Clinical trial results:
A Randomized, Blinded, Placebo-controlled, Two-Phase, Sequential Cohort, Dose Finding Study to Assess the Safety and Efficacy of an Oral Thrombopoietin Receptor Agonist, Eltrombopag (SB-497115-GR), Administered to Patients with Solid Tumors Receiving Gemcitabine monotherapy or Gemcitabine Plus Carboplatin or Cisplatin.

Summary

EudraCT number	2009-014858-15
Trial protocol	BE DE IE GR FI HU CZ
Global end of trial date	16 March 2015

Results information

Result version number	v1 (current)
This version publication date	25 March 2016
First version publication date	25 March 2016

Trial information

Trial identification

Sponsor protocol code	TRC112765

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Phase I of the study is to assess the safety and tolerability of eltrombopag compared to placebo when administered to subjects with solid tumors receiving gemcitabine monotherapy or the combination of gemcitabine plus carboplatin or cisplatin.The primary objective of Phase II of the study is to evaluate the efficacy of the dose of eltrombopag selected from Phase I compared to placebo on platelet counts when administered to subjects with solid tumors receiving gemcitabine monotherapy or the combination of gemcitabine plus carboplatin or cisplatin who experienced thrombocytopenia in a previous cycle.

Protection of trial subjects:

1. Frequent review of ICF to ensure it includes updated data.
2. Protocol mandated frequent monitoring of the subjects by the investigator, which includes physical exam, laboratory assessments, ECG.
3. Regular safety review by the medical monitor and, if needed, by a back-up secondary medical monitor.
4. Regular safety review by the project team safety review teams.
5. Thromboembolic events review by the independent external Clinical Events Committee.
6. Several safety review panel meetings which included internal GSK employees and an independent external physician.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	India: 3
Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Poland: 21
Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Ireland: 1

Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	108
EEA total number of subjects	66

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)	51
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) with solid tumors receiving gemcitabine monotherapy or the combination of gemcitabine plus carboplatin or cisplatin were eligible for enrollment into the study.

Pre-assignment

Screening details:

The study comprised of 2 phases (I & II), with 108 eligible participants being randomized to receive placebo or eltrombopag in each phase. A maximum of 6 cycles (with some exceptions) of chemotherapy with eltrombopag/placebo were allowed in each phase (either 21-day or 28-day cycle) followed by the 30 day Follow-up visit.

Period 1

Period 1 title	Overall Study (Phase 1 and Phase 2) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Phase 1 treatment arms were Double blind (Subject, Investigator and Monitor). Phase II treatment arms were Double blind (Subject, Investigator, Monitor, Data analyst, Carer and Assessor).

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase I: 21-Day Cycle Placebo

Arm description:

Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

Arm type	Placebo Comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Phase 1: Placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine: 1000-1250 mg/m2 IV, given on Day +1 and Day +8

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin: 4 -7 x AUC IV on Day +1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin: 50-80 mg/m2 IV on Day +1 (or divided on Day +1 and Day +8)

Arm title	Phase I: 21-Day Cycle Eltrombopag 100 mg

Arm description:

Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered eltrombopag 100 milligrams (mg) once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

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

Dosage and administration details:

Phase 1: 100 milligrams mg once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine: 1000-1250 mg/m2 IV, given on Day +1 and Day +8

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin: 4 -7 x AUC IV on Day +1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin: 50-80 mg/m2 IV on Day +1 (or divided on Day +1 and Day +8)

Arm title	Phase I: 28-Day Cycle Placebo

Arm description:

Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

Arm type	Placebo Comparator

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Phase 1: Placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles
Phase II: 100 milligrams mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine monotherapy: 1000-1250 mg/m2 IV, given on Day +1, Day +8, and Day +15

Arm title	Phase I: 28-Day Cycle Eltrombopag 100 mg

Arm description:

Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

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

Dosage and administration details:

Phase 1: 100 milligrams mg once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles
Phase II: 100 milligrams mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine monotherapy: 1000-1250 mg/m2 IV, given on Day +1, Day +8, and Day +15

Arm title	Phase II: Placebo

Arm description:

Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Phase II: 100 milligrams mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy

cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

For subjects receiving chemotherapy on a 21-days cycle: Gemcitabine: 1000-1250 mg/m2 IV, given on Day +1 and Day +8
For subjects receiving chemotherapy on a 28-days cycle:Gemcitabine monotherapy: 1000-1250 mg/m2 IV, given on Day +1, Day +8, and Day +15

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin: 4 -7 x AUC IV on Day +1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin: 50-80 mg/m2 IV on Day +1 (or divided on Day +1 and Day +8)

Arm title	Phase II: Eltrombopag 100 mg

Arm description:

Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).

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

Dosage and administration details:

Phase II: 100 milligrams mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

For subjects receiving chemotherapy on a 21-days cycle:
Gemcitabine: 1000-1250 mg/m2 IV, given on Day +1 and Day +8
For subjects receiving chemotherapy on a 28-days cycle:
Gemcitabine monotherapy: 1000-1250 mg/m2 IV, given on Day +1, Day +8, and Day +15

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin: 4 -7 x AUC IV on Day +1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin: 50-80 mg/m2 IV on Day +1 (or divided on Day +1 and Day +8)

Number of subjects in period 1[1]	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo
Started	3	9	4
Completed	2	8	2
Not completed	1	1	2
Adverse event, serious fatal	-	-	-
Physician decision	-	1	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Ongoing	-	-	-
Lost to follow-up	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1[1]	Phase I: 28-Day Cycle Eltrombopag 100 mg	Phase II: Placebo	Phase II: Eltrombopag 100 mg
Started	10	23	52
Completed	5	7	19
Not completed	5	16	33
Adverse event, serious fatal	-	1	-
Physician decision	-	5	11
Consent withdrawn by subject	3	7	15
Adverse event, non-fatal	1	2	6
Ongoing	-	1	-
Lost to follow-up	1	-	-
Protocol deviation	-	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 108 participants were enrolled and 101 participants received at least one dose of IP.

Baseline characteristics

Reporting groups	
Reporting group title	Phase I: 21-Day Cycle Placebo
Reporting group description:	
Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase I: 21-Day Cycle Eltrombopag 100 mg
Reporting group description:	
Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered eltrombopag 100 milligrams (mg) once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase I: 28-Day Cycle Placebo
Reporting group description:	
Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase I: 28-Day Cycle Eltrombopag 100 mg
Reporting group description:	
Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase II: Placebo
Reporting group description:	
Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).	
Reporting group title	Phase II: Eltrombopag 100 mg
Reporting group description:	
Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).	

Reporting group values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo
Number of subjects	3	9	4
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.3	53.8	61.8
standard deviation	± 3.79	± 11.27	± 22.82
Gender categorical Units: Subjects			
Female	1	7	3
Male	2	2	1

Race Units: Subjects			
African American/African Heritage	1	1	0
White	2	8	3
Central/South Asian Heritage	0	0	1
Japanese/East Asian Heritage/South East Asian	0	0	0

Reporting group values	Phase I: 28-Day Cycle Eltrombopag 100 mg	Phase II: Placebo	Phase II: Eltrombopag 100 mg
Number of subjects	10	23	52
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	65.6	64.4	66.3
standard deviation	± 8.41	± 9.96	± 8.98
Gender categorical Units: Subjects			
Female	3	13	23
Male	7	10	29
Race Units: Subjects			
African American/African Heritage	0	1	0
White	8	22	52
Central/South Asian Heritage	0	0	0
Japanese/East Asian Heritage/South East Asian	2	0	0

Reporting group values	Total		
Number of subjects	101		
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	50		
Male	51		
Race Units: Subjects			
African American/African Heritage	3		
White	95		
Central/South Asian Heritage	1		
Japanese/East Asian Heritage/South East Asian	2		

End points

End points reporting groups

Reporting group title	Phase I: 21-Day Cycle Placebo
Reporting group description:	
Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase I: 21-Day Cycle Eltrombopag 100 mg
Reporting group description:	
Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered eltrombopag 100 milligrams (mg) once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase I: 28-Day Cycle Placebo
Reporting group description:	
Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase I: 28-Day Cycle Eltrombopag 100 mg
Reporting group description:	
Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.	
Reporting group title	Phase II: Placebo
Reporting group description:	
Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).	
Reporting group title	Phase II: Eltrombopag 100 mg
Reporting group description:	
Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).	

Primary: Number of participants with any adverse event (AE) or serious adverse event (SAE): Pre-therapy, On-therapy + 30 days and Post-therapy in Phase I

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE): Pre-therapy, On-therapy + 30 days and Post-therapy in Phase I[1][2]
End point description:	
AEs are coded using the standard Medical Dictionary for Regulatory Activities (MedDRA) and were graded by the investigator according to National Cancer Institute (NCI) Common Terminology Criteria for AEs (CTCAE), version 4.0. AE is any untoward medical occurrence temporally associated with the use of a medicinal product (MP), whether or not considered related to the MP. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a MP. For marketed MPs, this also includes failure to produce expected benefits, abuse, or misuse. SAE event is any untoward medical occurrence that, at any dose: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or, is a congenital anomaly/birth defect.	
End point type	Primary
End point timeframe:	
From Cycle 1, Day 1 (C1D1) until at least 30 days post-investigational product discontinuation (longer for AEs considered related to study participation)	

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: There are no statistical data to report.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[3]	9[4]	4[5]	10[6]
Units: Participants				
Any AE Pre-therapy	3	8	4	9
Any SAE Pre-therapy	1	0	0	1
Any AE On-therapy+30 days	3	9	3	10
Any SAE On-therapy+30 days	1	5	1	2
Any AE Post-therapy	0	0	0	3
Any SAE Post-therapy	0	0	0	1
Treatment-related AEs On-therapy+30 days	2	3	1	6
>=Grade 3 AEs On-therapy+30 days	2	7	2	3
Liver AEs On-therapy+30 days	0	2	0	2
Renal AEs On-therapy+30 days	0	3	2	0
Thromboembolic events On-therapy+30 days	0	2	0	1
Cardiac AEs On-therapy+30 days	0	1	1	1
Neutropenia On-therapy+30 days	3	4	2	5
Anemia On-therapy+30 days	1	4	1	4
Thrombocytopenia On-therapy+30 days	2	3	3	3
Leukopenia On-therapy+30 days	1	2	2	3
Thrombocytosis On-therapy+30 days	2	2	1	2
Platelet count increased On-therapy+30 days	0	0	0	3

Notes:

[3] - Safety Population

[4] - Safety Population

[5] - Safety Population

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with indicated maximum toxicity grades for the indicated hematology parameters, at anytime post-Baseline in Phase I

End point title	Number of participants with indicated maximum toxicity grades for the indicated hematology parameters, at anytime post-Baseline in Phase I[7][8]

End point description:

Hematology parameters with a related NCI CTCAE (version 4.0) toxicity grading were summarized by toxicity grade at each scheduled assessment, the maximum toxicity grade reached by a participant post-Baseline was summarized. Hematology parameters included hemoglobin (increased), hemoglobin (anemia), lymphocytes (increased), lymphocytes (decreased), total absolute neutrophil count (ANC),

platelets (PLT) and white blood cells (WBC). The Baseline value is defined as the value reported immediately prior to the administration of the first dose of chemotherapy in Cycle 1. Post-Baseline is defined as any time after the first dose of chemotherapy in Cycle 1 up to and including all follow-up visits. Only those participant available at the indicated time points were analyzed (represented by n=X,X,X,X in the category titles).

End point type	Primary

End point timeframe:

After Baseline (C1D1), on-treatment and 30 day follow-up

Notes:

[7] - 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: There are no statistical data to report.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[9]	9[10]	4[11]	10[12]
Units: Participants				
Hemoglobin (Increased), Grade 0, n=3,9,4,10	3	9	4	10
Hemoglobin (Anemia), Grade 1, n=3,9,4,10	2	1	0	3
Hemoglobin (Anemia), Grade 2, n=3,9,4,10	0	6	2	4
Hemoglobin (Anemia), Grade 3, n=3,9,4,10	1	2	2	3
Lymphocytes (Increased), Grade 0, n=3,9,4,10	3	8	4	10
Lymphocytes (Increased), Grade 2, n=3,9,4,10	0	1	0	0
Lymphocytes (Decreased), Grade 0, n=3,9,4,10	1	1	0	3
Lymphocytes (Decreased), Grade 1, n=3,9,4,10	0	2	0	0
Lymphocytes (Decreased), Grade 2, n=3,9,4,10	1	1	1	4
Lymphocytes (Decreased), Grade 3, n=3,9,4,10	1	5	3	2
Lymphocytes (Decreased), Grade 4, n=3,9,4,10	0	0	0	1
Total ANC, Grade 0, n=1,2,1,2	0	2	1	0
Total ANC, Grade 1, n=1,2,1,2	1	0	0	2
PLT, Grade 0, n=3,9,4,10	0	1	0	2
PLT, Grade 1, n=3,9,4,10	0	1	1	3
PLT, Grade 2, n=3,9,4,10	0	3	1	3
PLT, Grade 3, n=3,9,4,10	1	2	2	1
PLT, Grade 4, n=3,9,4,10	2	2	0	1
WBC, Grade 0, n=3,9,4,10	0	0	1	2
WBC, Grade 1, n=3,9,4,10	0	1	0	2
WBC, Grade 2, n=3,9,4,10	2	2	1	2
WBC, Grade 3, n=3,9,4,10	1	5	2	3
WBC, Grade 4, n=3,9,4,10	0	1	0	1

Notes:

[9] - Safety Population

[10] - Safety Population

[11] - Safety Population

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with indicated maximum toxicity grades for the indicated clinical chemistry laboratory parameters, at anytime post-Baseline in Phase I

End point title	Number of participants with indicated maximum toxicity grades for the indicated clinical chemistry laboratory parameters, at anytime post-Baseline in Phase I[13][14]

End point description:

Clinical chemistry laboratory parameters with a related NCI CTCAE (version 4.0) toxicity grading were summarized by toxicity grade at each scheduled assessment. Clinical chemistry laboratory parameters included albumin (Alb), urea/blood urea nitrogen (BUN), creatinine, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin (TB), direct bilirubin (DB) and international normalized ratio/Prothrombin time (PT). The Baseline value is defined as the value reported immediately prior to the administration of the first dose of chemotherapy in Cycle 1. Post-Baseline is defined as any time after the first dose of chemotherapy in Cycle 1 up to and including all follow-up visits. Only those participants available at the indicated time points were analyzed (represented by n=X,X,X,X in the category titles).

End point type	Primary

End point timeframe:

After Baseline (C1D1), on-treatment and 30 day follow-up

Notes:

[13] - 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: There are no statistical data to report.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[15]	9[16]	4[17]	10[18]
Units: Participants				
Alb, Grade 0, n=3,9,4,10	2	4	0	4
Alb, Grade 1, n=3,9,4,10	1	2	2	5
Alb, Grade 2, n=3,9,4,10	0	3	1	1
Alb, Grade 3, n=3,9,4,10	0	0	1	0
ALP, Grade 0, n=3,9,4,10	2	3	3	6
ALP, Grade 1, n=3,9,4,10	1	5	1	1
ALP, Grade 2, n=3,9,4,10	0	1	0	2
ALP, Grade 3, n=3,9,4,10	0	0	0	1
ALT, Grade 0, n=3,9,4,10	2	3	3	4
ALT, Grade 1, n=3,9,4,10	1	4	1	5
ALT, Grade 2, n=3,9,4,10	0	2	0	0

ALT, Grade 3, n=3,9,4,10	0	0	0	1
AST, Grade 0, n=3,9,4,10	2	4	2	5
AST, Grade 1, n=3,9,4,10	1	3	2	3
AST, Grade 2, n=3,9,4,10	0	1	0	1
AST, Grade 3, n=3,9,4,10	0	1	0	1
TB, Grade 0, n=3,9,4,10	3	5	3	8
TB, Grade 1, n=3,9,4,10	0	2	0	0
TB, Grade 2, n=3,9,4,10	0	2	1	0
TB, Grade 3, n=3,9,4,10	0	0	0	2
Ca (hypercalcemia), Grade 0, n=3,9,4,10	3	8	4	10
Ca (hypercalcemia), Grade 1, n=3,9,4,10	0	1	0	0
Ca (hypercalcemia), Grade 2, n=3,9,4,10	0	0	0	0
Ca (hypercalcemia), Grade 3, n=3,9,4,10	0	0	0	0
Ca (hypocalcemia), Grade 0, n=3,9,4,10	2	7	3	9
Ca (hypocalcemia), Grade 1, n=3,9,4,10	1	1	0	0
Ca (hypocalcemia), Grade 2, n=3,9,4,10	0	1	1	1
Ca (hypocalcemia), Grade 3, n=3,9,4,10	0	0	0	0
Creatinine, Grade 0, n=3,9,4,10	3	7	4	9
Creatinine, Grade 1, n=3,9,4,10	0	1	0	1
Creatinine, Grade 2, n=3,9,4,10	0	1	0	0
Creatinine, Grade 3, n=3,9,4,10	0	0	0	0
Glu (hyperglycemia), Grade 0, n=3,9,4,10	2	3	1	2
Glu (hyperglycemia), Grade 1, n=3,9,4,10	0	4	2	4
Glu (hyperglycemia), Grade 2, n=3,9,4,10	1	2	1	4
Glu (hyperglycemia), Grade 3, n=3,9,4,10	0	0	0	0
Glu (hypoglycemia), Grade 0, n=3,9,4,10	3	8	4	8
Glu (hypoglycemia), Grade 1, n=3,9,4,10	0	0	0	1
Glu (hypoglycemia), Grade 2, n=3,9,4,10	0	1	0	1
Glu (hypoglycemia), Grade 3, n=3,9,4,10	0	0	0	0
K (hyperkalemia), Grade 0, n=3,9,4,10	1	8	3	9
K (hyperkalemia), Grade 1, n=3,9,4,10	2	1	0	0
K (hyperkalemia), Grade 2, n=3,9,4,10	0	0	1	1
K (hyperkalemia), Grade 3, n=3,9,4,10	0	0	0	0
K (hypokalemia), Grade 0, n=3,9,4,10	2	5	3	7
K (hypokalemia), Grade 1, n=3,9,4,10	1	3	1	3
K (hypokalemia), Grade 2, n=3,9,4,10	0	0	0	0
K (hypokalemia), Grade 3, n=3,9,4,10	0	1	0	0
Na (hypernatremia), Grade 0, n=3,9,4,10	2	9	3	10
Na (hypernatremia), Grade 1, n=3,9,4,10	1	0	1	0
Na (hypernatremia), Grade 2, n=3,9,4,10	0	0	0	0
Na (hypernatremia), Grade 3, n=3,9,4,10	0	0	0	0

Na (hyponatremia), Grade 0, n=3,9,4,10	2	4	2	5
Na (hyponatremia), Grade 1, n=3,9,4,10	1	4	0	5
Na (hyponatremia), Grade 2, n=3,9,4,10	0	0	0	0
Na (hyponatremia), Grade 3, n=3,9,4,10	0	1	2	0

Notes:

[15] - Safety Population

[16] - Safety Population

[17] - Safety Population

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with a change from Baseline in creatinine of >=26.5 micromoles/liter (UMOL/L) in Phase I

End point title	Number of participants with a change from Baseline in creatinine of >=26.5 micromoles/liter (UMOL/L) in Phase I[19][20]

End point description:

The number of participants with at least 1 change from Baseline in creatinine, with an increase >=26.5 UMOL/L are reported. Creatinine clearance is estimated using the Cockcroft-Gault formula which is a method to approximate kidney function. The Baseline value is defined as the value reported immediately prior to the administration of the first dose of chemotherapy in Cycle 1.

End point type	Primary

End point timeframe:

After Baseline (C1D1), on-treatment and 30 day follow-up

Notes:

[19] - 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: There are no statistical data to report.

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[21]	9[22]	4[23]	10[24]
Units: Participants	0	3	1	2

Notes:

[21] - Safety Population

[22] - Safety Population

[23] - Safety Population

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of the participants with Eastern Cooperative Oncology Group (ECOG) performance status scores at the indicated time points in Phase I

End point title	Number of the participants with Eastern Cooperative Oncology Group (ECOG) performance status scores at the indicated time points in Phase I[25][26]

End point description:

ECOG-Zubrod scores for the performance status are defined as follows: Score 0: Fully active, 1: restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, 2: ambulatory and capable of all self-care but unable to carry out any work activities, 3: capable of only limited self-care, 4: completely disabled, 5: dead. The data is presented for the participants with the ECOG performance score at the indicated time points during the study. Not available (NA) is presented as "99999".

End point type	Primary

End point timeframe:

Screening, C1D1, C2D1, C2D8, C2D15, C3D1, C4D1, C4D22, C5D1, C5D8, C6D1, C6D15

Notes:

[25] - 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: There are no statistical data to report.

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[27]	9[28]	4[29]	10[30]
Units: Participants				
Screening, Score 0, n=3,9,4,10	3	5	1	3
Screening, Score 1, n=3,9,4,10	0	3	3	7
Screening, Score 2, n=3,9,4,10	0	1	0	0
Screening, Score 3, n=3,9,4,10	0	0	0	0
C1D1, Score 0, n=3,9,4,10	3	5	2	3
C1D1, Score 1, n=3,9,4,10	0	3	2	7
C1D1, Score 2, n=3,9,4,10	0	1	0	0
C1D1, Score 3, n=3,9,4,10	0	0	0	0
C2D1, Score 0, n=3,8,4,10	1	3	2	2
C2D1, Score 1, n=3,8,4,10	1	4	1	8
C2D1, Score 2, n=3,8,4,10	1	1	1	0
C2D1, Score 3, n=3,8,4,10	0	0	0	0
C2D8, Score 0, n=1,0,1,0	1	99999	0	99999
C2D8, Score 1, n=1,0,1,0	0	99999	0	99999
C2D8, Score 2, n=1,0,1,0	0	99999	1	99999
C2D8, Score 3, n=1,0,1,0	1	99999	0	99999
C2D15, Score 0, n=0,1,0,1	99999	0	99999	0
C2D15, Score 1, n=0,1,0,1	99999	0	99999	1
C2D15, Score 2, n=0,1,0,1	99999	1	99999	0
C2D15, Score 3, n=0,1,0,1	99999	0	99999	0
C3D1, Score 0, n=2,6,2,7	1	2	2	4
C3D1, Score 1, n=2,6,2,7	1	2	0	3
C3D1, Score 2, n=2,6,2,7	0	1	0	0
C3D1, Score 3, n=2,6,2,7	0	1	0	0

C4D1, Score 0, n=2,6,1,7	1	1	0	4
C4D1, Score 1, n=2,6,1,7	1	3	1	3
C4D1, Score 2, n=2,6,1,7	0	1	0	0
C4D1, Score 3, n=2,6,1,7	0	1	0	0
C4D22, Score 0, n=0,0,0,1	99999	99999	99999	0
C4D22, Score 1, n=0,0,0,1	99999	99999	99999	0
C4D22, Score 2, n=0,0,0,1	99999	99999	99999	1
C4D22, Score 3, n=0,0,0,1	99999	99999	99999	0
C5D1, Score 0, n=1,3,1,4	0	0	0	2
C5D1, Score 1, n=1,3,1,4	1	1	1	2
C5D1, Score 2, n=1,3,1,4	0	1	0	0
C5D1, Score 3, n=1,3,1,4	0	1	0	0
C5D8, Score 0, n=0,1,0,0	99999	0	99999	99999
C5D8, Score 1, n=0,1,0,0	99999	0	99999	99999
C5D8, Score 2, n=0,1,0,0	99999	0	99999	99999
C5D8, Score 3, n=0,1,0,0	99999	1	99999	99999
C6D1, Score 0, n=1,1,1,4	0	1	0	2
C6D1, Score 1, n=1,1,1,4	1	0	1	2
C6D1, Score 2, n=1,1,1,4	0	0	0	0
C6D1, Score 3, n=1,1,1,4	0	0	0	0
C6D15, Score 0, n=0,0,0,1	99999	99999	99999	0
C6D15, Score 1, n=0,0,0,1	99999	99999	99999	1
C6D15, Score 2, n=0,0,0,1	99999	99999	99999	0
C6D15, Score 3, n=0,0,0,1	99999	99999	99999	0

Notes:

[27] - Safety Population

[28] - Safety Population

[29] - Safety Population

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with electrocardiogram (ECG) findings at anytime post-Baseline in Phase I

End point title	Number of participants with electrocardiogram (ECG) findings at anytime post-Baseline in Phase I[31][32]

End point description:

A single safety 12-lead ECG was performed using a standard 12-lead ECG machine at screening and post-dose on C2D4. Three further ECGs were carried out at C2D8, C5D8 and C6D15. Change in ECG findings were categorized as 'Clinically significant change: favorable', 'No change or insignificant change' or 'Clinically significant change (CSC): unfavorable' as determined by the investigator. The Baseline value is defined as the value reported immediately prior to the administration of the first dose of chemotherapy in Cycle 1. Any time post-Baseline is defined by counting the participants under the worst result experienced post-Baseline. The best to worst order is 'Clinically significant change: favorable', 'No change or insignificant change', and then 'Clinically significant change (CSC): unfavorable. Only those participants available at the indicated time points were analyzed (represented by n=X,X,X,X in the category titles).

End point type	Primary

End point timeframe:

C2D4, C2D8, C5D8, C6D15

Notes:

[31] - 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: There are no statistical data to report.

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[33]	9[34]	4[35]	10[36]
Units: Participants				
No change or insignificant change n=3,9,3,8	3	8	3	7
CSC: unfavorable, n=3,9,3,8	0	1	0	1

Notes:

[33] - Safety Population

[34] - Safety Population

[35] - Safety Population

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Mean Day 1 scheduled pre-chemotherapy platelet count evaluated across Cycles 1 to 6 in Phase II

End point title	Mean Day 1 scheduled pre-chemotherapy platelet count evaluated across Cycles 1 to 6 in Phase II[37]

End point description:

Scheduled pre-chemotherapy platelet count is defined within each cycle as the platelet count assessment on which the decision to give or delay chemotherapy was made. This was averaged for each participant across Cycles 1 to 6 and a natural log transformation was applied to the average. The log-transformed values were compared between eltrombopag and placebo groups using an analysis of covariance (ANCOVA) model adjusting for cycle duration (21-day vs. 28-day), Baseline loge(platelet count) and part of study (part 1 or 2 of phase II). Only those participants available at indicated time points were analyzed (represented by n=X,X).

End point type	Primary

End point timeframe:

Day 1 (averaged across cycles 1 to 6)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[38]	48[39]		
Units: Giga (10^9) cells per liter (Gi/L)				
geometric mean (geometric coefficient of variation)	193.34 (± 54.5)	246.2 (± 49.8)		

Notes:

[38] - Intent-to Treat (ITT) Population: all randomized participants.

[39] - Intent-to Treat (ITT) Population: all randomized participants.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase II: Placebo v Phase II: Eltrombopag 100 mg
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	ANCOVA
Parameter estimate	Percent difference
Point estimate	21.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	52.5

Secondary: Average pre-chemotherapy platelet count at the indicated time points in Phase I

End point title	Average pre-chemotherapy platelet count at the indicated time points in Phase I[40]

End point description:

Pre-chemotherapy platelet count is defined for Cycle 1 as the platelet count (from central laboratory data) immediately preceding the first dose of chemotherapy within Cycle 1. For all subsequent cycles it is defined as the platelet count (from central laboratory data) immediately preceding, but limited to within 2 days prior to the first dose of chemotherapy at Day 1. For 21-Day Cycle, the chemotherapy cycle consisted of 21 days and for 28-Day Cycle, the chemotherapy cycle consisted of 28 days. Blood samples were collected to estimate platelet count at the following time points: 21-Day Cycle; Days 1 and 8 of Cycles 1 to 6. 28-Day Cycle; Days 1, 8 and 15 of Cycles 1 to 6. Only those participants available at indicated time points were analyzed (represented by n=X, X, X, X). (Not available (NA)" is presented as "99999").

End point type	Secondary

End point timeframe:

C1D1, C1D8, C1D15, C2D1, C2D8, C2D15, C3D1, C3D8, C3D15, C4D1,C4D8, C4D15, C5D1,C5D8, C5D15, C6D1,C6D8 and C6D15

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[41]	9[42]	4[43]	10[44]
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)				
C1 D1, n=3,9,4,9	239.3 (± 75.87)	244.8 (± 48.47)	223.8 (± 79.96)	207.7 (± 65.51)
C1 D8, n=3,6,3,9	180.7 (± 65.03)	143.8 (± 33.88)	144 (± 44.17)	135.6 (± 52.52)
C1 D15, n=0,0,2, 6	99999 (± 99999)	99999 (± 99999)	135 (± 84.85)	97.5 (± 39.15)
C2 D1, n=2,9,4,8	443 (± 168.29)	545.8 (± 131.66)	284.8 (± 84.11)	473.3 (± 117.07)
C2 D8, n=2,7,3,9	221 (± 94.75)	335.6 (± 134.06)	163.3 (± 35.3)	333 (± 146.59)
C2 D15, n=0,0,2,6	99999 (± 99999)	99999 (± 99999)	80.5 (± 0.71)	142.7 (± 63.14)
C3 D1, n=2,5,2,7	464 (± 36.77)	484.6 (± 188.16)	290.5 (± 180.31)	435.4 (± 145.57)
C3 D8, n=2,6,2,5	285 (± 39.6)	292.2 (± 161.11)	293 (± 199.4)	465.2 (± 260.2)
C3 D15, n=0,0,2,5	99999 (± 99999)	99999 (± 99999)	92 (± 45.25)	183.4 (± 119.12)
C4 D1, n=1,6,1,6	298 (± 99999)	394.7 (± 154.28)	609 (± 99999)	388.3 (± 166.07)
C4 D8, n=1,5,1,6	261 (± 99999)	249.8 (± 122.29)	335 (± 99999)	366.5 (± 143.75)
C4 D15, n=0,0,1,6	99999 (± 99999)	99999 (± 99999)	86 (± 99999)	169.8 (± 120.56)
C5 D1, n=1,2,1,4	245 (± 99999)	529.5 (± 340.12)	337 (± 99999)	406 (± 174.89)
C5 D8, n=1,1,1,4	144 (± 99999)	123 (± 99999)	311 (± 99999)	403.5 (± 195.31)
C5 D15, n=0,0,1,4	99999 (± 99999)	99999 (± 99999)	75 (± 99999)	140.5 (± 42.93)
C6 D1, n=1,1,1,3	512 (± 99999)	123 (± 99999)	440 (± 99999)	360.3 (± 133.45)
C6 D8, n=1,1,0,3	251 (± 99999)	137 (± 99999)	99999 (± 99999)	428 (± 210.71)
C6 D15, n=0,0,1,2	99999 (± 99999)	99999 (± 99999)	113 (± 99999)	101 (± 48.08)

Notes:

[41] - Safety Population

[42] - Safety Population

[43] - Safety Population

[44] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Average within-subject central laboratory platelet count prior to scheduled chemotherapy across Cycles 2 to 6 in Phase I

End point title	Average within-subject central laboratory platelet count prior to scheduled chemotherapy across Cycles 2 to 6 in Phase I[45]

End point description:

Within-subject platelet count for each participant was calculated by summing up the visit platelet counts from each of Cycles 1 to 6 and dividing it by the number of cycles in which the participant had data. The average within a treatment group was calculated by summing up the values from each participant within the treatment 21-Day Cycle and dividing it by the number of participants. These platelet counts are different from the pre-chemotherapy platelet counts for cycles where the chemotherapy dose was delayed. Average within-subject central laboratory platelet count prior to scheduled chemotherapy across Cycles 2 to 6 are summarized. Blood samples were collected on Days 1 and 8 of Cycles 2 to 6 for 21-Day Cycle and on Days 1, 8 and 15 from Cycles 2 to 6 for 28-Day Cycle to estimate the average within subject platelet count prior to scheduled chemotherapy. Only those participants available at the indicated time points were analyzed (represented by n=X,X,X,X in the category titles).

End point type	Secondary

End point timeframe:

Day 1 (averaged across Cycles 2 to 6), Day 8 (averaged across Cycles 2 to 6)

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[46]	9[47]	4[48]	10[49]
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)				
G+Cb, Day 1, n=1,3,0,0	296.8 (± 99999)	275 (± 144.253)	99999 (± 99999)	99999 (± 99999)
G+Cb, Day 8, n=1,3,0,0	235 (± 99999)	232.1 (± 77.329)	99999 (± 99999)	99999 (± 99999)
G+Cis, Day 1, n=2,6,0,0	322.5 (± 82.731)	526 (± 86.408)	99999 (± 99999)	99999 (± 99999)
G+Cis, Day 8, n=2,6,0,0	326.85 (± 119.006)	296.75 (± 119.342)	99999 (± 99999)	99999 (± 99999)
Gm, Day1, n=0,0,4,9	99999 (± 99999)	99999 (± 99999)	309.2 (± 123.133)	442.79 (± 114.593)
Gm, Day8, n=0,0,4,10	99999 (± 99999)	99999 (± 99999)	204.2 (± 80.822)	355.09 (± 148.539)
Gm, Day15, n=0,0,3,10	99999 (± 99999)	99999 (± 99999)	75.37 (± 18.292)	164.24 (± 94.905)

Notes:

[46] - Safety Population (Not available (NA)" is presented as "99999")

[47] - Safety Population (Not available (NA)" is presented as "99999")

[48] - Safety Population (Not available (NA)" is presented as "99999")

[49] - Safety Population (Not available (NA)" is presented as "99999")

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet count nadir for each chemotherapy cycle in Phase I

End point title	Platelet count nadir for each chemotherapy cycle in Phase I[50]

End point description:

Platelet nadir is defined as the lowest platelet count (from central laboratory data) reported after the first dose of chemotherapy within each cycle. Platelet count nadir is defined for each cycle. For 21-Day Cycle, the chemotherapy cycle consisted of 21 days and for 28-Day Cycle, the chemotherapy cycle

consisted of 28 days. Blood samples were collected to estimate platelet nadir count at the following time points: 21-Day Cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 and 2, at Days 1, 4, 8, 15 and 17 of Cycle 3 to 6. 28-Day Cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6. Only those participants available at indicated time points were analyzed (represented by n=X, X, X, X). (Not available (NA)" is presented as "99999")

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[51]	9[52]	4[53]	10[54]
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)				
Cycle 1, n=3,9,4,10	30.67 (± 20.404)	106.56 (± 113.338)	60.5 (± 22.664)	99 (± 75.7)
Cycle 2, n=2,9,4,10	66 (± 9.899)	122.44 (± 115.794)	103.5 (± 62.952)	135.5 (± 73.951)
Cycle 3, n=2,7,2,7	47 (± 4.243)	88.29 (± 71.807)	78.5 (± 43.134)	151 (± 111.946)
Cycle 4, n=2,6,1,7	76.5 (± 4.95)	87.5 (± 79.173)	86 (± 99999)	142.86 (± 91.908)
Cycle 5, n=1,2,1,4	14 (± 99999)	148 (± 182.434)	75 (± 99999)	113.25 (± 34.683)
Cycle 6, n=1,1,1,4	24 (± 99999)	13 (± 99999)	110 (± 99999)	122.75 (± 63.163)

Notes:

[51] - Safety Population

[52] - Safety Population

[53] - Safety Population

[54] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Central Laboratory average daily area under the curve platelet-time course across Cycles 2 to 6 in Phase I

End point title	Central Laboratory average daily area under the curve platelet-time course across Cycles 2 to 6 in Phase I[55]

End point description:

Average daily area under the curve platelet-time course is defined as the area-under-the-curve (calculated using the trapezoidal rule) divided by total duration. It was calculated across all cycles. For 21-Day Cycle, the chemotherapy cycle consisted of 21 days and for 28-Day Cycle, the chemotherapy cycle consisted of 28 days. Blood samples were collected to estimate thrombocytes at the following time points: 21-Day Cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-Day Cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6.

End point type	Secondary

End point timeframe:

All assessments from Cycle 2 Day 1 to last assessment in Cycle 6

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[56]	9[57]	4[58]	10[59]
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)	260.97 (± 67.581)	307.59 (± 95.11)	183.68 (± 55.366)	291.18 (± 99.718)

Notes:

[56] - Safety Population

[57] - Safety Population

[58] - Safety Population

[59] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with thrombocytopenia of Grade 1, 2, 3 or 4 across all the chemotherapy cycles in Phase I, using central laboratory platelet count

End point title	Number of participants with thrombocytopenia of Grade 1, 2, 3 or 4 across all the chemotherapy cycles in Phase I, using central laboratory platelet count[60]

End point description:

As per the CTCAE version 4.0, par. with a platelet count <LLN but >=75 x 10^9/L (Gi/L) were considered to have Grade 1 thrombocytopenia; par. with a platelet count <75Gi/L, but >=50Gi/L were considered to have Grade 2 thrombocytopenia; par. with a platelet count <50Gi/L, but >=25Gi/L were considered to have Grade 3 thrombocytopenia and par. with a platelet count <25Gi/L were considered to have Grade 4 thrombocytopenia. Blood samples were collected to estimate thrombocytes at the following time points: For 21-Day Cycle, the chemotherapy cycle consisted of 21 days and for 28-Day Cycle, the chemotherapy cycle consisted of 28 days. Blood samples were collected to estimate thrombocytes at the following time points: 21-Day Cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-Day Cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6. Par. experiencing thrombocytopenia (Platelets <150Gi/L) at least once within a cycle are presented in the category title as n=X,X,X,X.

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[61]	9[62]	4[63]	10[64]
Units: Participants				
Grade 1, n=3,9,4,10	0	2	1	3
Grade 2, n=3,9,4,10	0	3	1	4
Grade 3, n=3,9,4,10	1	1	1	0
Grade 4, n=3,9,4,10	1	2	0	0
Grade 0 / None, n=3,9,4,10	1	1	1	3

Notes:

[61] - Safety Population

[62] - Safety Population

[63] - Safety Population

[64] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum duration of thrombocytopenia across Cycles 2 to 6 in Phase I, estimated using central laboratory platelet counts

End point title	Maximum duration of thrombocytopenia across Cycles 2 to 6 in Phase I, estimated using central laboratory platelet counts[65]

End point description:

Duration of thrombocytopenia is defined as a period of time in days from the first report of a platelet count with NCI CTCAE Grade 1-4 until the first subsequent report of a platelet count no longer meeting those criteria, regardless of rescue medication usage. It was assessed between Day 1 of Cycle 2 and up to and including any Conclusion/Early Withdrawal visit assigned to the same cycle for participants completing up to 6 cycles, and between Day 1 of Cycle 2 and up to and including the end of Cycle 6 for participants continuing beyond 6 cycles. The chemotherapy cycle for 21-Day Cycle was 21 days and for 28-Day Cycle was 28 days. Blood samples were collected to estimate thrombocytes at the following time points: 21-Day Cycle; Days 1, 4, 8, 15 and 17 of Cycles 2 to 6. 28-Day Cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 2 to 6.(Participants experiencing thrombocytopenia with subsequent increase in platelet count to >=150Gi/L are included)

End point type	Secondary

End point timeframe:

Cycle 2 to Cycle 6

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[66]	8[67]	3[68]	7[69]
Units: Days				
arithmetic mean (standard deviation)	11 (± 4.24)	10.6 (± 5.63)	14.7 (± 7.77)	13.4 (± 5.06)

Notes:

[66] - Safety Population

[67] - Safety Population

[68] - Safety Population

[69] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Central Laboratory platelet count for time taken to reach platelet nadir for each chemotherapy cycle in Phase I

End point title	Central Laboratory platelet count for time taken to reach platelet nadir for each chemotherapy cycle in Phase I[70]

End point description:

Platelet nadir is defined within each cycle as the lowest platelet count reported after the Day 1 chemotherapy dose. The time taken to reach platelet nadir is defined within each cycle. For 21-Day Cycle, the chemotherapy cycle consisted of 21 days and for 28-Day Cycle, the chemotherapy cycle consisted of 28 days. Blood samples were collected to estimate platelet nadir count at the following time points: 21-Day Cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-Day Cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6. Only those participants available at indicated time points were analyzed (represented by n=X, X, X, X). (Not available (NA)" is presented as "99999").

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[71]	9[72]	4[73]	10[74]
Units: Days				
arithmetic mean (standard deviation)				
Cycle 1, n=3,9,4,10	15.7 (± 0.58)	11.4 (± 5.53)	13.8 (± 6.13)	13.8 (± 4.73)
Cycle 2, n=2,9,4,10	15 (± 1.41)	12.9 (± 4.68)	14 (± 5.72)	19.2 (± 4.42)
Cycle 3, n=2,7,2,7	15 (± 1.41)	12.9 (± 3.02)	23.5 (± 0.71)	17.6 (± 4.5)
Cycle 4, n=2,6,1,7	14 (± 0)	13.5 (± 3.33)	14 (± 99999)	17.4 (± 6.16)
Cycle 5, n=1,2,1,4	15 (± 99999)	11.5 (± 6.36)	14 (± 99999)	21.5 (± 1)
Cycle 6, n=1,1,1,4	16 (± 99999)	14 (± 99999)	23 (± 99999)	15.5 (± 5.2)

Notes:

[71] - Safety Population

[72] - Safety Population

[73] - Safety Population

[74] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to recovery from platelet nadir for each chemotherapy cycle in Phase I, estimated using central laboratory platelet counts

End point title	Time to recovery from platelet nadir for each chemotherapy cycle in Phase I, estimated using central laboratory platelet counts[75]

End point description:

Platelet nadir is defined within each cycle as the lowest platelet count reported after the Day 1 chemotherapy dose. Time to recovery (TR) (>100Gi/L or >150Gi/L) from platelet nadir is defined within each cycle as the time in days from the platelet nadir to the time at which platelet count returns to >=100Gi/L or >=150Gi/L within the same cycle or up to and including Day 1 of the next cycle. For the last cycle in the study, time to recovery was calculated in the same manner but up to and including any Conclusion/Early Withdrawal visit which has been assigned to the same cycle. For 21-Day Cycle, the chemotherapy cycle consisted of 21 days and for 28-Day Cycle, the chemotherapy cycle consisted of 28 days. Blood samples were collected to estimate platelet count at: 21-Day Cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-Day Cycle; Days 1, 4, 8, 15, 22, and 24 of Cycles 1 to 6. Only those participants available at indicated time points were analyzed (represented by n=X, X, X, X).

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6 (Not available (NA)" is presented as "99999")

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[76]	9[77]	4[78]	10[79]
Units: Days				
arithmetic mean (standard deviation)				
TR(<100Gi/L to >=100Gi/L), Cycle 1, n=3,6,4,7	5.3 (± 0.58)	7.2 (± 2.56)	7 (± 0)	7.7 (± 2.87)
TR(<100Gi/L to >=100Gi/L), Cycle 2, n=2,5,3,4	6.5 (± 2.12)	6.6 (± 3.65)	6 (± 4)	7 (± 5.1)
TR(<100Gi/L to >=100Gi/L), Cycle 3, n=1,4,0,2	7 (± 99999)	8.5 (± 3.7)	99999 (± 99999)	6 (± 1.41)
TR(<100Gi/L to >=100Gi/L), Cycle 4, n=1,4,1,2	2 (± 99999)	6.5 (± 5.2)	14 (± 99999)	5 (± 2.83)
TR(<100Gi/L to >=100Gi/L), Cycle 5, n=1,1,1,1	5 (± 99999)	5 (± 99999)	9 (± 99999)	7 (± 99999)
TR(<100Gi/L to >=100Gi/L), Cycle 6, n=0,1,0,0	99999 (± 99999)	7 (± 99999)	99999 (± 99999)	99999 (± 99999)
TR(<150Gi/L to >=150Gi/L), Cycle 1, n=3,7,4,8	5.3 (± 0.58)	7.6 (± 2.57)	7 (± 0)	8.5 (± 3.46)
TR(<150Gi/L to >=150Gi/L), Cycle 2, n=2,4,3,5	6.5 (± 2.12)	7.8 (± 2.99)	9 (± 4.36)	9.4 (± 4.28)
TR(<150Gi/L to >=150Gi/L), Cycle 3, n=1,6,1,5	7 (± 99999)	8 (± 2.97)	7 (± 99999)	6.2 (± 1.1)
TR(<150Gi/L to >=150Gi/L), Cycle 4, n=1,4,1,4	8 (± 99999)	7.8 (± 4.27)	14 (± 99999)	8.3 (± 3.95)
TR(<150Gi/L to >=150Gi/L), Cycle 5, n=1,0,1,3	5 (± 99999)	99999 (± 99999)	14 (± 99999)	4.7 (± 2.52)
TR(<150Gi/L to >=150Gi/L), Cycle 6, n=0,0,1,0	99999 (± 99999)	99999 (± 99999)	5 (± 99999)	99999 (± 99999)

Notes:

[76] - Safety Population

[77] - Safety Population

[78] - Safety Population

[79] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Dose intensity of gemcitabine plus cisplatin (G+Cis)/gemcitabine plus carboplatin (G+Cb) and gemcitabine across chemotherapy Cycles 1 to 6 in Phase I

End point title	Dose intensity of gemcitabine plus cisplatin (G+Cis)/gemcitabine plus carboplatin (G+Cb) and gemcitabine across chemotherapy Cycles 1 to 6 in Phase I[80]

End point description:

Dose intensity of chemotherapy is defined as the actual dose of chemotherapy given as a percentage of the scheduled C1D1/C1D8 dose, as applicable, within this study: Cycle Dose Intensity (%) = Total Actual dose (mg/m^2) within Cycle *100/ Total Scheduled dose (mg/m^2) in Cycle 1; wherein Actual Dose (mg/m^2) = Actual dose (mg)/Body Surface Area reported on electronic case report form (eCRF). (Not available (NA)" is presented as "99999").

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[81]	9[82]	4[83]	10[84]
Units: Dose Intensity (%)				
arithmetic mean (standard deviation)				
G+Cis, Gemcitabine, Cycle 1, n=2,5,0,0	100 (± 0)	99.8 (± 0.45)	99999 (± 99999)	99999 (± 99999)
G+Cis, Gemcitabine, Cycle 2, n=1,5,0,0	100 (± 99999)	92.8 (± 24.83)	99999 (± 99999)	99999 (± 99999)
G+Cis, Gemcitabine, Cycle 3, n=1,4,0,0	100 (± 99999)	104.3 (± 8.5)	99999 (± 99999)	99999 (± 99999)
G+Cis, Gemcitabine, Cycle 4, n=1,3,0,0	100 (± 99999)	83.3 (± 28.87)	99999 (± 99999)	99999 (± 99999)
G+Cis, Cisplatin, Cycle 1, n=2,6,0,0	100 (± 0)	100.3 (± 1.03)	99999 (± 99999)	99999 (± 99999)
G+Cis, Cisplatin, Cycle 2, n=1,6,0,0	100 (± 99999)	102.8 (± 6.05)	99999 (± 99999)	99999 (± 99999)
G+Cis, Cisplatin, Cycle 3, n=1,5 ,0,0	100 (± 99999)	93.8 (± 24.34)	99999 (± 99999)	99999 (± 99999)
G+Cis, Cisplatin, Cycle 4, n=1,4,0,0	100 (± 99999)	100.3 (± 0.96)	99999 (± 99999)	99999 (± 99999)
G+Cis, Cisplatin, Cycle 5, n=0,1,0,0	99999 (± 99999)	50 (± 99999)	99999 (± 99999)	99999 (± 99999)
G+Cb, Gemcitabine, Cycle 1, n=1,2,0,0	99 (± 99999)	100 (± 0)	99999 (± 99999)	99999 (± 99999)

G+Cb, Gemcitabine, Cycle 2, n=1,2,0,0	99 (± 99999)	88.5 (± 17.68)	99999 (± 99999)	99999 (± 99999)
G+Cb, Gemcitabine, Cycle 3, n=1,2,0,0	99 (± 99999)	100 (± 0)	99999 (± 99999)	99999 (± 99999)
G+Cb, Gemcitabine, Cycle 4, n=1,2,0,0	49 (± 99999)	99.5 (± 0.71)	99999 (± 99999)	99999 (± 99999)
G+Cb, Gemcitabine, Cycle 5, n=1,1,0,0	99 (± 99999)	74 (± 99999)	99999 (± 99999)	99999 (± 99999)
G+Cb, Gemcitabine, Cycle 6, n=1,1,0,0	99 (± 99999)	74 (± 99999)	99999 (± 99999)	99999 (± 99999)
G+Cb, Carboplatin, Cycle 1, n=1,3,0,0	101 (± 99999)	88.7 (± 14.05)	99999 (± 99999)	99999 (± 99999)
G+Cb, Carboplatin, Cycle 2, n=1,3,0,0	100 (± 99999)	103 (± 5.2)	99999 (± 99999)	99999 (± 99999)
G+Cb, Carboplatin, Cycle 3, n=1,2,0,0	93 (± 99999)	105 (± 5.66)	99999 (± 99999)	99999 (± 99999)
G+Cb, Carboplatin, Cycle 4, n=1,2,0,0	91 (± 99999)	107.5 (± 2.12)	99999 (± 99999)	99999 (± 99999)
G+Cb, Carboplatin, Cycle 5, n=1,1,0,0	100 (± 99999)	71 (± 99999)	99999 (± 99999)	99999 (± 99999)
G+Cb, Carboplatin, Cycle 6, n=1,1,0,0	87 (± 99999)	79 (± 99999)	99999 (± 99999)	99999 (± 99999)
Gemcitabine, Cycle 1, n=0,0,1,7	99999 (± 99999)	99999 (± 99999)	100 (± 99999)	94.7 (± 6.75)
Gemcitabine, Cycle 2, n=0,0,1,7	99999 (± 99999)	99999 (± 99999)	100 (± 99999)	85 (± 17.48)
Gemcitabine, Cycle 3, n=0,0,1,4	99999 (± 99999)	99999 (± 99999)	100 (± 99999)	79.5 (± 21.44)
Gemcitabine, Cycle 4, n=0,0,0,4	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	94.8 (± 4.11)
Gemcitabine, Cycle 5, n=0,0,0,3	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	93.7 (± 3.79)
Gemcitabine, Cycle 6, n=0,0,0,3	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	72.7 (± 17.01)

Notes:

[81] - Safety Population

[82] - Safety Population

[83] - Safety Population

[84] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one delay in their scheduled dose of chemotherapy in any cycle in Phase I

End point title	Number of participants with at least one delay in their scheduled dose of chemotherapy in any cycle in Phase I[85]

End point description:

Any delay in a scheduled dose of gemcitabine monotherapy or the combination of gemcitabine plus carboplatin or cisplatin was evaluated for eltrombopag and placebo treated participants.

End point type	Secondary

End point timeframe:

All time on chemotherapy treatment

Notes:

[85] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo	Phase I: 28-Day Cycle Eltrombopag 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1[86]	3[87]	4[88]	10[89]
Units: Participants	1	2	2	1

Notes:

[86] - Safety Population

[87] - Safety Population

[88] - Safety Population

[89] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any bleeding and significant bleeding as assessed using the World Health Organization (WHO) bleeding scale, across cycles 1-6 in Phase II

End point title	Number of participants with any bleeding and significant bleeding as assessed using the World Health Organization (WHO) bleeding scale, across cycles 1-6 in Phase II[90]

End point description:

The WHO Bleeding Scale is a measure of bleeding severity with the following grades: Grade 0=no bleeding; Grade 1=petechiae; Grade 2=mild blood loss; Grade 3=gross bleeding; Grade 4=debilitating blood loss. The WHO grades were further classified into the following categories: no bleeding=Grade 0; any bleeding=Grades 1 to 4; no clinically significant bleeding=Grades 0 to 1; clinically significant bleeding=Grades 2 to 4. Baseline is defined as the Day 1 assessment or the latest possible screening assessment. Across Cycles 1-6 included all assessments after first dose of chemotherapy up to the end of Cycle 6. Data exclused for participants taking drugs that affect platelet function or anticoagulants, from the time that the medication was started.

End point type	Secondary

End point timeframe:

Screening, Day -5, Day 1 and 8 of Cycles 1 to 6 of 21-day cycle schedule, Day 1, 8 and 15 of cycles 1 to 6 of 28-day schedule, treatment withdrawal and 30-day follow-up

Notes:

[90] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12[91]	35[92]		
Units: Participants				
Grade 0	11	34		
Grade 1	1	0		
Grade 2	0	0		
Grade 3	0	0		
Grade 4	0	1		

Notes:

[91] - ITT Population: Participants with at least one visit within the cycle.

[92] - ITT Population: Participants with at least one visit within the cycle.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants requiring a platelet transfusion in Phase II

End point title	Number of participants requiring a platelet transfusion in Phase II[93]

End point description:

Platelet transfusion was used as a rescue medication for the treatment of thrombocytopenia. Number of participants requiring a platelet transfusion during Cycles 1-6 was summarized and compared between treatment groups using a logistic regression model adjusted for cycle duration. Each cycle included assessments starting at Day 1 of the cycle.

End point type	Secondary

End point timeframe:

Screening, Day -5, throughout cycles 1 to 6 and up to 30 days after IP discontinuation

Notes:

[93] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[94]	52[95]		
Units: Participants				
Cycle 1	0	4		
Cycle 2	2	3		
Cycle 3	0	2		
Cycle 4	1	1		
Cycle 5	0	0		
Cycle 6	0	0		

Notes:

[94] - ITT Population

[95] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one delay in their scheduled dose of chemotherapy in any cycle in Phase II

End point title	Number of participants with at least one delay in their scheduled dose of chemotherapy in any cycle in Phase II[96]

End point description:

Any delay in scheduled dose of gemcitabine monotherapy or the combination of gemcitabine plus carboplatin or cisplatin was evaluated for eltrombopag and placebo treated participants. Number of participants with any delay in dose during 21-day cycle or 28-day cycle, in part 1 or part 2 of the study is summarized and presented. Only those participants who actually received chemotherapy are included for the cisplatin and carboplatin components and all participants are included for the gemcitabine components (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[96] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[97]	52[98]		
Units: Participants				
Gemcitabine, 21-day cycle, n=11,22	5	7		
Carboplatin, 21-day cycle, n=4,12	4	5		
Cisplatin, 21-day cycle, n=7,9	1	2		
Gemcitabine, 28-day cycle, n=12,30	4	4		

Notes:

[97] - ITT Population

[98] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any dose reduction in their scheduled dose of chemotherapy in any cycle in Phase II

End point title	Number of participants with any dose reduction in their scheduled dose of chemotherapy in any cycle in Phase II[99]

End point description:

Dose reductions are required following potential drug-related toxicities. Number of participants with any dose reduction during 21-day cycle or 28-day cycle, in part 1 or part 2 of the study is summarized and presented. Only participants who actually received chemotherapy were included for the cisplatin and carboplatin components. All participants were included for the gemcitabine components.

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[99] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[100]	52[101]		
Units: Participants				
Gemcitabine, 21-day cycle, n=11,22	7	6		
Carboplatin, 21-day cycle, n=4,12	2	2		
Cisplatin, 21-day cycle, n=7,9	0	3		
Gemcitabine, 28-day cycle, n=12,30	8	8		

Notes:

[100] - ITT Population

[101] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Dose intensity of gemcitabine plus cisplatin(G+Cis)/gemcitabine plus carboplatin (G+Cb) and gemcitabine across chemotherapy cycles 1-6 in Phase II

End point title	Dose intensity of gemcitabine plus cisplatin(G+Cis)/gemcitabine plus carboplatin (G+Cb) and gemcitabine across chemotherapy cycles 1-6 in Phase II[102]

End point description:

Dose intensity of chemotherapy is defined as the actual dose of chemotherapy given as a percentage of the scheduled C1D1/C1D8 dose, as applicable, within this study: cycle Dose Intensity (%) = Total Actual dose (mg/m^2) within cycle *100/ Total Scheduled dose (mg/m^2) in Cycle 1; wherein Actual Dose (mg/m^2) = Actual dose (mg)/Body Surface Area reported on eCRF. The average chemotherapy dose intensity at Day 1 across Cycles 1 to 6, Day 8 across Cycles 1 to 6 and Day 15 across Cycles 1 to 6 was summarized and compared between treatment groups using an ANCOVA model adjusted for cycle duration and part of the study.

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[102] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[103]	52[104]		
Units: Dose Intensity (%)				
arithmetic mean (standard deviation)				
Cycle 1, n=23,48	96.6 (± 10.65)	97.9 (± 6.19)		
Cycle 2, n=19,37	113.1 (± 33.91)	97.8 (± 24.99)		
Cycle 3, n=13,26	102.6 (± 42.2)	98.7 (± 35.77)		
Cycle 4, n=11,19	96.6 (± 27.65)	90.7 (± 30)		
Cycle 5, n=6,12	102.2 (± 31.88)	81.3 (± 25.39)		
Cycle 6, n=5,7	84.4 (± 21.92)	65.2 (± 25.48)		
Cycle 1-6, n=23,49	98.5 (± 18.26)	94.6 (± 15.71)		

Notes:

[103] - ITT Population

[104] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with indicated maximum toxicity grades for the indicated hematology parameters, at anytime post-Baseline in Phase II

End point title	Number of participants with indicated maximum toxicity grades for the indicated hematology parameters, at anytime post-Baseline in Phase II[105]

End point description:

Hematology parameters with a related NCI CTCAE (version 4.0) toxicity grading were summarized by

toxicity grade at each scheduled assessment, the maximum toxicity grade reached by a participant post-Baseline was summarized. Hematology parameters included Hemoglobin (Hb) increased, Anemia, Lymphocyte count (Lym), platelet count, White Blood Cell count (WBC) and Total Absolute Neutrophil Count (Total ANC). The Baseline value is defined as the value reported immediately prior to the administration of the first dose of chemotherapy in Cycle 1. Post-Baseline is defined as any time after the first dose of chemotherapy in Cycle 1 up to and including all follow-up visits. participants with missing Baseline value were assumed to have normal Baseline value. Only those Participant available at the indicated time points were analyzed (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

After baseline (C1D1), on-treatment and 30 day follow-up

Notes:

[105] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[106]	52[107]		
Units: Participants				
Hb (Increased), Grade 0, n=23,52	23	52		
Hb (Increased), Grade 1, n=23,52	0	0		
Hb (Increased), Grade 2, n=23,52	0	0		
Hb (Increased), Grade 3, n=23,52	0	0		
Hb (Increased), Grade 4, n=23,52	0	0		
Hb (Anemia), Grade 0, n=23,52	0	4		
Hb (Anemia), Grade 1, n=23,52	4	16		
Hb (Anemia), Grade 2, n=23,52	13	16		
Hb (Anemia), Grade 3, n=23,52	6	16		
Hb (Anemia), Grade 4, n=23,52	0	0		
Lym (Increased), Grade 0, n=23,52	22	47		
Lym (Increased), Grade 1, n=23,52	0	0		
Lym (Increased), Grade 2, n=23,52	1	2		
Lym (Increased), Grade 3, n=23,52	0	1		
Lym (Increased), Grade 4, n=23,52	0	0		
Lym (Decreased), Grade 0, n=23,52	1	7		
Lym (Decreased), Grade 1, n=23,52	3	10		
Lym (Decreased), Grade 2, n=23,52	8	14		
Lym (Decreased), Grade 3, n=23,52	9	16		
Lym (Decreased), Grade 4, n=23,52	2	3		
Total ANC, Grade 0, n=23,52	4	16		
Total ANC, Grade 1, n=23,52	1	4		
Total ANC, Grade2, n=23,52	3	17		
Total ANC, Grade 3, n=23,52	10	10		
Total ANC, Grade 4, n=23,52	5	3		
Platelet count, Grade 0, n=23,52	0	7		
Platelet count, Grade 1, n=23,52	4	9		
Platelet count, Grade 2, n=23,52	3	9		
Platelet count, Grade 3, n=23,52	6	15		
Platelet count, Grade 4, n=23,52	10	12		
WBC count, Grade 0, n=23,52	4	14		
WBC count, Grade 1, n=23,52	3	10		

WBC count, Grade 2, n=23,52	8	17		
WBC count, Grade 3, n=23,52	6	11		
WBC count, Grade 4, n=23,52	2	0		

Notes:

[106] - Safety Population

[107] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with indicated worst-case change from Baseline in clinical chemistry laboratory parameters using CTCAE toxicity grading, at anytime post-Baseline in Phase II

End point title	Number of participants with indicated worst-case change from Baseline in clinical chemistry laboratory parameters using CTCAE toxicity grading, at anytime post-Baseline in Phase II[108]

End point description:

Clinical chemistry laboratory parameters with a related CTCAE (version 4.0) toxicity grading were summarized by toxicity grade at each scheduled assessment. Worst-case grade change of the laboratory parameters at anytime post-Baseline is presented as Any grade increase, Increase to Grade 3 or Grade 4. Clinical chemistry laboratory parameters included Albumin (Al), creatinine, AST, ALT, ALP, TB, Calcium hypercalcemia (CaHy)/hypocalcemia (CaHo), Glucose hyperglycemia (GluHy)/hypoglycemia (GluHo), Potassium hypernatremia (KHy)/hyponatremia (KHo) and Sodium hypernatremia (NaHy)/hyponatremia (NaHo). The Baseline value is defined as the value reported immediately prior to the administration of the first dose of chemotherapy in Cycle 1. Post-Baseline is defined as any time after the first dose of chemotherapy in Cycle 1 up to and including all follow-up visits. Only those Participant available at the indicated time points were analyzed (represented by n=X,X in the category

End point type	Secondary

End point timeframe:

After baseline (C1D1), on-treatment (collected on days 1 and 8 for subjects on 21-day cycle and on days 1, 8 and 15 for subjects on 28-day cycle) and 30 day follow-up

Notes:

[108] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[109]	52[110]		
Units: Participants				
Al, Any grade increase, n=23,51	10	22		
Al, Increase to Grade 3, n=23,51	0	2		
Al, Increase to Grade 4, n=23,51	0	0		
ALP, Any grade increase, n=23,52	11	16		
ALP, Increase to Grade 3, n=23,52	1	2		
ALP, Increase to Grade 4, n=23,52	0	0		
ALT, Any grade increase, n=23,52	12	16		
ALT, Increase to Grade 3, n=23,52	3	2		
ALT, Increase to Grade 4, n=23,52	0	0		
AST, Any grade increase, n=23,52	11	15		
AST, Increase to Grade 3, n=23,52	3	2		
AST, Increase to Grade 4, n=23,52	0	0		

TB, Any grade increase, n=23,52	5	11		
TB, Increase to Grade 3, n=23,52	3	2		
TB, Increase to Grade 4, n=23,52	0	0		
CaHy, Any grade increase, n=23,51	0	1		
CaHy, Increase to Grade 3, n=23,51	0	0		
CaHy, Increase to Grade 4, n=23,51	0	0		
CaHo, Any grade increase, n=23,51	3	10		
CaHo, Increase to Grade 3, n=23,51	1	2		
CaHo, Increase to Grade 4, n=23,51	0	0		
Creatinine, Any grade increase, n=23,52	5	11		
Creatinine, Increase to Grade 3, n=23,52	1	0		
Creatinine, Increase to Grade 4, n=23,52	0	0		
GluHy, Any grade increase, n=23,52	13	31		
GluHy, Increase to Grade 3, n=23,52	2	3		
GluHy, Increase to Grade 4, n=23,52	0	0		
GluHo, Any grade increase, n=23,52	2	4		
GluHo, Increase to Grade 3, n=23,52	0	0		
GluHo, Increase to Grade 4, n=23,52	1	0		
NaHy, Any grade increase, n=23,52	0	2		
NaHy, Increase to Grade 3, n=23,52	0	0		
NaHy, Increase to Grade 4, n=23,52	0	0		
NaHo, Any grade increase, n=23,52	4	15		
NaHo, Increase to Grade 3, n=23,52	1	1		
NaHo, Increase to Grade 4, n=23,52	0	0		
KHy, Any grade increase, n=23,52	4	10		
KHy, Increase to Grade 3, n=23,52	1	1		
KHy, Increase to Grade 4, n=23,52	0	0		
KHo, Any grade increase, n=23,52	5	11		
KHo, Increase to Grade 3, n=23,52	1	4		
KHo, Increase to Grade 4, n=23,52	0	1		

Notes:

[109] - Safety Population

[110] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Change from Baseline in Creatinine of >=26.5 UMOL/L in Phase II

End point title	Number of participants with Change from Baseline in Creatinine of >=26.5 UMOL/L in Phase II[111]

End point description:

Number of participants with at least 1 assessment of change from Baseline in creatinine, with increase >=26.5 UMOL/L are presented. The Baseline value is defined as the value reported immediately prior to the administration of the first dose of IP

End point type	Secondary

End point timeframe:

After baseline (C1D1), on-treatment (collected on days 1 and 8 for subjects on 21-day cycle and on days 1, 8 and 15 for subjects on 28-day cycle) and 30 day follow-up

Notes:

[111] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[112]	52[113]		
Units: Participants	5	11		

Notes:

[112] - Safety Population

[113] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of the participants with Eastern Cooperative Oncology Group (ECOG) performance status scores at the indicated time points in Phase II

End point title	Number of the participants with Eastern Cooperative Oncology Group (ECOG) performance status scores at the indicated time points in Phase II[114]

End point description:

ECOG-Zubrod scores for the Performance Status were defined as follows: 0: Fully active, 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, 2: Ambulatory and capable of all self-care but unable to carry out any work activities, 3: Capable of only limited self-care, 4: Completely disabled, 5 and Unknown: Dead. The data is presented for the participants with the ECOG performance score at different time points during the study. Only those participants available at the indicated time points were analyzed (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

Screening, C1D1, C2D1, C3D1, C4D1, C5D1, C6D1, C7D1, C8D1, C9D1, C10D1, C11D1, C12D1, C13D1, C14D1, C15D1, C16D1 and C17D1

Notes:

[114] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[115]	52[116]		
Units: Participants				
Screening, Score 0, n=23,52	3	19		
Screening, Score 1, n=23,52	19	32		
Screening, Score 2, n=23,52	1	1		
C1D1, Score 0, n=23,49	4	20		
C1D1, Score 1, n=23,49	17	28		
C1D1, Score 2, n=23,49	0	1		
C1D1, Unknown, n=23,49	2	0		
C2D1, Score 0, n=19,36	4	16		

C2D1, Score 1, n=19,36	13	18		
C2D1, Score 2, n=19,36	2	2		
C3D1, Score 0, n=13,27	3	9		
C3D1, Score 1, n=13,27	9	16		
C3D1, Score 2, n=13,27	1	2		
C4D1, Score 0, n=11,19	4	8		
C4D1, Score 1, n=11,19	7	10		
C4D1, Score 2, n=11,19	0	1		
C5D1, Score 0, n=6,12	2	5		
C5D1, Score 1, n=6,12	4	6		
C5D1, Score 2, n=6,12	0	1		
C6D1, Score 0, n=6,7	2	3		
C6D1, Score 1, n=6,7	4	4		
C7D1, Score 0, n=3,2	1	0		
C7D1, Score 1, n=3,2	2	2		
C8D1, Score 0, n=2,1	1	0		
C8D1, Score 1, n=2,1	1	1		
C9D1, Score 1, n=2,1	2	1		
C10D1, Score1 n=2,0	2	0		
C11D1, Score 1, n=2,0	1	0		
C11D1, Score 2, n=2,0	1	0		
C12D1, Score 1, n=2,0	2	0		
C13D1, Score 0, n=2,0	1	0		
C13D1, Score 1, n=2,0	1	0		
C14D1, Score 0, n=2,0	1	0		
C14D1, Score 1, n=2,0	1	0		
C15D1, Score 1, n=2,0	2	0		
C16D1, Score 0, n=1,0	1	0		
C17D1, Score 2, n=1,0	1	0		

Notes:

[115] - Safety Population

[116] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with electrocardiogram (ECG) findings at Cycle 1 Day 4 (2 to 6 hours post-dose) in phase II

End point title	Number of participants with electrocardiogram (ECG) findings at Cycle 1 Day 4 (2 to 6 hours post-dose) in phase II[117]

End point description:

A single safety 12-lead ECG was performed using a standard 12-lead ECG machine at screening and 2 to 6 hours post-dose on C1D4. Change in ECG findings were categorized as 'Clinically significant change (CSC): favorable', 'No change or insignificant change' or 'Clinically significant change (CSC): unfavorable' as determined by the investigator. The Baseline value is defined as the value reported immediately prior to the administration of the first dose of investigational product. Only those participants available at the indicated time points were analyzed (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

C1D4

Notes:

[117] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[118]	52[119]		
Units: Participants				
CSC favorable, n=22,45	0	2		
No change or insignificant change, n=22,45	20	42		
CSC: unfavorable, n=22,45	0	1		

Notes:

[118] - Safety Population

[119] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Day 8 scheduled pre-chemotherapy platelet counts evaluated across Cycles 1 to 6 in Phase II

End point title	Mean Day 8 scheduled pre-chemotherapy platelet counts evaluated across Cycles 1 to 6 in Phase II[120]

End point description:

Scheduled pre-chemotherapy platelet count is defined within each cycle as the platelet count assessment on which the decision to give or delay chemotherapy was made. This was averaged for each subject across cycles 1 to 6 and a natural log transformation was applied to the average. The log-transformed values were compared between eltrombopag and placebo groups using an analysis of covariance (ANCOVA) model adjusting for cycle duration (21-day vs. 28-day), baseline loge(platelet count) and part of study (part 1 or 2 of phase II). The number of participants analyzed is the number with a Day 8 scheduled platelet count.

End point type	Secondary

End point timeframe:

Day 8 (averaged across cycles 1 to 6)

Notes:

[120] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[121]	42[122]		
Units: Giga (10^9) cells per liter (G cells/L)				
geometric mean (geometric coefficient of variation)	162.18 (± 74.2)	180.65 (± 59.1)		

Notes:

[121] - ITT Population

[122] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase II: Placebo v Phase II: Eltrombopag 100 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.407
Method	ANCOVA
Parameter estimate	Percent difference
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.6
upper limit	51.1

Secondary: Mean Day 15 scheduled pre-chemotherapy platelet counts evaluated across Cycles 1 to 6 in Phase II

End point title	Mean Day 15 scheduled pre-chemotherapy platelet counts evaluated across Cycles 1 to 6 in Phase II[123]

End point description:

Scheduled pre-chemotherapy platelet count is defined within each cycle as the platelet count assessment on which the decision to give or delay chemotherapy was made. This was averaged for each subject across cycles 1 to 6 and a natural log transformation was applied to the average. The log-transformed values were compared between eltrombopag and placebo groups using an analysis of covariance (ANCOVA) model adjusting for cycle duration (21-day vs. 28-day), baseline loge(platelet count) and part of study (part 1 or 2 of phase II). The number of participants analyzed is the number with a Day 15 scheduled platelet count.

End point type	Secondary

End point timeframe:

Day 15 (averaged across cycles 1 to 6)

Notes:

[123] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[124]	22[125]		
Units: Giga (10^9) cells per liter (G cells/L)				
geometric mean (geometric coefficient of variation)	95.1 (± 23.3)	95.29 (± 52.1)		

Notes:

[124] - ITT Population

[125] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase II: Placebo v Phase II: Eltrombopag 100 mg
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.802
Method	ANCOVA
Parameter estimate	Percent difference
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.5
upper limit	37.4

Secondary: Mean within-subject platelet count prior to scheduled chemotherapy across Cycles 1 to 6 in Phase II

End point title	Mean within-subject platelet count prior to scheduled chemotherapy across Cycles 1 to 6 in Phase II[126]

End point description:

Within-subject platelet count for each par. was calculated by summing up the visit platelet counts from each of Cycles 1 to 6 and dividing it by the number of cycles in which the par. had data. The average within a treatment group was calculated by summing up the values from each par. within the treatment 21-day cycle dividing it by the number of par. These platelet counts are different from the pre-chemotherapy platelet counts for cycles where the chemotherapy dose was delayed. Average within-subject central laboratory platelet count prior to scheduled chemotherapy across Cycles 1 to 6 are summarized. Blood samples were collected on Day 1 and 8 of Cycles 1 to 6 for 21-day cycle and on Day 1, 8 and 15 from Cycles 1 to 6 for 28-day cycle to estimate the average within subject platelet count prior to scheduled chemotherapy. Only those participants available at the indicated time points were analyzed (represented by n=X,X in the category titles).

End point type	Secondary

End point timeframe:

Day 1, Day 8, Day 15 (all averaged across cycles 1 to 6)

Notes:

[126] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[127]	52[128]		
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)				
Day1, n=23,48	221 (± 128.23)	272.9 (± 120.92)		
Day 8, n=20,42	201 (± 143.75)	207.4 (± 110.93)		
Day 15, n=9,22	97.5 (± 24.82)	106.7 (± 54.73)		

Notes:

[127] - ITT Population

[128] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet count nadir for each chemotherapy cycle in Phase II

End point title	Platelet count nadir for each chemotherapy cycle in Phase II[129]

End point description:

Platelet nadir is defined as the lowest platelet count reported after the first dose of chemotherapy within each cycle. Platelet count nadir is defined for each cycle. Blood samples were collected to estimate platelet nadir count at the following time points: 21-day cycle; Day 1, Day 4, Day 8, Day 15 and Day 17 of Cycles 1 to 6. 28-day cycle; Day 1, Day 4, Day 8, Day 15, Day 22, Day 24 of Cycles 1 to 6. Only those participants available at indicated time points were analyzed (represented by n=X, X).

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[129] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[130]	52[131]		
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)				
Cycle 1, n=23,48	68.3 (± 47.74)	77.2 (± 76.43)		
Cycle 2, n=19,37	61.5 (± 35.82)	68.5 (± 48.92)		
Cycle 3, n=13,26	71.6 (± 53.8)	84.7 (± 60.03)		
Cycle 4, n=11, 19	89.7 (± 116.73)	86.9 (± 56.11)		
Cycle 5, n=6,11	51.7 (± 12.23)	83 (± 58.63)		
Cycle 6, n=5,5	69.6 (± 62.76)	136.6 (± 151.88)		

Notes:

[130] - ITT Population

[131] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Average daily area under the platelet-time course across cycles 1 to 6 in phase II

End point title	Average daily area under the platelet-time course across cycles 1 to 6 in phase II[132]

End point description:

Average daily area under the curve platelet-time course is defined as the area-under-the-curve (calculated using the trapezoidal rule) divided by total duration. It was calculated across all cycles. Blood samples were collected to estimate platelet count at the following time points: 21-day cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-day cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6.

End point type	Secondary

End point timeframe:

All assessments from Cycle 1 Day 1 to last assessment in Cycle 6

Notes:

[132] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[133]	48[134]		
Units: Giga (10^9) cells per liter (G cells/L)				
arithmetic mean (standard deviation)	153 (± 96.079)	189.48 (± 79.583)		

Notes:

[133] - ITT Population:Participants with platelet count data in at least one cycle in the study.

[134] - ITT Population:Participants with platelet count data in at least one cycle in the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with thrombocytopenia of Grade 1, 2, 3 or 4 across cycles 1 to 6 in Phase II

End point title	Number of participants with thrombocytopenia of Grade 1, 2, 3 or 4 across cycles 1 to 6 in Phase II[135]

End point description:

As per the CTCAE version 4.0, participants with a platelet count <LLN but >=75 x 10^9/L (Gi/L) were considered to have Grade 1 thrombocytopenia; participants with a platelet count <75Gi/L, but >=50Gi/L were considered to have Grade 2 thrombocytopenia; participants with a platelet count <50Gi/L, but >=25Gi/L were considered to have Grade 3 thrombocytopenia and participants with a platelet count <25Gi/L were considered to have Grade 4 thrombocytopenia. Blood samples were collected to estimate thrombocytes at the following time points: 21-day cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-day cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6. Participants experiencing thrombocytopenia (Platelets <150Gi/L) at least once within cycle are presented in the category title as n=X,X.

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[135] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[136]	50[137]		
Units: Participants				
Grade 1	4	9		
Grade 2	3	9		
Grade 3	8	15		
Grade 4	8	12		
None	0	5		

Notes:

[136] - ITT Population

[137] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum duration of thrombocytopenia across Cycles 1 to 6 in Phase II

End point title	Maximum duration of thrombocytopenia across Cycles 1 to 6 in Phase II[138]

End point description:

Duration of thrombocytopenia is defined as a period of time in days from the first report of a platelet count with NCI CTCAE Grade 1-4 until the first subsequent report of a platelet count no longer meeting those criteria, regardless of rescue medication usage. It was assessed between Day 1 of Cycle 2 and up to and including any Conclusion/Early Withdrawal visit assigned to the same cycle for participants completing up to 6 cycles, and between Day 1 of Cycle 2 and up to and including the end of Cycle 6 for participants continuing beyond 6 cycles. The chemotherapy cycle for 21-day cycle was 21 days and for 28-day cycle was 28 days. Blood samples were collected to estimate thrombocytes at the following time points: 21-day cycle; Days 1, 4, 8, 15 and 17 of Cycles 2 to 6. 28-day cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 2 to 6. (Participants with at least one period of thrombocytopenia where duration could be calculated)

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6 (ITT Population: Participants with at least one period of thrombocytopenia where duration could be calculated)

Notes:

[138] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[139]	45[140]		
Units: Days				
arithmetic mean (standard deviation)	32.6 (± 20.31)	23.5 (± 18.68)		

Notes:

[139] - ITT Population

[140] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time taken to reach platelet nadir for each chemotherapy cycle in Phase II

End point title	Time taken to reach platelet nadir for each chemotherapy cycle in Phase II[141]

End point description:

Platelet nadir is defined within each cycle as the lowest platelet count reported after the Day 1 chemotherapy dose. The time taken to reach platelet nadir is defined within each cycle. Blood samples were collected to estimate platelet nadir count at the following time points: 21-day cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-day cycle; Days 1, 4, 8, 15, 22 and 24 of Cycles 1 to 6. Only those participants available at indicated time points were analyzed (represented by n=X, X). (Not available (NA)" is presented as "99999")

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[141] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[142]	52[143]		
Units: Days				
arithmetic mean (standard deviation)				
Cycle 1, n=23,48	14.7 (± 4.85)	15.7 (± 6.12)		
Cycle 2, n=19,37	15.1 (± 4.41)	15.4 (± 3.62)		
Cycle 3, n=13,26	15.8 (± 5.64)	14.3 (± 4.76)		
Cycle 4, n=11,19	15.4 (± 5.48)	14.7 (± 5.19)		
Cycle 5, n=6,11	15.5 (± 6.38)	13.8 (± 4.45)		
Cycle 6, n=5,5	13.6 (± 7.37)	10.4 (± 6.31)		
Cycle 7,n=2,2	15 (± 0)	7.5 (± 0.71)		
Cycle 8, n=2,1	12.5 (± 3.54)	8 (± 99999)		
Cycle 9, n=2,0	12.5 (± 3.54)	99999 (± 99999)		

Notes:

[142] - ITT Population

[143] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to recovery from platelet nadir for each chemotherapy cycle in Phase II

End point title	Time to recovery from platelet nadir for each chemotherapy cycle in Phase II[144]

End point description:

Platelet nadir is defined within each cycle as the lowest platelet count reported after the Day 1 chemotherapy dose. TR (>100Gi/L or >150Gi/L) from platelet nadir is defined within each cycle as the time in days from the platelet nadir to the time at which platelet count returns to >=100Gi/L or >=150Gi/L within the same cycle or up to and including Day 1 of the next cycle. For the last cycle in

the study, time to recovery was calculated in the same manner but up to and including any Conclusion/Early Withdrawal visit which has been assigned to the same cycle. Blood samples were collected to estimate platelet count at: 21-day cycle; Days 1, 4, 8, 15 and 17 of Cycles 1 to 6. 28-day cycle; Days 1, 4, 8, 15, 22, and 24of Cycles 1 to 6. Time to recover censored if platelet count did not return to >=100/150 Gi/L. Censored results are excluded from calculation of summary statistics. Only those participants available at indicated time points were analyzed (represented by n=X, X).

End point type	Secondary

End point timeframe:

Cycle 1 to Cycle 6

Notes:

[144] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[145]	52[146]		
Units: Days				
arithmetic mean (standard deviation)				
TR(<100Gi/L to >=100Gi/L), Cycle 1, n=17, 32	8.1 (± 3.15)	8.5 (± 3.7)		
TR(<150Gi/L to >=150Gi/L), Cycle 1, n=12, 29	9.3 (± 3.89)	9.1 (± 3.26)		
TR(<100Gi/L to >=100Gi/L), Cycle 2, n=13, 24	9.9 (± 3.64)	8.3 (± 2.56)		
TR(<150Gi/L to >=150Gi/L), Cycle 2, n=11, 21	10.5 (± 4.5)	9 (± 3.31)		
TR(<100Gi/L to >=100Gi/L), Cycle 3, n=9, 12	10.1 (± 5.01)	8.8 (± 3.16)		
TR(<150Gi/L to >=150Gi/L), Cycle 3, n=7, 14	10.4 (± 5.74)	9.6 (± 3.43)		
TR(<100Gi/L to >=100Gi/L), Cycle 4, n=8, 10	10 (± 5.63)	10.9 (± 4.77)		
TR(<150Gi/L to >=150Gi/L), Cycle 4, n=5, 11	10.2 (± 6.65)	10.6 (± 5.39)		
TR(<100Gi/L to >=100Gi/L), Cycle 5, n=5,6	7.8 (± 1.1)	8.8 (± 4.79)		
TR(<150Gi/L to >=150Gi/L), Cycle 5, n=2,4	8 (± 0)	7.3 (± 1.5)		
TR(<100Gi/L to >=100Gi/L), Cycle 6, n=2,2	10.5 (± 6.36)	8.5 (± 0.71)		
TR(<150Gi/L to >=150Gi/L), Cycle 6, n=2,1	10.5 (± 6.36)	8 (± 99999)		
TR(<100Gi/L to >=100Gi/L), Cycle 7, n=1,1	15 (± 99999)	22 (± 99999)		
TR(<150Gi/L to >=150Gi/L), Cycle 7, n=1,1	15 (± 99999)	22 (± 99999)		
TR(<100Gi/L to >=100Gi/L), Cycle 8, n=1,1	14 (± 1.41)	20 (± 99999)		
TR(<150Gi/L to >=150Gi/L), Cycle 8, n=1,0	15 (± 99999)	99999 (± 99999)		
TR(<100Gi/L to >=100Gi/L), Cycle 9, n=2,0	14 (± 11.31)	99999 (± 99999)		
TR(<150Gi/L to >=150Gi/L), Cycle 9, n=0,0	99999 (± 99999)	99999 (± 99999)		

Notes:

[145] - ITT Population (NA is presented as "99999")

[146] - ITT Population (NA is presented as "99999")

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE): Pre-therapy, On-therapy + 30 days and Post-therapy in Phase II

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE): Pre-therapy, On-therapy + 30 days and Post-therapy in Phase II[147]

End point description:

AEs are coded using the standard MedDRA and were graded by the investigator according to NCI CTCAE, version 4.0. AE is any untoward medical occurrence temporally associated with the use of a medicinal product (MP), whether or not considered related to the MP. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a MP. For marketed MPs, this also includes failure to produce expected benefits, abuse, or misuse. SAE event is any untoward medical occurrence that, at any dose: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or, is a congenital anomaly/birth defect.

End point type	Secondary

End point timeframe:

From first dose of investigational product (IP) until 30 days after discontinuation of IP (Longer for AEs related to study participation)

Notes:

[147] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Phase II: Placebo	Phase II: Eltrombopag 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[148]	52[149]		
Units: Participants				
Any AE Pre Therapy	0	1		
Any SAE Pre Therapy	0	0		
Any AE On Therapy+30 days	23	48		
Any SAE On Therapy+30 days	12	16		
Any AE Post Therapy	4	2		
Any SAE Post Therapy	2	1		
Blood/lymphatic system disorders On-therapy+30 day	21	40		
Thrombocytopenia On-therapy+30 days	11	19		
Anemia On-therapy+30 days	16	26		
Neutropenia On-therapy+30 days	13	21		
Gastrointestinal disorders On-therapy+30 days	12	25		
Blood Creatinine increased On-therapy+30 days	3	2		
Vascular disorders On-therapy+30 days	2	6		

Cardiac disorders On-therapy+30 days	1	3		
Pulmonary embolism On-therapy+30 days	0	1		
Portal vein thrombosis On-therapy+30 days	1	0		
Deaths On-therapy+30 days	9	13		

Notes:

[148] - Safety Population

[149] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from Cycle 1, Day 1 for Phase I; and from the time the first dose of investigational product (IP) is administered for Phase II; up to 30 days following discontinuation of IP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Phase I: 21-Day Cycle Placebo

Reporting group description:

Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

Reporting group title	Phase I: 21-Day Cycle Eltrombopag 100 mg

Reporting group description:

Participants receiving gemcitabine on Day 1 and Day 8 plus carboplatin (G+Cb) or cisplatin (G+Cis) on Day 1 (Cis may be divided on Day 1 and Day 8) as a part of the 21-day chemotherapy cycle were administered eltrombopag 100 milligrams (mg) once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

Reporting group title	Phase I: 28-Day Cycle Placebo

Reporting group description:

Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

Reporting group title	Phase I: 28-Day Cycle Eltrombopag 100 mg

Reporting group description:

Participants receiving gemcitabine on Day 1, Day 8 and Day 15 as a part of the 28-day chemotherapy cycle, were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of Cycle 2 and subsequent chemotherapy cycles.

Reporting group title	Phase II: Placebo

Reporting group description:

Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle, were administered placebo once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).

Reporting group title	Phase II: Eltrombopag 100 mg

Reporting group description:

Participants receiving gemcitabine plus carboplatin or cisplatin as a part of 21-day chemotherapy cycle or gemcitabine alone as a part of the 28-day chemotherapy cycle were administered eltrombopag 100 mg once daily for 5 days before and 5 days after Day 1 of each chemotherapy cycle (up to a maximum of 6 cycles).

Serious adverse events	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	5 / 9 (55.56%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device damage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure cluster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic coma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase I: 28-Day Cycle Eltrombopag 100 mg	Phase II: Placebo	Phase II: Eltrombopag 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	13 / 23 (56.52%)	17 / 52 (32.69%)
number of deaths (all causes)	0	9	13
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device damage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	1 / 23 (4.35%)	0 / 52 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 23 (8.70%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure cluster			
subjects affected / exposed	1 / 10 (10.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic coma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	4 / 52 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 23 (8.70%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
subjects affected / exposed	0 / 10 (0.00%)	2 / 23 (8.70%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	3 / 52 (5.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Arthritis infective			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
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	Phase I: 21-Day Cycle Placebo	Phase I: 21-Day Cycle Eltrombopag 100 mg	Phase I: 28-Day Cycle Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	9 / 9 (100.00%)	4 / 4 (100.00%)
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Platelet count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Headache			

subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Polyneuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 9 (44.44%)	3 / 4 (75.00%)
occurrences (all)	3	7	4
Leukopenia			
subjects affected / exposed	2 / 3 (66.67%)	2 / 9 (22.22%)	2 / 4 (50.00%)
occurrences (all)	4	4	2
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
Neutropenia			
subjects affected / exposed	3 / 3 (100.00%)	5 / 9 (55.56%)	2 / 4 (50.00%)
occurrences (all)	9	14	6
Thrombocytopenia			
subjects affected / exposed	3 / 3 (100.00%)	3 / 9 (33.33%)	4 / 4 (100.00%)
occurrences (all)	11	6	10
Thrombocytosis			
subjects affected / exposed	2 / 3 (66.67%)	2 / 9 (22.22%)	1 / 4 (25.00%)
occurrences (all)	4	3	3
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	2 / 4 (50.00%)
occurrences (all)	1	1	2
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	2 / 4 (50.00%)
occurrences (all)	0	1	2
Pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	2 / 4 (50.00%)
occurrences (all)	1	1	4
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	4 / 9 (44.44%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	6 / 9 (66.67%)	1 / 4 (25.00%)
occurrences (all)	2	7	2
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	3	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	2 / 4 (50.00%)
occurrences (all)	0	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	2
Diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 4 (25.00%)
occurrences (all)	0	1	1

Non-serious adverse events	Phase I: 28-Day Cycle Eltrombopag 100 mg	Phase II: Placebo	Phase II: Eltrombopag 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	22 / 23 (95.65%)	47 / 52 (90.38%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	5 / 52 (9.62%)
occurrences (all)	1	2	5
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	3 / 52 (5.77%)
occurrences (all)	3	2	3
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 10 (20.00%)	3 / 23 (13.04%)	4 / 52 (7.69%)
occurrences (all)	2	3	5
Blood bilirubin increased			

subjects affected / exposed	1 / 10 (10.00%)	1 / 23 (4.35%)	3 / 52 (5.77%)
occurrences (all)	1	1	3
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	3 / 23 (13.04%)	2 / 52 (3.85%)
occurrences (all)	0	7	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 10 (0.00%)	3 / 23 (13.04%)	6 / 52 (11.54%)
occurrences (all)	0	3	8
Neutrophil count decreased			
subjects affected / exposed	0 / 10 (0.00%)	3 / 23 (13.04%)	3 / 52 (5.77%)
occurrences (all)	0	3	5
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	5 / 23 (21.74%)	6 / 52 (11.54%)
occurrences (all)	0	5	13
Platelet count increased			
subjects affected / exposed	3 / 10 (30.00%)	1 / 23 (4.35%)	1 / 52 (1.92%)
occurrences (all)	4	1	1
White blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	3 / 23 (13.04%)	4 / 52 (7.69%)
occurrences (all)	0	3	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	1 / 52 (1.92%)
occurrences (all)	4	2	1
Headache			
subjects affected / exposed	2 / 10 (20.00%)	1 / 23 (4.35%)	2 / 52 (3.85%)
occurrences (all)	3	1	2
Polyneuropathy			
subjects affected / exposed	0 / 10 (0.00%)	2 / 23 (8.70%)	1 / 52 (1.92%)
occurrences (all)	0	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 10 (50.00%)	15 / 23 (65.22%)	24 / 52 (46.15%)
occurrences (all)	16	18	30
Leukopenia			

subjects affected / exposed	3 / 10 (30.00%)	2 / 23 (8.70%)	9 / 52 (17.31%)
occurrences (all)	12	4	11
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)	5 / 23 (21.74%)	7 / 52 (13.46%)
occurrences (all)	0	17	13
Neutropenia			
subjects affected / exposed	6 / 10 (60.00%)	13 / 23 (56.52%)	21 / 52 (40.38%)
occurrences (all)	24	27	41
Thrombocytopenia			
subjects affected / exposed	5 / 10 (50.00%)	10 / 23 (43.48%)	18 / 52 (34.62%)
occurrences (all)	10	16	31
Thrombocytosis			
subjects affected / exposed	2 / 10 (20.00%)	2 / 23 (8.70%)	4 / 52 (7.69%)
occurrences (all)	2	3	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	4 / 23 (17.39%)	8 / 52 (15.38%)
occurrences (all)	1	4	9
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)	3 / 23 (13.04%)	13 / 52 (25.00%)
occurrences (all)	5	3	14
Oedema peripheral			
subjects affected / exposed	2 / 10 (20.00%)	1 / 23 (4.35%)	5 / 52 (9.62%)
occurrences (all)	2	1	5
Pain			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	2 / 52 (3.85%)
occurrences (all)	1	2	2
Peripheral swelling			
subjects affected / exposed	0 / 10 (0.00%)	5 / 23 (21.74%)	3 / 52 (5.77%)
occurrences (all)	0	5	3
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	4 / 23 (17.39%)	3 / 52 (5.77%)
occurrences (all)	0	10	4
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	3 / 23 (13.04%)	7 / 52 (13.46%)
occurrences (all)	1	4	8
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	4 / 52 (7.69%)
occurrences (all)	0	1	6
Constipation			
subjects affected / exposed	1 / 10 (10.00%)	4 / 23 (17.39%)	4 / 52 (7.69%)
occurrences (all)	1	4	4
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	4 / 23 (17.39%)	5 / 52 (9.62%)
occurrences (all)	2	6	5
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	4 / 52 (7.69%)
occurrences (all)	0	0	4
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 23 (0.00%)	5 / 52 (9.62%)
occurrences (all)	0	0	6
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	10 / 52 (19.23%)
occurrences (all)	1	2	12
Vomiting			
subjects affected / exposed	3 / 10 (30.00%)	3 / 23 (13.04%)	5 / 52 (9.62%)
occurrences (all)	4	3	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	2 / 52 (3.85%)
occurrences (all)	2	2	2
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	5 / 52 (9.62%)
occurrences (all)	1	5	5
Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	1 / 52 (1.92%)
occurrences (all)	1	2	1
Productive cough			

subjects affected / exposed	1 / 10 (10.00%)	2 / 23 (8.70%)	1 / 52 (1.92%)
occurrences (all)	3	3	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 23 (4.35%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	4 / 52 (7.69%)
occurrences (all)	0	1	4
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	4 / 23 (17.39%)	4 / 52 (7.69%)
occurrences (all)	0	4	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	5 / 23 (21.74%)	2 / 52 (3.85%)
occurrences (all)	0	5	2
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 23 (8.70%)	7 / 52 (13.46%)
occurrences (all)	0	3	8
Musculoskeletal chest pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 23 (8.70%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)	1 / 23 (4.35%)	5 / 52 (9.62%)
occurrences (all)	1	1	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	5 / 23 (21.74%)	0 / 52 (0.00%)
occurrences (all)	0	6	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 10 (20.00%)	6 / 23 (26.09%)	7 / 52 (13.46%)
occurrences (all)	2	6	8
Diabetes mellitus			

subjects affected / exposed	0 / 10 (0.00%)	3 / 23 (13.04%)	1 / 52 (1.92%)
occurrences (all)	0	3	1
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	2 / 52 (3.85%)
occurrences (all)	0	1	2
Hypocalcaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 23 (4.35%)	4 / 52 (7.69%)
occurrences (all)	0	8	4
Hypokalaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 23 (4.35%)	7 / 52 (13.46%)
occurrences (all)	1	1	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2012	Updates to the protocol to make changes for Phase II of the study to include: •Modification to the primary endpoint •Addition of a secondary endpoint •Changes to the study design •Modify the inclusion criteria •Removal of assessments and exploratory endpoint for QoL •Modification to the sample size •Reduction of the more extensive renal monitoring
27 May 2014	Amendment No.: 02 •Modification to the sample size for Phase II Part 2 •Removal of long-term follow-up visits •Addition of open-label eltrombopag dosing in Cycle 7 and beyond •Pooling of Part 1 and Part 2 of Phase II data •Corrections to clerical errors

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported