Clinical trial results:
A rollover study to provide continued treatment with eltrombopag

Summary

EudraCT number	2013-001371-20
Trial protocol	IE ES BE GR PL NL
Global end of trial date	23 February 2022

Results information

Result version number	v1 (current)
This version publication date	21 December 2022
First version publication date	21 December 2022

Trial information

Trial identification

Sponsor protocol code	200170

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01957176
WHO universal trial number (UTN)	-
Other trial identifiers	CETB115A2X01B: Novartis

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	23 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2022
Global end of trial reached?	Yes
Global end of trial date	23 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to provide continued treatment with eltrombopag for subjects who were participating in a Novartis-sponsored investigational study with eltrombopag (parent studies 114968/ASPIRE (NCT01440374), PMA112509 (NCT00903422), and TRA105325/EXTEND (NCT00351468), receiving clinical benefit without unacceptable toxicity and to collect long-term safety data.

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	15 October 2013
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	Belgium: 1
Country: Number of subjects enrolled	China: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Tunisia: 6
Worldwide total number of subjects	22
EEA total number of subjects	8

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)	9
From 65 to 84 years	12
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

22 subjects were enrolled in 14 centers in 12 countries (Belgium, China, France, Greece, Hong Kong, Ireland, Korea, Republic of., Netherlands, Peru, Poland, Romania, Tunisia).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A (MDS/AML adult subjects)

Arm description:

All subjects in this cohort received eltrombopag (ELT) at the dose that they were receiving at the time of the transition visit, except in the case where the subject required a dose modification. The range of doses of ELT that were used in this cohort were from 50 to 300 mg once daily (OD) for subjects of non-East Asian heritage. The dose ranges for subjects of East Asian heritage (i.e., Japanese, Chinese, Taiwanese, Thai and Korean) were 25 to 150 mg. Dose adjustments (if required) were done depending on each subject's platelet counts.

Arm type	Experimental
Investigational medicinal product name	Eltrombopag (ELT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with the same formulation of eltrombopag that was administered in the parent study. Eltrombopag tablets are white, round film-coated tablets containing eltrombopag olamine equivalent to 12.5 mg, 25 mg, 50 mg, 75 mg, and 100 mg of eltrombopag.

Arm title	Cohort B (ITP adult subjects)

Arm description:

All subjects in this cohort received ELT at the dose that they were receiving at the time of the transition visit, except in the case where the subject required a dose modification. The range of doses of ELT that were used in this cohort were from 12.5 to 75 mg. Dose adjustments (if required) were done depending on each subject's platelet counts.

Arm type	Experimental
Investigational medicinal product name	Eltrombopag (ELT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with the same formulation of eltrombopag that was administered in the parent study. Eltrombopag tablets are white, round film-coated tablets containing eltrombopag olamine equivalent to 12.5 mg, 25 mg, 50 mg, 75 mg, and 100 mg of eltrombopag.

Number of subjects in period 1	Cohort A (MDS/AML adult subjects)	Cohort B (ITP adult subjects)
Started	8	14
Completed	3	13
Not completed	5	1
Physician decision	2	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A (MDS/AML adult subjects)
Reporting group description:	
All subjects in this cohort received eltrombopag (ELT) at the dose that they were receiving at the time of the transition visit, except in the case where the subject required a dose modification. The range of doses of ELT that were used in this cohort were from 50 to 300 mg once daily (OD) for subjects of non-East Asian heritage. The dose ranges for subjects of East Asian heritage (i.e., Japanese, Chinese, Taiwanese, Thai and Korean) were 25 to 150 mg. Dose adjustments (if required) were done depending on each subject's platelet counts.	
Reporting group title	Cohort B (ITP adult subjects)
Reporting group description:	
All subjects in this cohort received ELT at the dose that they were receiving at the time of the transition visit, except in the case where the subject required a dose modification. The range of doses of ELT that were used in this cohort were from 12.5 to 75 mg. Dose adjustments (if required) were done depending on each subject's platelet counts.	

Reporting group values	Cohort A (MDS/AML adult subjects)	Cohort B (ITP adult subjects)	Total
Number of subjects	8	14	22
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	9	9
From 65-84 years	7	5	12
85 years and over	1	0	1
Age Continuous Units: Years			
arithmetic mean	73.8	59.5	
standard deviation	± 7.57	± 13.18	-
Sex: Female, Male Units: Participants			
Female	3	12	15
Male	5	2	7
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	2	2
Asian - East Asian Heritage	1	5	6
White - Arabic/North African Heritage	0	6	6
White - White/Caucasian/European Heritage	7	1	8

End points

End points reporting groups

Reporting group title	Cohort A (MDS/AML adult subjects)

Reporting group description:

All subjects in this cohort received eltrombopag (ELT) at the dose that they were receiving at the time of the transition visit, except in the case where the subject required a dose modification. The range of doses of ELT that were used in this cohort were from 50 to 300 mg once daily (OD) for subjects of non-East Asian heritage. The dose ranges for subjects of East Asian heritage (i.e., Japanese, Chinese, Taiwanese, Thai and Korean) were 25 to 150 mg. Dose adjustments (if required) were done depending on each subject's platelet counts.

Reporting group title	Cohort B (ITP adult subjects)

Reporting group description:

All subjects in this cohort received ELT at the dose that they were receiving at the time of the transition visit, except in the case where the subject required a dose modification. The range of doses of ELT that were used in this cohort were from 12.5 to 75 mg. Dose adjustments (if required) were done depending on each subject's platelet counts.

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[1]

End point description:

The distribution of adverse events was done via the analysis of frequencies for Adverse Events (AEs) and Serious Adverse Events (SAEs), through the monitoring of relevant clinical and laboratory safety parameters. Only descriptive analysis performed.

End point type	Primary

End point timeframe:

From the time of transition visit until 30 days after last dose of study treatment, assessed up to approximately 100 months.

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: Only descriptive analysis performed.

End point values	Cohort A (MDS/AML adult subjects)	Cohort B (ITP adult subjects)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	14		
Units: Participants				
Adverse Events (AEs)	7	12		
Serious Adverse Events (SAEs)	6	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of transition visit until 30 days after last dose of study treatment, assessed up to approximately 100 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	24.1

Reporting groups

Reporting group title	MDS/AML Adult

Reporting group description:

MDS/AML Adult

Reporting group title	All Subjects

Reporting group description:

All Subjects

Reporting group title	ITP Adult

Reporting group description:

ITP Adult

Serious adverse events	MDS/AML Adult	All Subjects	ITP Adult
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	13 / 22 (59.09%)	7 / 14 (50.00%)
number of deaths (all causes)	3	5	2
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural hygroma			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			

subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 8 (25.00%)	2 / 22 (9.09%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MDS/AML Adult	All Subjects	ITP Adult
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	19 / 22 (86.36%)	12 / 14 (85.71%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	2	3	1
Hot flush			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)	5 / 22 (22.73%)	4 / 14 (28.57%)
occurrences (all)	1	6	5
Hypertensive crisis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 8 (12.50%)	3 / 22 (13.64%)	2 / 14 (14.29%)
occurrences (all)	1	3	2
Chest pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Chills			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Discomfort			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	3	3
Face oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	2	2
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)	2 / 22 (9.09%)	0 / 14 (0.00%)
occurrences (all)	2	2	0
Inflammation			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Mucosal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Oedema peripheral			

subjects affected / exposed	3 / 8 (37.50%)	4 / 22 (18.18%)	1 / 14 (7.14%)
occurrences (all)	3	4	1
Pyrexia			
subjects affected / exposed	4 / 8 (50.00%)	7 / 22 (31.82%)	3 / 14 (21.43%)
occurrences (all)	4	9	5
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Heavy menstrual bleeding			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	8	8
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Scrotal oedema			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Bronchial irritation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Dyspnoea exertional			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Pleuritic pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Productive cough			

subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Rales			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Wheezing			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Confusional state			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	3	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	4 / 22 (18.18%)	3 / 14 (21.43%)
occurrences (all)	2	7	5
Apolipoprotein E abnormal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	4 / 22 (18.18%)	3 / 14 (21.43%)
occurrences (all)	1	7	6
Blood albumin decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	3 / 22 (13.64%)	3 / 14 (21.43%)
occurrences (all)	0	4	4
Blood glucose increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Blood pressure increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Blood urea increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Globulins increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Haematocrit increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Haemoglobin decreased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	2	2	0
Haemoglobin increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Neutrophil count increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2

Platelet count increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	7	7
Protein total increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	2	2
Urinary occult blood positive			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Urine ketone body present			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
White blood cell count increased			
subjects affected / exposed	2 / 8 (25.00%)	4 / 22 (18.18%)	2 / 14 (14.29%)
occurrences (all)	3	6	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Humerus fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Injury			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Procedural pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Rib fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Scratch			

subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Vaccination complication			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Nervous system disorders			
Diabetic neuropathy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	3	3
Headache			
subjects affected / exposed	1 / 8 (12.50%)	6 / 22 (27.27%)	5 / 14 (35.71%)
occurrences (all)	1	8	7
Lethargy			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	4 / 22 (18.18%)	2 / 14 (14.29%)
occurrences (all)	2	7	5
Eosinophilia			
subjects affected / exposed	0 / 8 (0.00%)	5 / 22 (22.73%)	5 / 14 (35.71%)
occurrences (all)	0	31	31
Iron deficiency anaemia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 22 (13.64%)	3 / 14 (21.43%)
occurrences (all)	0	8	8
Leukocytosis			

subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	10	10
Lymphadenopathy			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	4	4	0
Monocytosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Neutrophilia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Eye disorders			
Cataract			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Conjunctivitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Diabetic retinopathy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Ocular hyperaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Abdominal distension			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	3	3
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Anal fissure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Ascites			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	5 / 22 (22.73%)	4 / 14 (28.57%)
occurrences (all)	1	7	6
Duodenitis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Epigastric discomfort			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Gastric haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal angiodysplasia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Gingival bleeding			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	2	2
Hiatus hernia			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Inguinal hernia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Large intestine polyp			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Melaena			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	8	7
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	2	2
Odynophagia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	10	10
Rectal haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Stomatitis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Toothache			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	4	3
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	2	2
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0

Jaundice			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Ocular icterus			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Ingrowing nail			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Night sweats			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Petechiae			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	3	4	1
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Purpura			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Skin lesion			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	2	2	0
Pollakiuria			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	5	5
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	6 / 22 (27.27%)	5 / 14 (35.71%)
occurrences (all)	1	17	16
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	3 / 22 (13.64%)	2 / 14 (14.29%)
occurrences (all)	1	4	3
Intervertebral disc protrusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	2	2	0
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	2	2
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Osteoporosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Pain in extremity			

subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Rotator cuff syndrome			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Tendon pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	4	4
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	3	3
Ear infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	3 / 22 (13.64%)	3 / 14 (21.43%)
occurrences (all)	0	3	3
Genital infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Gingivitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1

Influenza			
subjects affected / exposed	1 / 8 (12.50%)	4 / 22 (18.18%)	3 / 14 (21.43%)
occurrences (all)	1	4	3
Kidney infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Lip infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	2 / 14 (14.29%)
occurrences (all)	0	11	11
Onychomycosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Oral herpes			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Paronychia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Periodontitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Pharyngotonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Pneumonia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1

Sinusitis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Tooth infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	6	6
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	6 / 22 (27.27%)	5 / 14 (35.71%)
occurrences (all)	1	10	9
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	3 / 22 (13.64%)	3 / 14 (21.43%)
occurrences (all)	0	9	9
Vaginal infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	3	2
Diabetes mellitus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Gout			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hyperuricaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypoalbuminaemia			

subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 14 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2016	The purpose of this amendment was (following the acquisition of SB-497115/eltrombopag from GSK): • To delete or replace references to GSK or its staff with that of Novartis and its authorized agents to align with the change of sponsorship; • Make administrative changes to align with Novartis processes and procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported