Clinical trial results:
A non-randomized, open label, multi-center, Phase II study to assess the safety and efficacy of eltrombopag in combination with rabbit anti-thymocyte globulin (r-ATG) and cyclosporine A (CsA) in East-Asian patients with treatment naive severe aplastic anemia (REACTS)

Summary

EudraCT number	2024-000602-14
Trial protocol	Outside EU/EEA
Global end of trial date	06 December 2024

Results information

Result version number	v2 (current)
This version publication date	06 August 2025
First version publication date	20 June 2025
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CETB115G2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04328727
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of eltrombopag in combination with r-ATG and CsA in terms of complete response (CR) rate at 6 months in East-Asian patients with treatment naive severe aplastic anemia (SAA).

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

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	04 November 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 26
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Korea, Republic of: 3
Worldwide total number of subjects	36
EEA total number of subjects	0

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)	4
Adolescents (12-17 years)	4
Adults (18-64 years)	26
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 12 sites in 4 different countries

Pre-assignment

Screening details:

there was an up to 30 days screening period (day -30 to -1) before first treatment (day 1).

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 received eltrombopag in combination with r-ATG and CsA. • Eltrombopag was administered orally once daily with initial doses of 75mg/day for ≥ 12 years old and 37.5 mg/day for participants between ≥ 6 and < 12 years. Doses could be adjusted based on platelet count • r-ATG was administered intravenously at a dose of 2.5 to 3.5 mg/kg/day on Days 1-5 • CsA was administered orally every 12 h at a starting dose of 3-6 mg/kg/day

Arm type	Experimental
Investigational medicinal product name	eltrombopag
Investigational medicinal product code	ETB115
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eltrombopag was administered orally once daily with initial doses of 75mg/day for ≥ 12 years old and 37.5 mg/day for participants between ≥ 6 and < 12 years. Doses could be adjusted based on platelet count

Investigational medicinal product name	cyclosporine A
Investigational medicinal product code	
Other name	CsA
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

CsA was administered orally every 12 h at a starting dose of 3-6 mg/kg/day

Investigational medicinal product name	rabbit anti-thymocyte globulin
Investigational medicinal product code	
Other name	r-ATG
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

r-ATG was administered intravenously at a dose of 2.5 to 3.5 mg/kg/day on Days 1-5

Number of subjects in period 1	eltrombopag
Started	36
Started extension part	28
Started long term follow up	34
Completed	28
Not completed	8
Participant decision	4
Death	3
Guardian Decision	1

Baseline characteristics

Reporting groups	
Reporting group title	eltrombopag
Reporting group description:	
Participants received eltrombopag in combination with r-ATG and CsA. • Eltrombopag was administered orally once daily with initial doses of 75mg/day for ≥ 12 years old and 37.5 mg/day for participants between ≥ 6 and < 12 years. Doses could be adjusted based on platelet count • r-ATG was administered intravenously at a dose of 2.5 to 3.5 mg/kg/day on Days 1-5 • CsA was administered orally every 12 h at a starting dose of 3-6 mg/kg/day	

Reporting group values	eltrombopag	Total	
Number of subjects	36	36	
Age Categorical Units: participants			
<=18 years	8	8	
Between 18 and 65 years	26	26	
>=65 years	2	2	
Age Continuous Units: years			
arithmetic mean	34.7		
standard deviation	± 18.97	-	
Sex: Female, Male Units: participants			
Female	21	21	
Male	15	15	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	36	36	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	eltrombopag

Reporting group description:

Participants received eltrombopag in combination with r-ATG and CsA. • Eltrombopag was administered orally once daily with initial doses of 75mg/day for ≥ 12 years old and 37.5 mg/day for participants between ≥ 6 and < 12 years. Doses could be adjusted based on platelet count • r-ATG was administered intravenously at a dose of 2.5 to 3.5 mg/kg/day on Days 1-5 • CsA was administered orally every 12 h at a starting dose of 3-6 mg/kg/day

Primary: Complete response (CR) rate at week 26

End point title	Complete response (CR) rate at week 26[1]

End point description:

Complete response rate was defined as percentage of patients achieving complete response (CR).

Complete response was defined as subjects meeting all the three criteria on two consecutive serial blood count measurements at least one week apart but not more than four weeks apart:
- Absolute neutrophil count > 1.0 ×10^9/L
- Platelet count > 100 ×10^9/L
- Hemoglobin > 100 g/L

The participants who discontinued from the trial before Week 26 and those that received blood products prior to response assessment (7 days prior for platelet transfusions, 14 days for RBC transfusion and 21 days for growth factors) were treated as non-responders.

No hypothesis test was planned for this primary outcome.

End point type	Primary

End point timeframe:

Week 26 (6 months after starting study treatment)

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: No statistical hypothesis test was planned for this primary outcome

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percentage of participants				
number (confidence interval 95%)				
All participants	16.7 (6.4 to 32.8)			
< 18 years	25 (3.2 to 65.1)			
18-64 years	15.4 (4.4 to 34.9)			
≥ 65 years	0 (0.0 to 84.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete response (CR) rate

End point title	Complete response (CR) rate

End point description:

Complete response rate was defined as percentage of patients achieving complete response (CR).

Complete response was defined as subjects meeting all the three criteria on two consecutive serial blood count measurements at least one week apart but not more than four weeks apart:
- Absolute neutrophil count > 1.0 ×10^9/L
- Platelet count > 100 ×10^9/L
- Hemoglobin > 100 g/L

The participants who discontinued from the trial before Week 26 and those that received blood products prior to response assessment (7 days prior for platelet transfusions, 14 days for RBC transfusion and 21 days for growth factors) were treated as non-responders.

End point type	Secondary

End point timeframe:

Week 13 (3 months), Week 52 (12 months) and yearly after up to 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percentage of participants				
number (confidence interval 95%)				
Week 13	5.6 (0.7 to 18.7)			
Week 52	30.6 (16.3 to 48.1)			
Year 2	30.6 (16.3 to 48.1)			
Year 3	30.6 (16.3 to 48.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response (ORR) rate

End point title	Overall response (ORR) rate

End point description:

Overall response rate was defined as percentage of patients achieving complete response (CR) or partial response (PR).

Partial response (PR) was defined as blood counts no longer meeting the standard criteria for severe pancytopenia in SAA, equivalent to at least 2 of the 3 criteria below, but not sufficient for a CR:
- Absolute neutrophil count ≥ 0.5 × 10^9/L
- Platelet count ≥ 20 × 10^9/L
- Reticulocyte count ≥ 20 × 10^9/L

Complete response (CR) was defined as subjects meeting all the three criteria on two consecutive serial

blood count measurements at least one week apart but not more than four weeks apart:
- Absolute neutrophil count > 1.0 ×10^9/L
- Platelet count > 100 ×10^9/L
- Hemoglobin > 100 g/L

End point type	Secondary

End point timeframe:

Week 13 (3 months), 26 weeks (6 months), 52 weeks and yearly after up to 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percentage of participants				
number (confidence interval 95%)				
Week 13	66.7 (49.0 to 81.4)			
Week 26	77.8 (60.8 to 89.9)			
Week 52	66.7 (49.0 to 81.4)			
Year 2	50.0 (32.9 to 67.1)			
Year 3	41.7 (25.5 to 59.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of complete response

End point title	Duration of complete response

End point description:

Duration of response was derived as the time from first documented and confirmed complete response (CR) until the time of relapse or death, whichever occurred first. Duration of response was estimated using Kaplan-Meier method.

Clinical relapse was considered as the occurrence of any of the following events in a participant who had achieved a hematological response (CR) but had subsequently lost response (not explained by any other independent concomitant medical conditions) in one blood count measurements:
- Meeting again the criteria for SAA
- Requirement for transfusion again for subjects who had been transfusion independent
- Decrease in any of the peripheral blood counts to absolute neutrophil count < 0.5 x10^9/L or platelets < 20 x10^9/L.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Up to aproximately 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	11[2]			
Units: months				
number (confidence interval 95%)	999 (999 to 999)			

Notes:

[2] - Not estimable due to insufficient number of participants with relapse or death

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS was defined as the time from the date of the first dose of study treatment to the date of death due to any cause. If a subject was not known to have died, survival was censored at the date of last contact. The distribution function of OS was estimated using the Kaplan- Meier method.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Up to approximately 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	36[3]			
Units: Months				
median (confidence interval 95%)	999 (999 to 999)			

Notes:

[3] - Not estimable due to median duration of OS being not evaluable from the Kaplan-Meyer analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) rate

End point title	Overall survival (OS) rate

End point description:

OS was defined as the time from the date of the first dose of study treatment to the date of death due to any cause. The OS rate is the estimated probability that a patient will remain event-free up to the specified time point and was obtained from the Kaplan-Meier survival estimates. If a subject was not known to have died, survival was censored at the date of last contact.

End point type	Secondary

End point timeframe:

Week 26, Week 52 and yearly after up to 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percent probability				
number (confidence interval 95%)				
Week 26	97.2 (81.9 to 99.6)			
Week 52	97.2 (81.9 to 99.6)			
Year 2	94.1 (78.3 to 95.5)			
Year 3	90.9 (74.4 to 97.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of overall response

End point title	Duration of overall response

End point description:

Duration of response was derived as the time from first documented and confirmed response (either CR or PR) until the time of relapse or death, whichever occurred first. Duration of response was estimated using Kaplan-Meier method.

Clinical relapse was considered as the occurrence of any of the following events in a participant who had achieved a hematological response (CR or PR) but had subsequently lost response (not explained by any other independent concomitant medical conditions) in one blood count measurements:
- Meeting again the criteria for SAA
- Requirement for transfusion again for subjects who had been transfusion independent
- Decrease in any of the peripheral blood counts to absolute neutrophil count < 0.5 x10^9/L or platelets < 20 x10^9/L.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating ‘not applicable’). Therefore, not applicable values are indicated as ‘999’.

End point type	Secondary

End point timeframe:

Up to aproximately 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	31[4]			
Units: months				
number (confidence interval 95%)	999 (3.1 to 999)			

Notes:

[4] - Not estimable due to median duration of overall response not being achieved from the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Red blood cells (RBC) and platelet transfusion-free interval before Week 13 and 26

End point title	Red blood cells (RBC) and platelet transfusion-free interval before Week 13 and 26

End point description:

Transfusion-free interval was defined as the time from most recent RBC/platelet transfusion preceding response assessment to the date of response assessment.

End point type	Secondary

End point timeframe:

Week 13, 26

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: days				
arithmetic mean (standard deviation)				
RBC transfusion-free interval - Week 13 n=34	36.3 (± 25.62)			
RBC transfusion-free interval - Week 26 n=32	98.9 (± 57.97)			
Platelet transfusion-free interval - Week 13 n=34	34.0 (± 25.64)			
Platelet transfusion-free interval - Week 26 n=32	97.3 (± 58.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pharmacokinetics (PK) parameters of eltrombopag: AUClast

End point title	Plasma pharmacokinetics (PK) parameters of eltrombopag: AUClast

End point description:

AUClast is the area under the curve from time zero to the last measurable concentration sampling time.

Blood samples were collected from patients to assess the plasma concentrations of eltrombopag using a validated liquid chromatography – tandem mass spectrometry assay (LC-MS/MS) approach.

End point type	Secondary

End point timeframe:

Pre-dose, and 2, 4, 6, 8 and 24 hours post-dose on Day 14 after initial dose

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ng*h/mL				
arithmetic mean (standard deviation)	602000 (± 239000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who become platelet transfusion independent

End point title	Percentage of participants who become platelet transfusion independent

End point description:

Transfusion independent participants were defined as those participants who were transfusion dependent at baseline but became transfusion free for a period of ≥ 4 weeks post-baseline for platelets.

End point type	Secondary

End point timeframe:

From date of first dose to approximately 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (not applicable)	88.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who become RBC transfusion independent

End point title	Percentage of participants who become RBC transfusion independent

End point description:

Transfusion independent participants were defined as those participants who were transfusion dependent at baseline but became transfusion free for a period of ≥ 8 weeks post-baseline for RBCs.

End point type	Secondary

End point timeframe:

From date of first dose to approximately 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage of participants				
number (not applicable)	86.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Time from the date of first dose of investigational treatment to the date of first occurrence of any clonal evolution events

End point title	Time from the date of first dose of investigational treatment to the date of first occurrence of any clonal evolution events

End point description:

Clonal evolution events were assessed by karyotyping (G-banding) and FISH (Fluorescence in situ hybridization) targeting abnormalities including, but not restricted to chromosome 3q del,5q del, monosomy 7, trisomy 8 and those associated with SAA (Severe aplastic anemia), MDS (Myelodysplastic syndrome), AML (Acute myeloid leukemia). Time to clonal evolution was to be estimated using the Kaplan-Meier method.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating ‘not applicable’). Therefore, not applicable values are indicated as ‘999’.

End point type	Secondary

End point timeframe:

From date of first dose to approximately 3 years

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	2[5]			
Units: weeks				
number (confidence interval 95%)	999 (999 to 999)			

Notes:

[5] - Not estimable due to insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pharmacokinetics (PK) parameters of eltrombopag: Tmax

End point title	Plasma pharmacokinetics (PK) parameters of eltrombopag:

	Tmax

End point description:

Tmax is the time to reach maximum (peak) plasma drug concentration after dose administration.

Blood samples were collected from patients to assess the plasma concentrations of eltrombopag using a validated liquid chromatography – tandem mass spectrometry assay (LC-MS/MS) approach.

End point type	Secondary

End point timeframe:

Pre-dose, and 2, 4, 6, 8 and 24 hours post-dose on Day 14 after initial dose

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: hours				
arithmetic mean (standard deviation)	5.59 (± 5.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pharmacokinetics (PK) parameters of eltrombopag: Ctrough

End point title	Plasma pharmacokinetics (PK) parameters of eltrombopag: Ctrough

End point description:

Cthrough is the pre-dose concentration at the end of dose interval.

Blood samples were collected to assess the plasma concentrations of eltrombopag using a validated liquid chromatography – tandem mass spectrometry assay (LC-MS/MS) approach.

Eltrombopag was administered orally once daily with initial doses of 75mg/day for ≥ 12 years old and 37.5 mg/day for participants between ≥ 6 and < 12 years.
Doses could be adjusted based on platelet count every 2 weeks by decreasing it by 25 mg/day (12.5 mg/day, for participants below 12 years old) if the platelet count was above 200×10^9/L. or interrupted if platelet count rose above 400×10^9/L. In partial response participants dose could be restarted or increased to that before the decrease if platelet counts < 30 x10^9/L, Hb< 90 g/L, ANC< 0.5 x 10^9/L or participant needed transfusion. In complete response participants dose could be restarted or increased to that before decrease if blood counts dropped to not meet CR criteria.

End point type	Secondary

End point timeframe:

Pre-dose on day 15 after initation of eltrombopag and and pre-dose on the 15th day after each new dose up to week 26

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	26[6]			
Units: ng/mL				
arithmetic mean (standard deviation)	20200 (± 9410)			

Notes:

[6] - Number of measurements 36

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pharmacokinetics (PK) parameters of eltrombopag: AUCtau

End point title	Plasma pharmacokinetics (PK) parameters of eltrombopag: AUCtau

End point description:

AUCtau is area under the curve calculated to the end of a dosing interval (tau) at steady-state

Blood samples were collected from patients to assess the plasma concentrations of eltrombopag using a validated liquid chromatography – tandem mass spectrometry assay (LC-MS/MS) approach.

End point type	Secondary

End point timeframe:

Pre-dose, and 2, 4, 6, 8 and 24 hours post-dose on Day 14 after initial dose

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng*h/mL				
arithmetic mean (standard deviation)	585000 (± 231000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pharmacokinetics (PK) parameters of eltrombopag: CLss/F

End point title	Plasma pharmacokinetics (PK) parameters of eltrombopag: CLss/F

End point description:

CLss/F is Apparent systemic (or total body) clearance at steady state from plasma.

Blood samples were collected from patients to assess the plasma concentrations of eltrombopag using a validated liquid chromatography – tandem mass spectrometry assay (LC-MS/MS) approach.

End point type	Secondary

End point timeframe:

Pre-dose, and 2, 4, 6, 8 and 24 hours post-dose on Day 14 after initial dose

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Liter/hour				
arithmetic mean (standard deviation)	0.148 (± 0.0618)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pharmacokinetics (PK) parameters of eltrombopag: Cmax

End point title	Plasma pharmacokinetics (PK) parameters of eltrombopag: Cmax

End point description:

Cmax is the The maximum (peak) observed plasma drug concentration after dose administration.

Blood samples were collected from patients to assess the plasma concentrations of eltrombopag using a validated liquid chromatography – tandem mass spectrometry assay (LC-MS/MS) approach.

End point type	Secondary

End point timeframe:

Pre-dose, and 2, 4, 6, 8 and 24 hours post-dose on Day 14 after initial dose

End point values	eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ng/mL				
median (standard deviation)	32500 (± 12300)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Mortality: from 1st dose of eltrombopag up to 2 years after last dose including post-treatment long term follow-up up to 3.1 years approximately.

AEs and SAEs: from first dose of eltrombopag until 30 days after last dose up to 1.1 years approximately.

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	27.1

Reporting groups

Reporting group title	eltrombopag

Reporting group description:

Participants received eltrombopag in combination with r-ATG and CsA.

Serious adverse events	eltrombopag		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 36 (38.89%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Breast hyperplasia				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Heavy menstrual bleeding				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperuricaemia			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	eltrombopag		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 36 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	10		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	4		
Chest pain			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	12 / 36 (33.33%)		
occurrences (all)	20		
Immune system disorders			
Allergy to immunoglobulin therapy			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Hypersensitivity			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	8		
Immunodeficiency			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Serum sickness			
subjects affected / exposed	9 / 36 (25.00%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Productive cough			

subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	3		
Rhinitis allergic			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 36 (36.11%)		
occurrences (all)	19		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	8		
Bilirubin conjugated increased			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	6		
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Blood bilirubin increased			
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	11		
Blood creatinine increased			
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	10		
Blood glucose increased			
subjects affected / exposed	13 / 36 (36.11%)		
occurrences (all)	21		
Blood pressure increased			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	6		
Blood urea increased			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	8		
Gamma-glutamyltransferase increased			

subjects affected / exposed occurrences (all)	10 / 36 (27.78%) 14		
Injury, poisoning and procedural complications Allergic transfusion reaction subjects affected / exposed occurrences (all)	 4 / 36 (11.11%) 4		
Cardiac disorders Cardiac failure subjects affected / exposed occurrences (all)	 2 / 36 (5.56%) 4		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 2 / 36 (5.56%) 2 4 / 36 (11.11%) 4		
Blood and lymphatic system disorders Febrile neutropenia subjects affected / exposed occurrences (all)	 3 / 36 (8.33%) 3		
Eye disorders Cataract subjects affected / exposed occurrences (all)	 3 / 36 (8.33%) 3		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Diarrhoea	 8 / 36 (22.22%) 8 2 / 36 (5.56%) 5 2 / 36 (5.56%) 3		

subjects affected / exposed	9 / 36 (25.00%)		
occurrences (all)	10		
Vomiting			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Mouth ulceration			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Haemorrhoids			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Gastrointestinal disorder			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	5		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Hyperbilirubinaemia			
subjects affected / exposed	11 / 36 (30.56%)		
occurrences (all)	32		
Skin and subcutaneous tissue disorders			
Dry skin			

subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Acne			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	7		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	5		
Renal failure			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Renal impairment			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Infections and infestations			
Cytomegalovirus infection reactivation			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Infection			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	7		
Neutropenic infection			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Oral infection			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	3		
Pneumonia			

subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Upper respiratory tract infection			
subjects affected / exposed	8 / 36 (22.22%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	6		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Fluid retention			
subjects affected / exposed	9 / 36 (25.00%)		
occurrences (all)	9		
Hypercholesterolaemia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	5		
Hyperglycaemia			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	15		
Hyperlipidaemia			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	6		
Hypertriglyceridaemia			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	10		
Hyperuricaemia			
subjects affected / exposed	14 / 36 (38.89%)		
occurrences (all)	49		
Hypoalbuminaemia			
subjects affected / exposed	10 / 36 (27.78%)		
occurrences (all)	14		
Hypocalcaemia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	5		

Hypokalaemia subjects affected / exposed occurrences (all)	18 / 36 (50.00%) 27		
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Hyponatraemia subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 9		
Hypoproteinaemia subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 7		
Sodium retention subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2020	The primary purpose of this amendment was to change the level of AST/ALT from > 8 × ULN to > 5 × ULN and to change the recommended action from "dose interruption" to "treatment discontinuation" in Table 6-7 of protocol, 'Guidelines for eltrombopag dose modification based on liver function abnormalities and thrombosis/embolism' in response to concerns raised by Korean Health Authority.
22 December 2021	The purpose of this amendment was to harmonize and clarify several inconsistencies in the protocol and add risk mitigation procedures during public health emergency declared by local or regional authorities. The updates were not triggered by any safety issues or new safety data becoming available. The assessment of the Benefit/Risk identified no additional risks related to COVID 19 and no changes have been made as a result.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: