Clinical trial results:
A Three-Part Study of Eltrombopag in Thrombocytopenic Subjects with Myelodysplastic Syndromes or Acute Myeloid Leukemia (Part 1: Open-Label, Part 2: Randomized, Double-Blind, Part 3: Extension).

Summary

EudraCT number	2011-000114-19
Trial protocol	BE DE CZ GR ES IE PL HU IT NL
Global end of trial date	21 December 2015

Results information

Result version number	v1 (current)
This version publication date	04 January 2017
First version publication date	04 January 2017

Trial information

Trial identification

Sponsor protocol code	CETB115D2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01440374
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2015
Global end of trial reached?	Yes
Global end of trial date	21 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1 open-label, 8 week first part of the study are:
• To evaluate the safety and tolerability of eltrombopag.
• To determine optimal dose escalation scheme for use in Part 2 of the study by assessing the dose of eltrombopag required to achieve platelet count response.
• To characterize plasma eltrombopag pharmacokinetics (steady-state plasma eltrombopag Cmax, tmax, AUC(0-τ), CL/F, and half-life).
Part 2: • The primary objective of this study is to determine reduction in the number of clinically relevant thrombocytopenic events (CRTE) in subjects with MDS or AML who have Grade 4 thrombocytopenia (<25 Gi/L) and are treated with eltrombopag compared to those treated with placebo.
Part 3: The objectives of Part 3 of the study are to evaluate the long-term durability of clinical benefit as well as overall survival, the long-term safety and tolerability of eltrombopag in subjects with MDS and AML.”

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Greece: 13
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Ireland: 11
Country: Number of subjects enrolled	Israel: 24
Country: Number of subjects enrolled	Italy: 9

Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	162
EEA total number of subjects	89

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)	34
From 65 to 84 years	120
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

Part 1, 17 subjects received open-label eltrombopag. Part 2, 145 subjects were randomized to receive eltrombopag plus SOC (N=98) or placebo plus SOC (N=47).
Part 3, 59 subjects from Part 2 entered Part 3. SOC was allowed as needed throughout the study. Subjects could receive disease-modifying therapy as needed.

Pre-assignment

Screening details:

Participants with myelodysplastic syndromes (MDS) or acute myeloid leukemia (AML) and Grade 4 thrombocytopenia due to bone marrow insufficiency and had at least one of the following: platelet count <10 Giga cells per liter, platelet transfusion or symptomatic hemorrhagic event during the 4 weeks prior to enrollment, were enrolled in the study.

Period 1

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

Blinding implementation details:

Part 1: Open-label Phase
Part 2: Double-blind Phase
Part 3: Extension

Arms

Are arms mutually exclusive?	No
Arm title	Part 1: Eltrombopag

Arm description:

The eltrombopag starting dose the participants received was 100 milligrams (mg) daily (50 mg for participants of East Asian heritage). The dose of eltrombopag was escalated from 100 mg to 200 mg (50 mg to 100 mg for East Asians) and further from 200 mg to 300 mg once daily (100 mg to 150 mg for East Asians) based on the platelet response and safety data after two weeks of current dose level. After all participants finished the 8 week treatment period, platelet response and safety were analyzed before initiating Part 2 of the study. Supportive standard of care was allowed as needed. The duration of Part 1 was 8 weeks.

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

Dosage and administration details:

Eltrombopag 100 mg once daily was selected as the starting dose for this study (50 mg for East Asian subjects), with subsequent dose adjustments dependent on each subject's platelet counts.
Eltrombopag was to be taken on an empty stomach (1 hour before or 2 hours after a meal) or with food containing little (<50 mg) or preferably no calcium or dairy products. At least a 4-hour interval between eltrombopag and other medications or products containing polyvalent cations.

Arm title	Part 2: Placebo

Arm description:

Participants received eltrombopag matching placebo once daily (3 tablets). Supportive standard of care was allowed as needed throughout the study.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

In Part 2 of the study, the duration of placebo administration required before dose escalation was based on platelet response and safety assessed during Part 1 of the study. The maximum dose of study medication was 300 mg once daily (150 mg for East Asian subjects).
Placebo was to be taken on an empty stomach (1 hour before or 2 hours after a meal) or with food containing little (<50 mg) or preferably no calcium or dairy products. At least a 4-hour interval between placebo and other medications or products containing polyvalent cations (e.g., calcium, magnesium, aluminum, zinc, selenium, or iron), such as antacids, dairy products, and mineral supplements, should be allowed to avoid significant (70% to 75%) reduction in absorption due to chelation.

Arm title	Part 2: Eltrombopag

Arm description:

The eltrombopag starting dose the participants received was 100 mg daily (50 mg for participants of East Asian heritage). The duration of treatment with the initial dose level prior to first dose escalation was determined based on the platelet response and toxicity observed in Part 1. The dose of eltrombopag was escalated from 100 mg to 200 mg (50 mg to 100 mg for East Asians) and further from 200 mg to 300 mg once daily (100 mg to 150 mg for East Asians) based on the platelet response and safety data after two weeks of current dose level. Supportive standard of care was allowed as needed throughout the study.

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

Dosage and administration details:

In Part 2 of the study, the duration of eltrombopag administration required before dose escalation was based on platelet response and safety assessed during Part 1 of the study. The maximum dose of study medication was 300 mg once daily (150 mg for East Asian subjects).
Eltrombopag was to be taken on an empty stomach (1 hour before or 2 hours after a meal) or with food containing little (<50 mg) or preferably no calcium or dairy products. At least a 4-hour interval between eltrombopag and other medications or products containing polyvalent cations (e.g., calcium, magnesium, aluminum, zinc, selenium, or iron), such as antacids, dairy products, and mineral supplements, should be allowed to avoid significant (70% to 75%) reduction in eltrombopag absorption due to chelation.

Arm title	Part 3: Eltrombopag

Arm description:

23 subjects of the 47 randomized to the placebo group in Part 2 entered part 3. 36 subjects of the 98 randomized to the Etrombopag group in Part 2 entered part 3. All subjects received eltrombopag. Part 3 subjects could also have received treatment for their disease per local SOC, including azacitidine, decitabine, lenalidomide, and chemotherapy. The duration of Part 3 was to be 10 months for subjects from Part 1and 9 months for subjects from Part 2.

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

Dosage and administration details:

Eltrombopag 100 mg once daily was selected as the starting dose for this study (50 mg for East Asian subjects), with subsequent dose adjustments dependent on each subject’s platelet counts.
Eltrombopag was to be taken on an empty stomach (1 hour before or 2 hours after a meal) or with food containing little (<50 mg) or preferably no calcium or dairy products. At least a 4-hour interval between eltrombopag and other medications or products containing polyvalent cations.

Number of subjects in period 1	Part 1: Eltrombopag	Part 2: Placebo	Part 2: Eltrombopag
Started	17	47	98
Completed	11	27	43
Not completed	6	20	55
Physician decision	1	8	17
Consent withdrawn by subject	-	4	5
Adverse event, non-fatal	5	7	31
Lack of efficacy	-	1	-
Not treated	-	-	1
Protocol deviation	-	-	1

Number of subjects in period 1	Part 3: Eltrombopag
Started	59
Completed	27
Not completed	32
Physician decision	14
Consent withdrawn by subject	5
Adverse event, non-fatal	13
Lack of efficacy	-
Not treated	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Eltrombopag

Reporting group description:

The eltrombopag starting dose the participants received was 100 milligrams (mg) daily (50 mg for participants of East Asian heritage). The dose of eltrombopag was escalated from 100 mg to 200 mg (50 mg to 100 mg for East Asians) and further from 200 mg to 300 mg once daily (100 mg to 150 mg for East Asians) based on the platelet response and safety data after two weeks of current dose level. After all participants finished the 8 week treatment period, platelet response and safety were analyzed before initiating Part 2 of the study. Supportive standard of care was allowed as needed. The duration of Part 1 was 8 weeks.

Reporting group title	Part 2: Placebo

Reporting group description:

Participants received eltrombopag matching placebo once daily (3 tablets). Supportive standard of care was allowed as needed throughout the study.

Reporting group title	Part 2: Eltrombopag

Reporting group description:

The eltrombopag starting dose the participants received was 100 mg daily (50 mg for participants of East Asian heritage). The duration of treatment with the initial dose level prior to first dose escalation was determined based on the platelet response and toxicity observed in Part 1. The dose of eltrombopag was escalated from 100 mg to 200 mg (50 mg to 100 mg for East Asians) and further from 200 mg to 300 mg once daily (100 mg to 150 mg for East Asians) based on the platelet response and safety data after two weeks of current dose level. Supportive standard of care was allowed as needed throughout the study.

Reporting group title	Part 3: Eltrombopag

Reporting group description:

23 subjects of the 47 randomized to the placebo group in Part 2 entered part 3. 36 subjects of the 98 randomized to the Etrombopag group in Part 2 entered part 3. All subjects received eltrombopag. Part 3 subjects could also have received treatment for their disease per local SOC, including azacitidine, decitabine, lenalidomide, and chemotherapy. The duration of Part 3 was to be 10 months for subjects from Part 1and 9 months for subjects from Part 2.

Reporting group values	Part 1: Eltrombopag	Part 2: Placebo	Part 2: Eltrombopag
Number of subjects	17	47	98
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	71.5	70.6	72.3
standard deviation	± 10.78	± 10.72	± 8.94
Gender categorical Units: Subjects			
Female	7	16	32
Male	10	31	66
RaceEthnicityOther Units: Subjects			
African American/African Heritage	0	0	1
Asian - East Asian Heritage	3	5	9
Asian - South East Asian Heritage	0	2	2
White - Arabic/North African Heritage	0	1	5

White - White/Caucasian/European Heritage	14	39	81

Reporting group values	Part 3: Eltrombopag	Total	
Number of subjects	59	221	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	72.2		
standard deviation	± 9.27	-	
Gender categorical Units: Subjects			
Female	19	74	
Male	40	147	
RaceEthnicityOther Units: Subjects			
African American/African Heritage	0	1	
Asian - East Asian Heritage	9	26	
Asian - South East Asian Heritage	0	4	
White - Arabic/North African Heritage	0	6	
White - White/Caucasian/European Heritage	50	184	

End points

End points reporting groups

Reporting group title	Part 1: Eltrombopag

Reporting group description:

The eltrombopag starting dose the participants received was 100 milligrams (mg) daily (50 mg for participants of East Asian heritage). The dose of eltrombopag was escalated from 100 mg to 200 mg (50 mg to 100 mg for East Asians) and further from 200 mg to 300 mg once daily (100 mg to 150 mg for East Asians) based on the platelet response and safety data after two weeks of current dose level. After all participants finished the 8 week treatment period, platelet response and safety were analyzed before initiating Part 2 of the study. Supportive standard of care was allowed as needed. The duration of Part 1 was 8 weeks.

Reporting group title	Part 2: Placebo

Reporting group description:

Participants received eltrombopag matching placebo once daily (3 tablets). Supportive standard of care was allowed as needed throughout the study.

Reporting group title	Part 2: Eltrombopag

Reporting group description:

The eltrombopag starting dose the participants received was 100 mg daily (50 mg for participants of East Asian heritage). The duration of treatment with the initial dose level prior to first dose escalation was determined based on the platelet response and toxicity observed in Part 1. The dose of eltrombopag was escalated from 100 mg to 200 mg (50 mg to 100 mg for East Asians) and further from 200 mg to 300 mg once daily (100 mg to 150 mg for East Asians) based on the platelet response and safety data after two weeks of current dose level. Supportive standard of care was allowed as needed throughout the study.

Reporting group title	Part 3: Eltrombopag

Reporting group description:

23 subjects of the 47 randomized to the placebo group in Part 2 entered part 3. 36 subjects of the 98 randomized to the Etrombopag group in Part 2 entered part 3. All subjects received eltrombopag. Part 3 subjects could also have received treatment for their disease per local SOC, including azacitidine, decitabine, lenalidomide, and chemotherapy. The duration of Part 3 was to be 10 months for subjects from Part 1and 9 months for subjects from Part 2.

Primary: Number of participants with platelet response up to Week 8 during Part 1

End point title	Number of participants with platelet response up to Week 8 during Part 1[1][2]

End point description:

A participant was considered as a responder if he/she met the following response criteria: a Baseline platelet count <20 Giga cells per liter (Gi/L) and a post-Baseline increased to >20 Gi/L and at least 2 times the Baseline value; or a Baseline platelet count >=20 Gi/L and a post-Baseline absolute platelet count increased to >=50 Gi/L and at least 2 times the Baseline value. The response criteria was evaluated at each visit. Increase in platelet count observed up to 3 days after a platelet transfusion was not considered as a platelet response. The Part 1 Population was comprised of all participants enrolled into Part 1.

End point type	Primary

End point timeframe:

From Baseline up to Week 8 during Part 1

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: Statistics were not reported for this endpoint.

[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: Statistics are not reported for all arms in this study.

End point values	Part 1: Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Participants	4			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with clinically relevant thrombocytopenic events (CRTE) from Week 5 up to Week 12 during Part 2

End point title	Percentage of participants with clinically relevant thrombocytopenic events (CRTE) from Week 5 up to Week 12 during Part 2[3]

End point description:

A participant was considered to have a CRTE at a given assessment if he/she had platelet counts <10 Gi/L, or platelet transfusions, or >=Grade 3 hemorrhagic adverse events. CRTEs during Weeks 5 to 12 were compared between treatments using a generalized linear mixed model. Average of weekly proportion of subjects with CRTE during Week 5 to 12 was estimated for each treatment. Intent to Treat (ITT) Population was comprised of all randomized participants during Part 2.

End point type	Primary

End point timeframe:

From Week 5 up to Week 12 during Part 2

Notes:

[3] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Percentage				
arithmetic mean (confidence interval 95%)	69 (57 to 80)	54 (43 to 64)		

Statistical analyses

Statistical analysis title	clinically relevant thrombocytopenic events
Comparison groups	Part 2: Placebo v Part 2: Eltrombopag
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0315
Method	Generalized Linear Mixed Models
Parameter estimate	Odds ratio (OR)
Point estimate	0.202

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.047
upper limit	0.868

Secondary: Plasma Eltrombopag Pharmacokinetic Concentration-Time Data - by Visit (Part 1 Subjects)

End point title	Plasma Eltrombopag Pharmacokinetic Concentration-Time Data - by Visit (Part 1 Subjects)[4]

End point description:

End point type	Secondary

End point timeframe:

Day 1 to week 8

Notes:

[4] - 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: Statistics are not reported for all arms in this study.

End point values	Part 1: Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: ug/mL				
arithmetic mean (standard deviation)				
Baseline/day 1 (Pre-dose PK)	0 (± 0)			
Day8 week 1 (Pre-dose PK)	7.7 (± 3.96)			
Day15 week 2 (Pre-dose PK)	7.2 (± 5.17)			
Day22 week 3 (Pre-dose PK)	14.3 (± 10.63)			
Day29 week 3 (2-6hrs post-dose PK)	20.8 (± 14.98)			
Day36 week 5 (Pre-dose PK)	20.2 (± 16.37)			
Day43 week6 (2-6hrs post-dose PK)	41.2 (± 32.56)			
Day50 week 7 (Pre-dose PK)	30.4 (± 27.95)			
Day57 week 8 (2-6hrs post-dose PK)	30.1 (± 18.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Eltrombopag Pharmacokinetic Concentration-Time Data - by Visit (Part 2 Subjects)

End point title	Plasma Eltrombopag Pharmacokinetic Concentration-Time Data - by Visit (Part 2 Subjects)[5]

End point description:

End point type	Secondary

End point timeframe:

Day 1 to week 12

Notes:

[5] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: ug/mL				
arithmetic mean (standard deviation)				
Baseline/day 1 (Pre-dose PK)	0 (± 0)			
Day15 week 2 (Pre-dose PK)	10.1 (± 5.54)			
Day22 week 3 (2-6hrs post-dose PK)	24 (± 14.6)			
Day29 week 4 (Pre-dose PK)	20.2 (± 13.61)			
Day43 week 6 (Pre-dose PK)	29 (± 18.13)			
Day50 week 7 (2-6hrs post-dose PK)	42.9 (± 22.37)			
Day57 week8 (Pre-dose PK)	36.3 (± 20.91)			
Day71 week 10 (Pre-dose PK)	33.5 (± 20.4)			
Day78 week 11 (2-6hrs post-dose PK)	41.2 (± 24.91)			
Day85 week12 (Pre-dose PK)	30.7 (± 18.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of Platelet Transfusions

End point title	Mean Number of Platelet Transfusions[6]

End point description:

End point type	Secondary

End point timeframe:

Weeks 5 to 12

Notes:

[6] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Number of platelet transfusions				
arithmetic mean (standard deviation)	15.7 (± 20.36)	18.8 (± 18.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Hematologic Improvement

End point title	Hematologic Improvement[7]

End point description:

End point type	Secondary

End point timeframe:

Weeks 5 to 12

Notes:

[7] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Number of subjects				
Any Improvement	4	10		
Platelets	2	8		
Neutrophils	4	4		
Hemoglobin	0	0		
Platelets and neutrophils	2	2		
Platelets and hemoglobin	0	0		
Platelets, hemoglobin and neutrophils	0	0		
Neutrophils and hemoglobin	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Mean Platelet Count

End point title	Change in Mean Platelet Count[8]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Gi/L				
arithmetic mean (standard deviation)				
Day8 week1	1.66 (± 6.249)	3.36 (± 11.795)		
Day15 week2	3.06 (± 9.675)	10.41 (± 60.225)		
Day22 week3	2.13 (± 9.258)	6.23 (± 22.872)		
Day29 week4	2.44 (± 11.215)	5.63 (± 17.582)		
Day36 week5	5.9 (± 16)	8.58 (± 22.504)		
Day43 week6	5.93 (± 21.96)	8.64 (± 19.779)		
Day50 week7	6.74 (± 31.074)	9.91 (± 25.561)		
Day57 week8	7.84 (± 34.213)	9.67 (± 23.243)		
Day64 week9	6.75 (± 31.709)	12.84 (± 27.272)		
Day71 week10	6.23 (± 30.941)	15.97 (± 33.866)		
Day78 week11	6.92 (± 26.906)	14.42 (± 36.901)		
Day 85 week12	4.85 (± 26.219)	9.06 (± 28.259)		

Statistical analyses

No statistical analyses for this end point

Secondary: MeanMaximum Duration of Platelet Transfusion Independence

End point title	MeanMaximum Duration of Platelet Transfusion

End point description:

End point type	Secondary

End point timeframe:

Weeks 5 to 12

Notes:

[9] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Number of platelet transfusions				
arithmetic mean (standard deviation)	25.4 (± 19.7)	26.3 (± 21.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Bleeding Grade According to World Health Organization on Bleeding Scale

End point title	Maximum Bleeding Grade According to World Health Organization on Bleeding Scale[10]

End point description:

End point type	Secondary

End point timeframe:

Weeks 5 to 12

Notes:

[10] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Number of subjects				
Grade 0 (no bleeding)	4	15		
Grade 1 (petechiae)	22	31		
Grade 2 (mild blood loss)	14	41		
Grade 3 (gross blood loss)	3	5		
Grade 4 (debilitating blood loss)	3	1		
Grades 0 – 1	26	46		
Grades 0 – 4	42	78		
Grades 2 - 4	20	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Independent Reviewer-Assessed Best Response

End point title	Independent Reviewer-Assessed Best Response[11]

End point description:

End point type	Secondary

End point timeframe:

up to week 12

Notes:

[11] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Number of subjects				
Responder	1	1		
Complete response (CR)	0	0		
Morphologic CR	1	0		
Morphologic leukemia-free state	0	0		
Marrow CR	0	1		
Cytogenetic CR	0	0		
Molecular CR	0	0		
Non-responder	46	97		
Partial response	0	0		
Stable disease (non-responder)	10	18		
Progressive disease (non-responder)	28	41		
Not evaluable (non-responder)	8	36		
Missing (non-responder)	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Independent Reviewer Assessed Disease Progression

End point title	Independent Reviewer Assessed Disease Progression[12]

End point description:

End point type	Secondary

End point timeframe:

Up to week 12

Notes:

[12] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Number of subjects				
Disease progression	36	61		
No disease progression	6	12		
Not evaluable	5	23		
Missing	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Overall Survival

End point title	Median Overall Survival[13]

End point description:

End point type	Secondary

End point timeframe:

Up to week 12

Notes:

[13] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Months				
median (confidence interval 95%)	4.6 (3.29 to 7.82)	4.27 (2.96 to 7.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Health Outcomes

End point title	Summary of Health Outcomes[14]

End point description:

The number of subject with medical resource utilization (MRU) data are reported in this table. MRU included number of emergency room visits, number of home healthcare visits, number of hospitalization days, number of medication or surgery specialist visits, number of procedures inpatient, number of procedures outpatient, number of non-study radiology visits, number of non-study laboratory visits, number of nurse practitioner/physician assistance/nurse visits, number of primary care physician visits, number of telephone consultations.

End point type	Secondary

End point timeframe:

week 12

Notes:

[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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: week				
Number of emergency room visits (n=17, n=10)	0	1		
Number of home healthcare visits (n=17, n=10)	1	2		
Number of hospitalization days (n=17, n=10)	4	5		
Number of med/surg specialist visits (n=17, n=10)	3	1		
Number of procedures inpatient (n=17, n=10)	1	2		
Number of procedures outpatient (n=17, n=10)	1	1		
Number of non-study radiology visits (n=2, n=2)	2	2		
Number of nurse prac/pa/nurse visits (n=17, n=10)	3	5		
Number of primary care physician visits (n=17,10)	1	7		
Number of telephone consultations (n=17, n=10)	0	1		
Number of non-study laboratory visits (n=17, n=10)	6	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Assessment of Cancer Therapy (FACT)

End point title	Functional Assessment of Cancer Therapy (FACT)[15]

End point description:

FACT-Th-18 questionnaire is the most widely used and accepted tool evaluating health-related quality-of-life outcomes in cancer patients with chronically low platelets (where Th designates thrombocytopenia). The entire FACT-Th-18 was used in this trial, which includes the 18-item thrombocytopenia subscale used to assess the impact of symptoms, signs, and functional consequences of thrombocytopenia in MDS and AML subjects. The FACT-Th-18 is a validated and reliable instrument with known psychometric properties [Cella, 2006]. The core questionnaire measures general health and well-being across 4 dimensions: physical, social and family, emotional, and functional well-being. FACT-Th-18 Trial Outcome Index (TOI) and FACT-G (global) scores.

End point type	Secondary

End point timeframe:

Change from baseline, up to week 12

Notes:

[15] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Adjusted mean change from baseline				
arithmetic mean (standard error)				
FACTG week 5 (n=61. n=34)	-3.15 (± 2.19)	-0.79 (± 1.64)		
FACTG week 9 (n=46. n=28)	-2.76 (± 2.34)	-4.83 (± 1.82)		
FACTG week12 (n=37. n=26)	-4.17 (± 2.39)	-3.38 (± 1.94)		
FACTHTOI week 5 (n=61, n=34)	-2.28 (± 2.74)	0.91 (± 2.04)		
FACTHTOI week 9 (n=46, n=28)	0.19 (± 2.89)	-1.69 (± 2.24)		
FACTHTOI week 12 (n=37, n=26)	-1.56 (± 2.95)	-0.26 (± 2.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D Utility Score Analysis

End point title	EQ-5D Utility Score Analysis[16]

End point description:

A summary of the number and percentage of subjects responding at each level for each dimension or item of the EQ-5D was displayed by visit and by treatment group. The EQ-5D measures mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Responses to each of the 5 health states are measured on a 3-point scale.

End point type	Secondary

End point timeframe:

Change from baseline, up to week 12

Notes:

[16] - 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: Statistics are not reported for all arms in this study.

End point values	Part 2: Placebo	Part 2: Eltrombopag		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	98		
Units: Adjusted mean change from baseline				
arithmetic mean (standard error)				
Week 5 (n=55. n=34)	-0.15 (± 0.05)	-0.01 (± 0.04)		
Week 9 (n=43. n=27)	-0.06 (± 0.05)	-0.08 (± 0.04)		
Week 12 (n=36. n=26)	-0.11 (± 0.05)	-0.09 (± 0.05)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Part 1 Eltrombopag
Reporting group description:	
Part 1 Eltrombopag	
Reporting group title	Part 2 Placebo
Reporting group description:	
Part 2 Placebo	
Reporting group title	Part 2 Eltrombopag
Reporting group description:	
Part 2 Eltrombopag	
Reporting group title	Part 2 subjects in Part 3 Eltrombopag
Reporting group description:	
Part 2 subjects in Part 3 Eltrombopag	

Serious adverse events	Part 1 Eltrombopag	Part 2 Placebo	Part 2 Eltrombopag
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 17 (52.94%)	32 / 47 (68.09%)	56 / 97 (57.73%)
number of deaths (all causes)	5	13	35
number of deaths resulting from adverse events	0	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung neoplasm			

subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Thrombophlebitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Chest discomfort			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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

Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Disease progression			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 17 (0.00%)	2 / 47 (4.26%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Multi-organ failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)	2 / 47 (4.26%)	0 / 97 (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
Pyrexia			

subjects affected / exposed	2 / 17 (11.76%)	6 / 47 (12.77%)	7 / 97 (7.22%)
occurrences causally related to treatment / all	0 / 3	0 / 8	1 / 8
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Sudden death			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (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
Lung consolidation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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

Lung disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory distress			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
International normalised ratio increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Head injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Subdural haematoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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

Subdural haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Wound haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
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			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Palpitations			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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			
Cerebral haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (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

Diabetic neuropathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Febrile neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	7 / 47 (14.89%)	7 / 97 (7.22%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Haemolytic anaemia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Lymphadenopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Splenic artery thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Splenic infarction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenomegaly			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			

subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal hypomotility			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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 ischaemia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Melaena			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral mucosal blistering			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cholangitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Bone pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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			
Abscess neck			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Appendicitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Catheter site cellulitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
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	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Clostridium difficile colitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Cystitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (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
Device related infection			

subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Endocarditis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Enteritis infectious			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Escherichia sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Herpes zoster			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Osteomyelitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Otitis externa			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	5 / 47 (10.64%)	14 / 97 (14.43%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 17
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 4
Respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (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
Sepsis			
subjects affected / exposed	4 / 17 (23.53%)	5 / 47 (10.64%)	8 / 97 (8.25%)
occurrences causally related to treatment / all	0 / 7	0 / 9	0 / 15
deaths causally related to treatment / all	0 / 3	0 / 4	0 / 7
Septic shock			

subjects affected / exposed	2 / 17 (11.76%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Splenic abscess			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Staphylococcal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Streptococcal sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (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
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	3 / 97 (3.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urosepsis			

subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral oesophagitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 subjects in Part 3 Eltrombopag		
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 59 (66.10%)		
number of deaths (all causes)	24		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Chest discomfort			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Death			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Malaise			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multi-organ failure			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Non-cardiac chest pain			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	7 / 59 (11.86%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Sudden death			

subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngeal oedema			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung consolidation			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary alveolar haemorrhage				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Blood bilirubin increased				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoglobin decreased				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
International normalised ratio increased				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
White blood cell count increased				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Subdural haemorrhage				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Transfusion reaction			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Myocardial infarction			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic neuropathy			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Generalised tonic-clonic seizure				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Seizure				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	3 / 59 (5.08%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Febrile neutropenia				
subjects affected / exposed	6 / 59 (10.17%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Haemolytic anaemia				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				

subjects affected / exposed	3 / 59 (5.08%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 2			
Lymphadenopathy				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic artery thrombosis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic infarction				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Splenomegaly				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal vein occlusion				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vitreous haemorrhage				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				

Abdominal pain			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal hypomotility			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal ischaemia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Melaena			

subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral mucosal blistering				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haemorrhage				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	2 / 59 (3.39%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Acute kidney injury				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Haematuria				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal disorder				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	2 / 59 (3.39%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess neck				

subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	4 / 59 (6.78%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Catheter site cellulitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis infective				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				

subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Enteritis infectious				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				

subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Lung infection				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis externa				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	10 / 59 (16.95%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 5			
Respiratory tract infection				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	6 / 59 (10.17%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 6			
Septic shock				

subjects affected / exposed	3 / 59 (5.08%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 2			
Splenic abscess				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal sepsis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tooth infection				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	5 / 59 (8.47%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Urosepsis				

subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral oesophagitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1 Eltrombopag	Part 2 Placebo	Part 2 Eltrombopag
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	44 / 47 (93.62%)	89 / 97 (91.75%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	9 / 47 (19.15%)	7 / 97 (7.22%)
occurrences (all)	0	12	7
Haemorrhage			
subjects affected / exposed	2 / 17 (11.76%)	4 / 47 (8.51%)	4 / 97 (4.12%)
occurrences (all)	2	4	7
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	6 / 97 (6.19%)
occurrences (all)	0	0	7
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	3 / 97 (3.09%)
occurrences (all)	1	1	3

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 17 (17.65%)	5 / 47 (10.64%)	4 / 97 (4.12%)
occurrences (all)	6	9	4
Catheter site related reaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	3 / 47 (6.38%)	23 / 97 (23.71%)
occurrences (all)	1	4	28
Oedema peripheral			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	9 / 97 (9.28%)
occurrences (all)	0	3	9
Pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences (all)	1	1	2
Pyrexia			
subjects affected / exposed	4 / 17 (23.53%)	10 / 47 (21.28%)	18 / 97 (18.56%)
occurrences (all)	12	25	29
Xerosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences (all)	1	0	6
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Cough			

subjects affected / exposed	1 / 17 (5.88%)	4 / 47 (8.51%)	13 / 97 (13.40%)
occurrences (all)	1	5	16
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)	5 / 47 (10.64%)	9 / 97 (9.28%)
occurrences (all)	1	6	10
Epistaxis			
subjects affected / exposed	5 / 17 (29.41%)	11 / 47 (23.40%)	27 / 97 (27.84%)
occurrences (all)	6	18	46
Haemoptysis			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	6 / 97 (6.19%)
occurrences (all)	0	3	7
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	0 / 97 (0.00%)
occurrences (all)	1	2	0
Productive cough			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Rales			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences (all)	1	1	0
Sputum increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences (all)	1	0	2
Confusional state			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences (all)	0	1	1
Initial insomnia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Investigations			
Activated partial thromboplastin time prolonged			

subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 17 (17.65%)	5 / 47 (10.64%)	10 / 97 (10.31%)
occurrences (all)	4	7	17
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	5 / 47 (10.64%)	3 / 97 (3.09%)
occurrences (all)	1	7	3
Blood albumin decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences (all)	1	2	2
Blood bilirubin increased			
subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	6 / 97 (6.19%)
occurrences (all)	3	3	9
Blood phosphorus decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Blood sodium increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	2 / 97 (2.06%)
occurrences (all)	0	3	2
Body temperature fluctuation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Liver function test abnormal			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences (all)	2	1	0
Platelet count decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	2	0	1

Serum ferritin increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	2	0	1
Weight decreased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences (all)	2	1	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 17 (5.88%)	3 / 47 (6.38%)	4 / 97 (4.12%)
occurrences (all)	2	17	7
Fall			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	1 / 97 (1.03%)
occurrences (all)	2	1	1
Laceration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Post procedural haematoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Transfusion reaction			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	2 / 97 (2.06%)
occurrences (all)	0	4	2
Wound			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Nervous system disorders			
Aphonia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Balance disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0

Dizziness			
subjects affected / exposed	2 / 17 (11.76%)	4 / 47 (8.51%)	9 / 97 (9.28%)
occurrences (all)	2	5	10
Headache			
subjects affected / exposed	3 / 17 (17.65%)	3 / 47 (6.38%)	3 / 97 (3.09%)
occurrences (all)	3	3	3
Mental impairment			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	2	0	0
Poor quality sleep			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	2 / 17 (11.76%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 17 (17.65%)	2 / 47 (4.26%)	8 / 97 (8.25%)
occurrences (all)	14	5	12
Blood disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Febrile neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	4 / 97 (4.12%)
occurrences (all)	1	0	4
Haemolysis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Leukocytosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	3 / 97 (3.09%)
occurrences (all)	0	1	4
Neutropenia			

subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	2 / 97 (2.06%)
occurrences (all)	4	4	2
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences (all)	1	1	0
Vertigo			
subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	1 / 97 (1.03%)
occurrences (all)	3	2	1
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	4 / 47 (8.51%)	2 / 97 (2.06%)
occurrences (all)	1	4	2
Eye haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	5 / 97 (5.15%)
occurrences (all)	0	0	5
Ocular hyperaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Ocular icterus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	3 / 47 (6.38%)	6 / 97 (6.19%)
occurrences (all)	1	4	8
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	2 / 47 (4.26%)	6 / 97 (6.19%)
occurrences (all)	0	3	9
Colitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	3 / 17 (17.65%)	0 / 47 (0.00%)	12 / 97 (12.37%)
occurrences (all)	3	0	20
Diarrhoea			

subjects affected / exposed	4 / 17 (23.53%)	5 / 47 (10.64%)	20 / 97 (20.62%)
occurrences (all)	5	5	29
Gingival bleeding			
subjects affected / exposed	1 / 17 (5.88%)	8 / 47 (17.02%)	13 / 97 (13.40%)
occurrences (all)	2	15	14
Gingival swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	7 / 47 (14.89%)	9 / 97 (9.28%)
occurrences (all)	0	13	12
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	8 / 47 (17.02%)	13 / 97 (13.40%)
occurrences (all)	1	9	20
Vomiting			
subjects affected / exposed	2 / 17 (11.76%)	5 / 47 (10.64%)	6 / 97 (6.19%)
occurrences (all)	2	6	8
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	2	0	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	3 / 97 (3.09%)
occurrences (all)	2	0	3
Skin and subcutaneous tissue disorders			
Blood blister			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences (all)	0	2	0
Decubitus ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Dry skin			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Ecchymosis			

subjects affected / exposed	2 / 17 (11.76%)	6 / 47 (12.77%)	7 / 97 (7.22%)
occurrences (all)	3	13	17
Petechiae			
subjects affected / exposed	6 / 17 (35.29%)	11 / 47 (23.40%)	41 / 97 (42.27%)
occurrences (all)	9	16	56
Pruritus			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences (all)	2	1	2
Purpura			
subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	0 / 97 (0.00%)
occurrences (all)	3	2	0
Rash			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences (all)	1	3	0
Skin discolouration			
subjects affected / exposed	2 / 17 (11.76%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences (all)	2	0	2
Skin haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	2 / 97 (2.06%)
occurrences (all)	0	4	2
Skin ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	4 / 47 (8.51%)	1 / 97 (1.03%)
occurrences (all)	2	4	1
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	4 / 47 (8.51%)	11 / 97 (11.34%)
occurrences (all)	0	5	11
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	5 / 47 (10.64%)	6 / 97 (6.19%)
occurrences (all)	0	5	6
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Arthritis infective			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Bacterial infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	2 / 97 (2.06%)
occurrences (all)	0	3	2
Escherichia infection			
subjects affected / exposed	1 / 17 (5.88%)	1 / 47 (2.13%)	0 / 97 (0.00%)
occurrences (all)	1	1	0
Klebsiella sepsis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Otitis externa			

subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	4 / 17 (23.53%)	1 / 47 (2.13%)	3 / 97 (3.09%)
occurrences (all)	4	1	3
Skin infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 17 (17.65%)	2 / 47 (4.26%)	2 / 97 (2.06%)
occurrences (all)	3	2	2
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	5 / 97 (5.15%)
occurrences (all)	2	4	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 17 (11.76%)	7 / 47 (14.89%)	14 / 97 (14.43%)
occurrences (all)	3	7	15
Dehydration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 47 (2.13%)	2 / 97 (2.06%)
occurrences (all)	0	2	2
Hyperkalaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 47 (4.26%)	7 / 97 (7.22%)
occurrences (all)	1	3	8
Hypocalcaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	4 / 97 (4.12%)
occurrences (all)	2	0	5
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	3 / 47 (6.38%)	9 / 97 (9.28%)
occurrences (all)	0	5	12
Hypomagnesaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	5 / 97 (5.15%)
occurrences (all)	2	0	5

Hypophagia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 47 (0.00%)	2 / 97 (2.06%)
occurrences (all)	1	0	2

Non-serious adverse events	Part 2 subjects in Part 3 Eltrombopag		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 59 (91.53%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	9 / 59 (15.25%)		
occurrences (all)	10		
Haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	17		
Catheter site related reaction			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	9 / 59 (15.25%)		
occurrences (all)	11		
Oedema peripheral			
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	9		

Pain			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	12 / 59 (20.34%)		
occurrences (all)	20		
Xerosis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	8		
Dyspnoea			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	6		
Epistaxis			
subjects affected / exposed	12 / 59 (20.34%)		
occurrences (all)	21		
Haemoptysis			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	3		
Oropharyngeal pain			

subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Productive cough			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Sputum increased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Confusional state			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Initial insomnia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Blood albumin decreased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	4		
Blood bilirubin increased			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	7		
Blood phosphorus decreased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Blood sodium increased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	3		
Body temperature fluctuation			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Liver function test abnormal			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Serum ferritin increased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	5		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	12		
Fall			

subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Laceration			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Post procedural haematoma			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Transfusion reaction			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Balance disorder			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Mental impairment			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	2		
Poor quality sleep			

subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0 1 / 59 (1.69%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Blood disorder subjects affected / exposed occurrences (all) Disseminated intravascular coagulation subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all) Haemolysis subjects affected / exposed occurrences (all) Leukocytosis subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 2 / 59 (3.39%) 5 0 / 59 (0.00%) 0 0 / 59 (0.00%) 0 2 / 59 (3.39%) 2 0 / 59 (0.00%) 0 4 / 59 (6.78%) 11 3 / 59 (5.08%) 3		
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	 0 / 59 (0.00%) 0 2 / 59 (3.39%) 2		
Eye disorders			

Conjunctival haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Eye haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Ocular icterus			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	5		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	5		
Abdominal pain upper			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Colitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	11 / 59 (18.64%)		
occurrences (all)	19		
Gingival bleeding			
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	8		
Gingival swelling			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Mouth haemorrhage			

subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	13		
Nausea			
subjects affected / exposed	14 / 59 (23.73%)		
occurrences (all)	14		
Vomiting			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	7		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Hyperbilirubinaemia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Blood blister			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Decubitus ulcer			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Ecchymosis			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	7		
Petechiae			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	15		
Pruritus			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Purpura			

subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	2		
Skin discolouration			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Skin haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Skin ulcer			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Infections and infestations			

Acute sinusitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Arthritis infective				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Bacterial infection				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	2 / 59 (3.39%)			
occurrences (all)	2			
Escherichia infection				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Klebsiella sepsis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	7 / 59 (11.86%)			
occurrences (all)	9			
Otitis externa				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	2 / 59 (3.39%)			
occurrences (all)	2			
Skin infection				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences (all)	0			

Urinary tract infection subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	10 / 59 (16.95%) 12		
Dehydration subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3		
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0		
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 8		
Hypokalaemia subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 12		
Hypomagnesaemia subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3		
Hypophagia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2011	The Czech Republic Regulatory Authority requested revisions to the protocol to comply with local country standards for liver chemistry inclusion criteria and liver chemistry discontinuation/withdrawal criteria.
25 May 2012	Selection of dose escalation scheme based on Part 1 results; added secondary endpoint of overall survival and separate endpoints to assess disease progression and response; addition of external adjudication committee to review disease progression and disease response; modifications to simplify dose adjustment guidelines; addition of guidelines to allow rechallenge with study medication after a subject met a liver stopping criteria.
17 January 2013	Modified to allow continued access to study medication in Part 3 for up to an additional 12 months. The amendment applied only to subjects in Israel.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported