Clinical trial results:
A PHASE 2, MULTICENTER STUDY TO DETERMINE THE EFFICACY AND SAFETY OF BB2121 IN SUBJECTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA.

Summary

EudraCT number	2017-002245-29
Trial protocol	DE BE FR ES IT
Global end of trial date	20 December 2023

Results information

Result version number	v1 (current)
This version publication date	28 December 2024
First version publication date	28 December 2024

Trial information

Trial identification

Sponsor protocol code	BB2121-MM-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	20 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy, as defined as overall response rate (ORR), of bb2121 in subjects with relapsed and refractory multiple myeloma (RRMM)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2017
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	Belgium: 3
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United States: 94
Worldwide total number of subjects	137
EEA total number of subjects	33

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)	91
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

137 participants treated

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	BB2121

Arm description:

BB2121

Arm type	Experimental
Investigational medicinal product name	BB2121
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravascular use

Dosage and administration details:

dose ranging from 150 to 450 × 106 CAR+ T cells/infusion.

Number of subjects in period 1	BB2121
Started	137
Completed	36
Not completed	101
Adverse event, serious fatal	77
Consent withdrawn by subject	20
Lost to follow-up	4

Baseline characteristics

Reporting groups	
Reporting group title	BB2121
Reporting group description:	
BB2121	

Reporting group values	BB2121	Total	
Number of subjects	137	137	
Age categorical Units: Subjects			
Adults (18-64 years)	91	91	
From 65-84 years	46	46	
Age Continuous Units: Years			
arithmetic mean	59.4		
standard deviation	± 9.53	-	
Sex: Female, Male Units: Participants			
Female	54	54	
Male	83	83	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	12	12	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	6	6	
White	103	103	
More than one race	0	0	
Unknown or Not Reported	16	16	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11	11	
Not Hispanic or Latino	112	112	
Unknown or Not Reported	14	14	

End points

End points reporting groups

Reporting group title	BB2121
Reporting group description:	
BB2121	

Primary: Overall Response Rate

End point title	Overall Response Rate[1]
End point description:	
Number of participants who achieved partial response (PR) or better according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an independent response committee (IRC).	
End point type	Primary
End point timeframe:	
From first dose to 24 Months	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analysis done for this endpoint	

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Percentage of Participants				
number (confidence interval 95%)	74.5 (67.1 to 81.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate

End point title	Complete Response Rate
End point description:	
Percentage of participants who achieved CR or sCR according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an IRC.	
End point type	Secondary
End point timeframe:	
From first dose to 24 Months	

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: Percentage of participants				
number (confidence interval 95%)	34.3 (26.4 to 42.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response

End point title	Time to response

End point description:

Time from first bb2121 infusion to first documentation of response of PR or better.

End point type	Secondary

End point timeframe:

From first dose to initial response (approximately on average 1.2 months, max of 8.8 months)

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Months				
median (full range (min-max))	1.0 (0.5 to 8.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with safety related events

End point title	Number of participants with safety related events

End point description:

Number of participants with adverse events (AEs), adverse events of special interest (AESI), serious adverse events (SAEs), cytokine release syndrome, neurotoxicity, infection and clinically significantt laboratory abnormalities.

End point type	Secondary

End point timeframe:

From screening to the end of follow up (approximately 5 years and 2 months)

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Participants				
Any Grade AE	137			
Grade 3 or 4 AE	136			
SAEs	98			
AEs of Special Interest	136			
Cytokine Release Syndrome	116			
Neurotoxicity	53			
Infections	95			
Clinically Significant Laboratory Abnormalities	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Time from first bb2121 infusion to time of death due to any cause.

End point type	Secondary

End point timeframe:

From screening to the end of follow up (approximately 5 years and 2 months)

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Months				
median (confidence interval 95%)	28.25 (20.21 to 38.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)

End point description:

Time from first bb2121 infusion to first documentation of progressive disease (PD), or death due to any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

From first dose to 24 months after first dose

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Months				
median (confidence interval 95%)	10.38 (6.11 to 12.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Time from first bb2121 infusion to first documentation of progressive disease (PD), or death due to any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

From first dose to 24 months after first dose

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Months				
median (confidence interval 95%)	8.90 (6.01 to 11.86)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Time from first documentation of response or PR or better to first documentation of disease progression or death from any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

From first dose to 24 months after first dose

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Months				
median (confidence interval 95%)	11.04 (9.92 to 12.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC 0-9M

End point title	AUC 0-9M

End point description:

Cmax

End point type	Secondary

End point timeframe:

From first dose to the end of follow up (Approximately 5 years)

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: copies*days/ug				
arithmetic mean (standard deviation)				
Total	8634034.70 (± 9909488.82)			
450x10^6 cells	10599751.18 (± 10833877.42)			
300x10^6 cells	6604279.35 (± 8523928.48)			
150x10^6 cells	10555200.59 (± 13555457.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax

End point title	Cmax

End point description: Cmax	
End point type	Secondary
End point timeframe: From first dose to the end of follow up (Approximately 5 years)	

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: copies/ug				
arithmetic mean (standard deviation)				
Total	388150.65 (± 372280.64)			
450x10^6 cells	449826.92 (± 375293.18)			
300x10^6 cells	335916.20 (± 369546.39)			
150x10^6 cells	317793.50 (± 284926.30)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-CAR-Antibodies

End point title	Number of Participants with Anti-CAR-Antibodies
End point description: Number of Participants with Anti-CAR-Antibodies. Pre-positive is defined by last value before or on bb2121 infusion date is positive Post-positive is defined by at least one positive value post bb2121 infusion.	
End point type	Secondary
End point timeframe: From first dose to the end of follow up (Approximately 5 years)	

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Participants				
Pre-Positive (pre-positive and post-positive)	6			
Pre-Positive (pre-positive and post-negative)	0			
Pre-Positive (missing post data)	0			
Pre-Negative (pre-negative and post-positive)	69			

Pre-Negative (pre-negative and post-negative)	60			
Pre-Negative (missing post data)	1			
Missing Pre data (post-positive)	1			
Missing Pre data (post-negative)	0			
Missing Pre Data (missing post data)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax

End point title	Tmax

End point description:

Tmax

End point type	Secondary

End point timeframe:

From first dose to the end of follow up (Approximately 5 years)

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: Days				
arithmetic mean (standard deviation)				
Total	12.07 (± 4.114)			
450x10^6 cells	12.37 (± 4.513)			
300x10^6 cells	11.74 (± 3.830)			
150x10^6 cells	13.25 (± 1.500)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-C30 - Pain

End point title	Mean change from baseline on the EORTC QLQ-C30 - Pain

End point description:

Mean change from baseline on the EORTC QLQ-C30

Mean change from baseline on the EORTC QLQ-C30

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”)

to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	-3.8 (± 19.46)			
Month 1	-8.9 (± 26.02)			
Month 3	-12.0 (± 26.65)			
Month 6	-14.5 (± 26.15)			
Month 9	-17.5 (± 24.26)			
Month 12	-17.3 (± 26.05)			
Month 18	-16.7 (± 25.39)			
Month 24	-13.1 (± 16.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieved >= VGPR and MRD negative status

End point title	Percentage of participants who achieved >= VGPR and MRD negative status

End point description:

Percentage of Subjects Who Achieved >= VGPR and MRD Negative Status at Any Time Point from within 3 Months prior to
Achieving VGPR or above to until Time of Progression/Death (Exclusive) based on IRC Review

End point type	Secondary

End point timeframe:

From screening to the end of follow up (Approximately 5 years and 2 months)

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Percentage of Participants				
number (confidence interval 95%)				
10^(-4) Sensitivity	41.6 (33.3 to 50.3)			
10^(-5) Sensitivity	40.9 (32.6 to 49.6)			
10^(-6) Sensitivity	24.8 (17.8 to 32.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-C30 - Physical Functioning

End point title	Mean change from baseline on the EORTC QLQ-C30 - Physical Functioning

End point description:

Mean change from baseline on the EORTC QLQ-C30

Mean change from baseline on the EORTC QLQ-C30

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”) to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	-0.4 (± 18.13)			
Month 1	2.1 (± 22.27)			
Month 3	9.8 (± 18.54)			
Month 6	13.9 (± 18.47)			
Month 9	13.1 (± 19.02)			
Month 12	13.3 (± 19.16)			
Month 18	12.8 (± 15.99)			
Month 24	3.8 (± 13.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-C30 - Cognitive Functioning

End point title	Mean change from baseline on the EORTC QLQ-C30 - Cognitive Functioning

End point description:

Mean change from baseline on the EORTC QLQ-C30

Mean change from baseline on the EORTC QLQ-C30

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”) to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	-0.4 (± 16.66)			
Month 1	2.8 (± 20.10)			
Month 3	5.4 (± 17.42)			
Month 6	6.4 (± 16.55)			
Month 9	6.8 (± 14.88)			
Month 12	4.2 (± 17.63)			
Month 18	3.8 (± 19.61)			
Month 24	3.6 (± 16.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-C30 - Global heath/QoL

End point title	Mean change from baseline on the EORTC QLQ-C30 - Global heath/QoL

End point description:

Mean change from baseline on the EORTC QLQ-C30

Mean change from baseline on the EORTC QLQ-C30

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”) to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	-4.7 (± 17.03)			
Month 1	4.3 (± 19.95)			
Month 3	8.8 (± 20.31)			
Month 6	12.5 (± 19.12)			
Month 9	15.7 (± 20.88)			
Month 12	14.1 (± 21.57)			
Month 18	10.6 (± 17.25)			
Month 24	7.1 (± 14.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-MY20 - Disease Symptoms

End point title	Mean change from baseline on the EORTC QLQ-MY20 - Disease Symptoms

End point description:

Mean change from baseline on the EORTC QLQ-MY20

The EORTC has developed a myeloma module referred to as QLQ- MY20, to be administered alongside the core QLQ-C30. The QLQ-MY20 is a 20-item myeloma module intended for use among patients varying in disease stage and treatment modality.

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”) to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	-0.8 (± 14.11)			
Month 1	-10.2 (± 18.54)			
Month 3	-10.8 (± 20.32)			
Month 6	-12.6 (± 20.81)			
Month 9	-14.4 (± 20.29)			
Month 12	-15.7 (± 23.28)			
Month 18	-12.0 (± 20.47)			
Month 24	-13.1 (± 19.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-MY20 - Side Effects

End point title	Mean change from baseline on the EORTC QLQ-MY20 - Side Effects

End point description:

Mean change from baseline on the EORTC QLQ-MY20

The EORTC has developed a myeloma module referred to as QLQ- MY20, to be administered alongside the core QLQ-C30. The QLQ-MY20 is a 20-item myeloma module intended for use among patients varying in disease stage and treatment modality.

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”) to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	2.5 (± 9.51)			
Month 1	0.0 (± 11.95)			
Month 3	-2.6 (± 11.45)			
Month 6	-4.7 (± 10.16)			
Month 9	-6.5 (± 10.28)			
Month 12	-4.0 (± 11.87)			
Month 18	-3.4 (± 9.96)			
Month 24	-3.2 (± 7.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EQ-5D-5L Index

End point title	Mean change from baseline on the EQ-5D-5L Index

End point description:

Mean change from baseline on the EQ-5D-5L Index

EQ-5D is a standardized measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal. The descriptive system comprises dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). Each dimension has 5 levels (no problems, slight problems, moderate problems, severe problems, extreme problems).

The lower the score the the better.

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	0.0314 (± 0.1760)			
Month 1	0.0528 (± 0.2473)			
Month 3	0.0998 (± 0.1956)			
Month 6	0.0974 (± 0.1798)			
Month 9	0.1067 (± 0.2334)			

Month 12	0.1097 (± 0.2287)			
Month 18	0.1101 (± 0.2027)			
Month 24	0.0383 (± 0.1604)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline on the EORTC QLQ-C30 - Fatigue.

End point title	Mean change from baseline on the EORTC QLQ-C30 - Fatigue.

End point description:

Mean change from baseline on the EORTC QLQ-C30

The QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories “Not at all”, “A little”, “Quite a bit” and “Very much”. The two items assessing global health status/ HRQoL utilize a 7-point scale ranging from 1(“Very Poor”) to 7 (“Excellent”)

End point type	Secondary

End point timeframe:

At Day 1 and at specific time points up to month 24

End point values	BB2121			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Day 1	4.4 (± 18.56)			
Month 1	1.1 (± 24.38)			
Month 3	-10.1 (± 24.32)			
Month 6	-15.1 (± 24.39)			
Month 9	-21.5 (± 24.58)			
Month 12	-16.4 (± 25.02)			
Month 18	-18.4 (± 19.10)			
Month 24	-7.9 (± 15.97)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening to the end of follow up (approximately 5 years and 2 months)

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	BB2121

Reporting group description:

BB2121

Serious adverse events	BB2121		
Total subjects affected by serious adverse events			
subjects affected / exposed	108 / 137 (78.83%)		
number of deaths (all causes)	82		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Plasmablastic lymphoma			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Plasma cell leukaemia			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Anal cancer			

subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	5 / 137 (3.65%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Myelodysplastic syndrome			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Distributive shock			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Asthenia				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Chills				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	30 / 137 (21.90%)			
occurrences causally related to treatment / all	0 / 33			
deaths causally related to treatment / all	0 / 28			
Localised oedema				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	8 / 137 (5.84%)			
occurrences causally related to treatment / all	2 / 11			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				

Acute graft versus host disease				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemophagocytic lymphohistiocytosis				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Cytokine release syndrome				
subjects affected / exposed	22 / 137 (16.06%)			
occurrences causally related to treatment / all	27 / 27			
deaths causally related to treatment / all	1 / 1			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Upper airway obstruction				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	4 / 137 (2.92%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	4 / 137 (2.92%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
Mood altered				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				

subjects affected / exposed	3 / 137 (2.19%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	3 / 137 (2.19%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	3 / 137 (2.19%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Coronavirus test positive				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Compression fracture				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyphaema				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stress fracture				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Toxicity to various agents				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vascular access complication				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Coronary artery disease				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	3 / 137 (2.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pericarditis				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Paraesthesia				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lethargy				

subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Hypotonia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	4 / 137 (2.92%)			
occurrences causally related to treatment / all	5 / 6			
deaths causally related to treatment / all	0 / 0			
Dysarthria				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Cerebral haematoma				

subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Cauda equina syndrome				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ataxia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Amnesia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Disseminated intravascular coagulation				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hyperviscosity syndrome				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				

subjects affected / exposed	12 / 137 (8.76%)			
occurrences causally related to treatment / all	5 / 16			
deaths causally related to treatment / all	0 / 0			
Thrombotic microangiopathy				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	9 / 137 (6.57%)			
occurrences causally related to treatment / all	7 / 9			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	6 / 137 (4.38%)			
occurrences causally related to treatment / all	8 / 9			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Diplopia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Melaena				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Urticaria				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				

subjects affected / exposed	5 / 137 (3.65%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal pain			

subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 1		
Bacteraemia			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Clostridium difficile colitis			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related bacteraemia			

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterococcal bacteraemia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemophilus infection				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis E				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypopyon				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	5 / 137 (3.65%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Listeriosis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection viral				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	15 / 137 (10.95%)			
occurrences causally related to treatment / all	4 / 19			
deaths causally related to treatment / all	0 / 2			
Pneumonia aspiration				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	3 / 137 (2.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	3 / 137 (2.19%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Arthritis infective				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Serratia bacteraemia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Typhoid fever				

subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Acidosis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Adult failure to thrive				
subjects affected / exposed	2 / 137 (1.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolic acidosis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour lysis syndrome				

subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	BB2121		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	137 / 137 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	24 / 137 (17.52%)		
occurrences (all)	35		
Hypertension			
subjects affected / exposed	19 / 137 (13.87%)		
occurrences (all)	44		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	22 / 137 (16.06%)		
occurrences (all)	32		
Chills			
subjects affected / exposed	20 / 137 (14.60%)		
occurrences (all)	22		
Fatigue			
subjects affected / exposed	53 / 137 (38.69%)		
occurrences (all)	91		
Malaise			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	9		
Oedema peripheral			
subjects affected / exposed	27 / 137 (19.71%)		
occurrences (all)	39		
Pain			
subjects affected / exposed	9 / 137 (6.57%)		
occurrences (all)	9		

Pyrexia			
subjects affected / exposed	36 / 137 (26.28%)		
occurrences (all)	77		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	110 / 137 (80.29%)		
occurrences (all)	170		
Hypogammaglobulinaemia			
subjects affected / exposed	32 / 137 (23.36%)		
occurrences (all)	36		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	34 / 137 (24.82%)		
occurrences (all)	47		
Dyspnoea			
subjects affected / exposed	14 / 137 (10.22%)		
occurrences (all)	20		
Dyspnoea exertional			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	10		
Epistaxis			
subjects affected / exposed	11 / 137 (8.03%)		
occurrences (all)	12		
Nasal congestion			
subjects affected / exposed	11 / 137 (8.03%)		
occurrences (all)	11		
Oropharyngeal pain			
subjects affected / exposed	13 / 137 (9.49%)		
occurrences (all)	14		
Pleural effusion			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	10		
Rhinorrhoea			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	7		
Psychiatric disorders			

Anxiety			
subjects affected / exposed	19 / 137 (13.87%)		
occurrences (all)	27		
Confusional state			
subjects affected / exposed	16 / 137 (11.68%)		
occurrences (all)	20		
Insomnia			
subjects affected / exposed	14 / 137 (10.22%)		
occurrences (all)	15		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	14		
Alanine aminotransferase increased			
subjects affected / exposed	22 / 137 (16.06%)		
occurrences (all)	33		
Aspartate aminotransferase increased			
subjects affected / exposed	26 / 137 (18.98%)		
occurrences (all)	40		
Blood alkaline phosphatase increased			
subjects affected / exposed	18 / 137 (13.14%)		
occurrences (all)	36		
Blood creatinine increased			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	14		
C-reactive protein increased			
subjects affected / exposed	15 / 137 (10.95%)		
occurrences (all)	29		
International normalised ratio increased			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	9		
Weight decreased			
subjects affected / exposed	19 / 137 (13.87%)		
occurrences (all)	38		
Weight increased			

subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	16		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	9 / 137 (6.57%)		
occurrences (all)	9		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	22 / 137 (16.06%)		
occurrences (all)	44		
Nervous system disorders			
Dizziness			
subjects affected / exposed	23 / 137 (16.79%)		
occurrences (all)	27		
Headache			
subjects affected / exposed	47 / 137 (34.31%)		
occurrences (all)	68		
Somnolence			
subjects affected / exposed	10 / 137 (7.30%)		
occurrences (all)	11		
Tremor			
subjects affected / exposed	12 / 137 (8.76%)		
occurrences (all)	14		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	104 / 137 (75.91%)		
occurrences (all)	706		
Leukopenia			
subjects affected / exposed	70 / 137 (51.09%)		
occurrences (all)	531		
Lymphopenia			
subjects affected / exposed	49 / 137 (35.77%)		
occurrences (all)	284		
Neutropenia			
subjects affected / exposed	130 / 137 (94.89%)		
occurrences (all)	1018		

Thrombocytopenia subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all)	95 / 137 (69.34%) 719 19 / 137 (13.87%) 24		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 45 / 137 (32.85%) 63 61 / 137 (44.53%) 81 10 / 137 (7.30%) 11 12 / 137 (8.76%) 15 85 / 137 (62.04%) 123 34 / 137 (24.82%) 43		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 11 / 137 (8.03%) 11 9 / 137 (6.57%) 9 12 / 137 (8.76%) 21		
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	11 / 137 (8.03%)		
occurrences (all)	12		
Pollakiuria			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	32 / 137 (23.36%)		
occurrences (all)	48		
Back pain			
subjects affected / exposed	29 / 137 (21.17%)		
occurrences (all)	36		
Bone pain			
subjects affected / exposed	18 / 137 (13.14%)		
occurrences (all)	23		
Muscle spasms			
subjects affected / exposed	9 / 137 (6.57%)		
occurrences (all)	13		
Musculoskeletal chest pain			
subjects affected / exposed	11 / 137 (8.03%)		
occurrences (all)	26		
Myalgia			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	10		
Pain in extremity			
subjects affected / exposed	12 / 137 (8.76%)		
occurrences (all)	15		
Infections and infestations			
Influenza			
subjects affected / exposed	9 / 137 (6.57%)		
occurrences (all)	11		
Candida infection			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	9		
Nasopharyngitis			

subjects affected / exposed	10 / 137 (7.30%)		
occurrences (all)	12		
Pneumonia			
subjects affected / exposed	9 / 137 (6.57%)		
occurrences (all)	9		
Respiratory tract infection			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	10		
Sinusitis			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	9		
Upper respiratory tract infection			
subjects affected / exposed	21 / 137 (15.33%)		
occurrences (all)	37		
Urinary tract infection			
subjects affected / exposed	8 / 137 (5.84%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	41 / 137 (29.93%)		
occurrences (all)	58		
Hypercalcaemia			
subjects affected / exposed	12 / 137 (8.76%)		
occurrences (all)	19		
Hyperglycaemia			
subjects affected / exposed	15 / 137 (10.95%)		
occurrences (all)	49		
Hyperkalaemia			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	7		
Hyperuricaemia			
subjects affected / exposed	13 / 137 (9.49%)		
occurrences (all)	16		
Hypoalbuminaemia			
subjects affected / exposed	26 / 137 (18.98%)		
occurrences (all)	60		

Hypocalcaemia			
subjects affected / exposed	37 / 137 (27.01%)		
occurrences (all)	118		
Hypokalaemia			
subjects affected / exposed	56 / 137 (40.88%)		
occurrences (all)	93		
Hypomagnesaemia			
subjects affected / exposed	35 / 137 (25.55%)		
occurrences (all)	59		
Hyponatraemia			
subjects affected / exposed	30 / 137 (21.90%)		
occurrences (all)	72		
Hypophosphataemia			
subjects affected / exposed	46 / 137 (33.58%)		
occurrences (all)	106		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2019	• Moved minimal residual disease (MRD) assessment by EuroFlow to Exploratory Objectives and Exploratory Endpoints. Updated the term "vector copy number" (VCN). • Separated the secondary objective of characterization of the expansion of CAR+ T cells in the peripheral blood and bone marrow into two objectives. Evaluation of CAR+ T cells in the peripheral blood will remain as a secondary objective while evaluation in the bone marrow will be an exploratory objective. Evaluation in the bone marrow was also added as an exploratory endpoint. • Removed the secondary objective and secondary endpoint, "Evaluate cytokine induction in the blood of subjects after infusion of bb2121", and removed cytokines as a key safety assessment. • Moved the secondary objective and secondary endpoint, "Evaluate the percentage of B-cell maturation antigen (BCMA)-expressing (BCMA+) cells and levels of BCMA expression in bone marrow, and the level of circulating soluble BCMA" to exploratory objectives and exploratory endpoints. • Clarified the definition of "cellular kinetics".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported