Clinical trial results:
Phase 1-2 Study Investigating Safety, Tolerability, Pharmacokinetics and Preliminary Antitumor Activity of Anti-PD-L1 Monoclonal Antibody BGB-A333 Alone and in Combination with Anti-PD-1 Monoclonal Antibody Tislelizumab in Patients with Advanced Solid Tumors

Summary

EudraCT number	2018-000265-37
Trial protocol	ES
Global end of trial date	08 September 2020

Results information

Result version number	v2 (current)
This version publication date	24 November 2021
First version publication date	19 September 2021
Version creation reason	• Correction of full data set Errors in time frame were corrected

Trial information

Trial identification

Sponsor protocol code	BGB-900-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03379259
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BeiGene, Ltd
Sponsor organisation address	BeiGene, Ltd., c/o BeiGene USA, Inc. 2955 Campus Drive, Suite 200 , San Mateo, California, United States, 94403
Public contact	BeiGene DDT Call Center, BeiGene Ltd., 1-877 828-5568, clinicaltrials@beigene.com
Scientific contact	BeiGene DDT Call Center, BeiGene Ltd., 1-877 828-5568, clinicaltrials@beigene.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	04 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 September 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

1) For Phase 1:
• To assess the safety and tolerability of BGB-A333 alone and in combination with tislelizumab in patients with advanced solid tumors
• To determine the MTD, if any, and RP2D for BGB-A333 alone and in combination with tislelizumab

2) For Phase 2: To assess ORR per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 of BGB-A333 alone and in combination with tislelizumab in patients with selected tumor types

Protection of trial subjects:

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of GCP as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki. The IEC/IRB-approved ICF was signed and dated by the subject or the subject's legally authorized representative before his or her participation in the study. A copy of each signed ICF was provided to the subject or the subject's legally authorized representative. All signed and dated ICFs were retained in each patient's study file or in the site file. For any updated or revised ICFs, written informed consent was obtained using the IEC/IRB-approved updated/revised ICFs for continued participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 28
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Spain: 7
Worldwide total number of subjects	39
EEA total number of subjects	7

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	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 8 study centers in Australia, 1 study center in New Zealand, and 3 study centers in Spain.

Pre-assignment

Screening details:

A total of 39 patients were enrolled in the study and all received ≥ 1 dose of study drug.

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

Are arms mutually exclusive?	Yes
Arm title	Phase 1A: BGB-A333 450 mg

Arm description:

BGB-A333 450 mg, intravenously, every 3 weeks

Arm type	Experimental
Investigational medicinal product name	BGB-A333
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose ranging from 450 mg to 1800 mg, administered every three weeks

Arm title	Phase 1A: BGB-A333 900 mg

Arm description:

BGB-A333 900 mg, intravenously, every 3 weeks

Arm type	Experimental
Investigational medicinal product name	BGB-A333
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose ranging from 450 mg to 1800 mg, administered every three weeks

Arm title	Phase 1A: BGB-A333 1350 mg

Arm description:

BGB-A333 1350 mg, intravenously, every 3 weeks

Arm type	Experimental
Investigational medicinal product name	BGB-A333
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Dose ranging from 450 mg to 1800 mg, administered every three weeks	

Arm title	Phase 1A: BGB-A333 1800 mg
Arm description: BGB-A333 1800 mg, intravenously, every 3 weeks	
Arm type	Experimental
Investigational medicinal product name	BGB-A333
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dose ranging from 450 mg to 1800 mg, administered every three weeks	
Arm title	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg
Arm description: BGB-A333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks	
Arm type	Experimental
Investigational medicinal product name	BGB-A333
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dose ranging from 450 mg to 1800 mg, administered every three weeks	
Investigational medicinal product name	BGB-A317
Investigational medicinal product code	
Other name	Tislelizumab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Tislelizumab 200 mg, intravenously, every 3 weeks	
Arm title	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Arm description: BGB-A333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks (Urothelial Carcinoma Cohort)	
Arm type	Experimental
Investigational medicinal product name	BGB-A333
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dose ranging from 450 mg to 1800 mg, administered every three weeks	
Investigational medicinal product name	BGB-A317
Investigational medicinal product code	
Other name	Tislelizumab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Tislelizumab 200 mg, intravenously, every 3 weeks

Number of subjects in period 1	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg
Started	3	3	6
Completed	2	2	3
Not completed	1	1	3
Consent withdrawn by subject	-	-	1
Disease progression	-	-	-
Death	-	1	2
Study terminated by sponsor	-	-	-
Deteriorating condition	-	-	-
Commenced new anti-cancer therapy	1	-	-
Study terminated by sponsor	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Phase 1A: BGB-A333 1800 mg	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Started	3	12	12
Completed	0	3	5
Not completed	3	9	7
Consent withdrawn by subject	-	2	-
Disease progression	1	-	1
Death	1	4	2
Study terminated by sponsor	1	-	4
Deteriorating condition	-	1	-
Commenced new anti-cancer therapy	-	-	-
Study terminated by sponsor	-	1	-
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1A: BGB-A333 450 mg
Reporting group description: BGB-A333 450 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 900 mg
Reporting group description: BGB-A333 900 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 1350 mg
Reporting group description: BGB-A333 1350 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 1800 mg
Reporting group description: BGB-A333 1800 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg
Reporting group description: BGB-A333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks	
Reporting group title	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Reporting group description: BGB-A333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks (Urothelial Carcinoma Cohort)	

Reporting group values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg
Number of subjects	3	3	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	56.0	60.3	58.8
standard deviation	± 7.21	± 11.24	± 14.52
Gender categorical Units: Subjects			
Female	2	2	4
Male	1	1	2
PD-L1 Status Units: Subjects			
Positive	0	2	2

Negative	2	1	3
Missing	1	0	1

Reporting group values	Phase 1A: BGB-A333 1800 mg	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Number of subjects	3	12	12
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	58.0	65.3	67.5
standard deviation	± 16.52	± 10.85	± 8.52
Gender categorical Units: Subjects			
Female	2	7	1
Male	1	5	11
PD-L1 Status Units: Subjects			
Positive	1	4	6
Negative	2	7	6
Missing	0	1	0

Reporting group values	Total		
Number of subjects	39		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			

standard deviation	-		

Gender categorical Units: Subjects			
Female	18		
Male	21		
PD-L1 Status Units: Subjects			
Positive	15		
Negative	21		
Missing	3		

End points

End points reporting groups

Reporting group title	Phase 1A: BGB-A333 450 mg
Reporting group description: BGB-A333 450 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 900 mg
Reporting group description: BGB-A333 900 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 1350 mg
Reporting group description: BGB-A333 1350 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 1800 mg
Reporting group description: BGB-A333 1800 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg
Reporting group description: BGB-A333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks	
Reporting group title	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Reporting group description: BGB-A333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks (Urothelial Carcinoma Cohort)	
Subject analysis set title	Phase 1A: BGB-A333 Monotherapy Dose Escalation
Subject analysis set type	Safety analysis
Subject analysis set description: Dose escalation cohorts	

Primary: Phase 1 and Phase 2: Number of Subjects with Adverse Events and Serious Adverse Events

End point title	Phase 1 and Phase 2: Number of Subjects with Adverse Events and Serious Adverse Events[1]
End point description: Adverse events were assessed per the National Cancer Institute Common Terminology Criteria for Adverse Events NCI-CTCAE Version 4.03 SAEs were monitored from the date of informed consent. All adverse events (AEs) and SAEs, were reported until either 30 days after the last dose of study drug or until initiation of a new anticancer therapy, whichever occurred first.	
End point type	Primary
End point timeframe: Up to 33.5 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 summary statistics available for discrete values.

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Subjects				
Any Treatment Emergent Adverse Event (TEAE)	1	2	6	3

Serious TEAE	0	1	3	1

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects				
Any Treatment Emergent Adverse Event (TEAE)	12	12		
Serious TEAE	5	3		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1 and Phase 2: Number of Subjects with Abnormalities During Physical Examinations- Ophthalmology Findings

End point title	Phase 1 and Phase 2: Number of Subjects with Abnormalities During Physical Examinations- Ophthalmology Findings[2]

End point description:

Complete physical examination including an evaluation of 1) head, eyes, ears, nose, throat, 2) cardiovascular, 3) dermatological, 4) musculoskeletal, 5) respiratory, 6) gastrointestinal, and 7) neurological systems was required to be performed at Screening. At subsequent visits (or as clinically indicated), limited, symptom-directed physical examinations were performed. Clinically significant Ophthalmology abnormalities were collected from case report forms. All AEs and SAEs, were reported until either 30 days after the last dose of study drug or until initiation of a new anticancer therapy, whichever occurred first.

End point type	Primary

End point timeframe:

Up to 33.5 months

Notes:

[2] - 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 summary statistics available for discrete values.

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Subjects	0	0	0	0

End point values	Phase 1B: BGB-A333 1350 mg +	Phase 2B: BGB-A333 1350 mg +		

	Tislelizumab 200 mg	Tislelizumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1 and Phase 2: Number of Subjects with Abnormal Electrocardiograms (ECG)

End point title	Phase 1 and Phase 2: Number of Subjects with Abnormal Electrocardiograms (ECG)[3]

End point description:

Central ECG data was used and the abnormality was determined by the evaluator (Investigating physician). Multiple tests such as QT, HR, PR, RR were used by the evaluator to determine abnormality. All AEs and SAEs, were reported until either 30 days after the last dose of study drug or until initiation of a new anticancer therapy, whichever occurred first.

End point type	Primary

End point timeframe:

Up to 33.5 months

Notes:

[3] - 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 summary statistics available for discrete values.

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Subjects	0	1	5	2

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects	1	9		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1 and Phase 2: Number of Subjects with Abnormal Lab Assessment Results

End point title	Phase 1 and Phase 2: Number of Subjects with Abnormal Lab Assessment Results[4]

End point description:

Lab abnormality was based on ANRIND: if the measurement value > ULN (upper limit of normal), it was considered Abnormal. All AEs and SAEs, were reported until either 30 days after the last dose of study drug or until initiation of a new anticancer therapy, whichever occurred first.

End point type	Primary

End point timeframe:

Up to 33.5 months

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No summary statistics available for discrete values

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Subjects	3	3	6	3

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects	12	12		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2B: Overall Response Rate (ORR) Determined by Investigators Based on RECIST Version 1.1

End point title	Phase 2B: Overall Response Rate (ORR) Determined by Investigators Based on RECIST Version 1.1[5][6]

End point description:

The ORR is defined as the percentage of participants who had confirmed Complete Response (CR) or Partial response (PR) assessed by investigator using RECIST version 1.1

End point type	Primary

End point timeframe:

Up to 33.5 months

Notes:

[5] - 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 summary statistics available for discrete values

[6] - 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 summary statistics available for discrete values.

End point values	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (confidence interval 95%)	41.7 (15.17 to 72.33)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1A: Recommended Phase 2 Dose (RP2D) for BGB-A333

End point title	Phase 1A: Recommended Phase 2 Dose (RP2D) for BGB-

End point description:

RP2D for BGB-A333 alone and in combination with tislelizumab was the maximum tolerated dose (MTD) or less, which was determined by testing increasing doses up to 1800 mg.

End point type	Primary

End point timeframe:

Up to 28 months

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No summary statistics available for discrete values

End point values	Phase 1A: BGB-A333 Monotherapy Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: Milligrams	1350			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1A and Phase 1B: Overall Response Rate (ORR) Determined by

Investigators Based on RECIST Version 1.1

End point title	Phase 1A and Phase 1B: Overall Response Rate (ORR) Determined by Investigators Based on RECIST Version 1.1[8]

End point description:

ORR is defined as the percentage of participants who had confirmed CR or PR assessed by investigator using RECIST version 1.1

End point type	Secondary

End point timeframe:

Up to 33.5 months

Notes:

[8] - 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:
Not all arms in the Baseline Period are applicable for this endpoint.

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.00 to 70.76)	33.3 (0.84 to 90.57)	50.0 (11.81 to 88.19)	33.3 (0.84 to 90.57)

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (confidence interval 95%)	16.7 (2.09 to 48.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2B: Duration of Response (DOR) Determined by Investigators Based on RECIST Version 1.1

End point title	Phase 2B: Duration of Response (DOR) Determined by Investigators Based on RECIST Version 1.1[9]

End point description:

DOR was defined as the time from the first determination of an objective response per RECIST version 1.1, until the first documentation of progression or death, whichever occurs first. DOR was not evaluable in Phase 1A and Phase 1B. 9999 = Data not estimable due to insufficient number of participants with events

End point type	Secondary

End point timeframe:

Up to 33.5 months

Notes:

[9] - 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 summary statistics available for discrete values.

End point values	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Months				
median (confidence interval 95%)	9.6 (6.0 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: Disease Control Rate (DCR) Determined by Investigators Based on RECIST Version 1.1

End point title	Phase 1 and Phase 2: Disease Control Rate (DCR) Determined by Investigators Based on RECIST Version 1.1

End point description:

DCR is defined as the proportion of participants with best overall response of CR, PR and Stable Disease.

End point type	Secondary

End point timeframe:

Up to 33.5 months

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Percentage of subjects				
number (confidence interval 95%)	33.3 (0.84 to 90.57)	33.3 (0.84 to 90.57)	66.7 (22.28 to 95.67)	66.7 (9.43 to 99.16)

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage of subjects				
number (confidence interval 95%)	58.3 (27.67 to 84.83)	75.0 (42.81 to 94.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2B: Progression-free Survival (PFS) Determined by Investigators Based on RECIST Version 1.1

End point title	Phase 2B: Progression-free Survival (PFS) Determined by Investigators Based on RECIST Version 1.1[10]

End point description:

PFS was defined as the time from the date of the first dose of study drug(s) to the date of the first documentation of disease progression assessed by investigator using RECIST v1.1 or death, whichever occurs first

End point type	Secondary

End point timeframe:

Up to 33.5 months

Notes:

[10] - 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: Not all arms in the Baseline Period are applicable for this endpoint

End point values	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Months				
median (confidence interval 95%)	6.1 (1.9 to 11.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximum Plasma Concentration (Cmax) of BGB-A333

End point title	Phase 1: Maximum Plasma Concentration (Cmax) of BGB-

End point description:

PK parameters were derived only for Phase 1A and Phase 1B. Phase 2B PK parameters were not estimated due to limited sampling. Actual observed time values for PK sampling, have an allowable time deviation
(+/- 3 days) from the planned nominal time as pre-specified in the Visit Window section of the study protocol.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Pre-dose, End of infusion, 6 hours), Day 2, Day 4, Day 8, Day 15 and Day 21

Notes:

[11] - 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: Not all arms in the Baseline Period are applicable for this endpoint.

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: ug/mL				
arithmetic mean (standard deviation)	167 (± 42.4)	351 (± 151)	466 (± 91.0)	594 (± 150)

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ug/mL				
arithmetic mean (standard deviation)	450 (± 127)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to Cmax (Tmax) of BGB-A333

End point title	Phase 1: Time to Cmax (Tmax) of BGB-A333[12]

End point description:

PK parameters were derived only for Phase 1A and Phase 1B. Phase 2B PK parameters were not estimated due to limited sampling.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Pre-dose, End of infusion, 6 hours), Day 2, Day 4, Day 8, Day 15 and Day 21

Notes:

[12] - 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: Not all arms in the Baseline Period are applicable for this endpoint.

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Day				
median (full range (min-max))	0.05 (0.04 to 0.21)	0.06 (0.05 to 0.06)	0.05 (0.05 to 0.22)	0.06 (0.06 to 0.21)

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Day				
median (full range (min-max))	0.21 (0.05 to 0.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Trough Serum Concentration (Ctrough) of BGB-A333

End point title	Phase 1: Trough Serum Concentration (Ctrough) of BGB-

End point description:

PK parameters were derived only for Phase 1A and Phase 1B. Phase 2B PK parameters were not estimated due to limited sampling.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Pre-dose, End of infusion, 6 hours), Day 2, Day 4, Day 8, Day 15 and Day 21

Notes:

[13] - 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: Not all arms in the Baseline Period are applicable for this endpoint

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: ug/mL				
arithmetic mean (standard deviation)	21.3 (± 5.69)	47.0 (± 26.7)	90.7 (± 24.2)	81.4 (± 23.9)

End point values	Phase 1B: BGB-A333			

	1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ug/mL				
arithmetic mean (standard deviation)	80.0 (± 22.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to Last Observed Concentration (Tlast) of BGB-A333

End point title	Phase 1: Time to Last Observed Concentration (Tlast) of BGB-A333[14]

End point description:

PK parameters were derived only for Phase 1A and Phase 1B. Phase 2B PK parameters were not estimated due to limited sampling.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Pre-dose, End of infusion, 6 hours), Day 2, Day 4, Day 8, Day 15 and Day 21

Notes:

[14] - 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: Not all arms in the Baseline Period are applicable for this endpoint

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Day				
median (full range (min-max))	22.0 (21.0 to 22.0)	21.0 (14.1 to 21.0)	21.0 (14.0 to 22.0)	21.0 (21.0 to 24.0)

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Day				
median (full range (min-max))	21.0 (7.10 to 24.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Concentration-time Curve From 9 to 21 Days Post-dose (AUC0-21day) of BGB-A333

End point title	Phase 1: Area Under the Concentration-time Curve From 9 to 21 Days Post-dose (AUC0-21day) of BGB-A333[15]

End point description:

PK parameters were derived only for Phase 1A and Phase 1B. Phase 2B PK parameters were not estimated due to limited sampling.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Pre-dose, End of infusion, 6 hours), Day 2, Day 4, Day 8, Day 15 and Day 21

Notes:

[15] - 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: Not all arms in the Baseline Period are applicable for this endpoint

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	5	3
Units: ug*day/mL				
arithmetic mean (standard deviation)	1095 (± 141)	2913 (± 320)	3823 (± 566)	4141 (± 648)

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ug*day/mL				
arithmetic mean (standard deviation)	3546 (± 814)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1A and Phase 2: Number of Subjects with Detectable Treatment-emergent Anti-BGB-A333 Antibodies

End point title	Phase 1A and Phase 2: Number of Subjects with Detectable Treatment-emergent Anti-BGB-A333 Antibodies

End point description:

Treatment-emergent anti drug antibodies (ADA) was the sum of both treatment-induced ADA and treatment-boosted ADA, synonymous with "ADA incidence"

End point type	Secondary

End point timeframe:

Up to 33.5 months

End point values	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg	Phase 1A: BGB-A333 1800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: Subjects	1	1	1	0

End point values	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Subjects	0	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the date of consent until study termination (approximately 33.5 months)	
Adverse event reporting additional description:	
All adverse events were reported until either 30 days after the last dose of study drug or until initiation of a new anticancer therapy, whichever occurred first.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Phase 1A: BGB-A333 450 mg
Reporting group description:	
BGB-333 450 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 900 mg
Reporting group description:	
BGB-333 900 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 1350 mg
Reporting group description:	
BGB-333 1350 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1A: BGB-A333 1800 mg
Reporting group description:	
BGB-333 1800 mg, intravenously, every 3 weeks	
Reporting group title	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg
Reporting group description:	
BGB-333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks	
Reporting group title	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Reporting group description:	
BGB-333 1350 mg, intravenously, + Tislelizumab 200 mg, intravenously, every 3 weeks (Urothelial Carcinoma Cohort)	

Serious adverse events	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	3 / 6 (50.00%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1A: BGB-A333 1800 mg	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	5 / 12 (41.67%)	3 / 12 (25.00%)
number of deaths (all causes)	1	4	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Phase 1A: BGB-A333 450 mg	Phase 1A: BGB-A333 900 mg	Phase 1A: BGB-A333 1350 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	6 / 6 (100.00%)
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Perineal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	4
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	3 / 6 (50.00%)
occurrences (all)	0	1	3
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	5	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			

Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1A: BGB-A333 1800 mg	Phase 1B: BGB-A333 1350 mg + Tislelizumab 200 mg	Phase 2B: BGB-A333 1350 mg + Tislelizumab 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	12 / 12 (100.00%)	12 / 12 (100.00%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	2 / 12 (16.67%)	2 / 12 (16.67%)
occurrences (all)	2	3	2
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Perineal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 3 (33.33%)	3 / 12 (25.00%)	0 / 12 (0.00%)
occurrences (all)	1	3	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 12 (25.00%)	1 / 12 (8.33%)
occurrences (all)	1	4	2
Eye disorders			
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)	2 / 12 (16.67%)
occurrences (all)	1	4	4
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
Vomiting			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	9	1
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Rash			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	5	0	1
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	3
Arthralgia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	7	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Oral candidiasis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Hypercalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2018	• BGB-A317 was replaced with its generic name tislelizumab. • The study design was revised so that for Phase 2A and Phase 2B, approximately 20 patients with UC were to be enrolled. The sponsor may have considered other tumor types including but not limited to non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck, gastric cancer, MSI-high cancer, etc. Eligibility criteria for these cohorts was to be defined in future protocol amendments based on emerging clinical data. Sample size for Phase 2A and Phase 2B was adjusted. • The safety follow-up period was modified to include telephone contacts at Day 60 and Day 90 to assess immune-mediated AEs and concomitant medications, regardless of whether or not the patient started a new anticancer therapy. • The survival follow-up period was removed. • A requirement of antiviral therapy in patients with active hepatitis B was added, as was viral load testing. • Restrictions of hepatotoxic drugs, alcohol, and addictive drugs in patients with hepatocellular carcinoma were added. • Eye examinations were added. • The inclusion and exclusion criteria were revised. Patients who had detectable hepatitis B virus DNA at screening were to have the viral load test performed every 4 cycles, at the end of treatment visit, and when clinically indicated. • Tumor and response evaluations were revised so that tumor response would be assessed by the investigators using RECIST v1.1, and additional information on new lesions was collected according to iRECIST. The sponsor was to derive tumor response using iRECIST as an exploratory assessment. Imaging of the brain at screening was required for all patients. • The documentation method for SAE reporting was modified. • Creatine kinase and creatine kinase-MB tests were added. • The American Society of Clinical Oncology guideline and regulatory feedback on other studies of tislelizumab was added. • Child-Pugh classification was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 September 2020	The sponsor decided not to pursue BGB-A333 as a monotherapy beyond the completion of dose escalation in Phase 1A. As such, Phase 2A was not conducted. Phase 1B was opened for dose expansion and enrolled 12 patients. For Phase 2B, only 1 cohort was opened for dose expansion and a total of 12 patients were treated in the metastatic UC arm. The sponsor terminated the study after Protocol Amendment 1 since the primary objective of assessing objective response rate (ORR) had been achieved.	-

Notes:

Limitations and caveats

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

Phase 2A of the study was not initiated nor conducted since BGB-A333 as a monotherapy treatment beyond the completion of dose escalation in Phase 1A was not pursued.

Notes: