 indicates severe fatigue. The higher the score, the better the
quality of life (less fatigue).

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	5.42 (± 9.700)			
6 Months	6.15 (± 8.779)			
9 Months	6.89 (± 9.291)			
12 Months	7.90 (± 9.064)			
15 Months	7.12 (± 11.720)			
18 Months	8.87 (± 11.644)			
21 Months	8.80 (± 11.112)			
24 Months	8.69 (± 10.635)			
end of treatment visit	5.40 (± 10.116)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Functional Assessment of Cancer Therapy-Thrombocytopenia (FACT-Th6) questionnaire

End point title	Change from baseline in Functional Assessment of Cancer Therapy- Thrombocytopenia (FACT-Th6) questionnaire

End point description:

FACT-Th6 instrument is used to measure worry/concern about bleeding and bruising, and the impact of this worry/concern on physical and social activity (Cella 2006). FACT-Th6 is a 6-item subset of the more

detailed FACT-Th, which is an 18-item subscale of the validated FACT that specifically measures concerns related to thrombocytopenia in the past 7 days. The FACT-Th6 is scored using a 5-level Likert scale (0=not at all to 4=very much) and is calculated by summing scores for the 6-items; therefore, scores can range from 0–24, with higher scores representing better HRQoL

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	3.80 (± 5.130)			
6 Months	4.35 (± 6.312)			
9 Months	5.60 (± 6.114)			
12 Months	5.62 (± 6.505)			
15 Months	5.44 (± 8.949)			
18 Months	7.04 (± 7.654)			
21 Months	7.32 (± 7.351)			
24 Months	7.08 (± 7.048)			
end of treatment visit	4.15 (± 6.631)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Bodily Pain (BP) Score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Bodily Pain (BP) Score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	7.55 (± 24.199)			
6 Months	2.75 (± 24.636)			
9 Months	3.82 (± 21.507)			
12 Months	7.53 (± 25.547)			
15 Months	1.96 (± 36.697)			
18 Months	13.61 (± 26.662)			
21 Months	3.00 (± 20.967)			
24 Months	9.27 (± 29.090)			
end of treatment visit	5.19 (± 29.460)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: General Health (GH) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: General Health (GH) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				

3 Months	4.12 (± 18.894)			
6 Months	5.39 (± 20.646)			
9 Months	7.40 (± 17.990)			
12 Months	7.62 (± 18.420)			
15 Months	11.17 (± 20.470)			
18 Months	14.78 (± 26.801)			
21 Months	14.36 (± 25.541)			
24 Months	13.92 (± 19.577)			
end of treatment visit	3.80 (± 18.122)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Mental Health (MH) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Mental Health (MH) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	6.74 (± 15.775)			
6 Months	6.97 (± 18.149)			
9 Months	9.78 (± 15.074)			
12 Months	10.26 (± 16.125)			

15 Months	7.08 (± 22.259)			
18 Months	15.22 (± 22.334)			
21 Months	14.32 (± 20.948)			
24 Months	12.50 (± 17.103)			
end of treatment visit	6.82 (± 17.058)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Physical Functioning (PF) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Physical Functioning (PF) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	8.48 (± 23.842)			
6 Months	10.90 (± 26.069)			
9 Months	12.67 (± 28.074)			
12 Months	14.31 (± 28.767)			
15 Months	11.87 (± 37.469)			
18 Months	19.35 (± 33.449)			
21 Months	24.09 (± 31.983)			
24 Months	16.54 (± 35.882)			

end of treatment visit	9.00 (± 29.376)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Role Emotional (RE) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Role Emotional (RE) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	4.42 (± 22.371)			
6 Months	6.15 (± 23.270)			
9 Months	8.89 (± 22.361)			
12 Months	10.20 (± 23.260)			
15 Months	4.86 (± 27.022)			
18 Months	13.04 (± 26.211)			
21 Months	16.29 (± 25.520)			
24 Months	16.03 (± 20.128)			
end of treatment visit	7.25 (± 22.078)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Role Physical (RP) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Role Physical (RP) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	13.26 (± 22.958)			
6 Months	9.43 (± 27.066)			
9 Months	17.36 (± 24.165)			
12 Months	19.94 (± 29.232)			
15 Months	15.89 (± 37.454)			
18 Months	22.55 (± 32.680)			
21 Months	27.27 (± 33.604)			
24 Months	29.81 (± 32.849)			
end of treatment visit	15.88 (± 33.332)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Social Functioning (SF) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-

	36v2) questionnaire: Social Functioning (SF) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	6.06 (± 24.143)			
6 Months	7.17 (± 26.951)			
9 Months	10.00 (± 22.863)			
12 Months	16.38 (± 26.408)			
15 Months	14.58 (± 30.986)			
18 Months	26.63 (± 24.514)			
21 Months	20.45 (± 26.318)			
24 Months	25.96 (± 22.617)			
end of treatment visit	11.18 (± 26.236)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Vitality (VT) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Vitality (VT) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	7.48 (± 18.418)			
6 Months	6.45 (± 20.696)			
9 Months	12.78 (± 20.982)			
12 Months	14.33 (± 22.398)			
15 Months	8.33 (± 26.237)			
18 Months	12.23 (± 27.918)			
21 Months	17.33 (± 26.087)			
24 Months	11.06 (± 24.705)			
end of treatment visit	8.97 (± 22.503)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Physical Component Summary (PCS) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Physical Component Summary (PCS) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	3.46 (± 7.445)			
6 Months	2.72 (± 8.165)			
9 Months	3.92 (± 7.608)			
12 Months	4.85 (± 8.946)			
15 Months	4.37 (± 11.754)			
18 Months	6.77 (± 9.950)			
21 Months	6.65 (± 8.017)			
24 Months	6.63 (± 9.627)			
end of treatment visit	3.30 (± 9.728)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Mental Component Summary (MCS) score

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire: Mental Component Summary (MCS) score

End point description:

The SF-36 Scale is a 36-item, patient-reported survey which measures overall quality of life. It consists of 8 subscales (bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role emotional (SE), role physical (RP), social role functioning (SF) and vitality (VT)) which can be aggregated to derive a physical-component summary (PCS) score and a mental-component score (MCS). The SF-36 is scored using norm-based scoring procedures: each sub-scale score ranges from 0 to 10, and the composite score ranges from 0 to 100. Higher scores indicative of better HRQoL.

End point type	Secondary

End point timeframe:

Baseline to month 3, 6, 9, 12 (End of Treatment Visit for non-responders), 15, 18, 21 and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
3 Months	2.34 (± 8.443)			
6 Months	2.85 (± 9.451)			
9 Months	4.52 (± 7.815)			

12 Months	5.33 (± 8.719)			
15 Months	3.28 (± 11.083)			
18 Months	7.12 (± 11.312)			
21 Months	7.18 (± 11.143)			
24 Months	6.87 (± 9.081)			
end of treatment visit	3.53 (± 9.002)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with worst post-baseline value in Functional Assessment of Cancer Therapy-G (GP5)

End point title	Percentage of participants with worst post-baseline value in Functional Assessment of Cancer Therapy-G (GP5)

End point description:

The GP5 is a single question used to assess the overall bothersomeness of treatment side effects. The GP5 is scored using a 5-point rating scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; and 4 = very much), where lower scores reflect less bothersomeness from treatment side effects.

End point type	Secondary

End point timeframe:

Baseline to end of treatment visit, assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Participants				
Rating 0	51			
Rating 1	15			
Rating 2	10			
Rating 3	2			
Rating 4	5			
Missing	22			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall change of treatment satisfaction using Treatment Satisfaction Questionnaire (TSQM-9)

End point title	Overall change of treatment satisfaction using Treatment Satisfaction Questionnaire (TSQM-9)

End point description:

The Treatment Satisfaction Questionnaire for Medication (TSQM-9) is a psychometric measure of a patient's satisfaction with medication. It consists of 3 subscales: effectiveness, convenience and global satisfaction. The scores were computed by adding items for each domain, i.e. 1 to 3 for effectiveness, 4 - 6 for convenience and 7 to 9 for global satisfaction. The lowest possible score (1 for each item and 3 for all 3 subscales) was subtracted from the composite score and divided by the greatest possible score range. The greatest range was (7-1) X 3 items = 18 for the effectiveness and convenience, and (5-1) x 3 items = 12 for global satisfaction. This provided a transformed score between 0 and 1 that was then multiplied by 100. A positive change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline to month 12 (End of Treatment Visit for non-responders) and 24 (End of Treatment Visit for responders), assessed up to 12 months for non-responders and up to 24 months for responders

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Global Satisfaction change from BL at 12 months	17.78 (± 29.201)			
Global Satisfaction change from BL at 24 months	17.69 (± 26.110)			
Global Satisfaction change from BL at EOT	9.96 (± 33.966)			
Effectiveness change from BL at 12 months	18.82 (± 33.809)			
Effectiveness change from BL at 24 months	17.99 (± 29.913)			
Effectiveness change from BL at EOT	14.14 (± 36.673)			
Convenience change from BL at 12 months	17.69 (± 30.758)			
Convenience change from BL at 24 months	19.05 (± 25.189)			
Convenience change from BL at EOT	15.07 (± 30.253)			
Total score change from BL at 12 months	54.29 (± 78.218)			
Total score change from BL at 24 months	54.72 (± 75.463)			
Total score change from BL at EOT	39.17 (± 86.449)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

On-treatment deaths were reported from the date of first dose of eltrombopag to 30 days after the date

of the last non-zero dose of eltrombopag for patients who discontinued on or before month 12 (i.e., non-responders). For patients ongoing at month 12, the on-treatment period lasted until the cut-off date for the primary analysis (22-Oct-2021; approximately 35 months), as a patient could restart treatment at any time during study.
Post-treatment deaths were collected in the post treatment period from 31 days after last dose of study medication until the cut-off date for the primary analysis (22-Oct-2021; approximately 35 months). These are not considered Adverse Events.

End point type	Post-hoc

End point timeframe:

On-treatment deaths: Up to approximately 35 months. Post-treatment deaths: Up to approximately 35 months

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Participants				
On-treatment deaths	3			
Post-treatment deaths	1			
All deaths	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 35 months

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	25.1

Reporting groups

Reporting group title	All patients

Reporting group description:

All patients

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 105 (20.00%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Basal cell carcinoma			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Platelet count decreased			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Intentional product misuse			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Superficial vein thrombosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Central nervous system haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Carotid artery stenosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Thrombocytopenia			

subjects affected / exposed	3 / 105 (2.86%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Petechiae			

subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Tuberculosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cavernous sinus thrombosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonsillar abscess			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 105 (84.76%)		
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		

Deep vein thrombosis subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2		
Extravasation blood subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Hot flush subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Hypertension subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4		
Hypotension subjects affected / exposed occurrences (all)	3 / 105 (2.86%) 3		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	8 / 105 (7.62%) 10		
Fatigue subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 7		
Discomfort subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2		
Injection site swelling subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Malaise subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Mucosal disorder subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Mucosal haemorrhage			

subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	10		
Oedema peripheral			
subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	5 / 105 (4.76%)		
occurrences (all)	7		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Dysmenorrhoea			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Heavy menstrual bleeding			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	4		
Intermenstrual bleeding			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Uterine polyp			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Vaginal haemorrhage			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Cough			

subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	6		
Dysphonia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	5 / 105 (4.76%)		
occurrences (all)	11		
Lung infiltration			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Oropharyngeal discomfort			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
Productive cough			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		

Insomnia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Irritability subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Sleep disorder subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2		
Anxiety disorder subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	9 / 105 (8.57%) 10		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	7 / 105 (6.67%) 14		
Amylase increased subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Blood bilirubin increased subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2		
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4		
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Blood glucose increased			

subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
Blood phosphorus decreased			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Gamma-glutamyltransferase abnormal			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	3		
Platelet count increased			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Serum ferritin decreased			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Contusion			

subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	6		
Head injury			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Muscle strain			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Neck injury			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Periorbital haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Procedural dizziness			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Wrong technique in product usage process			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Gilbert's syndrome			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	6		
Tachycardia			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Nervous system disorders			

Headache				
subjects affected / exposed	23 / 105 (21.90%)			
occurrences (all)	45			
Vocal cord paralysis				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Anosmia				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Autonomic nervous system imbalance				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Cerebrovascular accident				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Cervical radiculopathy				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Dizziness				
subjects affected / exposed	3 / 105 (2.86%)			
occurrences (all)	5			
Dizziness postural				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Dysarthria				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Hypotonia				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Migraine				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Neuralgia				

subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 105 (6.67%)		
occurrences (all)	8		
Haemorrhagic diathesis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Bone marrow reticulin fibrosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Haemoglobinaemia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	16 / 105 (15.24%)		
occurrences (all)	31		
Hyperchromasia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		

Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Neutropenia subjects affected / exposed occurrences (all)	5 / 105 (4.76%) 7		
Neutrophilia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Platelet disorder subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Thrombocytosis subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 2		
Iron deficiency anaemia subjects affected / exposed occurrences (all)	3 / 105 (2.86%) 3		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	3 / 105 (2.86%) 3		
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Central serous chorioretinopathy subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2		
Eye haemorrhage subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Optic nerve cupping			

subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Photopsia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Retinal degeneration			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Retinal haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Scleral haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 105 (6.67%)		
occurrences (all)	10		
Diarrhoea			
subjects affected / exposed	10 / 105 (9.52%)		
occurrences (all)	13		
Gingival bleeding			
subjects affected / exposed	6 / 105 (5.71%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	8 / 105 (7.62%)		
occurrences (all)	10		
Vomiting			
subjects affected / exposed	6 / 105 (5.71%)		
occurrences (all)	9		

Mouth haemorrhage				
subjects affected / exposed	2 / 105 (1.90%)			
occurrences (all)	3			
Abdominal discomfort				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Abdominal pain upper				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	2 / 105 (1.90%)			
occurrences (all)	2			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	3			
Haematochezia				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Haemorrhoids				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Lip blister				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Odynophagia				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Stomatitis				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			

Oral pain subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1		
Hepatobiliary disorders Cholestasis subjects affected / exposed occurrences (all) Hepatic failure subjects affected / exposed occurrences (all) Hepatic function abnormal subjects affected / exposed occurrences (all) Hyperbilirubinaemia subjects affected / exposed occurrences (all) Hypertransaminasaemia subjects affected / exposed occurrences (all)	 1 / 105 (0.95%) 1 1 / 105 (0.95%) 1 1 / 105 (0.95%) 1 4 / 105 (3.81%) 5 1 / 105 (0.95%) 1		
Skin and subcutaneous tissue disorders Petechiae subjects affected / exposed occurrences (all) Night sweats subjects affected / exposed occurrences (all) Acne subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Dermatitis allergic subjects affected / exposed occurrences (all) Dry skin	 11 / 105 (10.48%) 18 1 / 105 (0.95%) 1 1 / 105 (0.95%) 1 5 / 105 (4.76%) 5 1 / 105 (0.95%) 2		

subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Ecchymosis			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
Eczema			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Onychoclasis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Pigmentation disorder			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	5		
Purpura			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	5 / 105 (4.76%)		
occurrences (all)	7		
Rash maculo-papular			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Skin reaction			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Skin haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Renal and urinary disorders			

Chromaturia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 105 (6.67%)		
occurrences (all)	10		
Back pain			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	5		
Bone pain			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Joint lock			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Lumbar spinal stenosis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	4		
Myalgia			

subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Infections and infestations			
Oral herpes			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Abscess limb			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Acute sinusitis			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Adenovirus infection			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
COVID-19			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Coronavirus infection			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Eye infection viral			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		

Furuncle				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	6			
Gastroenteritis				
subjects affected / exposed	2 / 105 (1.90%)			
occurrences (all)	2			
Gastrointestinal viral infection				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Helicobacter infection				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	4 / 105 (3.81%)			
occurrences (all)	7			
Nasopharyngitis				
subjects affected / exposed	5 / 105 (4.76%)			
occurrences (all)	6			
Onychomycosis				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Papilloma viral infection				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Periodontitis				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	3 / 105 (2.86%)			
occurrences (all)	4			
Subcutaneous abscess				
subjects affected / exposed	1 / 105 (0.95%)			
occurrences (all)	1			

Suspected COVID-19 subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1			
Tooth abscess subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2			
Tooth infection subjects affected / exposed occurrences (all)	3 / 105 (2.86%) 4			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1			
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 105 (2.86%) 4			
Viral infection subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2			
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1			
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1			
Dyslipidaemia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 2			
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1			
Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 105 (2.86%) 4			
Hyperkalaemia				

subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
Hyperuricaemia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	3		
Hypomagnesaemia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	6		
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2019	Amendment 01: The purpose was to update the pregnancy prevention language to align with CTFG recommendations, update the biomarker sample collection schedule, add a follow-up period of 12 Months, update the DILI guidance, and align with current eltrombopag program risk language.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported