Clinical trial results:
A randomized, double-blind, placebo-controlled phase II multi-center study of intravenous MBG453 added to hypomethylating agents in adult subjects with intermediate, high or very high-risk myelodysplastic syndrome (MDS) as per IPSS-R criteria

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results.
Please use https://www.novctrd.com for complete trial results.

Summary

EudraCT number	2018-004479-11
Trial protocol	ES FR GB DE CZ AT GR HU NO BE IT
Global end of trial date	15 July 2024

Results information

Result version number	v1 (current)
This version publication date	30 July 2025
First version publication date	30 July 2025

Trial information

Trial identification

Sponsor protocol code	CMBG453B12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03946670
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 Pharm, AG, 41 8613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharm, AG, 41 8613241111, 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	26 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if sabatolimab combined with standard HMA therapy improves PFS in subjects with intermediate, high or very high risk MDS.

To determine if sabatolimab combined with standard HMA therapy improves complete remission in subjects with intermediate, high, or very high risk MDS

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	04 June 2019
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	Austria: 3
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 17

Country: Number of subjects enrolled	Japan: 22
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 3
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Taiwan: 11
Country: Number of subjects enrolled	Türkiye: 8
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	127
EEA total number of subjects	58

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)	16
From 65 to 84 years	108
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

47 centers across 17 countries enrolled subjects in this study.

Pre-assignment

Screening details:

Informed consent was obtained from each subject in writing at screening before any study specific procedure was performed.

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	MBG453 + hypomethylating agents (HMA)

Arm description:

Patients were taking MBG453 plus hypomethylating agents

Arm type	Experimental
Investigational medicinal product name	Hypomethylating agent (HMA): decitabine or azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection, Powder for concentrate for solution for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Decitabine (IV) 20 mg/m^2 from Day 1 to Day 5, azacitidine (SC or IV) 75 mg/m^2 from Day 1 to Day 7 or Day 1 to Day 5 plus Day 8 to Day 9, per Investigator's choice based on system organ class (SOC)

Investigational medicinal product name	Sabatolimab (MBG453)
Investigational medicinal product code	MBG453
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Implantation

Dosage and administration details:

Sabatolimab solution for injection was supplied to the Investigators at dose strength of 100 mg/1mL and 400 mg/ 4 mL

Arm title	Placebo + hypomethylating agents (HMA)

Arm description:

Patients were taking placebo plus hypomethylating agents

Arm type	Placebo
Investigational medicinal product name	Hypomethylating agent (HMA): decitabine or azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection, Powder for concentrate for solution for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Decitabine (IV) 20 mg/m^2 from Day 1 to Day 5, azacitidine (SC or IV) 75 mg/m^2 from Day 1 to Day

7 or Day 1 to Day 5 plus Day 8 to Day 9, per Investigator's choice based on system organ class (SOC)

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Implantation

Dosage and administration details:

Placebo solution for injection was supplied to the Investigators at dose strength of 100 mg/1mL and 400 mg/ 4 mL

Number of subjects in period 1	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)
Started	65	62
Treated	64	61
Not treated	1	1
Discontinued from treatment	64	61
Completed	0	0
Not completed	65	62
Adverse event, serious fatal	5	8
Physician decision	6	5
Subject Decision	4	5
Adverse event, non-fatal	7	10
Study Terminated By Sponsor	2	-
Not Treated	1	1
Progressive Disease	34	27
New Therapy For Study Indication	1	-
HSCT Planned	5	6

Baseline characteristics

Reporting groups	
Reporting group title	MBG453 + hypomethylating agents (HMA)
Reporting group description:	
Patients were taking MBG453 plus hypomethylating agents	
Reporting group title	Placebo + hypomethylating agents (HMA)
Reporting group description:	
Patients were taking placebo plus hypomethylating agents	

Reporting group values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)	Total
Number of subjects	65	62	127
Age categorical Units: Subjects			
Adults (18-64 years)	6	10	16
From 65-84 years	57	51	108
85 years and over	2	1	3
Age Continuous Units: Years			
arithmetic mean	71.9	71.3	
standard deviation	± 6.70	± 9.64	-
Sex: Female, Male Units: Participants			
Female	24	17	41
Male	41	45	86
Race/Ethnicity, Customized Units: Subjects			
White	44	33	77
Asian	17	25	42
Black or African American	0	1	1
Unknown	4	3	7

End points

End points reporting groups

Reporting group title	MBG453 + hypomethylating agents (HMA)
Reporting group description: Patients were taking MBG453 plus hypomethylating agents	
Reporting group title	Placebo + hypomethylating agents (HMA)
Reporting group description: Patients were taking placebo plus hypomethylating agents	

Primary: Complete Remission (CR) Rate

End point title	Complete Remission (CR) Rate
End point description: 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%. Modified response criteria According to International Working Group (IWG) and as per World Health Organization (WHO) criteria for Myelodysplastic syndromes (MDS) as per investigator assessment.	
End point type	Primary
End point timeframe: average of 7 months	

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Percentage of participants				
number (confidence interval 95%)	21.5 (12.3 to 33.5)	17.7 (9.2 to 29.5)		

Statistical analyses

Statistical analysis title	CR rate Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.769
Method	Cochran-Mantel-Haenszel

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Defined as time from randomization to disease progression (including transformation to acute leukemia per WHO 2016 classification), relapse from CR according to IWG-MDS or death due to any cause, whichever occurs first, as per investigator assessment.

End point type	Primary

End point timeframe:

approx. 32 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: months				
median (confidence interval 95%)	11.07 (7.62 to 17.61)	8.48 (6.93 to 11.30)		

Statistical analyses

Statistical analysis title	PFS Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1022
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.749
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.479
upper limit	1.173

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Time from randomization to death due to any cause

End point type	Secondary

End point timeframe:

approx. 48 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Months				
median (confidence interval 95%)	19.12 (13.90 to 30.03)	18.00 (13.11 to 25.43)		

Statistical analyses

Statistical analysis title	OS Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.808
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.542
upper limit	1.205

Secondary: Progression Free Survival (PFS) - Final PFS

End point title	Progression Free Survival (PFS) - Final PFS

End point description:

Defined as time from randomization to disease progression (including transformation to acute leukemia per WHO 2016 classification), relapse from CR according to IWG-MDS or death due to any cause. This is an update of the Primary Outcome Measure PFS with data collected after assessment of the primary results.

End point type	Secondary

End point timeframe:

approx. 48 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: months				
median (confidence interval 95%)	11.07 (7.62 to 16.59)	8.48 (6.93 to 11.30)		

Statistical analyses

Statistical analysis title	Final PFS Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.795
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.521
upper limit	1.212

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 World Health Organization (WHO) 2016 classification) or diagnosis of extramedullary acute leukemia or death due to any cause.

End point type	Secondary

End point timeframe:

approx. 48 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Months				
median (confidence interval 95%)	16.82 (8.80 to 28.58)	13.63 (9.82 to 21.16)		

Statistical analyses

Statistical analysis title	LFS Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.906
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.44

Secondary: Event-free Survival (EFS)

End point title	Event-free Survival (EFS)
End point description:	
EFS is defined as the time from randomization to lack of reaching complete response (CR) within the first 6 months, relapse from CR or death due to any cause, whichever occurs first. CR and relapse from CR were defined according to International Working Group (IWG) for Myelodysplastic Syndromes (MDS) as per Investigator assessment. For participants not reaching CR within the first 6 months, an EFS event at day 1 was considered.	
End point type	Secondary
End point timeframe:	
approx. 48 months	

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Months				
median (confidence interval 95%)	0.03 (0 to 999)	0.03 (0 to 999)		

Statistical analyses

Statistical analysis title	EFS Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.589
upper limit	1.343

Secondary: Duration of Complete Remission

End point title	Duration of Complete Remission
End point description:	
Duration of complete response is the time from the date of the first documented CR to the date of first documented relapse from CR or death due to any cause, whichever occurs first.	
End point type	Secondary
End point timeframe:	
approx. 48 months	

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Months				
median (confidence interval 95%)	17.97 (10.87 to 27.17)	9.23 (5.09 to 17.97)		

Statistical analyses

Statistical analysis title	Duration of CR Analysis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.664
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	1.838

Secondary: Response Rate of Complete Remission (CR)/marrow Complete Remission (mCR)/Partial Remission (PR)/Hematopoietic Improvement (HI))

End point title	Response Rate of Complete Remission (CR)/marrow Complete Remission (mCR)/Partial Remission (PR)/Hematopoietic Improvement (HI))

End point description:

Percentage of complete remission (CR)/marrow Complete Remission (mCR)/partial remission (PR) & Hematological improvement (HI) as per investigator assessment according to IWG-MDS. 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: where the Bone marrow ≤5% blasts and blast count decrease by ≥50% compared to baseline 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. HI definition is based on modified Hematological Improvement per IWG-MDS criteria in MDS & is the combination of Erythroid response (HI-E), Platelet response (HI-P) & Neutrophil response (HI-N).

End point type	Secondary

End point timeframe:

approx. 32 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Percentage of participants				
number (confidence interval 95%)	67.7 (54.9 to 78.8)	61.3 (48.1 to 73.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants who are Red Blood Cells (RBC)/Platelets transfusion independent after randomization as per IWG-MDS

End point title	Percent of Participants who are Red Blood Cells (RBC)/Platelets transfusion independent after randomization as per IWG-MDS

End point description:

Improvement in RBC/platelets transfusion independence. RBC/Platelets transfusion independence rate is defined as the percentage of participants having received no RBC/Platelets transfusions during at least 8 consecutive weeks after randomization.

End point type	Secondary

End point timeframe:

approx. 48 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Percentage of participants				
number (confidence interval 95%)				
Red blood cells (RBC)	60.0 (47.1 to 72.0)	64.5 (51.3 to 76.3)		
Platelets	73.8 (61.5 to 84.0)	74.2 (61.5 to 84.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Complete Remission

End point title	Time to Complete Remission
End point description: Time from randomization to the first documented CR	
End point type	Secondary
End point timeframe: Average of 7 months	

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Months				
median (confidence interval 95%)	999 (999 to 999)	999 (999 to 999)		

Statistical analyses

Statistical analysis title	Time to CR Analyis
Comparison groups	MBG453 + hypomethylating agents (HMA) v Placebo + hypomethylating agents (HMA)

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.237
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.588
upper limit	2.601

Secondary: Red Blood Cells (RBC)/Platelets transfusion independence duration after randomization

End point title	Red Blood Cells (RBC)/Platelets transfusion independence duration after randomization

End point description:

The total duration of all transfusion independence periods is the sum of each period of the transfusion independence.
RBC/Platelets transfusions independence period is defined as the period for which participants having received no RBC/Platelets transfusions during at least 8 consecutive weeks after randomization.

End point type	Secondary

End point timeframe:

approx. 48 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	10		
Units: Weeks				
median (inter-quartile range (Q1-Q3))				
RBC	46.29 (22.86 to 113.00)	36.71 (20.29 to 65.36)		
Platelets	44.36 (22.29 to 107.43)	45.29 (25.14 to 80.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations for MBG453

End point title	Serum Concentrations for MBG453[1]

End point description:

Pharmacokinetics (PK) of MBG453 when given in combination with hypomethylating agents (HMA). Cycle - C, Day = D

End point type	Secondary

End point timeframe:

0hr pre-dose on Day 8 of each cycle until cycle 6 and on Day 8 of cycles 9, 12, 18 and 24, 2hr post-dose on Day 8 of C1 and C3, EOT (approx. 48 months) and up to 150 day of the safety follow up period; 1 cycle = 28 days

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	MBG453 + hypomethylating agents (HMA)			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: micro gram/mL				
arithmetic mean (standard deviation)				
C1 D8 at 0 hour (hr) (pre-dose) (n = 47)	0 (± 0)			
C1 D8 at 2 hr (n =37)	103 (± 72.4)			
C2 D8 at 0 hr (pre-dose) (n = 43)	38.8 (± 20.5)			
C3 D8 at 0 hr (pre-dose) (n = 49)	57.5 (± 32.1)			
C3 D8 at 2 hr (n = 44)	149 (± 49.6)			
C4 D8 at 0 hr (pre-dose) (n = 42)	70.7 (± 37.6)			
C5 D8 at 0 hr (pre-dose) (n = 42)	76.7 (± 38.4)			
C6 D8 at 0 hr (pre-dose) (n = 39)	85.0 (± 37.7)			
C9 D8 at 0 hr (pre-dose) (n = 30)	97.3 (± 49.3)			
C12 D8 at 0 hr (pre-dose) (n = 22)	103 (± 43.0)			
C18 D8 at 0 hr (pre-dose) (n = 11)	97.7 (± 42.4)			
C24 D8 at 0 hr (pre-dose) (n = 4)	134 (± 39.3)			
End of treatment (EOT) (n = 40)	50.0 (± 43.8)			
30 D Safety follow-up (f/u) (n = 11)	44.4 (± 46.6)			
150 D Safety f/u (n = 5)	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity of MBG453 when given in combination of hypomethylating agents: ADA Incidence

End point title	Immunogenicity of MBG453 when given in combination of hypomethylating agents: ADA Incidence[2]

End point description:

Anti-drug Antibody (ADA) incidence on-treatment. ADA incidence (i.e. ADA-positive subjects) was calculated as the number of subjects with at least 1 on-treatment ADA-positive sample divided by the number of participants with a determinant baseline IG sample and at least one determinant post-baseline IG sample.

End point type	Secondary

End point timeframe:

approx. 48 months

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	MBG453 + hypomethylating agents (HMA)			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Participants	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity (IG) of MBG453 when given in combination of hypomethylating agents: ADA prevalence

End point title	Immunogenicity (IG) of MBG453 when given in combination of hypomethylating agents: ADA prevalence[3]

End point description:

Number of subjects with at least one sample meeting the criteria either at baseline or post-baseline. Anti-drug Antibody (ADA) prevalence equals ADA-positive at baseline or post-baseline.

End point type	Secondary

End point timeframe:

at baseline

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	MBG453 + hypomethylating agents (HMA)			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Participants	11			

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 end of trial, approx. 48 months.

End point type	Post-hoc

End point timeframe:

from randomization until end of trial, approx. 48 months

End point values	MBG453 + hypomethylating agents (HMA)	Placebo + hypomethylating agents (HMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	62		
Units: Participants				
Pre-treatment deaths	0	1		
On-treatment deaths	5	13		
Post-treatment deaths	40	39		
Total deaths	45	53		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the date of 1st administration of study treatment to 30 days after the date of the last administration of study treatment, up to approx. 48 months. Deaths were collected from randomization until end of trial, approx. 48 months

Adverse event reporting additional description:

Adverse Event: Any sign or symptom that occurs during the study treatment + 30 days post treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Placebo + hypomethylating agents (HMA)

Reporting group description:

Patients are taking placebo plus hypomethylating agents

Reporting group title	MBG453 + hypomethylating agents (HMA)

Reporting group description:

Patients are taking MBG453 plus hypomethylating agents

Serious adverse events	Placebo + hypomethylating agents (HMA)	MBG453 + hypomethylating agents (HMA)	
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 63 (68.25%)	38 / 62 (61.29%)	
number of deaths (all causes)	53	45	
number of deaths resulting from adverse events	2	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to bone			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the hypopharynx			

subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral artery stenosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Death			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Condition aggravated			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chills			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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	9 / 63 (14.29%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	1 / 11	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Immune reconstitution inflammatory syndrome			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary hypertension			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pleural effusion			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Organising pneumonia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			

subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
General physical condition abnormal			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemoglobin decreased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
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	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile nonhaemolytic transfusion reaction			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
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	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dysarthria			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 63 (4.76%)	3 / 62 (4.84%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hyperleukocytosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	14 / 63 (22.22%)	16 / 62 (25.81%)	
occurrences causally related to treatment / all	10 / 22	11 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	1 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophilic dermatosis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Arthritis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Epiglottitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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	3 / 63 (4.76%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermo-hypodermitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival abscess			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	11 / 63 (17.46%)	9 / 62 (14.52%)	
occurrences causally related to treatment / all	5 / 15	5 / 14	
deaths causally related to treatment / all	1 / 4	0 / 0	
Pneumonia fungal			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 63 (1.59%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	8 / 63 (12.70%)	4 / 62 (6.45%)	
occurrences causally related to treatment / all	1 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal bacterial infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo + hypomethylating agents (HMA)	MBG453 + hypomethylating agents (HMA)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 63 (100.00%)	61 / 62 (98.39%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 63 (11.11%)	7 / 62 (11.29%)	
occurrences (all)	13	7	
Haematoma			
subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	
occurrences (all)	4	4	
Hypotension			
subjects affected / exposed	6 / 63 (9.52%)	3 / 62 (4.84%)	
occurrences (all)	9	3	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	7 / 63 (11.11%)	11 / 62 (17.74%)	
occurrences (all)	8	21	
Chest pain			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	5	2	
Fatigue			
subjects affected / exposed	8 / 63 (12.70%)	14 / 62 (22.58%)	
occurrences (all)	8	18	
Injection site erythema			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	4	2	
Injection site reaction			
subjects affected / exposed	10 / 63 (15.87%)	4 / 62 (6.45%)	
occurrences (all)	12	7	
Oedema			
subjects affected / exposed	5 / 63 (7.94%)	3 / 62 (4.84%)	
occurrences (all)	5	3	
Oedema peripheral			
subjects affected / exposed	7 / 63 (11.11%)	8 / 62 (12.90%)	
occurrences (all)	7	10	
Pain			
subjects affected / exposed	4 / 63 (6.35%)	3 / 62 (4.84%)	
occurrences (all)	4	3	
Pyrexia			
subjects affected / exposed	13 / 63 (20.63%)	17 / 62 (27.42%)	
occurrences (all)	17	27	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 63 (4.76%)	5 / 62 (8.06%)	
occurrences (all)	5	7	
Cough			
subjects affected / exposed	11 / 63 (17.46%)	8 / 62 (12.90%)	
occurrences (all)	14	9	
Dyspnoea			

subjects affected / exposed	12 / 63 (19.05%)	11 / 62 (17.74%)	
occurrences (all)	12	13	
Epistaxis			
subjects affected / exposed	6 / 63 (9.52%)	8 / 62 (12.90%)	
occurrences (all)	10	9	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	9 / 63 (14.29%)	9 / 62 (14.52%)	
occurrences (all)	10	9	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	12 / 63 (19.05%)	4 / 62 (6.45%)	
occurrences (all)	18	4	
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 63 (14.29%)	6 / 62 (9.68%)	
occurrences (all)	14	7	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	
occurrences (all)	4	4	
Blood bilirubin increased			
subjects affected / exposed	5 / 63 (7.94%)	1 / 62 (1.61%)	
occurrences (all)	8	1	
Blood creatinine increased			
subjects affected / exposed	5 / 63 (7.94%)	2 / 62 (3.23%)	
occurrences (all)	10	2	
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 63 (7.94%)	3 / 62 (4.84%)	
occurrences (all)	7	3	
Gamma-glutamyltransferase increased			
subjects affected / exposed	7 / 63 (11.11%)	2 / 62 (3.23%)	
occurrences (all)	8	2	
Lymphocyte count decreased			
subjects affected / exposed	5 / 63 (7.94%)	3 / 62 (4.84%)	
occurrences (all)	27	13	
Neutrophil count decreased			

subjects affected / exposed	23 / 63 (36.51%)	14 / 62 (22.58%)	
occurrences (all)	89	55	
Platelet count decreased			
subjects affected / exposed	19 / 63 (30.16%)	12 / 62 (19.35%)	
occurrences (all)	70	17	
SARS-CoV-2 test negative			
subjects affected / exposed	7 / 63 (11.11%)	5 / 62 (8.06%)	
occurrences (all)	9	13	
Weight decreased			
subjects affected / exposed	8 / 63 (12.70%)	10 / 62 (16.13%)	
occurrences (all)	12	10	
White blood cell count decreased			
subjects affected / exposed	17 / 63 (26.98%)	13 / 62 (20.97%)	
occurrences (all)	54	34	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 63 (0.00%)	6 / 62 (9.68%)	
occurrences (all)	0	6	
Procedural pain			
subjects affected / exposed	0 / 63 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Transfusion reaction			
subjects affected / exposed	5 / 63 (7.94%)	2 / 62 (3.23%)	
occurrences (all)	9	2	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	4 / 63 (6.35%)	0 / 62 (0.00%)	
occurrences (all)	4	0	
Atrial fibrillation			
subjects affected / exposed	2 / 63 (3.17%)	5 / 62 (8.06%)	
occurrences (all)	2	5	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 63 (7.94%)	8 / 62 (12.90%)	
occurrences (all)	7	13	
Headache			

subjects affected / exposed	7 / 63 (11.11%)	8 / 62 (12.90%)	
occurrences (all)	7	12	
Paraesthesia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	32 / 63 (50.79%)	22 / 62 (35.48%)	
occurrences (all)	70	36	
Thrombocytopenia			
subjects affected / exposed	13 / 63 (20.63%)	20 / 62 (32.26%)	
occurrences (all)	24	44	
Neutropenia			
subjects affected / exposed	20 / 63 (31.75%)	25 / 62 (40.32%)	
occurrences (all)	105	104	
Febrile neutropenia			
subjects affected / exposed	9 / 63 (14.29%)	11 / 62 (17.74%)	
occurrences (all)	12	21	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	5 / 63 (7.94%)	1 / 62 (1.61%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 63 (3.17%)	4 / 62 (6.45%)	
occurrences (all)	2	6	
Vomiting			
subjects affected / exposed	6 / 63 (9.52%)	7 / 62 (11.29%)	
occurrences (all)	7	10	
Toothache			
subjects affected / exposed	2 / 63 (3.17%)	4 / 62 (6.45%)	
occurrences (all)	2	5	
Stomatitis			
subjects affected / exposed	9 / 63 (14.29%)	4 / 62 (6.45%)	
occurrences (all)	11	9	
Haemorrhoids			

subjects affected / exposed	6 / 63 (9.52%)	6 / 62 (9.68%)	
occurrences (all)	6	9	
Diarrhoea			
subjects affected / exposed	15 / 63 (23.81%)	27 / 62 (43.55%)	
occurrences (all)	22	42	
Constipation			
subjects affected / exposed	26 / 63 (41.27%)	29 / 62 (46.77%)	
occurrences (all)	41	61	
Abdominal pain			
subjects affected / exposed	5 / 63 (7.94%)	5 / 62 (8.06%)	
occurrences (all)	5	6	
Nausea			
subjects affected / exposed	19 / 63 (30.16%)	15 / 62 (24.19%)	
occurrences (all)	39	26	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 63 (11.11%)	11 / 62 (17.74%)	
occurrences (all)	7	23	
Night sweats			
subjects affected / exposed	2 / 63 (3.17%)	6 / 62 (9.68%)	
occurrences (all)	4	6	
Erythema			
subjects affected / exposed	2 / 63 (3.17%)	6 / 62 (9.68%)	
occurrences (all)	3	20	
Rash			
subjects affected / exposed	8 / 63 (12.70%)	12 / 62 (19.35%)	
occurrences (all)	11	15	
Purpura			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	5	2	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 63 (4.76%)	5 / 62 (8.06%)	
occurrences (all)	3	5	
Dysuria			

subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	
occurrences (all)	3	7	
Haematuria			
subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	
occurrences (all)	6	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 63 (12.70%)	8 / 62 (12.90%)	
occurrences (all)	10	11	
Back pain			
subjects affected / exposed	7 / 63 (11.11%)	12 / 62 (19.35%)	
occurrences (all)	7	14	
Myalgia			
subjects affected / exposed	1 / 63 (1.59%)	6 / 62 (9.68%)	
occurrences (all)	1	10	
Pain in extremity			
subjects affected / exposed	6 / 63 (9.52%)	11 / 62 (17.74%)	
occurrences (all)	8	12	
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 63 (6.35%)	9 / 62 (14.52%)	
occurrences (all)	4	10	
Cellulitis			
subjects affected / exposed	4 / 63 (6.35%)	3 / 62 (4.84%)	
occurrences (all)	5	3	
Nasopharyngitis			
subjects affected / exposed	5 / 63 (7.94%)	0 / 62 (0.00%)	
occurrences (all)	5	0	
Oral herpes			
subjects affected / exposed	6 / 63 (9.52%)	3 / 62 (4.84%)	
occurrences (all)	6	3	
Pneumonia			
subjects affected / exposed	7 / 63 (11.11%)	2 / 62 (3.23%)	
occurrences (all)	8	3	
Respiratory tract infection			

subjects affected / exposed	0 / 63 (0.00%)	5 / 62 (8.06%)	
occurrences (all)	0	6	
Urinary tract infection			
subjects affected / exposed	3 / 63 (4.76%)	9 / 62 (14.52%)	
occurrences (all)	5	27	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 63 (9.52%)	13 / 62 (20.97%)	
occurrences (all)	6	14	
Hyperglycaemia			
subjects affected / exposed	9 / 63 (14.29%)	4 / 62 (6.45%)	
occurrences (all)	23	7	
Hyperkalaemia			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	9	2	
Hypernatraemia			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	9	2	
Hyperuricaemia			
subjects affected / exposed	2 / 63 (3.17%)	4 / 62 (6.45%)	
occurrences (all)	2	5	
Hypoalbuminaemia			
subjects affected / exposed	5 / 63 (7.94%)	6 / 62 (9.68%)	
occurrences (all)	8	6	
Hypocalcaemia			
subjects affected / exposed	4 / 63 (6.35%)	1 / 62 (1.61%)	
occurrences (all)	9	1	
Hypokalaemia			
subjects affected / exposed	13 / 63 (20.63%)	12 / 62 (19.35%)	
occurrences (all)	16	17	
Hypomagnesaemia			
subjects affected / exposed	4 / 63 (6.35%)	1 / 62 (1.61%)	
occurrences (all)	4	1	
Hyponatraemia			
subjects affected / exposed	8 / 63 (12.70%)	4 / 62 (6.45%)	
occurrences (all)	12	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2019	To add a general guideline for dosing modifications of the investigational drug (sabatolimab/placebo) in relation to nonhematologic non-immune-related toxicities that were clinically significant according to the Investigator and possibly attributable to the investigational drug. This guideline did not apply to nonhematologic non-immune-related toxicities that were attributable to decitabine/azacitidine or the MDS and its complications.
13 January 2020	The primary purpose of this amendment was to address Health Authorities' requests and SSC recommendations. Based on FDA feedback, EFS was added as a secondary endpoint, defined similarly to the EFS definition used for AML. Events included failure to achieve complete remission within the first 6 months, relapse from complete remission, or death from any cause, whichever occurred first. PK and IG sample collection were extended, with updated time points. The SSC recommended prohibiting the use of erythropoietin-stimulating agents and thrombopoietic agents during the study, as they could mask cytopenias. However, GCSF was not prohibited because it was part of the standard care in cases of infection or septicemia. The table for CR was updated accordingly; Confirmation of CR by peripheral blood at 4 weeks was removed. CR was considered confirmed if progression or relapse from CR was not observed within 4 weeks. Assessment of hematological improvements based on IWG 2006 criteria were added, and definitions of transfusion independence/dependence status were adapted to reflect the IWG 2018 criteria. Reference values to determine significant increases in blasts or decreases in blood values were added. The inclusion criterion for adequate renal function was updated to use the MDRD formula instead of the Cockcroft-Gault formula, as MDRD is more accurate below an eGFR of 60 mm/min/1.73 m^2 and better suited for identifying renal impairment in the older MDS population (median age around 70 years). The exclusion criterion related to previous cancer was clarified to specify that low-risk MDS subjects who adequately treated with lenalidomide and failed were eligible. Lenalidomide was not to be administered for intermediate, high, or very high-risk MDS. The safety information was updated to align with the Investigator Brochure Edition 5.1. Clarifications and corrections were made throughout the protocol, along with editorial changes to improve flow and consistency.
06 May 2020	The purpose of this amendment was to update the definitions of the RBC or platelet transfusion dependence and transfusion independence in Section 8.3, Table 8-2 based on FDA feedback. 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 high-risk MDS subjects at baseline. Transfusion independence was defined as absence of any transfusion during a given period of observation.

02 September 2021	The main purpose of this amendment was to clarify that long-term safety and efficacy data is collected until 4 years after last subject was randomized, which is the time of the end of study and the data cut-off date for the final OS analysis. Further, based on the observed pooled PFS events, the pooled rate of discontinuations without PFS event, the limited number of subjects that are still at risk to have a PFS event and the predictions of future PFS events, the target number of PFS events for the final PFS analysis might not be reached at all or within a reasonable time frame. Thus, the final PFS analysis data cut-off date is now planned to be approximately 4 months after the interim PFS (iPFS) analysis data cut-off date (or after approximately 108 PFS events are observed if this is earlier) if PFS is not already significant at iPFS analysis. The final PFS analysis if applicable, and the interim OS analysis will be performed approximately 4 months after the iPFS analysis data cut-off date. Based on FDA's recommendation, the alpha spending function for PFS and OS analyses were modified to use O'Brien and Fleming boundaries. Post Trial Access (PTA) language was included to clarify the provision of study treatment to trial subjects who complete participation in this trial and continue to derive clinical benefit from the treatment based on the Investigator's evaluation. Furthermore, new Novartis standard language, referred to as disruption proofing language, has been added to specify trial conduct during public health emergencies. The added language addresses study subject safety and trial integrity. Additional guidance for COVID-19 vaccinations was added to avoid overlapping adverse events with study treatment including update on risk and benefits session. Lastly, the definition of withdrawal of consent and management of biological samples was updated as per latest protocol template.

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.

127 subjects were randomized. However, only 125 were treated. 2 subjs in S+HMA arm received only HMA & were reported in P+HMA arm in the safety dataset. Therefore, the safety dataset included 62 subjs in the S+HMA arm & 63 subjects in the P+HMA arm.

Notes: