Clinical trial results:
A Phase 3 Randomized, Open-Label Clinical Study to Evaluate the Efficacy and Safety of Pembrolizumab plus Epacadostat, Pembrolizumab Monotherapy, and the EXTREME Regimen as First-line Treatment for Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (KEYNOTE-669/ECHO-304)

Summary

EudraCT number	2017-002311-34
Trial protocol	BE ES NL GB PL FR
Global end of trial date	10 August 2020

Results information

Result version number	v1 (current)
This version publication date	04 December 2021
First version publication date	04 December 2021

Trial information

Trial identification

Sponsor protocol code	KEYNOTE-672/ECHO-307

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte
Sponsor organisation address	1801 Augustine Cutoff drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, +1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, +1 8554633463, medinfo@incyte.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	10 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of pembrolizumab + epacadostat vs pembrolizumab + placebo in participants with cisplatin-ineligible urothelial carcinoma.

Protection of trial subjects:

This study was conducted in conformance with applicable country or local requirements regarding ethical committee review, informed consent, and other statutes or regulations regarding the protection of the rights and welfare of human participants in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 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	Australia: 4
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	93
EEA total number of subjects	35

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)	18
From 65 to 84 years	66
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 47 centers in 15 countries.

Pre-assignment

Screening details:

This study was conducted at 95 centers in 16 countries. Study enrollment was discontinued early and final efficacy was reported at the time of enrollment discontinuation. Only safety data was collected from ongoing participants until the study completion.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab 200 mg + Epacadostat 100 mg BID

Arm description:

Pembrolizumab administered intravenously every 3 weeks. Epacadostat administered orally twice daily.

Arm type	Experimental
Investigational medicinal product name	epacadostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral Twice a day

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

Dosage and administration details:

IV every 3 weeks

Arm title	Pembrolizumab 200 mg + Placebo BID

Arm description:

Pembrolizumab administered intravenously every 3 weeks. Matching placebo administered orally twice daily.

Arm type	Active comparator
Investigational medicinal product name	pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

IV every 3 weeks

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral Twice a day

Number of subjects in period 1	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Pembrolizumab 200 mg + Placebo BID
Started	44	49
Intention-to-Treat (ITT)	44	49
All Participants as Treated (APaT)	43	49
Completed	25	22
Not completed	19	27
Adverse event, serious fatal	17	18
Physician decision	1	9
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab 200 mg + Epacadostat 100 mg BID
Reporting group description:	
Pembrolizumab administered intravenously every 3 weeks. Epacadostat administered orally twice daily.	
Reporting group title	Pembrolizumab 200 mg + Placebo BID
Reporting group description:	
Pembrolizumab administered intravenously every 3 weeks. Matching placebo administered orally twice daily.	

Reporting group values	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Pembrolizumab 200 mg + Placebo BID	Total
Number of subjects	44	49	93
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	9	18
From 65-84 years	29	37	66
85 years and over	6	3	9
Age Continuous Units: years			
arithmetic mean	73.3	72.4	
standard deviation	± 9.5	± 8.9	-
Sex: Female, Male Units:			
Female	11	11	22
Male	33	38	71
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	2
Not Hispanic or Latino	35	42	77
Unknown or Not Reported	7	7	14
Race/Ethnicity, Customized Units: Subjects			
Asian	9	8	17
White	33	37	70
Missing	2	4	6
Metastasis Status at Screening Units: Subjects			
Metastatic	38	45	83
Advanced/Unresectable	6	4	10

End points

End points reporting groups

Reporting group title	Pembrolizumab 200 mg + Epacadostat 100 mg BID
Reporting group description:	
Pembrolizumab administered intravenously every 3 weeks. Epacadostat administered orally twice daily.	
Reporting group title	Pembrolizumab 200 mg + Placebo BID
Reporting group description:	
Pembrolizumab administered intravenously every 3 weeks. Matching placebo administered orally twice daily.	

Primary: Objective response rate (ORR) with pembrolizumab + epacadostat versus pembrolizumab + placebo

End point title	Objective response rate (ORR) with pembrolizumab + epacadostat versus pembrolizumab + placebo[1]
End point description:	
ORR was defined as the percentage of participants who had a confirmed complete response (CR) or partial response (PR) per RECIST v1.1 by investigator determination. Responses are based on Investigator assessments per RECIST 1.1 without confirmation using all scans up to the cutoff date.	
End point type	Primary
End point timeframe:	
Week 9	

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 for this endpoint.

End point values	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Pembrolizumab 200 mg + Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	49		
Units: percentage of participants				
number (confidence interval 95%)	31.8 (22.46 to 55.24)	24.5 (15.33 to 43.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability of Pembrolizumab + Epacadostat Versus Pembrolizumab + Placebo as Measured by Number of Participants Experiencing Adverse Events (AEs)

End point title	Safety and Tolerability of Pembrolizumab + Epacadostat Versus Pembrolizumab + Placebo as Measured by Number of Participants Experiencing Adverse Events (AEs)
End point description:	
AE is defined as any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment.	

End point type	Secondary

End point timeframe:

up to approximately 25 months

End point values	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Pembrolizumab 200 mg + Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	49		
Units: Number of Participants	43	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability of Pembrolizumab + Epacadostat Versus Pembrolizumab + Placebo as Measured by Number of Participants Discontinuing Study Treatment Due to AE

End point title	Safety and Tolerability of Pembrolizumab + Epacadostat Versus Pembrolizumab + Placebo as Measured by Number of Participants Discontinuing Study Treatment Due to AE

End point description:

AE is defined as any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment.

End point type	Secondary

End point timeframe:

up to approximately 25 months

End point values	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Pembrolizumab 200 mg + Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	49		
Units: Number of participants	11	15		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: up to approximately 25 months	
Adverse event reporting additional description: AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16

Reporting groups	
Reporting group title	Pembrolizumab 200 mg + Epacadostat 100 mg BID
Reporting group description: Pembrolizumab administered intravenously every 3 weeks. Epacadostat administered orally twice daily.	
Reporting group title	Total
Reporting group description: Total	
Reporting group title	Pembrolizumab 200 mg + Placebo BID
Reporting group description: Pembrolizumab administered intravenously every 3 weeks. Matching placebo administered orally twice daily.	

Serious adverse events	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Total	Pembrolizumab 200 mg + Placebo BID
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 43 (53.49%)	46 / 92 (50.00%)	23 / 49 (46.94%)
number of deaths (all causes)	17	36	19
number of deaths resulting from adverse events	10	16	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			

subjects affected / exposed	8 / 43 (18.60%)	13 / 92 (14.13%)	5 / 49 (10.20%)
occurrences causally related to treatment / all	0 / 9	0 / 14	0 / 5
deaths causally related to treatment / all	0 / 7	0 / 10	0 / 3
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 43 (2.33%)	2 / 92 (2.17%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Fatigue			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Product issues			
Device occlusion			
subjects affected / exposed	2 / 43 (4.65%)	2 / 92 (2.17%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract stoma complication			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Huntington's disease			

subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis cholestatic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	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 / 43 (0.00%)	2 / 92 (2.17%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic kidney disease			
subjects affected / exposed	0 / 43 (0.00%)	3 / 92 (3.26%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	2 / 43 (4.65%)	2 / 92 (2.17%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy toxic			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 43 (2.33%)	2 / 92 (2.17%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pathological fracture			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Encephalitis			

subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph gland infection			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 92 (1.09%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 92 (1.09%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	3 / 43 (6.98%)	9 / 92 (9.78%)	6 / 49 (12.24%)
occurrences causally related to treatment / all	0 / 3	0 / 13	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	2 / 43 (4.65%)	3 / 92 (3.26%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 92 (2.17%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pembrolizumab 200 mg + Epacadostat 100 mg BID	Total	Pembrolizumab 200 mg + Placebo BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 43 (97.67%)	89 / 92 (96.74%)	47 / 49 (95.92%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 43 (9.30%)	9 / 92 (9.78%)	5 / 49 (10.20%)
occurrences (all)	4	11	7
Amylase increased			
subjects affected / exposed	4 / 43 (9.30%)	8 / 92 (8.70%)	4 / 49 (8.16%)
occurrences (all)	8	12	4
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 43 (9.30%)	9 / 92 (9.78%)	5 / 49 (10.20%)
occurrences (all)	4	10	6
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 43 (4.65%)	7 / 92 (7.61%)	5 / 49 (10.20%)
occurrences (all)	2	7	5
Blood creatinine increased			
subjects affected / exposed	5 / 43 (11.63%)	8 / 92 (8.70%)	3 / 49 (6.12%)
occurrences (all)	6	12	6
Creatinine renal clearance decreased			
subjects affected / exposed	3 / 43 (6.98%)	3 / 92 (3.26%)	0 / 49 (0.00%)
occurrences (all)	3	3	0
Lipase increased			

subjects affected / exposed	4 / 43 (9.30%)	8 / 92 (8.70%)	4 / 49 (8.16%)
occurrences (all)	4	8	4
Weight decreased			
subjects affected / exposed	3 / 43 (6.98%)	7 / 92 (7.61%)	4 / 49 (8.16%)
occurrences (all)	3	7	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 43 (32.56%)	23 / 92 (25.00%)	9 / 49 (18.37%)
occurrences (all)	14	26	12
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 43 (20.93%)	19 / 92 (20.65%)	10 / 49 (20.41%)
occurrences (all)	9	19	10
Fatigue			
subjects affected / exposed	6 / 43 (13.95%)	14 / 92 (15.22%)	8 / 49 (16.33%)
occurrences (all)	7	16	9
Oedema peripheral			
subjects affected / exposed	3 / 43 (6.98%)	10 / 92 (10.87%)	7 / 49 (14.29%)
occurrences (all)	4	14	10
Pyrexia			
subjects affected / exposed	5 / 43 (11.63%)	11 / 92 (11.96%)	6 / 49 (12.24%)
occurrences (all)	6	14	8
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 43 (4.65%)	8 / 92 (8.70%)	6 / 49 (12.24%)
occurrences (all)	2	8	6
Constipation			
subjects affected / exposed	7 / 43 (16.28%)	14 / 92 (15.22%)	7 / 49 (14.29%)
occurrences (all)	10	17	7
Diarrhoea			
subjects affected / exposed	10 / 43 (23.26%)	17 / 92 (18.48%)	7 / 49 (14.29%)
occurrences (all)	14	23	9
Dry mouth			
subjects affected / exposed	0 / 43 (0.00%)	4 / 92 (4.35%)	4 / 49 (8.16%)
occurrences (all)	0	4	4
Nausea			

subjects affected / exposed	6 / 43 (13.95%)	12 / 92 (13.04%)	6 / 49 (12.24%)
occurrences (all)	9	15	6
Vomiting			
subjects affected / exposed	4 / 43 (9.30%)	11 / 92 (11.96%)	7 / 49 (14.29%)
occurrences (all)	4	13	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 43 (9.30%)	9 / 92 (9.78%)	5 / 49 (10.20%)
occurrences (all)	4	10	6
Dyspnoea			
subjects affected / exposed	5 / 43 (11.63%)	8 / 92 (8.70%)	3 / 49 (6.12%)
occurrences (all)	5	8	3
Pneumonitis			
subjects affected / exposed	4 / 43 (9.30%)	4 / 92 (4.35%)	0 / 49 (0.00%)
occurrences (all)	4	4	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	10 / 43 (23.26%)	16 / 92 (17.39%)	6 / 49 (12.24%)
occurrences (all)	13	20	7
Rash			
subjects affected / exposed	10 / 43 (23.26%)	24 / 92 (26.09%)	14 / 49 (28.57%)
occurrences (all)	12	26	14
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 43 (6.98%)	6 / 92 (6.52%)	3 / 49 (6.12%)
occurrences (all)	3	6	3
Haematuria			
subjects affected / exposed	4 / 43 (9.30%)	11 / 92 (11.96%)	7 / 49 (14.29%)
occurrences (all)	5	14	9
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 43 (6.98%)	5 / 92 (5.43%)	2 / 49 (4.08%)
occurrences (all)	3	5	2
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	3 / 43 (6.98%)	7 / 92 (7.61%)	4 / 49 (8.16%)
occurrences (all)	3	7	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 43 (6.98%)	6 / 92 (6.52%)	3 / 49 (6.12%)
occurrences (all)	3	8	5
Back pain			
subjects affected / exposed	7 / 43 (16.28%)	15 / 92 (16.30%)	8 / 49 (16.33%)
occurrences (all)	7	16	9
Flank pain			
subjects affected / exposed	1 / 43 (2.33%)	4 / 92 (4.35%)	3 / 49 (6.12%)
occurrences (all)	1	4	3
Musculoskeletal pain			
subjects affected / exposed	1 / 43 (2.33%)	4 / 92 (4.35%)	3 / 49 (6.12%)
occurrences (all)	1	4	3
Pain in extremity			
subjects affected / exposed	2 / 43 (4.65%)	5 / 92 (5.43%)	3 / 49 (6.12%)
occurrences (all)	2	5	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 43 (0.00%)	4 / 92 (4.35%)	4 / 49 (8.16%)
occurrences (all)	0	4	4
Pneumonia			
subjects affected / exposed	3 / 43 (6.98%)	5 / 92 (5.43%)	2 / 49 (4.08%)
occurrences (all)	3	5	2
Urinary tract infection			
subjects affected / exposed	5 / 43 (11.63%)	16 / 92 (17.39%)	11 / 49 (22.45%)
occurrences (all)	5	19	14
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 43 (11.63%)	13 / 92 (14.13%)	8 / 49 (16.33%)
occurrences (all)	7	15	8
Hyperkalaemia			
subjects affected / exposed	3 / 43 (6.98%)	7 / 92 (7.61%)	4 / 49 (8.16%)
occurrences (all)	3	9	6
Hyperuricaemia			

subjects affected / exposed	3 / 43 (6.98%)	3 / 92 (3.26%)	0 / 49 (0.00%)
occurrences (all)	7	7	0
Hypoalbuminaemia			
subjects affected / exposed	5 / 43 (11.63%)	7 / 92 (7.61%)	2 / 49 (4.08%)
occurrences (all)	5	7	2
Hypocalcaemia			
subjects affected / exposed	4 / 43 (9.30%)	5 / 92 (5.43%)	1 / 49 (2.04%)
occurrences (all)	6	7	1
Hypokalaemia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 92 (3.26%)	3 / 49 (6.12%)
occurrences (all)	0	4	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2018	Enrollment was permanently stopped on 02May2018 as a strategic decision. For participants who are considered to be obtaining ongoing clinical benefit, continued study treatment will be at the discretion of the investigator after a discussion with the participant of the results from KEYNOTE-252/ECHO-301 study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported