Clinical trial results:
A randomized, double-blind, placebo-controlled phase III multi-center study of azacitidine with or without MBG453 for the treatment of patients with intermediate, high or very high risk myelodysplastic syndrome (MDS) as per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2)

Summary

EudraCT number	2019-002089-11
Trial protocol	DE FR CZ BE IT ES AT GB PT FI LT NL GR
Global end of trial date	02 October 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	CMBG453B12301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04266301
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	Lichtstrasse 35, Basel, Switzerland, 4056
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare overall survival (OS) in the MBG453 plus azacitidine arm vs. placebo plus azacitidine arm

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	08 June 2020
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: 2
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	Austria: 10
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Brazil: 9
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	China: 74
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Greece: 8
Country: Number of subjects enrolled	India: 12
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Japan: 49
Country: Number of subjects enrolled	Korea, Republic of: 31

Country: Number of subjects enrolled	Lebanon: 1
Country: Number of subjects enrolled	Lithuania: 4
Country: Number of subjects enrolled	Malaysia: 12
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Oman: 3
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	Saudi Arabia: 1
Country: Number of subjects enrolled	Singapore: 20
Country: Number of subjects enrolled	Spain: 41
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	Thailand: 21
Country: Number of subjects enrolled	Türkiye: 21
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	530
EEA total number of subjects	188

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)	126
From 65 to 84 years	381
85 years and over	23

Subject disposition

Recruitment

Recruitment details:

This study randomized participants in 149 centers in 36 participating countries.

Pre-assignment

Screening details:

Following completion of screening procedure, all eligible participants were randomized via Interactive Response Technology (IRT) to one of the treatment arms.

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Sabatolimab (MBG453) + Azacitidine

Arm description:

Participants were randomized to sabatolimab plus Azacitidine

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

100 mg or other locally available dose strengths was administeredaccording to local standard clinical practice. A standard dose ofazacitidine (75mg/m2) was given based on local azacitidinepackage insert every day for seven consecutive days on Days 1 to7 of a 28-day cycle, followed by sabatolimab.

Investigational medicinal product name	Sabatolimab
Investigational medicinal product code	MBG453
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sabatolimab 400 mg concentrate for solution for infusion wasadministered preferably over 30 minutes, with a maximumadministration time of 2 hours.

Arm title	Placebo + Azacitidine

Arm description:

Participants were randomized to placebo plus Azacitidine

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

100 mg or other locally available dose strengths was administeredaccording to local standard clinical practice. A standard dose ofazacitidine (75mg/m2) was given based on local azacitidinepackage insert

every day for seven consecutive days on Days 1 to7 of a 28-day cycle, followed by sabatolimab.

Investigational medicinal product name	Sabatolimab
Investigational medicinal product code	MBG453
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo 400 mg concentrate for solution for infusion wasadministered preferably over 30 minutes, with a maximumadministration time of 2 hours.

Number of subjects in period 1	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine
Started	265	265
Participants Treated	264	264
Participants Not treated	1	1
Discontinued from treatment	264	264
Entered post-treatment	68	71
Did not enter post-treatment	196	193
Discontinued from study	265	265
Full Analysis See (FAS)	265	265
Safety Set	263	265
Completed	0	0
Not completed	265	265
Adverse event, serious fatal	26	35
Participant Decision	22	28
Physician decision	14	9
Adverse event, non-fatal	41	43
Protocol Deviation	2	4
Progressive Disease	111	92
Participants Not Treated	1	1
Guardian Decision	1	-
Study Terminated by Sponsor	22	27
Lost to follow-up	1	-
HSCT Planned	22	22
New Therapy for Study Indication	2	4

Baseline characteristics

Reporting groups	
Reporting group title	Sabatolimab (MBG453) + Azacitidine
Reporting group description:	
Participants were randomized to sabatolimab plus Azacitidine	
Reporting group title	Placebo + Azacitidine
Reporting group description:	
Participants were randomized to placebo plus Azacitidine	

Reporting group values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine	Total
Number of subjects	265	265	530
Age categorical Units: Subjects			
Adults (18-64 years)	60	66	126
From 65-84 years	192	189	381
85 years and over	13	10	23
Age Continuous Units: Years			
arithmetic mean	70.2	69.1	
standard deviation	± 11.46	± 11.23	-
Sex: Female, Male Units: Participants			
Female	104	79	183
Male	161	186	347
Race/Ethnicity, Customized Units: Subjects			
White	150	134	284
Asian	111	124	235
Black or African American	3	4	7
American Indian or Alaska Native	1	2	3
Unknown	0	1	1
ECOG performance status			
Eastern Cooperative Oncology Group (ECOG) performance status scale is a widely used standard of care criteria used to assess the functional status of a patient with cancer to measure how the disease impacts the patient's daily living abilities. This scale has a range from 0 - 5. The higher the grade, the worse the patient's abilities: 0 implies fully active, able to carry on all pre-disease performance without restriction and 5 implies death.			
Units: Subjects			
ECOG performance status: 0	92	101	193
ECOG performance status: 1	161	141	302
ECOG performance status: 2	12	23	35

End points

End points reporting groups

Reporting group title	Sabatolimab (MBG453) + Azacitidine
Reporting group description: Participants were randomized to sabatolimab plus Azacitidine	
Reporting group title	Placebo + Azacitidine
Reporting group description: Participants were randomized to placebo plus Azacitidine	
Subject analysis set title	Sabatolimab (MBG453)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received sabatolimab.	
Subject analysis set title	Sabatolimab (MBG453)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received sabatolimab	
Subject analysis set title	Sabatolimab (MBG453)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received sabatolimab	

Primary: Overall Survival (OS) (Final efficacy results)

End point title	Overall Survival (OS) (Final efficacy results)
End point description: OS is the time from randomization until death due to any cause.	
End point type	Primary
End point timeframe: Up to 5 years after last participant randomized	

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Months				
median (confidence interval 95%)	22.18 (19.55 to 24.41)	18.83 (15.38 to 23.72)		

Statistical analyses

Statistical analysis title	OS Final Analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine

Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.863
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.693
upper limit	1.076

Primary: Overall Survival (OS) (Primary efficacy results)

End point title	Overall Survival (OS) (Primary efficacy results)
End point description:	
OS is the time from randomization until death due to any cause.	
End point type	Primary
End point timeframe:	
approx. 39 months after first participant randomized	

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Months				
median (confidence interval 95%)	22.31 (19.55 to 24.74)	18.83 (15.38 to 23.72)		

Statistical analyses

Statistical analysis title	OS Primary Analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0825 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.847
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.671
upper limit	1.07

Notes:

[1] - P Value is 1-sided

Secondary: Key secondary endpoint 1: Time to definitive deterioration of fatigue using Functional Assessment of Cancer Therapy (FACIT)-Fatigue score

End point title	Key secondary endpoint 1: Time to definitive deterioration of fatigue using Functional Assessment of Cancer Therapy (FACIT)-Fatigue score

End point description:

FACIT-Fatigue score is a 13-item questionnaire designed to assess fatigue in cancer participants. All items use a 5-point scale ranging from 0 to 4 (0=Not at All to 4=Very Much). The total score ranges from 0 to 52 with higher values representing better quality of life. Time to definitive deterioration of fatigue is defined as time from randomization to at least 3 points worsening from baseline in FACIT-fatigue scores with no subsequently observed improvement above this threshold, or death due to any cause, whichever occurred first.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Months				
median (confidence interval 95%)	13.37 (11.96 to 15.90)	11.76 (10.15 to 13.86)		

Statistical analyses

Statistical analysis title	Time to Def. Analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2132 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.921
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.13

Notes:

[2] - P Value is 1-sided

Secondary: Key secondary endpoint 2: Red Blood Cell (RBC) annualized transfusion

free rate for transfusion

End point title	Key secondary endpoint 2: Red Blood Cell (RBC) annualized transfusion free rate for transfusion

End point description:

Annualized transfusion free rate is defined as the average number of days in RBC transfusion-free intervals in a year (i.e., the total number of days in RBC transfusion-free intervals divided by the total days in the study multiplied by 365.25), where RBC transfusion-free intervals correspond to cumulative times of intervals with no evidence of RBC transfusion for at least 8 weeks at any point after randomization until death due to any cause.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: annualized transfusion-free rate (days)				
median (full range (min-max))	184.3 (0 to 365)	175.7 (0 to 365)		

Statistical analyses

Statistical analysis title	RBC annualized
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4692 [3]
Method	negative binomial regression model

Notes:

[3] - P Value is 1-sided

Secondary: Key secondary endpoint 4: Percentage of participants with at least 10 point confirmed improvement from baseline in physical functioning using European Organization for Research and Treatment of Cancer's Core Quality of Life Questionnaire (EORTC QLQ-C30)

End point title	Key secondary endpoint 4: Percentage of participants with at least 10 point confirmed improvement from baseline in physical functioning using European Organization for Research and Treatment of Cancer's Core Quality of Life Questionnaire (EORTC QLQ-C30)

End point description:

EORTC-QLQ-C30 is a 30-item questionnaire developed to assess the quality of life of cancer participants. Participants' responses to 5 questions about their physical functioning (Items 1-5) are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. A high score indicates a high / healthy level of functioning. The responder is defined as having 10 points improvement from baseline confirmed by a second improvement of 10 points at any time, regardless of preceding worsening. A participant who could not improve was considered as a non-responder.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Percentage of participants with response				
number (confidence interval 95%)	30.2 (24.7 to 36.1)	22.6 (17.7 to 28.2)		

Statistical analyses

Statistical analysis title	EORTC Analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5743 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.2

Notes:

[4] - P Value is 1-sided

Secondary: Key secondary endpoint 3: Percentage of participants with at least 3 point confirmed improvement from baseline in FACIT-fatigue scores

End point title	Key secondary endpoint 3: Percentage of participants with at least 3 point confirmed improvement from baseline in FACIT-fatigue scores

End point description:

FACIT-Fatigue score is a 13-item questionnaire designed to assess fatigue in cancer participants. All items use a 5-point scale ranging from 0 to 4 (0=Not at All to 4=Very Much). The total score ranges from 0 to 52 with higher values representing better quality of life. The responder is defined as having 3 points improvement from baseline confirmed by a second improvement of 3 points at any time, regardless of preceding worsening. A participant who could not improve was considered as a non-responder.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Percentage of participants with response				
number (confidence interval 95%)	39.6 (33.7 to 45.8)	40.8 (34.8 to 46.9)		

Statistical analyses

Statistical analysis title	FACIT analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4865 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.4

Notes:

[5] - P Value is 1-sided

Secondary: Percentage of participants with stable disease (SD) according to International Working Group for MDS (IWG-MDS) as per investigator assessment

End point title	Percentage of participants with stable disease (SD) according to International Working Group for MDS (IWG-MDS) as per investigator assessment

End point description:

Response rate of participants with stable disease. SD is the failure to achieve at least partial response (PR), but no evidence of progression for >8 weeks.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Percentage of participants				
number (not applicable)	20.0	19.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Key secondary endpoint 5: Percentage of participants with at least 10 point confirmed improvement from baseline in emotional functioning using EORTC-QLQ-C30

End point title	Key secondary endpoint 5: Percentage of participants with at least 10 point confirmed improvement from baseline in emotional functioning using EORTC-QLQ-C30

End point description:

EORTC-QLQ-C30 is a 30-item questionnaire developed to assess the quality of life of cancer participants. Participants' responses to 4 questions about their emotional functioning (Items 21-24) are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. A high score indicates a high / healthy level of functioning. The responder is defined as having 10 points improvement from baseline confirmed by a second improvement of 10 points at any time, regardless of preceding worsening. A participant who could not improve was considered as a non-responder.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Percentage of participants				
number (confidence interval 95%)	31.7 (26.1 to 37.7)	28.3 (23.0 to 34.1)		

Statistical analyses

Statistical analysis title	EORTC-QLQ-C30
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine

Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2126 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.7

Notes:

[6] - P Value is 1-sided

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS is defined as the time from randomization to disease progression (including transformation to acute leukemia per WHO 2016), relapse from CR (IWG-MDS), or death. Disease progression: bone marrow blasts increase ≥ 50% over baseline, to > 5% if initially < 5%, > 10% if 5%-<10%, or > 20% if 10%-<20%. Includes a peripheral blood count decrease ≥ 50% from maximum remission/response levels: neutrophils < 1.0x109/L, platelets < 100x109/L, or hemoglobin drop ≥ 2 g/dL to < 10 g/dL, becoming transfusion-dependent. Relapse from CR: baseline bone marrow blast % return, neutrophils decrease ≥ 50% to < 1.0x109/L, platelets decrease ≥ 50% to < 100x109/L, or hemoglobin drop ≥ 1.5 g/dL to < 10 g/dL, becoming transfusion-dependent. Leukemia transformation: > 20% blasts per WHO 2016 (Arber et al 2016).

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Months				
median (confidence interval 95%)	14.26 (12.22 to 17.74)	10.12 (8.64 to 11.14)		

Statistical analyses

Statistical analysis title	PFS Analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine

Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.576
upper limit	0.875

Secondary: Percentage of participants with either CR, or mCR, or PR, or HI in each treatment arm according to International Working Group for MDS (IWG-MDS) as per investigator assessment

End point title	Percentage of participants with either CR, or mCR, or PR, or HI in each treatment arm according to International Working Group for MDS (IWG-MDS) as per investigator assessment

End point description:

Response rate of participants with complete remission (CR), or marrow remission (mCR), or partial remission (PR), or hematologic improvement (HI). CR: where the Bone marrow: ≤ 5% blasts with normal maturation of all cell lineages and Peripheral blood: where Hgb ≥ 10 g/dL AND Platelets ≥ 100*109/L AND Neutrophils ≥ 1.0*109/L AND Peripheral blasts 0%. mCR: Bone marrow: ≤ 5% blasts and blast count decrease by ≥ 50% compared to baseline; Peripheralblood/transfusion: Marrow CR may be achieved with or without improved blood counts or with or without transfusions PR: All CR criteria except bone marrow: ≥50% decrease from baseline in blasts in bone marrow AND blast count in bone marrow >5%. HI: restoration or enhancement of the function of the body's blood cell-producing system that must last as least 8 weeks.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Percentage of participants				
number (confidence interval 95%)	58.1 (51.9 to 64.1)	47.5 (41.4 to 53.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who become Red Blood Cells (RBC)/platelets transfusion independence after randomization

End point title	Number of participants who become Red Blood Cells (RBC)/platelets transfusion independence after randomization

End point description:

Improvement in RBC/Platelets transfusion independence as per International Working Group for MDS (IWG-MDS) criteria. RBC/Platelets transfusion independence was defined as having received 0 units of RBC/Platelets transfusions during at least 8 consecutive weeks after randomization. The number of participants was shown in only those with transfusion dependence at baseline (BL).

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Participants				
At least 1 per. of packed RBC ind. at BL(n=96,108)	50	53		
At least 1 per. of PLTS ind. at BL (n=23,28)	11	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of MBG453 (parameter Cmax)

End point title	Pharmacokinetics of MBG453 (parameter Cmax)

End point description:

Cmax is the maximum (peak) observed drug concentration after single dose administration (mass x volume-1).

End point type	Secondary

End point timeframe:

0 hr (pre-dose) & 2 hrs (post-dose) of Cycle (C) 1 Day (D) 8, 0 hr (pre-dose) of C2D8, 0 hr (pre-dose) and 2 hrs (post-dose) of C3D8, 0 hr (pre-dose) in D8 of Cycle 4, 6, 9, 12 and every 6 cycles thereafter, EOT, 30 Day Follow up and 150 Day Follow up

End point values	Sabatolimab (MBG453)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: ug/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1	232 (± 20.9)			
Cycle 3 (n = 6)	239 (± 39.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Leukemia-free survival (LFS)

End point title	Leukemia-free survival (LFS)

End point description:

LFS is defined as the time from randomization to ≥ 20% blasts in bone marrow/peripheral blood (per WHO 2016 classification) or diagnosis of extramedullary acute leukemia, or death due to any cause

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Months				
median (confidence interval 95%)	19.84 (17.15 to 24.21)	13.73 (11.79 to 18.73)		

Statistical analyses

Statistical analysis title	LFS Analysis
Comparison groups	Sabatolimab (MBG453) + Azacitidine v Placebo + Azacitidine
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.815
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.038

Secondary: Pharmacokinetics of MBG453 (parameter AUC)

End point title	Pharmacokinetics of MBG453 (parameter AUC)

End point description:

AUCinf is the AUC from time zero to infinity (mass x time x volume-1).

End point type	Secondary

End point timeframe:

0 hr (pre-dose) & 2 hrs (post-dose) of Cycle (C) 1 Day (D) 8, 0 hr (pre-dose) of C2D8, 0 hr (pre-dose) & 2 hrs (post-dose) of C3D8, 0 hr (pre-dose) in Day 8 of Cycle 4, 6, 9, 12 and every 6 cycles thereafter, EOT, 30 Day Follow up and 150 Day Follow up

End point values	Sabatolimab (MBG453)			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: day*ug/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Cycle 3 (n = 3)	2670 (± 45.9) 4930 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: ADA prevalence at baseline and ADA incidence on-treatment

End point title	ADA prevalence at baseline and ADA incidence on-treatment

End point description:

ADA incidence (i.e. ADA-positive subjects) will be calculated as the number of subjects with at least one on-treatment ADA-positive sample divided by the number of subjects with a determinant baseline IG sample and at least one determinant post-baseline IG sample.

End point type	Secondary

End point timeframe:

Continuously collected for patients during treatment with sabatolimab up to 150 days after last treatment, approx. 39 months

End point values	Sabatolimab (MBG453)			
Subject group type	Subject analysis set			
Number of subjects analysed	249			
Units: Participants				
ADA prevalence (i.e. ADA positive) @ baseline (BL) ADA-positive participants on-treatment	24 34			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the European Quality of Life (EuroQol) - 5 Dimensions, 5 Level Questionnaire (EQ-5D-5L) score over time

End point title	Change from baseline in the European Quality of Life (EuroQol) - 5 Dimensions, 5 Level Questionnaire (EQ-5D-5L) score over time

End point description:

The EQ-5D-5L comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. For each of the 5 dimensions, subject's responses are scored on a 5-point scale (1=no problem to 5=extreme problems). Change from baseline is being presented for EQ Index score. Index score is defined as a weighted combination of the levels of the 5-dimention scales, ranging from 0 to 1. The United States value set from Pickard et al 2019 was used.

End point type	Secondary

End point timeframe:

Up to 5 years after last patient randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	245		
Units: change from baseline in utility				
arithmetic mean (standard deviation)				
Baseline (BL)	0.78 (± 0.204)	0.78 (± 0.239)		
Change from BL @ Cycle (C) 3 Day (D) 1 (n=205,199)	0.00 (± 0.215)	-0.03 (± 0.222)		
Change from BL at C6D1 (n = 163, 157)	-0.02 (± 0.260)	-0.02 (± 0.305)		
Change from BL at C9D1 (n = 129, 117)	0.03 (± 0.232)	-0.01 (± 0.226)		
Change from BL at C12D1 (n = 93, 88)	0.02 (± 0.163)	-0.05 (± 0.261)		
Change from BL at C15D1 (n = 84, 61)	-0.02 (± 0.238)	0.01 (± 0.221)		
Change from BL at C18D1 (n = 65, 53)	-0.02 (± 0.208)	0.00 (± 0.226)		
Change from BL at C21D1 (n = 47, 45)	0.00 (± 0.208)	0.00 (± 0.256)		
Change from BL at C24D1 (n = 45, 41)	0.00 (± 0.157)	0.02 (± 0.225)		
Change from BL at C27D1 (n = 34, 35)	-0.09 (± 0.283)	0.00 (± 0.213)		
Change from BL at C30D1 (n = 30, 25)	-0.03 (± 0.315)	0.02 (± 0.256)		
Change from BL at C33D1 (n = 22, 22)	-0.01 (± 0.211)	-0.02 (± 0.218)		
Change from BL at C36D1 (n = 18, 15)	-0.07 (± 0.333)	-0.07 (± 0.395)		
Change from BL at C39D1 (n = 14, 10)	-0.16 (± 0.360)	0.02 (± 0.143)		
Change from BL at C42D1 (n = 9, 4)	-0.09 (± 0.262)	-0.13 (± 0.309)		
Change from BL at C45D1 (n = 6, 2)	-0.12 (± 0.262)	0.17 (± 0.069)		
Change from BL at C48D1 (n = 1, 2)	-0.07 (± 0.000)	0.06 (± 0.087)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the European Quality of Life (EuroQoL) - 5 Dimensions, 5 Level Questionnaire (EQ-5D-5L) Visual Analogue Scale (VAS) over time

End point title	Change from baseline in the European Quality of Life (EuroQoL) - 5 Dimensions, 5 Level Questionnaire (EQ-5D-5L) Visual Analogue Scale (VAS) over time

End point description:

The EQ-5D-5L VAS records the participant's self-rated health on a visual analogue scale numbered from 0 to 100, with 0 being "the worst health you can imagine" and 100 being "the best health you can imagine". Change from baseline was presented.

End point type	Secondary

End point timeframe:

Up to 5 years after last participant randomized

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	245		
Units: Change from baseline in VAS value				
arithmetic mean (standard deviation)				
Baseline (BL)	68.91 (± 18.371)	68.04 (± 18.762)		
Change from BL @ Cycle 3 Day 1 (C3D1) (n=205,199)	1.39 (± 21.029)	0.40 (± 18.767)		
Change from BL at C6D1 (n = 163, 157)	2.60 (± 25.218)	2.08 (± 23.294)		
Change from BL at C9D1 (n = 129, 117)	5.28 (± 20.528)	2.55 (± 20.805)		
Change from BL at C12D1 (n = 93, 88)	5.55 (± 21.380)	1.18 (± 22.728)		
Change from BL at C15D1 (n = 84, 61)	2.87 (± 21.940)	3.72 (± 21.564)		
Change from BL at C18D1 (n = 65, 53)	3.80 (± 20.474)	6.87 (± 19.369)		
Change from BL at C21D1 (n = 47, 45)	3.70 (± 23.541)	5.71 (± 18.577)		
Change from BL at C24D1 (n = 45, 41)	1.73 (± 21.288)	7.68 (± 18.781)		
Change from BL at C27D1 (n = 34, 35)	-0.44 (± 21.139)	4.63 (± 19.792)		
Change from BL at C30D1 (n = 30, 25)	3.13 (± 26.829)	4.76 (± 14.998)		
Change from BL at C33D1 (n = 22, 22)	5.41 (± 26.923)	1.64 (± 17.705)		
Change from BL at C36D1 (n = 18, 15)	-1.50 (± 25.714)	-2.80 (± 29.617)		
Change from BL at C39D1 (n = 14, 10)	3.57 (± 28.281)	1.70 (± 20.078)		
Change from BL at C42D1 (n = 9, 4)	-11.89 (± 22.469)	-0.75 (± 26.550)		
Change from BL at C45D1 (n = 6, 2)	2.00 (± 15.113)	-2.00 (± 24.042)		
Change from BL at C48D1 (n = 1, 2)	7.00 (± 0.000)	5.50 (± 34.648)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of Global Health Status/Quality of Life scores using European Organization for Research and Treatment of Cancer's Core Quality of Life Questionnaire (EORTC-QLQ-C30).

End point title	Change from baseline of Global Health Status/Quality of Life scores using European Organization for Research and Treatment of Cancer's Core Quality of Life Questionnaire (EORTC-QLQ-C30).

End point description:

EORTC-QLQ-C30 is a 30-item questionnaire developed to assess the quality of life of cancer participants. Participant's responses to 2 questions (Items 29+30: "How would you rate your overall health during the past week?" and "How would you rate your overall quality of life during the past week?") are scored on a 7-point scale (1=Very Poor to 7=Excellent). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. A higher score indicates a better overall outcome. Change from baseline to Cycle 12 Day 1 as presented.

End point type	Secondary

End point timeframe:

Up to Cycle 12 Day 1 (C12D1) (1 cycle = 28 days)

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	62		
Units: scores on a scale				
arithmetic mean (standard deviation)	8.72 (± 23.071)	8.20 (± 19.932)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: All Collected Deaths

End point title	All Collected Deaths

End point description:

Deaths were collected from randomization until the end of the trial, approx. 52 months, including post-treatment survival follow up period.

End point type	Post-hoc

End point timeframe:

from randomization until end of trial, approx. 52 months

End point values	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	265		
Units: Participants				
Pre-treatment deaths	0	1		
On-treatment deaths	18	37		
Post-treatment deaths (n = 247, 228)	143	122		
All deaths	161	160		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: deaths were collected from first dose of study treatment up to approx. 52 months, including post-treatment survival follow up period. Serious and Other Adverse Events: from first dose of study treatment until 30 days after last dose

Adverse event reporting additional description:

Any sign or symptom that occurred during the conduct of the trial and the safety follow-up. Deaths in the post-treatment survival follow-up period are not considered adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Sabatolimab (MBG453) + Azacitidine

Reporting group description:

Participants received sabatolimab plus azacitidine.

Reporting group title	Placebo + Azacitidine

Reporting group description:

Participants received placebo plus azacitidine.

Serious adverse events	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine	
Total subjects affected by serious adverse events			
subjects affected / exposed	174 / 263 (66.16%)	164 / 265 (61.89%)	
number of deaths (all causes)	161	159	
number of deaths resulting from adverse events	7	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposarcoma			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodular melanoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine adenocarcinoma			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (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 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 263 (0.76%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White coat hypertension			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 263 (0.76%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			

subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Oedema			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	17 / 263 (6.46%)	19 / 265 (7.17%)	
occurrences causally related to treatment / all	9 / 21	7 / 20	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sudden death			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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			
Epistaxis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (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	2 / 263 (0.76%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Emphysema			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity pneumonitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung infiltration			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 263 (0.38%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	2 / 2	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary toxicity			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 263 (1.14%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anti-platelet antibody positive			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	5 / 263 (1.90%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	8 / 9	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	10 / 263 (3.80%)	7 / 265 (2.64%)	
occurrences causally related to treatment / all	12 / 12	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin T increased			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	3 / 263 (1.14%)	4 / 265 (1.51%)	
occurrences causally related to treatment / all	4 / 5	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	4 / 263 (1.52%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	3 / 263 (1.14%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 263 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Refractoriness to platelet transfusion			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site inflammation			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	4 / 263 (1.52%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			

subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	3 / 263 (1.14%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 263 (0.38%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	1 / 2	
Left ventricular dysfunction			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mitral valve incompetence			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (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	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	6 / 263 (2.28%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	2 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Altered state of consciousness			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system haemorrhage			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cerebrovascular accident			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Encephalopathy			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 263 (0.38%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic intolerance			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 263 (4.18%)	11 / 265 (4.15%)	
occurrences causally related to treatment / all	5 / 13	8 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agranulocytosis			
subjects affected / exposed	1 / 263 (0.38%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of malignant disease			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	49 / 263 (18.63%)	31 / 265 (11.70%)	
occurrences causally related to treatment / all	39 / 63	22 / 45	
deaths causally related to treatment / all	1 / 2	0 / 1	
Iron deficiency anaemia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			

subjects affected / exposed	0 / 263 (0.00%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	4 / 263 (1.52%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	4 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	3 / 263 (1.14%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	6 / 263 (2.28%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	4 / 6	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Haematotympanum			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Vision blurred			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 263 (0.76%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			

subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal ulcer			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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	2 / 263 (0.76%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal motility disorder			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids thrombosed			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 263 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overflow diarrhoea			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric dysplasia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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	0 / 263 (0.00%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema nodosum			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 263 (0.76%)	5 / 265 (1.89%)	
occurrences causally related to treatment / all	0 / 2	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Calculus bladder			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Joint effusion			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	6 / 263 (2.28%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	4 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 263 (0.00%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	12 / 263 (4.56%)	9 / 265 (3.40%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 2	
Herpes zoster			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	6 / 263 (2.28%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	4 / 263 (1.52%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Eyelid infection			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 263 (0.38%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes dermatitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	4 / 263 (1.52%)	9 / 265 (3.40%)	
occurrences causally related to treatment / all	0 / 4	1 / 9	
deaths causally related to treatment / all	0 / 1	0 / 2	
Infection			
subjects affected / exposed	1 / 263 (0.38%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	1 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Legionella infection			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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	3 / 263 (1.14%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	3 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Opportunistic infection			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	5 / 263 (1.90%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	3 / 5	1 / 2	
deaths causally related to treatment / all	1 / 2	0 / 0	
Pneumonia			

subjects affected / exposed	35 / 263 (13.31%)	36 / 265 (13.58%)	
occurrences causally related to treatment / all	19 / 38	16 / 36	
deaths causally related to treatment / all	3 / 3	2 / 7	
Pneumonia aspiration			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia bacterial			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia escherichia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mucormycosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 263 (0.00%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 263 (1.14%)	10 / 265 (3.77%)	
occurrences causally related to treatment / all	0 / 5	4 / 10	
deaths causally related to treatment / all	0 / 1	1 / 4	
Septic shock			
subjects affected / exposed	6 / 263 (2.28%)	8 / 265 (3.02%)	
occurrences causally related to treatment / all	4 / 6	4 / 8	
deaths causally related to treatment / all	1 / 1	2 / 3	
Sialoadenitis			

subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	7 / 263 (2.66%)	5 / 265 (1.89%)	
occurrences causally related to treatment / all	1 / 8	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	2 / 263 (0.76%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 263 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic infection			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
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	3 / 263 (1.14%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	2 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	2 / 263 (0.76%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	1 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			

subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 263 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 263 (0.38%)	0 / 265 (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	1 / 263 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 263 (0.76%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Sabatolimab (MBG453) + Azacitidine	Placebo + Azacitidine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	256 / 263 (97.34%)	255 / 265 (96.23%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	17 / 263 (6.46%)	14 / 265 (5.28%)	
occurrences (all)	28	19	
Hypertension			
subjects affected / exposed	21 / 263 (7.98%)	12 / 265 (4.53%)	
occurrences (all)	28	12	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	24 / 263 (9.13%)	33 / 265 (12.45%)	
occurrences (all)	29	43	
Asthenia			
subjects affected / exposed	31 / 263 (11.79%)	29 / 265 (10.94%)	
occurrences (all)	41	36	
Fatigue			
subjects affected / exposed	50 / 263 (19.01%)	33 / 265 (12.45%)	
occurrences (all)	58	36	
Injection site reaction			
subjects affected / exposed	16 / 263 (6.08%)	20 / 265 (7.55%)	
occurrences (all)	45	39	
Pyrexia			
subjects affected / exposed	71 / 263 (27.00%)	59 / 265 (22.26%)	
occurrences (all)	94	115	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	15 / 263 (5.70%)	17 / 265 (6.42%)	
occurrences (all)	26	30	
Dyspnoea			
subjects affected / exposed	24 / 263 (9.13%)	15 / 265 (5.66%)	
occurrences (all)	28	18	
Cough			

subjects affected / exposed	35 / 263 (13.31%)	27 / 265 (10.19%)	
occurrences (all)	45	37	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	29 / 263 (11.03%)	21 / 265 (7.92%)	
occurrences (all)	43	21	
Investigations			
Blood creatinine increased			
subjects affected / exposed	19 / 263 (7.22%)	12 / 265 (4.53%)	
occurrences (all)	39	12	
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 263 (4.56%)	18 / 265 (6.79%)	
occurrences (all)	20	37	
Alanine aminotransferase increased			
subjects affected / exposed	15 / 263 (5.70%)	24 / 265 (9.06%)	
occurrences (all)	29	40	
C-reactive protein increased			
subjects affected / exposed	18 / 263 (6.84%)	6 / 265 (2.26%)	
occurrences (all)	23	6	
White blood cell count decreased			
subjects affected / exposed	48 / 263 (18.25%)	52 / 265 (19.62%)	
occurrences (all)	182	205	
Weight decreased			
subjects affected / exposed	34 / 263 (12.93%)	25 / 265 (9.43%)	
occurrences (all)	38	26	
Platelet count decreased			
subjects affected / exposed	62 / 263 (23.57%)	56 / 265 (21.13%)	
occurrences (all)	207	216	
Neutrophil count decreased			
subjects affected / exposed	61 / 263 (23.19%)	54 / 265 (20.38%)	
occurrences (all)	213	241	
Lymphocyte count decreased			
subjects affected / exposed	14 / 263 (5.32%)	20 / 265 (7.55%)	
occurrences (all)	56	56	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	15 / 263 (5.70%)	5 / 265 (1.89%)	
occurrences (all)	17	5	
Nervous system disorders			
Dizziness			
subjects affected / exposed	21 / 263 (7.98%)	15 / 265 (5.66%)	
occurrences (all)	26	17	
Headache			
subjects affected / exposed	23 / 263 (8.75%)	20 / 265 (7.55%)	
occurrences (all)	32	25	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	67 / 263 (25.48%)	58 / 265 (21.89%)	
occurrences (all)	167	142	
Neutropenia			
subjects affected / exposed	96 / 263 (36.50%)	76 / 265 (28.68%)	
occurrences (all)	333	225	
Leukopenia			
subjects affected / exposed	17 / 263 (6.46%)	22 / 265 (8.30%)	
occurrences (all)	57	44	
Febrile neutropenia			
subjects affected / exposed	19 / 263 (7.22%)	21 / 265 (7.92%)	
occurrences (all)	19	34	
Anaemia			
subjects affected / exposed	107 / 263 (40.68%)	91 / 265 (34.34%)	
occurrences (all)	276	222	
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	14 / 263 (5.32%)	12 / 265 (4.53%)	
occurrences (all)	15	13	
Diarrhoea			
subjects affected / exposed	61 / 263 (23.19%)	46 / 265 (17.36%)	
occurrences (all)	90	67	
Constipation			
subjects affected / exposed	141 / 263 (53.61%)	114 / 265 (43.02%)	
occurrences (all)	218	179	
Abdominal pain			

subjects affected / exposed	26 / 263 (9.89%)	15 / 265 (5.66%)	
occurrences (all)	34	18	
Vomiting			
subjects affected / exposed	48 / 263 (18.25%)	45 / 265 (16.98%)	
occurrences (all)	61	70	
Nausea			
subjects affected / exposed	87 / 263 (33.08%)	66 / 265 (24.91%)	
occurrences (all)	114	94	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	30 / 263 (11.41%)	26 / 265 (9.81%)	
occurrences (all)	36	35	
Pruritus			
subjects affected / exposed	22 / 263 (8.37%)	18 / 265 (6.79%)	
occurrences (all)	36	23	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	43 / 263 (16.35%)	26 / 265 (9.81%)	
occurrences (all)	54	32	
Back pain			
subjects affected / exposed	31 / 263 (11.79%)	19 / 265 (7.17%)	
occurrences (all)	34	21	
Pain in extremity			
subjects affected / exposed	18 / 263 (6.84%)	9 / 265 (3.40%)	
occurrences (all)	21	10	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	24 / 263 (9.13%)	17 / 265 (6.42%)	
occurrences (all)	32	30	
Upper respiratory tract infection			
subjects affected / exposed	21 / 263 (7.98%)	20 / 265 (7.55%)	
occurrences (all)	31	25	
Pneumonia			
subjects affected / exposed	30 / 263 (11.41%)	27 / 265 (10.19%)	
occurrences (all)	30	29	
Cellulitis			

subjects affected / exposed	14 / 263 (5.32%)	12 / 265 (4.53%)	
occurrences (all)	15	15	
COVID-19			
subjects affected / exposed	44 / 263 (16.73%)	35 / 265 (13.21%)	
occurrences (all)	48	36	
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	16 / 263 (6.08%)	18 / 265 (6.79%)	
occurrences (all)	22	28	
Hyperglycaemia			
subjects affected / exposed	15 / 263 (5.70%)	25 / 265 (9.43%)	
occurrences (all)	28	35	
Decreased appetite			
subjects affected / exposed	26 / 263 (9.89%)	26 / 265 (9.81%)	
occurrences (all)	41	28	
Hypoalbuminaemia			
subjects affected / exposed	20 / 263 (7.60%)	23 / 265 (8.68%)	
occurrences (all)	33	52	
Hypokalaemia			
subjects affected / exposed	39 / 263 (14.83%)	33 / 265 (12.45%)	
occurrences (all)	60	57	
Hyponatraemia			
subjects affected / exposed	15 / 263 (5.70%)	13 / 265 (4.91%)	
occurrences (all)	31	33	
Hypocalcaemia			
subjects affected / exposed	7 / 263 (2.66%)	15 / 265 (5.66%)	
occurrences (all)	19	54	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2020	As of the release of this amendment, approximately 13 participants were randomized in this study. The purpose of this amendment was to clarify the inclusion criteria related to the eligibility for intensive chemotherapy and stem cell transplantation, as well as the exclusion criteria related to cardiac abnormalities. Additionally, as new treatment options were available for participants with AML, study treatment beyond progression in case of acute leukemia was not permitted. Definitions of the RBC or platelet transfusion dependence and transfusion independence were updated. The same pre-specified period of observation (i.e., 8 weeks) was used to determine the transfusion status throughout the study. The interval of 8 weeks was selected, as it was in line with the assessment of transfusions for hematologic improvement and was acceptable to evaluate the transfusion status of higher-risk MDS participants at baseline (IWG 2006, IWG 2018). Transfusion independence was defined as absence of any transfusion during a given period of observation. Clarifications about the estimand definition and methods for statistical analyses of PRO data were added. In addition, the need for TLS risk monitoring was further emphasized.
14 July 2021	As of the release of this amendment, approximately 324 participants were randomized in this study. The main purpose of this amendment was to clarify inclusion criterion related to MDS/CMML-2 status of the Participant and exclusion criterion related to myelofibrosis. It was clarified that the IPSS-R score used for MDS participants in this study was solely based on the publication Greenberg et al 2012 to ensure consistency across the participating sites. For CMML-2, it was clarified that in alignment with the WHO classification 2016. Furthermore, the new Novartis standard language, referred to as disruption proofing language, added to specify trial conduct during public health emergencies. The added language addressed study participant safety and trial integrity. Additional guidance for COVID-19 vaccinations was added to avoid overlapping adverse events with study treatment, and several updates were made to clarify the visit windows in case of delay of administration of study treatment and time windows for certain assessments. Lastly, the definition of withdrawal of consent and management of biological samples was updated as per latest protocol template.
23 June 2022	The purpose of this protocol amendment was to adjust the group-sequential statistical plan based on independent information that became available from the final progression free survival (PFS) analysis of CMBG453B12201 which was conducted in a similar participant population and study treatment. Based on these data, a delayed treatment effect was considered for this study which justified an increase in overall survival (OS) events to retain statistical power for the primary analysis at 85%. As of the release of this amendment, accrual was completed: 530 participants had been randomized. The DMC, who had been informed about the outcome of CMBG453B12201, had completed the safety & preplanned futility assessment of this study at 74 OS events (data cutoff as of 20-Nov-2021) and recommended to continue 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.

Two participants didn’t receive treatment and were excluded from the Safety Set. One withdrew consent, another progressed to AML before treatment. One sabatolimab participant progressed to AML, received azacitidine only, and was analyzed as placebo.

Notes: