Clinical trial results:
A randomized, double-blind, placebo-controlled, Phase III, multi-centre study of eltrombopag or placebo in combination with azacitidine in subjects with IPSS intermediate-1, intermediate-2 and high risk myelodysplastic syndromes (MDS)

Summary

EudraCT number	2013-000918-37
Trial protocol	IT SE DE DK AT CZ GR IE BE NO ES HU
Global end of trial date	28 April 2016

Results information

Result version number	v1 (current)
This version publication date	13 May 2017
First version publication date	13 May 2017

Trial information

Trial identification

Sponsor protocol code	CETB115D2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02158936
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	28 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2016
Global end of trial reached?	Yes
Global end of trial date	28 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine the effect of eltrombopag versus placebo on the proportion of patients who are platelet transfusion-free during the first 4 cycles of azacitidine therapy

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2014
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: 5
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 25
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Greece: 17
Country: Number of subjects enrolled	Hong Kong: 8
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Norway: 5

Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Puerto Rico: 1
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Spain: 56
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	Thailand: 11
Country: Number of subjects enrolled	Turkey: 18
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	356
EEA total number of subjects	179

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)	100
From 65 to 84 years	235
85 years and over	21

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 356 patients were enrolled in the study and 2 patients did not receive treatment.

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	Eltrombopag

Arm description:

Starting dose is 200 mg (100 mg for East Asian heritage). Dose modifications permitted by 100 mg increments (50 mg increments for East Asians) to a lowest dose of 100 mg (50 mg for East Asian heritage) or a maximum dose of 300 mg (150 mg for East Asian heritage) in order to maintain platelet counts at safe, effective level (level sufficient to avoid platelet transfusions and bleeding events). Subjects will receive Azacitidine 75 mg/meter^2 is administered subcutaneously once daily for 7 days every 28 days, for at least 6 cycles, if tolerated, until they are no longer receiving benefit (at least stable disease), disease progression, death, or unacceptable toxicity/adverse event. The subject may receive eltrombopag daily for the full 28 days each cycle if subject is receiving azacitidine

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

Dosage and administration details:

The starting dose of eltrombopag was 200mg once daily (100 mg for East Asian patients) It was adjustable by 100 mg increments (50 mg for East Asian patients) to a lowest dose of 100mg (50mg for East Asian patients) and to a maximum dose of 300 mg (150 mg for East Asian patients)

Investigational medicinal product name	Placebo -matching eltrombopag placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The starting dose of placebo was 200mg once daily (100 mg for East Asian patients) It was adjustable by 100 mg increments (50 mg for East Asian patients) to a lowest dose of 100mg (50mg for East Asian patients) and to a maximum dose of 300 mg (150 mg for East Asian patients)

Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Azacitidine was given subcutaneously at 75 mg/m2 per day for 7 days every 28 days, for at least 6 cycles

Arm title	Placebo

Arm description:

Subject will receive eltrombopag matching placebo. Subjects will receive azacitidine 75 mg/meter^2 subcutaneously once daily for 7 days (+/- 3 day treatment window permitted) every 28 days, for at least 6 cycles if tolerated and until they are no longer receiving benefit (defined as at least stable disease per the investigator's assessment) or until disease progression, death, or unacceptable toxicity/adverse event. The subject may receive matching placebo daily for the full 28 days each cycle for as long as the subject is receiving azacitidine

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

Dosage and administration details:

The starting dose of placebo was 200mg once daily (100 mg for East Asian patients) It was adjustable by 100 mg increments (50 mg for East Asian patients) to a lowest dose of 100mg (50mg for East Asian patients) and to a maximum dose of 300 mg (150 mg for East Asian patients)

Number of subjects in period 1	Eltrombopag	Placebo
Started	179	177
Treated	177	177
Untreated	2	0
Completed	0	0
Not completed	179	177
Consent withdrawn by subject	15	16
Physician decision	15	13
Azacitidine tx discontinued	53	46
Study closed/ terminated	57	77
Adverse event, non-fatal	39	24
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Eltrombopag
Reporting group description:	
Starting dose is 200 mg (100 mg for East Asian heritage). Dose modifications permitted by 100 mg increments (50 mg increments for East Asians) to a lowest dose of 100 mg (50 mg for East Asian heritage) or a maximum dose of 300 mg (150 mg for East Asian heritage) in order to maintain platelet counts at safe, effective level (level sufficient to avoid platelet transfusions and bleeding events). Subjects will receive Azacitidine 75 mg/meter^2 is administered subcutaneously once daily for 7 days every 28 days, for at least 6 cycles, if tolerated, until they are no longer receiving benefit (at least stable disease), disease progression, death, or unacceptable toxicity/adverse event. The subject may receive eltrombopag daily for the full 28 days each cycle if subject is receiving azacitidine	
Reporting group title	Placebo
Reporting group description:	
Subject will receive eltrombopag matching placebo. Subjects will receive azacitidine 75 mg/meter^2 subcutaneously once daily for 7 days (+/- 3 day treatment window permitted) every 28 days, for at least 6 cycles if tolerated and until they are no longer receiving benefit (defined as at least stable disease per the investigator's assessment) or until disease progression, death, or unacceptable toxicity/adverse event. The subject may receive matching placebo daily for the full 28 days each cycle for as long as the subject is receiving azacitidine	

Reporting group values	Eltrombopag	Placebo	Total
Number of subjects	179	177	356
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	51	49	100
From 65-84 years	118	117	235
85 years and over	10	11	21
Age Continuous Units: years			
arithmetic mean	68.3	69.4	
standard deviation	± 12.82	± 10.58	-
Gender, Male/Female Units: Subjects			
Female	69	53	122
Male	110	124	234
Race/Ethnicity, Customized Units: Subjects			
White	146	148	294
East Asian/Japanese/S.E. Asian	26	23	49
Central/South Asian	0	2	2
Other	4	4	8
Missing	3	0	3
IPSS risk score			

Units: Subjects			
Int - 1	64	61	125
Int - 2	77	83	160
High	38	33	71
Platelet Count Units: Subjects			
< 10	10	10	20
≥ 10 - <20	35	30	65
≥ 20 - <50	83	84	167
≥ 50 - <100	49	53	102
≥ 100	0	0	0
missing	2	0	2
Platelet trans dependence			
Platelet transfusion dependence			
Units: Subjects			
Yes	29	37	66
No	150	140	290

End points

End points reporting groups

Reporting group title	Eltrombopag

Reporting group description:

Starting dose is 200 mg (100 mg for East Asian heritage). Dose modifications permitted by 100 mg increments (50 mg increments for East Asians) to a lowest dose of 100 mg (50 mg for East Asian heritage) or a maximum dose of 300 mg (150 mg for East Asian heritage) in order to maintain platelet counts at safe, effective level (level sufficient to avoid platelet transfusions and bleeding events). Subjects will receive Azacitidine 75 mg/meter^2 is administered subcutaneously once daily for 7 days every 28 days, for at least 6 cycles, if tolerated, until they are no longer receiving benefit (at least stable disease), disease progression, death, or unacceptable toxicity/adverse event. The subject may receive eltrombopag daily for the full 28 days each cycle if subject is receiving azacitidine

Reporting group title	Placebo

Reporting group description:

Subject will receive eltrombopag matching placebo. Subjects will receive azacitidine 75 mg/meter^2 subcutaneously once daily for 7 days (+/- 3 day treatment window permitted) every 28 days, for at least 6 cycles if tolerated and until they are no longer receiving benefit (defined as at least stable disease per the investigator's assessment) or until disease progression, death, or unacceptable toxicity/adverse event. The subject may receive matching placebo daily for the full 28 days each cycle for as long as the subject is receiving azacitidine

Primary: Percentage of participants who were platelet transfusion independent during Cycles 1-4 of azacitidine therapy

End point title	Percentage of participants who were platelet transfusion independent during Cycles 1-4 of azacitidine therapy

End point description:

A subject is defined as being platelet transfusion independent if they received no platelet transfusions within the first 4 cycles of treatment with azacitidine. Subjects who died or withdrew from investigational product within the first four cycles were treated as failures (i.e. not transfusion independent) in the analysis

End point type	Primary

End point timeframe:

4 cycles (Cycle = 28 days)

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: Participants				
Yes - platelet transfusion independent	28	55		
No - platelet transfusion independent	151	122		

Statistical analyses

Statistical analysis title	Platelet infusion independent
Comparison groups	Eltrombopag v Placebo

Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	
P-value	= 1 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.65

Notes:

[1] - One sided p value

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival is defined as the time from randomization until death due to any cause and deaths have been presented. Subjects still alive at the time of the analysis and subjects who have withdrawn from the study will be censored at the time of last contact

End point type	Secondary

End point timeframe:

Randomization until death or end of study, approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: deaths (events)	57	51		

Statistical analyses

Statistical analysis title	Overall survival

Statistical analysis description:

Confidence Intervals estimated using the Brookmeyer-Crowley method. Hazard ratios are estimated using the Pike estimator. A hazard ratio <1 indicates a lower risk with eltrombopag compared with Placebo. Log-rank test stratified by IVRS stratification factors

Comparison groups	Eltrombopag v Placebo
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.164
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.08

Secondary: Summary of progression free survival from investigator assessment (ITT)

End point title	Summary of progression free survival from investigator assessment (ITT)

End point description:

Progression-free survival, defined as the time from randomization until either disease progression or death. The modified 2006 IWG criteria for MDS used for progression assessment

End point type	Secondary

End point timeframe:

First day of each cycle (Cycles 3+), at the end of therapy visit and every 3 months in follow-up for up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	66		
Units: participants				
Death	34	36		
Disease progression	38	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of progression free survival from central review (ITT)

End point title	Summary of progression free survival from central review (ITT)

End point description:

Progression-free survival, defined as the time from randomization until either disease progression or death. The modified 2006 IWG criteria for MDS used for progression assessment

End point type	Secondary

End point timeframe:

First day of each cycle (Cycles 3+), at the end of therapy visit and every 3 months in follow-up for up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	67		
Units: participants				
Death	44	41		
Disease progression	32	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of AML progression from investigator assessment and central review (ITT)

End point title	Summary of AML progression from investigator assessment and central review (ITT)

End point description:

Progression to AML in MDS patients with baseline bone marrow blast < 20% was defined as meeting definition of disease progression according to the modified 2006 IWG response criteria for MDS with the additional requirement that bone marrow blast or peripheral blast increases from < 20% at baseline to ≥ 20% postbaseline.

End point type	Secondary

End point timeframe:

First day of each cycle (Cycles 3+), at the end of therapy visit and every 3 months in follow-up

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: participants				
Events (AML progression) Investigator assessment	27	16		
Events (AML progression) Central Review	21	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Best disease response from investigator assessment (ITT)

End point title	Best disease response from investigator assessment (ITT)

End point description:

Best disease response is categorized as complete remission (CR), partial remission (PR), or marrow CR, stable disease, disease progression, or as non-evaluable; according to modified 2006 International Working Group (IWG) criteria for MDS

End point type	Secondary

End point timeframe:

At end of Cycle 6 (cycle=28 days) or end of therapy, whichever came first

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	150		
Units: participant				
Complete response - CR	15	26		
Marrow complete response	8	14		
Partial response - PR	13	22		
Stable disease	50	47		
Progressive disease	22	8		
Not evaluable	32	33		
Overall Response (CR+Marrow+PR	36	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Best disease response from central review (ITT)

End point title	Best disease response from central review (ITT)

End point description:

Best disease response is categorized as complete remission (CR), partial remission (PR), or marrow CR, stable disease, disease progression, or as non-evaluable; according to modified 2006 International Working Group (IWG) criteria for MDS

End point type	Secondary

End point timeframe:

At end of Cycle 6 (cycle=28 days) or end of therapy, whichever came first

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	105		
Units: participant				
Complete response - CR	11	7		
Marrow complete response	2	5		
Partial response - PR	2	7		
Stable disease	23	31		
Progressive disease	24	17		
Not evaluable	26	38		
Overall Response (CR+Marrow+PR)	15	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Hematologic improvement (HI) in platelets, neutrophils, and hemoglobin based on the modified IWG criteria for MDS (ITT)

End point title	Hematologic improvement (HI) in platelets, neutrophils, and hemoglobin based on the modified IWG criteria for MDS (ITT)

End point description:

HI based on the modified IWG criteria for MDS. HI – Platelets (BL <100Gi/L), response criteria= BL <20: increase to>20 and 100% at least for 56 days or BL >=20: absolute increase of >=30. HI – Neutrophils (BL <1.0 Gi/L), response criteria=100% increase and an absolute increase >0.5 Gi/L over BL for at least 56 days. HI-Hemoglobin (BL <g/dL), response criteria=Hgb increase by >=1.5 g/dL over BL, RBC transfusions(given for Hgb<=9.0) reduced by >=4 per 8w from BL

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up (samples collected weekly in Cycle 1, Days 1 and 15 in Cycles 2-6 and Day 1 of Cycles >=7) up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: participants				
Platelets	56	57		
Neutrophils	12	13		
Hemoglobin	1	1		
Platelets and neutrophils	10	11		
Platelets and hemoglobin	1	1		
Neutrophils and hemoglobin	1	1		
Platelets, neutrophils and hemoglobin	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who were platelet transfusion independent (ITT set)

End point title	Number of participants who were platelet transfusion independent (ITT set)

End point description:

Platelet transfusion independence is defined for each cycle as the number of participants who continue to the end of a cycle without requiring a platelet transfusion

End point type	Secondary

End point timeframe:

From Day 1 to end of study treatment up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: participants				
Screening (179,177)	127	121		
Cycle 1 (175,173)	68	87		
Cycle 2 (135,158)	62	87		
Cycle 3 (105,131)	68	94		
Cycle 4 (93,116)	58	91		
Cycle 5 (76,108)	49	76		
Cycle 6 (65,90)	41	62		
Cycle 7 (47,74)	29	50		
Cycle 8 (37,61)	20	42		
Cycle 9 (28,46)	19	36		
Cycle 10 (23,38)	18	28		
Cycle 11 (19,29)	13	20		
Cycle 12 (15,21)	10	15		
Cycle 13 (12,16)	7	10		
Cycle 14 (6,11)	3	6		
Cycle 15 (3,5)	2	3		
Cycle 16 (0,3)	0	3		
Cycle 17 (0,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Bleeding adverse events (AEs) >= Grade 3

End point title	Bleeding adverse events (AEs) >= Grade 3

End point description:

Bleeding will be assessed by recording AEs or serious adverse events (SAEs) as graded according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v4.0

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	177		
Units: participant				
Any event - Grade 3	9	12		
Any event - Grade 4	2	2		
Any event - Grade 5	1	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of of subjects with azacitidine dose delays, dose reductions, interruptions

End point title	Number of of subjects with azacitidine dose delays, dose reductions, interruptions

End point description:

The proportion of subjects with any delay, reduction or interruption in dosage of Azacitidine excluding those for non-medical reasons will be analyzed

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up, up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: participant				
Overall dose delay	82	88		
Overall dose reduction	7	16		
Overall dose interruption	3	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Response levels in all domains of Euroquol-5 Dimensions of Health, 3 Response Levels (EQ-5D-3L™)

End point title	Response levels in all domains of Euroquol-5 Dimensions of Health, 3 Response Levels (EQ-5D-3L™)

End point description:

The EQ-5D is a general health status and health utility measure which captures 5 dimensions of health state: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The survey also includes a visual analog scale (VAS or thermometer) measuring overall health state. (EQ-5D is a trademark of the Stichting EuroQol Group) .

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up, up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: participant				
Mobility C1, D1 (176, 173) L1- no problem walking	94	105		
Mobility C1,D1 (176, 173) L2- some problem walking	81	66		
Mobility C1, D1 (176,173) L3- confined to bed	1	2		
Mobility Wk 4 FU (71,72) L1- no problem walking	40	48		
Mobility Wk 4 FU (71,72) L2- some problem walking	29	22		
Mobility Wk 4 FU (71,72) L3- confined to bed	2	2		
Self-Care C1, D1 (176,173) L1-no problems	140	125		
Self-Care C1, D1 (176,173) L2-some problems	32	20		
Self-Care C1, D1 (176,173) L3-unable to	4	51		
Self-Care Wk4 FU (71,72) L1-no problems	56	62		
Self-Care Wk4 FU(71,72) L2-some problems	13	9		
Self-Care Wk4 FU (71,72) L2-unable to wash/dress	2	1		
Usual activities C1,D1(175,173) L1-no problem	97	94		
Usual activities C1,D1(175,173) L2-some problem	71	68		
Usual activities C1,D1(175,173) L3-unable to	7	11		
Usual activities Wk4 FU (71,72) L1-no problem	36	41		
Usual activities Wk4 FU (71,72) L1-some problem	29	25		
Usual activities Wk4 FU (71,72) L3-unable to	6	6		
Pain/discomfort C1,D1(176,173) L1-none	97	89		
Pain/discomfort C1,D1(176,173) L2-moderate	74	78		
Pain/discomfort C1,D1(176,173) L3-extreme	5	6		
Pain/discomfort Wk4 FU (71,72) L1-none	38	40		
Pain/discomfort Wk4 FU (71,72) L2-moderate	28	27		
Pain/discomfort Wk4 FU (71,72) L3-extreme	5	5		
Anxiety/depression C1 D1(176,173) L1-none	96	112		
Anxiety/depression C1 D1(176,173) L2-moderately	74	56		

Anxiety/depression C1 D1(176,173) L3-extremely	6	5		
Anxiety/depression Wk4 FU(71,72) L1-none	44	45		
Anxiety/depression Wk4 FU(71,72) L2-moderately	24	25		
Anxiety/depression Wk4 FU(71,72) Le-extremely	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Assessment of Chronic Disease Therapy-fatigue subscale (FACIT-Fatigue) (ITT)

End point title	Functional Assessment of Chronic Disease Therapy-fatigue subscale (FACIT-Fatigue) (ITT)

End point description:

The FACIT-Fatigue subscale measures severity and impact of fatigue on functioning and Health Related QoL experienced in the past 7 days (The FACIT Fatigue Scale is owned by David Cella, Ph.D.)

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up (Approximate median 9 Cycles+4 weeks follow-up) up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: scores				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (175,172)	17.401 (± 11.0279)	15.951 (± 10.9911)		
Week 4 Follow-up (68,70)	16.669 (± 10.7266)	14.898 (± 12.2362)		

Statistical analyses

No statistical analyses for this end point

Secondary: Medical resource utilization (MRU): Event -hospitalizations inpatient and outpatient

End point title	Medical resource utilization (MRU): Event -hospitalizations inpatient and outpatient

End point description:

MRU data will be collected for each subject. Events corresponding to unscheduled (not scheduled per protocol) hospitalizations

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up (Approximate median 9 Cycles+4 weeks follow-up) up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: days				
arithmetic mean (standard deviation)				
In-patient hospitalizations - entire study (91,66)	23.9 (± 24.33)	27.1 (± 33.81)		
Out-patient hospitalizations - entire study (4,2)	9.5 (± 16.34)	2.5 (± 0.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Medical resource utilization (MRU): Event and use of site specific medical resources - non-study laboratory tests

End point title	Medical resource utilization (MRU): Event and use of site specific medical resources - non-study laboratory tests

End point description:

MRU data will be collected for each subject. Events corresponding to unscheduled (not scheduled per protocol) hospitalizations, office visits including consultations, laboratory and diagnostic tests (lab results, imaging etc.), and procedures prior to therapy initiation and during therapy will be collected

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up (Approximate median 9 Cycles+4 weeks follow-up) up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: tests	88	105		

Statistical analyses

No statistical analyses for this end point

Secondary: Medical resource utilization (MRU): Event and use of site specific medical resources

End point title	Medical resource utilization (MRU): Event and use of site

	specific medical resources

End point description:

MRU data will be collected for each subject. Events corresponding to unscheduled (not scheduled per protocol) hospitalizations, office visits including consultations, laboratory and diagnostic tests (lab results, imaging etc.), and procedures prior to therapy initiation and during therapy will be collected

End point type	Secondary

End point timeframe:

From Day 1 to 4-week follow-up (Approximate median 9 Cycles+4 weeks follow-up) up to approximately 2 years

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: visits				
Medical or surgical specialist visits	49	58		
Home healthcare visits by medical professional	89	97		
Primary physician care visits	89	97		
Nurse practitioner, physic assistant, nurse visits	89	97		
Telephone consultations	89	97		
Emergency visits not resulting in hospital stay	89	97		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Post-Hoc estimates of steady-state eltrombopag Cmax and Cmin pharmacokinetic parameters for a 50 mg dose

End point title	Summary of Post-Hoc estimates of steady-state eltrombopag Cmax and Cmin pharmacokinetic parameters for a 50 mg dose[2]

End point description:

Eltrombopag concentrations were analyzed using a population PK model along with data from other studies in healthy volunteers and in patients with MDS and/or AML. Post-hoc PK parameters were derived. Only patients from this study were included (163). Geometric coefficient of variation should be presented as: Cmax, 36.8% and Cmin, 49.9%. (presented incorrectly due to acknowledged system error)

End point type	Secondary

End point timeframe:

Cycle 1, Week 2: Pre-dose, 1.5 and 3 hour post dose; Cycle 1, Week 3: 4, 5.5, and 7 hours post dose

Notes:

[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: Outcome measurement was for PK of eltrombopag only

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cmax	7.7 (± 36.8)			
Cmin	4.41 (± 49.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Post-Hoc estimates of steady-state eltrombopag AUC0 infinity pharmacokinetic parameters for a 50 mg dose

End point title	Summary of Post-Hoc estimates of steady-state eltrombopag AUC0 infinity pharmacokinetic parameters for a 50 mg dose[3]

End point description:

Eltrombopag concentrations were analyzed using a population PK model along with data from other studies in healthy volunteers and in patients with MDS and/or AML. Post-hoc PK parameters were derived. Only patients from this study were included (163). Geometric coefficient of variation should be presented as: AUC0 infinity, 43.1% (presented incorrectly in table due to acknowledged system error)

End point type	Secondary

End point timeframe:

Cycle 1, Week 2: Pre-dose, 1.5 and 3 hour post dose; Cycle 1, Week 3: 4, 5.5, and 7 hours post dose

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: Outcome measurement was for PK of eltrombopag only

End point values	Eltrombopag			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: hr.µg/mL				
geometric mean (geometric coefficient of variation)	135 (± 43.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-infinity -pharmacokinetic(s) parameter of azacitidine

End point title	AUC0-infinity -pharmacokinetic(s) parameter of azacitidine

End point description:

An analysis of variance (ANOVA) on AUC0-infinity. The PK parameters were log transformed prior to analysis. The model included treatment as a fixed effect. Point estimates and their associated 90% CI were constructed for the differences in PK parameter values. The point estimates and their associated 90% CI were then back transformed to provide point estimates and 90% CI for the azacitidine + eltrombopag:azacitidine + placebo PK parameter ratios. Geometric coefficient of variation should be presented as: AUC0 infinity for eltrombopag, 53.0% and placebo 67% (presented incorrectly in table

due to acknowledged system error)

End point type	Secondary

End point timeframe:

Cycle 2 Day 1: Pre-dose, 15 min, 0.5, 1, 2 and 4 hr post dose

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: hr.ng/mL				
geometric mean (geometric coefficient of variation)	840 (± 53)	641 (± 67)		

Statistical analyses

Statistical analysis title	AUC0 infinity
Comparison groups	Eltrombopag v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.99
upper limit	1.74

Secondary: Cmax -pharmacokinetic parameter of azacitidine

End point title	Cmax -pharmacokinetic parameter of azacitidine

End point description:

An analysis of variance (ANOVA) on Cmax . The PK parameters were log transformed prior to analysis. The model included treatment as a fixed effect. Point estimates and their associated 90% CI were constructed for the differences in PK parameter values. The point estimates and their associated 90% CI were then back transformed to provide point estimates and 90% CI for the azacitidine + ltrombopag:azacitidine + placebo PK parameter ratios. Geometric coefficient of variation should be presented as: Cmax for eltrombopag, 91.0% and placebo 89% (presented incorrectly in table due to acknowledged system error)

End point type	Secondary

End point timeframe:

Cycle 2 Day 1: Pre-dose, 15 min, 0.5, 1, 2 and 4 hr post dose

End point values	Eltrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	744 (± 91)	535 (± 89)		

Statistical analyses

Statistical analysis title	Cmax
Comparison groups	Eltrombopag v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.97
upper limit	1.99

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 resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Eltrombopag
Reporting group description:	
Eltrombopag	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	Eltrombopag	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	128 / 177 (72.32%)	100 / 177 (56.50%)	
number of deaths (all causes)	33	29	
number of deaths resulting from adverse events	12	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	4 / 177 (2.26%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
B-cell lymphoma			

subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelofibrosis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour associated fever			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic dilatation			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	3 / 177 (1.69%)	3 / 177 (1.69%)	
occurrences causally related to treatment / all	2 / 4	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Orthostatic hypotension			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	3 / 177 (1.69%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chest pain			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 177 (1.69%)	3 / 177 (1.69%)	
occurrences causally related to treatment / all	2 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Inflammation			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site haemorrhage			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 177 (0.56%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal haemorrhage			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	20 / 177 (11.30%)	8 / 177 (4.52%)	
occurrences causally related to treatment / all	6 / 20	1 / 9	
deaths causally related to treatment / all	0 / 2	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
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			
Acute pulmonary oedema			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 177 (1.13%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	1 / 2	0 / 1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epistaxis			
subjects affected / exposed	0 / 177 (0.00%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 177 (1.13%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary haemorrhage			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary hypertension			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	4 / 177 (2.26%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomania			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood osmolarity decreased			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fall			
subjects affected / exposed	1 / 177 (0.56%)	4 / 177 (2.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transfusion reaction			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 177 (1.13%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Angina pectoris			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	4 / 177 (2.26%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	2 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	3 / 177 (1.69%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	3 / 177 (1.69%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiovascular deconditioning			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary muscle infarction			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericardial effusion			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericarditis constrictive			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amnesia			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic stroke			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	5 / 177 (2.82%)	7 / 177 (3.95%)	
occurrences causally related to treatment / all	1 / 6	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytopenia			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	47 / 177 (26.55%)	33 / 177 (18.64%)	
occurrences causally related to treatment / all	46 / 75	21 / 50	
deaths causally related to treatment / all	2 / 4	0 / 4	
Leukocytosis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	3 / 177 (1.69%)	3 / 177 (1.69%)	
occurrences causally related to treatment / all	4 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 177 (1.13%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Cataract			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 177 (1.69%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 177 (0.00%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faeces discoloured			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 177 (0.56%)	5 / 177 (2.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gingival bleeding			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal ulcer haemorrhage			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Liver injury			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity vasculitis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petechiae			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	7 / 177 (3.95%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 7	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Haematuria			
subjects affected / exposed	0 / 177 (0.00%)	3 / 177 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal failure			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular disorder			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	0 / 177 (0.00%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Abscess			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 177 (0.56%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 177 (0.00%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arthritis infective			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bacteraemia			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	2 / 177 (1.13%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	6 / 177 (3.39%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 7	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epiglottitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 177 (0.56%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Extradural abscess			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			

subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fungal pharyngitis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Furuncle			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 177 (0.00%)	2 / 177 (1.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 177 (0.00%)	4 / 177 (2.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			

subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	3 / 177 (1.69%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	20 / 177 (11.30%)	17 / 177 (9.60%)	
occurrences causally related to treatment / all	6 / 20	4 / 17	
deaths causally related to treatment / all	1 / 5	1 / 6	
Pneumonia bacterial			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia necrotising			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyomyositis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 177 (1.13%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	10 / 177 (5.65%)	7 / 177 (3.95%)	
occurrences causally related to treatment / all	4 / 10	0 / 7	
deaths causally related to treatment / all	3 / 8	0 / 2	
Septic shock			
subjects affected / exposed	10 / 177 (5.65%)	5 / 177 (2.82%)	
occurrences causally related to treatment / all	3 / 10	2 / 5	
deaths causally related to treatment / all	0 / 6	2 / 5	
Skin infection			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic abscess			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic mycosis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue fungal infection			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
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	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 177 (2.26%)	5 / 177 (2.82%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 177 (1.69%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gout			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 177 (0.56%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperglycaemia			

subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 177 (0.00%)	1 / 177 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 177 (1.13%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron overload			
subjects affected / exposed	1 / 177 (0.56%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Eltrombopag	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 177 (89.83%)	153 / 177 (86.44%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 177 (5.65%)	3 / 177 (1.69%)	
occurrences (all)	11	3	
Blood bilirubin increased			
subjects affected / exposed	13 / 177 (7.34%)	2 / 177 (1.13%)	
occurrences (all)	17	2	
Neutrophil count decreased			

subjects affected / exposed	12 / 177 (6.78%)	11 / 177 (6.21%)	
occurrences (all)	15	12	
Platelet count decreased			
subjects affected / exposed	9 / 177 (5.08%)	5 / 177 (2.82%)	
occurrences (all)	15	6	
White blood cell count decreased			
subjects affected / exposed	10 / 177 (5.65%)	4 / 177 (2.26%)	
occurrences (all)	14	5	
Vascular disorders			
Haematoma			
subjects affected / exposed	10 / 177 (5.65%)	12 / 177 (6.78%)	
occurrences (all)	14	14	
Hypertension			
subjects affected / exposed	2 / 177 (1.13%)	11 / 177 (6.21%)	
occurrences (all)	2	14	
Hypotension			
subjects affected / exposed	12 / 177 (6.78%)	5 / 177 (2.82%)	
occurrences (all)	13	5	
Nervous system disorders			
Dizziness			
subjects affected / exposed	17 / 177 (9.60%)	14 / 177 (7.91%)	
occurrences (all)	19	15	
Headache			
subjects affected / exposed	20 / 177 (11.30%)	13 / 177 (7.34%)	
occurrences (all)	21	19	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	32 / 177 (18.08%)	19 / 177 (10.73%)	
occurrences (all)	59	36	
Febrile neutropenia			
subjects affected / exposed	13 / 177 (7.34%)	10 / 177 (5.65%)	
occurrences (all)	17	13	
Leukopenia			
subjects affected / exposed	9 / 177 (5.08%)	5 / 177 (2.82%)	
occurrences (all)	23	10	
Neutropenia			

subjects affected / exposed	52 / 177 (29.38%)	44 / 177 (24.86%)	
occurrences (all)	108	103	
Thrombocytopenia			
subjects affected / exposed	14 / 177 (7.91%)	14 / 177 (7.91%)	
occurrences (all)	26	19	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	28 / 177 (15.82%)	34 / 177 (19.21%)	
occurrences (all)	42	50	
Chills			
subjects affected / exposed	8 / 177 (4.52%)	11 / 177 (6.21%)	
occurrences (all)	11	11	
Fatigue			
subjects affected / exposed	31 / 177 (17.51%)	27 / 177 (15.25%)	
occurrences (all)	39	30	
Injection site pain			
subjects affected / exposed	7 / 177 (3.95%)	9 / 177 (5.08%)	
occurrences (all)	9	10	
Oedema peripheral			
subjects affected / exposed	22 / 177 (12.43%)	11 / 177 (6.21%)	
occurrences (all)	26	13	
Pyrexia			
subjects affected / exposed	44 / 177 (24.86%)	40 / 177 (22.60%)	
occurrences (all)	63	67	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 177 (3.95%)	12 / 177 (6.78%)	
occurrences (all)	12	13	
Abdominal pain upper			
subjects affected / exposed	9 / 177 (5.08%)	7 / 177 (3.95%)	
occurrences (all)	9	8	
Constipation			
subjects affected / exposed	48 / 177 (27.12%)	57 / 177 (32.20%)	
occurrences (all)	75	72	
Diarrhoea			

subjects affected / exposed	42 / 177 (23.73%)	25 / 177 (14.12%)	
occurrences (all)	59	30	
Gingival bleeding			
subjects affected / exposed	13 / 177 (7.34%)	9 / 177 (5.08%)	
occurrences (all)	15	9	
Nausea			
subjects affected / exposed	54 / 177 (30.51%)	46 / 177 (25.99%)	
occurrences (all)	68	65	
Stomatitis			
subjects affected / exposed	9 / 177 (5.08%)	3 / 177 (1.69%)	
occurrences (all)	9	3	
Vomiting			
subjects affected / exposed	33 / 177 (18.64%)	29 / 177 (16.38%)	
occurrences (all)	44	38	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 177 (12.99%)	29 / 177 (16.38%)	
occurrences (all)	26	32	
Dyspnoea			
subjects affected / exposed	24 / 177 (13.56%)	12 / 177 (6.78%)	
occurrences (all)	25	15	
Epistaxis			
subjects affected / exposed	14 / 177 (7.91%)	18 / 177 (10.17%)	
occurrences (all)	19	36	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	11 / 177 (6.21%)	6 / 177 (3.39%)	
occurrences (all)	13	6	
Petechiae			
subjects affected / exposed	11 / 177 (6.21%)	11 / 177 (6.21%)	
occurrences (all)	18	15	
Pruritus			
subjects affected / exposed	12 / 177 (6.78%)	12 / 177 (6.78%)	
occurrences (all)	15	16	
Rash			

subjects affected / exposed	19 / 177 (10.73%)	11 / 177 (6.21%)	
occurrences (all)	20	13	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 177 (9.04%)	9 / 177 (5.08%)	
occurrences (all)	17	9	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 177 (3.39%)	11 / 177 (6.21%)	
occurrences (all)	6	11	
Back pain			
subjects affected / exposed	13 / 177 (7.34%)	10 / 177 (5.65%)	
occurrences (all)	13	11	
Pain in extremity			
subjects affected / exposed	9 / 177 (5.08%)	14 / 177 (7.91%)	
occurrences (all)	12	16	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 177 (3.95%)	9 / 177 (5.08%)	
occurrences (all)	7	11	
Pneumonia			
subjects affected / exposed	12 / 177 (6.78%)	9 / 177 (5.08%)	
occurrences (all)	13	13	
Upper respiratory tract infection			
subjects affected / exposed	9 / 177 (5.08%)	11 / 177 (6.21%)	
occurrences (all)	11	13	
Urinary tract infection			
subjects affected / exposed	9 / 177 (5.08%)	8 / 177 (4.52%)	
occurrences (all)	11	9	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	27 / 177 (15.25%)	21 / 177 (11.86%)	
occurrences (all)	33	25	
Hypokalaemia			
subjects affected / exposed	19 / 177 (10.73%)	17 / 177 (9.60%)	
occurrences (all)	31	24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2014	Modified protocol to include ocular examinations, baseline assessment of aPTT/INR, collection of data pertaining to the development of leukemia cutis and myeloid sarcoma, and recommendation for male subjects to store sperm. Amended inclusion criteria regarding post-treatment contraception requirements for female subjects (3-months posttreatment). Amended liver chemistry stopping criteria. Clarifications throughout, including clarification to eligibility criteria and the definition of study completion. The main analysis of disease response and progression will be based on central bone marrow evaluation. -
24 July 2014	Modified protocol to include an azacitidine PK substudy. Added inclusion criteria to clarify that the diagnosis of MDS may be by WHO or FAB classification. Excluded subjects with proliferative type chronic myelomonocytic leukemia. Modified options for delay of azacitidine dosing. Modified the reporting of events that are part of the course of the disease under study. Added collection of Grade≥3 non-hematological laboratory abnormalities. Clarified bone marrow requirements and IP dosing
29 October 2014	Clarified definition of study completion. Corrected the Time and Events table to mark assessments which must be completed during Day 1 visits for Cycles 7+
29 January 2015	Clarified definition of Day 1 visit to align with Time and Events table and dose escalation. Updated drug restart/rechallenge guidance following liver event possibly related to IP. Updated throughout, to indicate that approximately 125 subjects will be randomized into the intermediate 1 risk MDS strata of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The IDMC recommended terminating the study for futility (primary) and safety (secondary). Due to early termination of the trial, the final analysis of OS took place at the same time as the final analysis of the primary end point.

Notes: