



Clinical trial results:

A Phase II, Multi Center Study of BGB324 in combination with Pembrolizumab in Patients with Previously Treated, Locally Advanced and Unresectable or Metastatic Triple Negative Breast Cancer (TNBC) or Triple Negative Inflammatory Breast Cancer (TN-IBC)

Summary

EudraCT number	2016-003608-30
Trial protocol	NO GB ES
Global end of trial date	20 August 2018

Results information

Result version number	v1 (current)
This version publication date	07 November 2021
First version publication date	07 November 2021

Trial information

Trial identification

Sponsor protocol code	BGBC007
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03184558
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BerGenBio ASA
Sponsor organisation address	Jonas Lies vei 91, Bergen, Norway, 5009
Public contact	BerGenBio Clinical Team, BerGenBio ASA, trialsites@bergenbio.com
Scientific contact	BerGenBio Clinical Team, BerGenBio ASA, trialsites@bergenbio.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 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 August 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the trial was to assess the anti-tumor activity of the combination treatment of BGB324 (bemcentinib) and pembrolizumab in subjects with previously treated, locally advanced and unresectable or metastatic TNBC or TN-IBC.

Protection of trial subjects:

The study was conducted in accordance with ICH GCP, the Declaration of Helsinki, the European Union Clinical Trials Directive 2001/20/EC, the GCP Directive 2005/28/EC, the requirements of local IEC/IRB, and the US Code of Federal Regulations, Title 21 CFR Part 50. Safety assessments included monitoring of adverse events, vital signs, safety laboratory and electrocardiogram.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 July 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	Norway: 1
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	29
EEA total number of subjects	20

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)	27
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 29 subjects were enrolled and received study medication in this study.

Period 1

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

Arms

Arm title	Bemcentinib + Pembrolizumab
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Arm description:

Subjects received Bemcentinib (BGB324) capsules orally once daily as a loading dose of 400 milligram (mg) on Days 1, 2, and 3. A dose of 200 mg pembrolizumab was given by intravenous infusion over 30 minutes every 3 weeks in all subjects. Dosing of both drugs commenced on Day 1. On days when both BGB324 and pembrolizumab were given, pembrolizumab was given first and subjects were observed for 1 hour after the end of infusion before BGB324 was administered. From Day 4 onward, subjects received a daily maintenance dose of 200 mg along with Pembrolizumab 200 mg intravenous (IV) infusion over 30 minutes every 3 weeks until disease progression, until an unacceptable toxicity occurred that required treatment withdrawal or withdrawal of consent or until 106 weeks had passed.

Arm type	Experimental
Investigational medicinal product name	Bemcentinib 400 mg
Investigational medicinal product code	
Other name	BGB324
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received Bemcentinib 400 mg capsules orally once daily on Days 1, 2, and 3.

Investigational medicinal product name	Bemcentinib 200 mg
Investigational medicinal product code	
Other name	BGB324
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received Bemcentinib 200 mg capsules orally once daily from Day 4 onward.

Investigational medicinal product name	Pembrolizumab 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subject received pembrolizumab 200 mg IV infusion over 30 minutes every 3 weeks.

Number of subjects in period 1	Bemcentinib + Pembrolizumab
Started	29
Completed	0
Not completed	29
Adverse event, serious fatal	16
Consent withdrawn by subject	2
Unspecified	9
Lost to follow-up	2

Baseline characteristics

Reporting groups

Reporting group title	Bemcentinib + Pembrolizumab
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Reporting group description:

Subjects received Bemcentinib (BGB324) capsules orally once daily as a loading dose of 400 milligram (mg) on Days 1, 2, and 3. A dose of 200 mg pembrolizumab was given by intravenous infusion over 30 minutes every 3 weeks in all subjects. Dosing of both drugs commenced on Day 1. On days when both BGB324 and pembrolizumab were given, pembrolizumab was given first and subjects were observed for 1 hour after the end of infusion before BGB324 was administered. From Day 4 onward, subjects received a daily maintenance dose of 200 mg along with Pembrolizumab 200 mg intravenous (IV) infusion over 30 minutes every 3 weeks until disease progression, until an unacceptable toxicity occurred that required treatment withdrawal or withdrawal of consent or until 106 weeks had passed.

Reporting group values	Bemcentinib + Pembrolizumab	Total	
Number of subjects	29	29	
Age categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	27	27	
>=65 years	2	2	
Gender categorical Units: Subjects			
Female	29	29	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	29	29	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Bemcentinib + Pembrolizumab
Reporting group description:	
Subjects received Bemcentinib (BGB324) capsules orally once daily as a loading dose of 400 milligram (mg) on Days 1, 2, and 3. A dose of 200 mg pembrolizumab was given by intravenous infusion over 30 minutes every 3 weeks in all subjects. Dosing of both drugs commenced on Day 1. On days when both BGB324 and pembrolizumab were given, pembrolizumab was given first and subjects were observed for 1 hour after the end of infusion before BGB324 was administered. From Day 4 onward, subjects received a daily maintenance dose of 200 mg along with Pembrolizumab 200 mg intravenous (IV) infusion over 30 minutes every 3 weeks until disease progression, until an unacceptable toxicity occurred that required treatment withdrawal or withdrawal of consent or until 106 weeks had passed.	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR) ^[1]
End point description:	
ORR is defined as the percentage of evaluable subjects who had at least one confirmed overall response of complete response (CR) or partial response (PR) according to the modified Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. CR: Disappearance of all target lesions (TLs) since baseline, any pathological lymph nodes selected as TLs must have a reduction in short axis to less than (<) 10 millimeter (mm). PR: At least a 30 percent decrease in the sum of the diameters of TLs, taking as reference the baseline sum of diameters. The Evaluable analysis set included all evaluable subjects who had received at least 1 combination dose of pembrolizumab and bemcentinib and who had measurable disease at entry, as determined by the investigator site assessment.	
End point type	Primary
End point timeframe:	
Until disease progression or death or withdrawal of consent whichever comes first, up to end of study (Up to 1 year)	
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: Endpoint was descriptive in nature, no inferential statistics was done.	

End point values	Bemcentinib + Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)
End point description:	
DOR is defined as the time from the date of first documented response until date of documented progression or death in the absence of disease progression (PD); the end of response should coincide with the date of progression or death from any cause. PD per modified RECIST 1.1 defined as: at least a	

20 percent increase in the sum of diameters of TLs and an absolute increase of at least 5 mm, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). Analysis performed on subjects in evaluable analysis set who had an objective response.

End point type	Secondary
End point timeframe:	
Until disease progression or death or withdrawal of consent whichever comes first, up to end of study (Up to 1 year)	

End point values	Bemcentinib + Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[2]			
Units: Weeks				
number (not applicable)				

Notes:

[2] - DOR could not be calculated as none of the subjects had an objective response.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description:	
DCR is defined as the percentage of subjects with a confirmed CR, PR, or stable disease (SD). CR: Disappearance of all target lesions (TLs) since baseline, any pathological lymph nodes selected as TLs must have a reduction in short axis to < 10 mm. PR: At least a 30 percent decrease in the sum of the diameters of TLs, taking as reference the baseline sum of diameters. SD per modified RECIST 1.1 defined as: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. The evaluable analysis set included all evaluable subjects who had received at least 1 combination dose of pembrolizumab and bemcentinib and who had measurable disease at entry, as determined by the investigator site assessment.	
End point type	Secondary
End point timeframe:	
Until disease progression or death or withdrawal of consent whichever comes first, up to end of study (Up to 1 year)	

End point values	Bemcentinib + Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Percentage of subjects				
number (not applicable)	3.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)
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End point description:

PFS was defined as the duration from start of treatment until the date of radiological disease progression (the date on which the confirmed progression was initially observed) or the date of death (regardless of cause of death), whichever was earlier. The evaluable analysis set included all evaluable subjects who had received at least 1 combination dose of pembrolizumab and bemcentinib and who had measurable disease at entry, as determined by the investigator site assessment.

End point type	Secondary
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End point timeframe:

Until disease progression or death or withdrawal of consent whichever comes first, up to end of study (Up to 1 year)

End point values	Bemcentinib + Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Weeks				
median (confidence interval 95%)	13.1 (12.4 to 18.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
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End point description:

OS was defined as the time from the first dose of study treatment until the date of death (from any cause and irrespective of any subsequent anti-cancer treatment given). The evaluable analysis set included all evaluable subjects who had received at least 1 combination dose of pembrolizumab and bemcentinib and who had measurable disease at entry, as determined by the investigator site assessment.

End point type	Secondary
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End point timeframe:

Until disease progression or death or withdrawal of consent whichever comes first, up to end of study (Up to 1 year)

End point values	Bemcentinib + Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Weeks				
median (confidence interval 95%)	32.0 (13.6 to 37.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 1 year

Adverse event reporting additional description:

The safety set included all subjects who were enrolled in the study and who received at least 1 dose of study product (BGB324 and/or pembrolizumab).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Bemcentinib + Pembrolizumab
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Reporting group description:

Subjects received Bemcentinib (BGB324) capsules orally once daily as a loading dose of 400 milligram (mg) on Days 1, 2, and 3. From Day 4 onward, subjects received a daily maintenance dose of 200 mg along with Pembrolizumab 200 mg intravenous (IV) infusion over 30 minutes every 3 weeks until disease progression, until an unacceptable toxicity occurred that required treatment withdrawal or until 106 weeks had passed.

Serious adverse events	Bemcentinib + Pembrolizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 29 (75.86%)		
number of deaths (all causes)	16		
number of deaths resulting from adverse events	2		
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Jugular vein thrombosis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphoedema			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Adverse drug reaction			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Face oedema			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumonitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Rash generalised			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Pruritus generalised			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash macular			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Septic shock			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Upper respiratory tract infection subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Bemcentinib + Pembrolizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Hypotension			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Jugular vein thrombosis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	12 / 29 (41.38%)		
occurrences (all)	16		
Pyrexia			
subjects affected / exposed	6 / 29 (20.69%)		
occurrences (all)	7		
Pain			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	5		
Oedema peripheral			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	3		
Influenza like illness			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Axillary pain			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Face oedema			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	3		
Suprapubic pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Facial pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Non-cardiac chest pain			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	6		
Pleural effusion			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	3		
Cough			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Pneumonitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Dyspnoea exertional			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	2		
Atelectasis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Sinus pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Upper-airway cough syndrome			

subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Affect lability			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	13 / 29 (44.83%)		
occurrences (all)	16		
Alanine aminotransferase increased			
subjects affected / exposed	11 / 29 (37.93%)		
occurrences (all)	18		
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	5		
Electrocardiogram QT prolonged			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	7		
White blood cell count decreased			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	10		
Neutrophil count decreased			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	7		
Platelet count decreased			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	4		
Lymphocyte count decreased			

subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	12		
Blood creatinine increased			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	3		
Transaminases increased			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Nervous system disorders			
Tremor			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Neuropathy peripheral			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Aphasia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Hemiparaesthesia			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Movement disorder			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Neurological symptom			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 29 (27.59%)		
occurrences (all)	14		
Thrombocytopenia			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	5		
Febrile neutropenia			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Eye disorders			
Eyelid ptosis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	13 / 29 (44.83%)		
occurrences (all)	22		
Nausea			
subjects affected / exposed	11 / 29 (37.93%)		
occurrences (all)	17		
Vomiting			
subjects affected / exposed	6 / 29 (20.69%)		
occurrences (all)	12		
Constipation			
subjects affected / exposed	6 / 29 (20.69%)		
occurrences (all)	8		
Abdominal distension			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	5		
Dyspepsia			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Hepatotoxicity			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Rash generalised subjects affected / exposed occurrences (all)	5 / 29 (17.24%) 10		
Rash maculo-papular subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 8		
Rash subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 6		
Pruritus subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1		
Incontinence subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1		
Renal impairment subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	5 / 29 (17.24%) 6		
Neck pain subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 4		
Muscular weakness subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3		
Arthralgia subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3		
Back pain			

subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	5		
Hypokalaemia			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	9		
Hypoalbuminaemia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	4		
Hypocalcaemia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	4		
Hyponatraemia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	3		
Dehydration			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	3		
Hypophosphataemia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2017	The amendment included the following changes: management of patients who require concomitant systemic steroidal intervention; revisions requested by other (European and USA) regulatory authorities during review; updates to pembrolizumab standard protocol text.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None of the subjects achieved CR or PR. As there were no responses, the study was terminated. It was planned to terminate the trial in favor of the null hypothesis of futility when 5 or fewer responses were observed in 28 subjects.

Notes: