Clinical trial results:
Study PMA112509, a Phase I/II Study of Eltrombopag in Thrombocytopenic Subjects with Advanced Myelodysplastic Syndrome (MDS) or secondary Acute Myeloid Leukemia after MDS (sAML/MDS)

Summary

EudraCT number	2009-015512-17
Trial protocol	DE FR DK GB
Global end of trial date	05 December 2013

Results information

Result version number	v1 (current)
This version publication date	08 April 2016
First version publication date	13 April 2015

Trial information

Trial identification

Sponsor protocol code	PMA112509

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 July 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of eltrombopag when administered to subjects with advanced MDS, sAML/MDS or de novo AML with 10-50% bone marrow blasts.

Protection of trial subjects:

Participants were monitored closely throughout the study related to changes to bone marrow changes and disease progression. Bone marrow samples were taken prior to first dose of study medication and throughout the study until the end of the study. Bone marrow samples were reviewed centrally by a central pathologist. To closely monitor disease progression, the study implemented a blinded adjudication of disease progression by use of an adjudication committee comprised of three external hematologists.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 May 2009
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	Hong Kong: 10
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Taiwan: 9
Worldwide total number of subjects	98
EEA total number of subjects	43

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)	19
From 65 to 84 years	72
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The initial on-therapy phase of the study involved treatment with study medication for up to 6 months. After completion of the dosing period, participants (par.) underwent follow-up assessments for 6 months after the final dose. The 6-month Follow up period was intended to assess the long-term safety of treatment with eltrombopag.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Matching placebo tablets were administered to participants once daily for 6 months.

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

Dosage and administration details:

placebo tablets orally once daily for 6 months

Arm title	Eltrombopag 50 mg

Arm description:

Participants initially received 50 milligram (mg) eltrombopag tablets orally once daily for 6 months. Intra-individual dose adjustments in a stepwise fashion to 100 mg, 200 mg, or 300 mg were allowed based on the participants' platelet and bone marrow blast counts. For participants of East Asian heritage, a maximum dose of 150 mg was allowed. Stepwise dose adjustments from 50 mg to 100 mg or 150 mg were permitted for East Asian participants.

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

Dosage and administration details:

50 milligram (mg) eltrombopag tablets orally once daily for 6 months. Intra-individual dose adjustments in a stepwise fashion to 100 mg, 200 mg, or 300 mg were allowed based on the participants' platelet and bone marrow blast counts. For participants of East Asian heritage, a maximum dose of 150 mg was allowed. Stepwise dose adjustments from 50 mg to 100 mg or 150 mg were permitted for East Asian participants.

Number of subjects in period 1	Placebo	Eltrombopag 50 mg
Started	34	64
Completed	3	11
Not completed	31	53
Consent withdrawn by subject	6	9
Physician decision	-	2
Adverse event, non-fatal	10	10
Disease Progression	10	21
Lack of efficacy	5	9
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo tablets were administered to participants once daily for 6 months.	
Reporting group title	Eltrombopag 50 mg
Reporting group description:	
Participants initially received 50 milligram (mg) eltrombopag tablets orally once daily for 6 months. Intra-individual dose adjustments in a stepwise fashion to 100 mg, 200 mg, or 300 mg were allowed based on the participants' platelet and bone marrow blast counts. For participants of East Asian heritage, a maximum dose of 150 mg was allowed. Stepwise dose adjustments from 50 mg to 100 mg or 150 mg were permitted for East Asian participants.	

Reporting group values	Placebo	Eltrombopag 50 mg	Total
Number of subjects	34	64	98
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median	71	73	
full range (min-max)	40 to 91	29 to 88	-
Gender categorical			
Units: Subjects			
Female	9	30	39
Male	25	34	59
Race			
Units: Subjects			
African American/African Heritage	2	2	4
Japanese/East Asian Heritage (EAH) /South EAH	7	18	25
White	25	43	68
African American/African Heritage & White	0	1	1
Number of participants with MDS or AML at Baseline per World Health Organization (WHO) Guidelines			
Two participants (1 placebo, 1 eltrombopag) had missing information.			
Units: Subjects			
Advanced Myelodysplastic Syndrome (AMS)	11	15	26
Acute Myeloid Leukemia (AML)	22	48	70
Missing	1	1	2
Number of participants with MDS or AML per French-American-Bristish Criteria			
Two participants (1 placebo, 1 eltrombopag) had missing information.			
Units: Subjects			
Advanced Myelodysplastic Syndrome	14	22	36
Acute Myeloid Leukemia	19	41	60
Missing	1	1	2

Median Bone Marrow Blast Counts at Baseline			
Bone marrow blasts are immature cells in the bone marrow.			
Units: percent			
median	20	25.5	
full range (min-max)	10 to 50	10 to 50	-
Median Absolute Neutrophil Count at Baseline			
Units: Giga (10^9) per Liter (Gi/L)			
median	0.55	0.85	
full range (min-max)	0 to 9.8	0 to 17.6	-
Median Platelet Count at Baseline			
Units: Gi/L			
median	12.3	17.4	
full range (min-max)	2 to 38	2 to 71	-
Median Hemoglobin Values at Baseline			
Units: grams per Liter			
median	85	88	
full range (min-max)	60 to 112	43 to 132	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Matching placebo tablets were administered to participants once daily for 6 months.	

Reporting group title	Eltrombopag 50 mg
Reporting group description:	
Participants initially received 50 milligram (mg) eltrombopag tablets orally once daily for 6 months. Intra-individual dose adjustments in a stepwise fashion to 100 mg, 200 mg, or 300 mg were allowed based on the participants' platelet and bone marrow blast counts. For participants of East Asian heritage, a maximum dose of 150 mg was allowed. Stepwise dose adjustments from 50 mg to 100 mg or 150 mg were permitted for East Asian participants.	

Primary: Number of participants with any Serious Adverse Event (SAE) and non-serious Adverse Event (AE)

End point title	Number of participants with any Serious Adverse Event (SAE) and non-serious Adverse Event (AE)[1]
End point description:	
An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is a Grade 4 (life threatening or disabling) non-hematologic laboratory abnormality assessed using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Refer to the general AE/SAE module for a complete list of AEs and SAEs.	
End point type	Primary
End point timeframe:	
From the start of study treatment plus 30 days post-treatment (average of 96.6 weeks)	

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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[2]	64[3]		
Units: Participants				
Any Adverse Event	32	63		
Any Serious Adverse Event	22	50		

Notes:

[2] - Safety Population: all randomized par. who received at least one dose of investigation product.

[3] - Safety Population: all randomized par. who received at least one dose of investigation product.

Statistical analyses

No statistical analyses for this end point

Primary: Bone marrow blast counts at Baseline, at Month 3, at Month 6, and at the

3-Month Follow-up visit, as Assessed by the Central Morphologist

End point title	Bone marrow blast counts at Baseline, at Month 3, at Month 6, and at the 3-Month Follow-up visit, as Assessed by the Central Morphologist[4]

End point description:

Bone marrow blast (immature cells in the bone marrow) counts were assessed every 3 months during the treatment and follow-up periods. Bone marrow exams occurring within 120 days of Baseline were slotted as Month 3, while those occurring after 120 days from Baseline were slotted as Month 6. Similar slotting was used for follow-up and extension periods. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed at different time points; thus, the overall number of participants analyzed reflects everyone in the Safety Population.

End point type	Primary

End point timeframe:

Baseline, Month 3, Month 6, and at the 3-Month Follow-up visit (up to Study Month 18)

Notes:

[4] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[5]	64[6]		
Units: percent				
median (inter-quartile range (Q1-Q3))				
Baseline, n=24, 56	29 (13.5 to 38)	31 (17 to 53.5)		
Month 3, n=14, 33	42.5 (25 to 66)	48 (21 to 73)		
Month 6, n=3, 10	50 (8 to 74)	38.5 (18 to 82)		
3-Month Follow-up visit, n=1, 6	28 (28 to 28)	49 (38 to 71)		

Notes:

[5] - Safety Population

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the indicated non-hematological laboratory toxicity >=Grade 3 post-Baseline

End point title	Number of participants with the indicated non-hematological laboratory toxicity >=Grade 3 post-Baseline[7]

End point description:

A grading (severity) scale is provided for each non-hematological laboratory toxicity. Grade refers to the severity of the toxicity. The CTCAE version 3.0 displays Grades 1 through 5, with unique clinical descriptions of the severity for each toxicity based on the general guideline: Grade 1, mild toxicity; Grade 2, moderate toxicity; Grade 3, severe toxicity; Grade 4, life-threatening or disabling toxicity; Grade 5, death related to toxicity.

End point type	Primary

End point timeframe:

From the start of study treatment plus 30 days post-treatment (average of 96.6 weeks)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical Analysis is not applicable for this Outcome Measure.

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[8]	64[9]		
Units: Participants				
Alanine Amino Tranferase	1	1		
Albumin	1	0		
Alkaline Phosphatase	1	0		
Creatinine	0	1		
Hyperkalemia	0	1		
Hypokalemia	2	9		
Hyponatremia	3	3		
Total Bilirubin	2	2		

Notes:

[8] - Safety Population

[9] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants classified as platelet responders

End point title	Number of participants classified as platelet responders

End point description:

Platelet responders were defined based on the modified International Working Group response criteria for hematological improvement as par. who had a Baseline platelet count <20 giga (10^9) cells per liter (Gi/L) and an increase to >20 Gi/L and at least a two times increase from Baseline, or a Baseline platelet count >=20 Gi/L and an increase to >=50 Gi/L and at least a two times increase from Baseline at any time during treatment with study medication (unless the increase in platelets is observed up to 3 days after a platelet transfusion). A durable platelet response is defined as a continuous platelet response of 4 weeks or longer. Analysis was performed by Stratified Cochrane-Mantel-haenszel chi-square test adjusting for the presence of a poor prognosis karyotype and bone marrow blast counts. Par. were evaluated according to the treatment to which they were randomized. Any participant who received a treatment randomization number was considered to have been randomized.

End point type	Secondary

End point timeframe:

Baseline through the end of treatment (up to Study Week 81)

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[10]	64[11]		
Units: Participants				
Platelet response, yes	10	18		
Durable response, yes	1	5		

Notes:

[10] - All Randomized Population: all randomized participants.

[11] - All Randomized Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Eltrombopag 50 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.9419
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.9658
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3811
upper limit	2.4476

Notes:

[12] - Statistical analysis for platelet response.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Eltrombopag 50 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.3586
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.7817
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2989
upper limit	25.8867

Notes:

[13] - Statistical analysis for durable platelet response.

Secondary: Number of participants with a platelet transfusion at the indicated study week

End point title	Number of participants with a platelet transfusion at the indicated study week

End point description:

The number of participants receiving platelet transfusions during the treatment period was assessed.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 8, 12, 16, 20, and 24

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32[14]	58[15]		
Units: Participants				
Week 1, n=32, 58	17	29		
Week 4, n=26, 48	12	20		
Week 8, n=19, 39	6	12		
Week 12, n=9, 22	4	6		
Week 16, n=5, 13	2	4		
Week 20, n=4, 11	2	5		
Week 24, n=2, 5	0	3		

Notes:

[14] - All Randomized Population. Par. with data available at the indicated time points were analyzed.

[15] - All Randomized Population. Par. with data available at the indicated time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum platelet transfusion independence of >=56 days

End point title	Number of participants with maximum platelet transfusion independence of >=56 days

End point description:

For participants who received study medication, the duration of platelet transfusion independence is defined as the duration of time during which participants don't receive any platelet transfusions during the treatment and 4-week follow up periods. Data are presented as the number of participants with platelet transfusion indpendence >=56 days. Analysis was performed by stratified Cochrane-Mantel-haenszel chi-square test adjusting for the presence of a poor prognosis karyotype and bone marrow blast counts.

End point type	Secondary

End point timeframe:

During treatment plus 4 weeks of follow-up (up to Study Week 68.6)

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[16]	64[17]		
Units: participants	7	24		

Notes:

[16] - All Randomized Population

[17] - All Randomized Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Eltrombopag 50 mg

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0979
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.277
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8558
upper limit	6.0585

Secondary: Number of participants with bleeding events of the indicated severity

End point title	Number of participants with bleeding events of the indicated severity

End point description:

The severity of bleeding events was assessed using the World Health Organization bleeding scale: Grade 0, no bleeding; Grade 1, petechiae (pinpoint-sized bleeding); Grade 2, mild blood loss; Grade 3, gross blood loss; Grade 4, debilitating blood loss.

End point type	Secondary

End point timeframe:

Day 1 and Weeks 4, 8, 12, 16, 20, and 24

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[18]	64[19]		
Units: Participants				
Day 1, Grade 0, n=34, 64	15	32		
Day 1, Grades, 1–4 n=34, 64	19	32		
Week 4, Grade 0, n=26, 45	9	23		
Week 4, Grades 1-4, n=26, 45	17	22		
Week 8, Grade 0, n=19, 28	6	21		
Week 8, Grades 1-4, n=19, 28	13	17		
Week 12, Grade 0, n=9, 21	3	13		
Week 12, Grades 1-4, n=9, 21	6	8		
Week 16, Grade 0, n=5, 13	3	5		
Week 16, Grades 1-4, n=5, 13	2	8		
Week 20, Grade 0, n=4, 11	2	5		
Week 20, Grades 1-4, n=4, 11	2	6		
Week 24, Grade 0, n=2, 5	1	3		
Week 24, Grades 1-4, n=2, 5	1	2		

Notes:

[18] - All Randomized Population. Par. with data available at the indicated time points were analyzed.

[19] - All Randomized Population. Par. with data available at the indicated time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival is defined as the time from randomization until death due to any cause. For surviving participants and participants who withdrew from the study, time to death was censored at the time of last contact. Overall survival was summarized using Kaplan-Meier survival curves, and compared between treatment arms using a stratified log-rank. Hazard ratio was estimated using the Pike Estimator. A hazard ratio <1 indicates a lower risk with eltrombopag compared with placebo.

End point type	Secondary

End point timeframe:

From randomization until death due to any cause (up to Study Week 96.6)

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[20]	64[21]		
Units: Weeks				
median (confidence interval 95%)	15.7 (9.6 to 26.3)	27 (16.4 to 34)		

Notes:

[20] - All Randomized Population

[21] - All Randomized Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Eltrombopag 50 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2079
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.27

Secondary: Mean steady-state plasma eltrombopag trough concentrations by dose level

End point title	Mean steady-state plasma eltrombopag trough concentrations by dose level[22]

End point description:

Mean steady-state plasma eltrombopag concentrations were estimated for different dose levels. Only those participants with data available at the indicated time points were analyzed. A single participant could have received more than one dose of eltrombopag.

End point type	Secondary

End point timeframe:

Steady-state (>=5 days on current dose) and within 6 hours of the planned sample time

Notes:

[22] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	Eltrombopag 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	64[23]			
Units: micrograms/milliliter				
arithmetic mean (standard deviation)				
50 mg, n=34	5.39 (± 3.03)			
100 mg, n=30	8.5 (± 5.45)			
125 mg, n=1	25.1 (± 5.92)			
150 mg, n=12	19.2 (± 10.8)			
200 mg, n=15	16 (± 10.7)			
300 mg, n=15	25.7 (± 14.9)			

Notes:

[23] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated on-therapy AEs of special interest

End point title	Number of participants with the indicated on-therapy AEs of special interest

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. On-therapy events are defined as those AEs with an onset on or after the start date of study medication and up to 30 days after the last dose of study medication. Refer to the general AE/SAE module for a complete list of AEs and SAEs.

End point type	Secondary

End point timeframe:

From the start of study treatment plus 30 days post-treatment (average of 96.6 weeks)

End point values	Placebo	Eltrombopag 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[24]	64[25]		
Units: Participants				
Any hepatobiliary events	5	12		
Any thromboembolic event	1	2		
Any renal event	2	8		
Any skin discoloration event	0	4		

Notes:

[24] - Safety Population

[25] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
On-treatment AEs	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo tablets were administered to participants once daily for 6 months	
Reporting group title	Eltrombopag 50 mg
Reporting group description:	
Participants initially received 50 milligram (mg) eltrombopag tablets orally once daily for 6 months. Intra-individual dose adjustments in a stepwise fashion to 100 mg, 200 mg or 300 mg were allowed based on the participants' platelet and bone marrow blast counts. For participants of East Asian heritage, a maximum dose of 150 mg was allowed. Stepwise dose adjustments from 50 mg to 100 mg or 150 mg were permitted for East Asian participants.	

Serious adverse events	Placebo	Eltrombopag 50 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 34 (67.65%)	53 / 64 (82.81%)	
number of deaths (all causes)	21	40	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Shock haemorrhagic			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 34 (2.94%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site granuloma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 34 (2.94%)	4 / 64 (6.25%)	
occurrences causally related to treatment / all	1 / 1	1 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Reproductive system and breast disorders			
Balanitis			

subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subcutaneous haematoma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericardial effusion			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic paroxysmal hemicrania			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Syncope			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	5 / 34 (14.71%)	4 / 64 (6.25%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Increased tendency to bruise			

subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival bleeding			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			

subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal stenosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hydronephrosis			

subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal failure acute			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoporosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	1 / 34 (2.94%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fascial infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 34 (2.94%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Klebsiella bacteraemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 34 (17.65%)	5 / 64 (7.81%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 2	
Pneumonia fungal			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis Escherichia coli			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			

subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 34 (5.88%)	4 / 64 (6.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 2	
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Eltrombopag 50 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 34 (88.24%)	58 / 64 (90.63%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 34 (5.88%)	6 / 64 (9.38%)	
occurrences (all)	4	15	
Haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	4	
Hypotension			
subjects affected / exposed	1 / 34 (2.94%)	4 / 64 (6.25%)	
occurrences (all)	1	4	
Orthostatic hypotension			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 34 (11.76%)	4 / 64 (6.25%)	
occurrences (all)	5	4	
Catheter site haematoma			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Catheter site phlebitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	
Chills			
subjects affected / exposed	0 / 34 (0.00%)	4 / 64 (6.25%)	
occurrences (all)	0	5	
Fatigue			

subjects affected / exposed	6 / 34 (17.65%)	15 / 64 (23.44%)	
occurrences (all)	6	20	
General physical health deterioration			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Injection site extravasation			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Oedema			
subjects affected / exposed	1 / 34 (2.94%)	3 / 64 (4.69%)	
occurrences (all)	1	3	
Oedema peripheral			
subjects affected / exposed	5 / 34 (14.71%)	9 / 64 (14.06%)	
occurrences (all)	5	11	
Pain			
subjects affected / exposed	2 / 34 (5.88%)	3 / 64 (4.69%)	
occurrences (all)	2	3	
Pyrexia			
subjects affected / exposed	9 / 34 (26.47%)	19 / 64 (29.69%)	
occurrences (all)	24	28	
Suprapubic pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Scrotal pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Cough			

subjects affected / exposed	2 / 34 (5.88%)	8 / 64 (12.50%)	
occurrences (all)	2	9	
Dyspnoea			
subjects affected / exposed	4 / 34 (11.76%)	5 / 64 (7.81%)	
occurrences (all)	6	5	
Dyspnoea exertional			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	3	0	
Epistaxis			
subjects affected / exposed	9 / 34 (26.47%)	10 / 64 (15.63%)	
occurrences (all)	16	15	
Haemoptysis			
subjects affected / exposed	2 / 34 (5.88%)	3 / 64 (4.69%)	
occurrences (all)	2	3	
Nasal obstruction			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	0 / 34 (0.00%)	5 / 64 (7.81%)	
occurrences (all)	0	6	
Pleural effusion			
subjects affected / exposed	2 / 34 (5.88%)	3 / 64 (4.69%)	
occurrences (all)	2	3	
Productive cough			
subjects affected / exposed	2 / 34 (5.88%)	3 / 64 (4.69%)	
occurrences (all)	3	3	
Pulmonary congestion			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Pulmonary oedema			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	3 / 34 (8.82%)	2 / 64 (3.13%)	
occurrences (all)	4	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 34 (5.88%)	2 / 64 (3.13%)	
occurrences (all)	2	3	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
Blood albumin decreased			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	5	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Blood bicarbonate decreased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
Blood potassium decreased			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Blood urea increased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
Blood urine present			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	
Hepatic enzyme increased			

subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 34 (2.94%)	4 / 64 (6.25%)	
occurrences (all)	1	4	
White blood cell count			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Eye contusion			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Periorbital contusion			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Transfusion reaction			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Arrhythmia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Atrioventricular block			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Cardiomegaly			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 34 (2.94%)	3 / 64 (4.69%)	
occurrences (all)	1	3	
Tachycardia			

subjects affected / exposed	3 / 34 (8.82%)	0 / 64 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 34 (2.94%)	9 / 64 (14.06%)	
occurrences (all)	1	10	
Dysgeusia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 34 (5.88%)	8 / 64 (12.50%)	
occurrences (all)	2	8	
Hypoaesthesia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Somnolence			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 34 (14.71%)	6 / 64 (9.38%)	
occurrences (all)	5	19	
Coagulopathy			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Haemorrhagic disorder			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Leukopenia			

subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
Lymphopenia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Neutropenia			
subjects affected / exposed	2 / 34 (5.88%)	2 / 64 (3.13%)	
occurrences (all)	2	2	
Thrombocytopenia			
subjects affected / exposed	1 / 34 (2.94%)	4 / 64 (6.25%)	
occurrences (all)	1	16	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	
Conjunctivitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	2 / 34 (5.88%)	6 / 64 (9.38%)	
occurrences (all)	2	6	
Abdominal pain upper			
subjects affected / exposed	1 / 34 (2.94%)	4 / 64 (6.25%)	
occurrences (all)	1	4	
Constipation			
subjects affected / exposed	3 / 34 (8.82%)	10 / 64 (15.63%)	
occurrences (all)	3	10	
Diarrhoea			

subjects affected / exposed	6 / 34 (17.65%)	18 / 64 (28.13%)	
occurrences (all)	8	24	
Diverticulum			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	2 / 34 (5.88%)	4 / 64 (6.25%)	
occurrences (all)	2	4	
Epigastric discomfort			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	3	0	
Flatulence			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Gastric ulcer			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Gingival bleeding			
subjects affected / exposed	1 / 34 (2.94%)	5 / 64 (7.81%)	
occurrences (all)	1	5	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	
Haemorrhoids			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	
Lip swelling			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Melaena			

subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Mouth ulceration			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Nausea			
subjects affected / exposed	5 / 34 (14.71%)	20 / 64 (31.25%)	
occurrences (all)	5	24	
Proctalgia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Rectal haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	1 / 34 (2.94%)	12 / 64 (18.75%)	
occurrences (all)	1	22	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 34 (5.88%)	2 / 64 (3.13%)	
occurrences (all)	2	2	
Ecchymosis			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Hyperhidrosis			

subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Petechiae			
subjects affected / exposed	3 / 34 (8.82%)	4 / 64 (6.25%)	
occurrences (all)	5	5	
Pruritus			
subjects affected / exposed	1 / 34 (2.94%)	3 / 64 (4.69%)	
occurrences (all)	1	3	
Rash			
subjects affected / exposed	4 / 34 (11.76%)	5 / 64 (7.81%)	
occurrences (all)	4	6	
Skin discolouration			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	
Urticaria			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 34 (8.82%)	3 / 64 (4.69%)	
occurrences (all)	3	4	
Back pain			
subjects affected / exposed	8 / 34 (23.53%)	8 / 64 (12.50%)	
occurrences (all)	8	9	
Bone pain			
subjects affected / exposed	1 / 34 (2.94%)	5 / 64 (7.81%)	
occurrences (all)	1	5	
Joint swelling			

subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 34 (5.88%)	2 / 64 (3.13%)	
occurrences (all)	2	2	
Musculoskeletal pain			
subjects affected / exposed	1 / 34 (2.94%)	3 / 64 (4.69%)	
occurrences (all)	1	3	
Myalgia			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Pain in extremity			
subjects affected / exposed	0 / 34 (0.00%)	5 / 64 (7.81%)	
occurrences (all)	0	5	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Candiduria			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	0 / 34 (0.00%)	4 / 64 (6.25%)	
occurrences (all)	0	6	
Cystitis			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	4	
Escherichia infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	

Herpes virus infection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
Infection			
subjects affected / exposed	2 / 34 (5.88%)	4 / 64 (6.25%)	
occurrences (all)	2	5	
Nasopharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Oral herpes			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 34 (2.94%)	3 / 64 (4.69%)	
occurrences (all)	2	3	
Respiratory tract infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Stomatococcal infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Streptococcal infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	

Tooth infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	6	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 34 (5.88%)	14 / 64 (21.88%)	
occurrences (all)	3	16	
Fluid retention			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Gout			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Hyperkalaemia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 34 (2.94%)	6 / 64 (9.38%)	
occurrences (all)	1	8	
Hypokalaemia			
subjects affected / exposed	3 / 34 (8.82%)	3 / 64 (4.69%)	
occurrences (all)	3	3	
Hypomagnesaemia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Hyponatraemia			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Hypophosphataemia			

subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Iron overload			
subjects affected / exposed	0 / 34 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 June 2010	Amendment No. 02: Modified inclusion criteria to include de novo AML patients and bone marrow blasts of 10-19%. Updated liver chemistry stopping criteria. Added interim analysis for completers. Provided additional details regarding extension treatment periods.
05 March 2012	Amendment No. 03: Modified definitions of disease progression, baseline platelet count, platelet response, and evaluable subjects. Addition of an external adjudication committee. Updated details for the Primary Safety and Efficacy Analysis (previously Interim Analysis). Included optional collection of genetic mutations information. Clarifications and corrections to existing language throughout, including clarification to planned subject randomization numbers and planned PK analyses.
25 October 2012	Amendment No. 04: Modified to allow continued access to eltrombopag for ongoing subjects in Extension Period 3. The amendment applied only to 3 ongoing subjects at the time that the amendment was issued.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported