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COMPLETED

Study of Pembrolizumab (MK-3475) in Participants With Advanced Solid Tumors (MK-3475-028/KEYNOTE-28)

ClinicalTrials.gov ID **NCT02054806**

Sponsor Merck Sharp & Dohme LLC

Information provided by Merck Sharp & Dohme LLC (Responsible Party)

Last Update Posted 2023-10-30

Results Posted Tab

Results Overview

Conditions

Solid Tumor

Intervention/Treatment

- Biological: Pembrolizumab

Other Study ID Numbers

- 3475-028
- 142515 (Registry Identifier) (REGISTRY: JAPIC-CTI)

Feedback

JHU 2080
Merck Sharp v. Johns Hopkins
IPR2024-00623

Study Design

Allocation: N/A
Interventional Model: Single Group Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Results Point of Contact

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme LLC
Phone: 1-800-672-6372
Email: ClinicalTrialsDisclosure@merck.com

Enrollment (Actual)

477

Study Type

Interventional

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2014-02-03

First Posted (Estimated)
2014-02-04

Results Reporting Dates

Results First Submitted
2022-04-19

Results First Posted
2023-10-30

Study Record Updates

Last Update Posted
2023-10-30

Last Verified
2023-02

Participant Flow

Recruitment Details

Participants with a histologically- or cytologically-confirmed diagnosis of 20 advanced (unresectable and/or metastatic) solid tumors, were recruited into a single arm.

Pre-assignment Details

Per protocol, response/progression or adverse events during the second pembrolizumab course were not counted towards efficacy outcome measures or safety outcome measures respectively.

Per protocol, analyses of disease type cohort was planned and conducted for efficacy outcome measures only.

Arm/Group Title	Pembrolizumab 10 mg/kg
Arm/Group Description	Participants received pembrolizumab 10 mg/kg intravenously (IV) over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. Qualified participants who completed the first course of pembrolizumab treatment but progressed after discontinuation were eligible for a second course of pembrolizumab at 10 mg/kg IV Q2W for up to ~1 additional year, at the Investigator's discretion. Per protocol participants were presented by treatment received in the single arm study.

Period Title: **Overall Study**

Started	477

Treated During First Course	475
Treated During Second Course	11
Completed	0
Not Completed	477

Reason Not Completed

Sponsor Decision	31
Withdrawal by Subject	43
Protocol Violation	2
Lost to Follow-up	10
Death	391

Baseline Characteristics

Arm/Group Title	Pembrolizumab (MK-3475) 10 mg/kg
Arm/Group Description	Participants received pembrolizumab 10 mg/kg IV over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. Qualified participants who completed the first course of pembrolizumab treatment but progressed after discontinuation were eligible for a second course of pembrolizumab at 10 mg/kg IV Q2W for up to ~1 additional year, at the Investigator's discretion. Per protocol participants were presented by treatment received in the single arm study.
Overall Number of Baseline Participants	475
Baseline Analysis Population Description	The analysis population consisted of all allocated participants who received at least one dose of study drug. Per protocol, Baseline Characteristics were summarized by treatment dose.

Expand all / Collapse all

Age, Continuous

Mean (Standard Deviation) | Unit of measure: Years

Number Analyzed	475 participants
	58.7 (11.7)

Sex: Female, Male

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	475 participants	
Female	281	59.2%
Male	194	40.8%

Ethnicity (NIH/OMB)

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	475 participants	
Hispanic or Latino	18	3.8%
Not Hispanic or Latino	380	80.0%
Unknown or Not Reported	77	16.2%

Race (NIH/OMB)

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	475 participants	
American Indian or Alaska Native	1	0.2%
Asian	99	20.8%
Native Hawaiian or Other Pacific Islander	0	0.0%
Black or African American	20	4.2%
White	280	58.9%
More than one race	2	0.4%

Unknown or Not Reported	73 15.4%

Outcome Measures

Expand all / Collapse all

1. Overall Response Rate (ORR)

Type: Primary | Time Frame: Up to approximately 86 months

Description	Overall response rate (ORR) was defined as the percentage of participants who experienced a complete response (CR; disappearance of all target lesions) or a Partial Response (PR; at least a 30% decrease in the sum of diameters of target lesions) and was assessed using modified Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 by the investigator.
Time Frame	Up to approximately 86 months
Analysis Population Description	The analysis population consisted of all participants who received at least 1 dose of study treatment, had a baseline scan with measurable disease per modified RECIST 1.1 and had the intended indication. Per protocol, participants were analyzed according to disease type.

Arm/Group Title	Cohort A1: Colon or Rectal Adenocarcinoma	Cohort A2: Anal Canal Squamo Cell Carcinoma
Arm/Group Description	Participants received pembrolizumab 10 mg/kg IV over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participants who enrolled with colon or rectal adenocarcinoma.	Participants received pembrolizumab 10 mg/kg IV ov 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participar who enrolled with anal canal squamous cell carcinoma.
Overall Number of Participants Analyzed	23	25
Measure Type: Number (95% Confidence Interval) | Unit of Measure: Percentage of Participants	4.3 (0.1 to 21.9)	20.0 (6.8 to 40.7)

2. Number of Participants Who Experienced an Adverse Event (AE)

Type: Secondary | Time Frame: Up to approximately 28 months

Description	An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The number of participants with at least one AE was assessed.
Time Frame	Up to approximately 28 months

Analysis Population Description	The analysis population consisted of all allocated participants who received at least one dose of study drug.
Arm/Group Title	Pembrolizumab (MK-3475) 10 mg/kg
Arm/Group Description	Participants received pembrolizumab 10 mg/kg intravenously (IV) over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. Per protocol participants were presented by treatment received in the single arm study.
Overall Number of Participants Analyzed	475
Measure Type: Count of Participants | Unit of Measure: Participants	456 96.0%

3. Number of Participants Who Discontinued From Study Treatment Due to an AE

Type: Secondary | Time Frame: Up to approximately 25 months

Description	An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The number of participants who discontinued treatment due to an AE was assessed.
Time Frame	Up to approximately 25 months
Analysis Population Description	The analysis population consisted of all allocated participants who received at least one dose of study drug.

Arm/Group Title	Pembrolizumab (MK-3475) 10 mg/kg
Arm/Group Description	Participants received pembrolizumab 10 mg/kg intravenously (IV) over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. Per protocol participants were presented by treatment received in the single arm study.
Overall Number of Participants Analyzed	475
Measure Type: Count of Participants | Unit of Measure: Participants	30 6.3%

4. Progression Free Survival (PFS)

Type: Secondary | Time Frame: Up to approximately 86 months

Description	PFS was defined as the time from the date of allocation to the date of the first documentation of disease progression, as determined by investigator per modified RECIST 1.1 or death due to any cause (whichever occurred first). Disease progression was defined as at least 20 percent (%) increase (including an absolute increase of at least 5 millimeter [mm]) in the sum of diameter of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. PFS was estimated and analyzed using Kaplan-Meier method.
Time Frame	Up to approximately 86 months
Analysis Population Description	The analysis population consisted of all participants who received at least 1 dose of study treatment, had a baseline scan with measurable disease per modified RECIST 1.1 and had the intended indication. Per protocol, participants were analyzed according to disease type.

Arm/Group Title	Cohort A1: Colon or Rectal Adenocarcinoma	Cohort A2: Anal Canal Squamo Cell Carcinoma
Arm/Group Description	Participants received pembrolizumab 10 mg/kg IV over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participants who enrolled with colon or rectal adenocarcinoma.	Participants received pembrolizumab 10 mg/kg IV ov 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participar who enrolled with anal canal squamous cell carcinoma.
Overall Number of Participants Analyzed	23	25
Median (95% Confidence Interval) | Unit of Measure: Months	1.7 (1.4 to 1.8)	3.1 (1.6 to 6.2)

5. Overall Survival (OS)

Type: Secondary | Time Frame: Up to approximately 86 months

Description	OS was defined as the time from the date of allocation to the date of death due to any cause. Participants who were lost to follow-up and those who were alive at the end of the trial were censored at the date of last assessment.
Time Frame	Up to approximately 86 months
Analysis Population Description	The analysis population consisted of all participants who received at least 1 dose of study treatment, had a baseline scan with measurable disease per modified RECIST 1.1 and had the intended indication. Per protocol, participants were analyzed according to disease type.

Arm/Group Title	Cohort A1: Colon or Rectal Adenocarcinoma	Cohort A2: Anal Canal Squamo Cell Carcinoma
Arm/Group Description	Participants received pembrolizumab 10 mg/kg IV over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participants who enrolled with colon or rectal adenocarcinoma.	Participants received pembrolizumab 10 mg/kg IV ov 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participar who enrolled with anal canal squamous cell carcinoma.
Overall Number of Participants Analyzed	23	25
Median (95% Confidence Interval) | Unit of Measure: Months	5.3 (2.2 to 10.9)	8.3 (5.8 to 16.2)

[1] NA = Upper limit not reached at time of data cut-off due to insufficient number of participants with an event.

6. Duration of Response (DOR)

Type: Secondary | Time Frame: Up to approximately 86 months

Description	For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR (at least a 30% decrease in the sum of diameters of target lesions) per modified RECIST 1.1, DOR was defined as the time from first documented evidence of a CR or PR until progressive disease (PD) or death. DOR for participants who had not progressed or died at the time of analysis was censored at the date of their last tumor assessment. Per modified RECIST 1.1, PD was defined as at least a 20% increase in the sum of diameters of target lesions. In

	addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered PD. DOR assessments were based on investigator with confirmation. The DOR according to modified RECIST 1.1 for all participants who experienced a confirmed CR or PR was reported. Per protocol, participants were analyzed according to disease type.
Time Frame	Up to approximately 86 months
Analysis Population Description	The analysis population consisted of all participants who received at least 1 dose of study treatment, had a baseline scan with measurable disease per modified RECIST 1.1, had the intended indication, and experienced a response. Per protocol-specified definition, DOR could not be analyzed in arms which did not have a confirmed response of CR or PR.

Arm/Group Title	Cohort A1: Colon or Rectal Adenocarcinoma	Cohort A2: Anal Canal Squamo Cell Carcinoma
Arm/Group Description	Participants received pembrolizumab 10 mg/kg IV over 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participants who enrolled with colon or rectal adenocarcinoma.	Participants received pembrolizumab 10 mg/kg IV ov 30 minutes once every 2 weeks (Q2W) for up to ~2 years. This cohort represents all participar who enrolled with anal canal squamous cell carcinoma.
Overall Number of Participants Analyzed	1	5
Median (Full Range) | Unit of Measure: Months	NA [1] (NA to NA)	28.9 [2] (3.8 to NA)

[1] NA = Median, upper limit, lower limit not reached at time of data cut-off due to insufficient number of responding participants with relapse.

[2] NA = Upper limit not reached at time of data cut-off due to insufficient number of responding participants with relapse.

[3] NA = Median, upper limit not reached at time of data cut-off due to insufficient number of responding participants with relapse.

Adverse Events

Time Frame
Up to ~28 months for first course and up to ~49 months for second course. All-cause mortality (ACM): Up to ~86 months for first and second course.

Adverse Event Reporting Description
ACM includes all randomized participants. Safety includes all participants receiving ≥1 dose of study treatment. Per protocol, AEs were collected and reported by treatment intervention irrespective of indication. Per protocol, MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to study treatment were excluded as AEs. Participants receiving a second course of pembrolizumab per protocol were monitored for ACM and safety separately.

Arm/Group Title	First Course Pembrolizumab 10 mg/kg	Second Course Pembrolizuma 10 mg/kg
Arm/Group Description	Participants received pembrolizumab 10 mg/kg IV over 30 minutes once every 2 weeks (Q2W) for up to ~2 years.	Qualified participants who completed the first course of pembrolizumab 10 mg/kg IV ov 30 minutes once every 2 weeks (Q2W) for up to ~2 years, but experienced disease progressi initiated a second course of pembrolizumab at the investigator's discretion, at 10 mg/kg IV Q2W for up to ~1 yea

All-Cause Mortality

Arm/Group Title	First Course Pembrolizumab 10 mg/kg	Second Course Pembrolizuma 10 mg/kg
	Affected / at Risk (%)	Affected / at Risk (%)
Total	426/477 (89.31%)	6/11 (54.55%)

Serious Adverse Events

Arm/Group Title	First Course Pembrolizumab 10 mg/kg		Second Course Pembrolizuma 10 mg/kg	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	160/475 (33.68%)		3/11 (27.27%)	
Blood and lymphatic system disorders				
Anaemia †1	5/475 (1.05%)	5	0/11 (0.00%)	0
Autoimmune haemolytic anaemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Thrombocytopenia †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Cardiac disorders				
Acute coronary syndrome †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Atrial fibrillation †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Atrial tachycardia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Atrioventricular block complete †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Myocardial infarction †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pericardial effusion †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pulseless electrical activity †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Ear and labyrinth disorders				
Ear haemorrhage †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Endocrine disorders				

Hypercalcaemia of malignancy †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Hypothyroidism †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Gastrointestinal disorders				
Abdominal pain †1	4/475 (0.84%)	4	0/11 (0.00%)	0
Abdominal pain upper †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Ascites †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Colitis †1	7/475 (1.47%)	8	0/11 (0.00%)	0
Constipation †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Diarrhoea †1	5/475 (1.05%)	5	0/11 (0.00%)	0
Enteritis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Enterocolitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Gastritis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Gastrointestinal haemorrhage †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Gastrointestinal ulcer †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Haemorrhoids †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Ileus †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Intestinal ischaemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Intestinal obstruction †1	3/475 (0.63%)	3	0/11 (0.00%)	0

Large intestinal haemorrhage †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Malignant gastrointestinal obstruction †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Melaena †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pancreatitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Small intestinal obstruction †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Subileus †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Upper gastrointestinal haemorrhage †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Vomiting †1	2/475 (0.42%)	2	0/11 (0.00%)	0
General disorders				
Chest pain †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Complication associated with device †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Death †1	4/475 (0.84%)	4	0/11 (0.00%)	0
General physical health deterioration †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Influenza like illness †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Malaise †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Non-cardiac chest pain †1	1/475 (0.21%)	2	0/11 (0.00%)	0
Oedema †1	1/475 (0.21%)	1	0/11 (0.00%)	0

Pyrexia †1	8/475 (1.68%)	11	0/11 (0.00%)	0
Hepatobiliary disorders				
Acute hepatic failure †1	0/475 (0.00%)	0	1/11 (9.09%)	1
Autoimmune hepatitis †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Biliary colic †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Biliary obstruction †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Cholangitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Cholestasis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hepatic cytolysis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hepatic failure †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hepatitis †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Hyperbilirubinaemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Jaundice †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Liver disorder †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Immune system disorders				
Cytokine release syndrome †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Infections and infestations				
Abdominal sepsis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Bacteraemia †1	3/475 (0.63%)	4	0/11 (0.00%)	0
Biliary sepsis †1	1/475 (0.21%)	1	0/11 (0.00%)	0

Cellulitis †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Clostridium difficile colitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Device related bacteraemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Device related infection †1	1/475 (0.21%)	2	0/11 (0.00%)	0
Device related sepsis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Escherichia sepsis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Gastroenteritis viral †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Helicobacter infection †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Infection †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Infectious mononucleosis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Infectious pleural effusion †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Liver abscess †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Lower respiratory tract infection †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Lower respiratory tract infection bacterial †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Meningitis bacterial †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Oropharyngeal candidiasis †1	1/475 (0.21%)	1	0/11 (0.00%)	0

Osteomyelitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Otitis media †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pelvic abscess †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Peritonitis †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Pneumonia †1	6/475 (1.26%)	6	0/11 (0.00%)	0
Pulmonary sepsis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Salmonellosis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Sepsis †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Septic shock †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Streptococcal sepsis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Subcutaneous abscess †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Urinary tract infection †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Wound infection †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Injury, poisoning and procedural complications				
Femoral neck fracture †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Gastroenteritis radiation †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Post procedural complication †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Investigations				

Alanine aminotransferase increased †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Aspartate aminotransferase increased †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Blood creatine phosphokinase increased †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Transaminases increased †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Metabolism and nutrition disorders				
Decreased appetite †1	5/475 (1.05%)	5	0/11 (0.00%)	0
Food intolerance †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hypercalcaemia †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Hypoglycaemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hypokalaemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hyponatraemia †1	0/475 (0.00%)	0	1/11 (9.09%)	1
Hypovolaemia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Type 2 diabetes mellitus †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Musculoskeletal and connective tissue disorders				
Arthralgia †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Arthritis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Back pain †1	2/475 (0.42%)	2	1/11 (9.09%)	1

Flank pain †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Joint effusion †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pain in extremity †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Rhabdomyolysis †1	1/475 (0.21%)	1	0/11 (0.00%)	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)

Cancer pain †1	5/475 (1.05%)	5	0/11 (0.00%)	0
Malignant melanoma †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Myelodysplastic syndrome †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Squamous cell carcinoma of skin †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Tumour associated fever †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Tumour compression †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Tumour pain †1	2/475 (0.42%)	2	0/11 (0.00%)	0

Nervous system disorders

Altered state of consciousness †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Epilepsy †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Guillain-Barre syndrome †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hydrocephalus †1	1/475 (0.21%)	1	0/11 (0.00%)	0

Ischaemic stroke †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Migraine †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Myelitis transverse †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Neuropathy peripheral †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Presyncope †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Seizure †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Syncope †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Product Issues				
Device occlusion †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Psychiatric disorders				
Anxiety †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Confusional state †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Depression †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Mental status changes †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Renal and urinary disorders				
Acute kidney injury †1	2/475 (0.42%)	2	1/11 (9.09%)	1
Haematuria †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hydronephrosis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Renal failure †1	2/475 (0.42%)	2	1/11 (9.09%)	1
Ureteric dilatation †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Urinary retention †1	1/475 (0.21%)	1	0/11 (0.00%)	0

Reproductive system and breast disorders				
Intermenstrual bleeding †1	1/475 (0.21%)	3	0/11 (0.00%)	0
Vaginal haemorrhage †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Vulvovaginal pain †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Respiratory, thoracic and mediastinal disorders				
Dyspnoea †1	3/475 (0.63%)	3	0/11 (0.00%)	0
Haemoptysis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Interstitial lung disease †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Noninfective bronchitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pleural effusion †1	8/475 (1.68%)	9	0/11 (0.00%)	0
Pneumonia aspiration †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pneumonitis †1	5/475 (1.05%)	5	0/11 (0.00%)	0
Pneumothorax †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Pulmonary embolism †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Respiratory distress †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Tracheal stenosis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Skin and subcutaneous tissue disorders				
Acute febrile neutrophilic	1/475 (0.21%)	1	0/11 (0.00%)	0

dermatosis †1				
Dermatitis †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Pemphigoid †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Rash †1	2/475 (0.42%)	2	0/11 (0.00%)	0
Vascular disorders				
Haemorrhage †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Hypotension †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Lymphoedema †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Lymphorrhoea †1	1/475 (0.21%)	1	0/11 (0.00%)	0
Orthostatic hypotension †1	0/475 (0.00%)	0	1/11 (9.09%)	1
Thrombosis †1	1/475 (0.21%)	1	0/11 (0.00%)	0

† Indicates events were collected by systematic assessment

1 Term from vocabulary, MedDRA 24.0

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%			
Arm/Group Title	First Course Pembrolizumab 10 mg/kg		Second Course Pembrolizuma 10 mg/kg	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	429/475 (90.32%)		10/11 (90.91%)	

Blood and lymphatic system disorders				
Anaemia †1	87/475 (18.32%)	101	0/11 (0.00%)	0
Iron deficiency anaemia †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Ear and labyrinth disorders				
Hypoacusis †1	2/475 (0.42%)	2	1/11 (9.09%)	1
Endocrine disorders				
Hypothyroidism †1	38/475 (8.00%)	39	0/11 (0.00%)	0
Eye disorders				
Cataract †1	5/475 (1.05%)	5	1/11 (9.09%)	1
Dry eye †1	11/475 (2.32%)	11	2/11 (18.18%)	2
Uveitis †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Gastrointestinal disorders				
Abdominal pain †1	54/475 (11.37%)	59	0/11 (0.00%)	0
Abdominal pain upper †1	28/475 (5.89%)	31	1/11 (9.09%)	1
Constipation †1	93/475 (19.58%)	105	1/11 (9.09%)	1
Diarrhoea †1	102/475 (21.47%)	177	3/11 (27.27%)	3
Dry mouth †1	29/475 (6.11%)	30	1/11 (9.09%)	1
Nausea †1	124/475 (26.11%)	149	0/11 (0.00%)	0

Vomiting †1	75/475 (15.79%)	99	1/11 (9.09%)	1
Oral pain †1	8/475 (1.68%)	9	1/11 (9.09%)	1
Abdominal pain lower †1	7/475 (1.47%)	7	1/11 (9.09%)	1
Stomatitis †1	14/475 (2.95%)	19	2/11 (18.18%)	2
General disorders				
Asthenia †1	59/475 (12.42%)	68	1/11 (9.09%)	1
Fatigue †1	165/475 (34.74%)	176	0/11 (0.00%)	0
Oedema peripheral †1	43/475 (9.05%)	47	1/11 (9.09%)	1
Pyrexia †1	74/475 (15.58%)	97	0/11 (0.00%)	0
Chest pain †1	20/475 (4.21%)	23	1/11 (9.09%)	1
Influenza like illness †1	11/475 (2.32%)	16	2/11 (18.18%)	3
Infections and infestations				
Conjunctivitis †1	7/475 (1.47%)	7	2/11 (18.18%)	2
Gingivitis †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Lower respiratory tract infection †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Oral candidiasis †1	7/475 (1.47%)	7	1/11 (9.09%)	1
Upper respiratory tract infection †1	21/475 (4.42%)	27	1/11 (9.09%)	1
Mucosal infection †1	0/475 (0.00%)	0	1/11 (9.09%)	1

Viral upper respiratory tract infection †1	0/475 (0.00%)	0	1/11 (9.09%)	1
Injury, poisoning and procedural complications				
Lumbar vertebral fracture †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Contusion †1	4/475 (0.84%)	4	1/11 (9.09%)	1
Investigations				
Alanine aminotransferase increased †1	31/475 (6.53%)	39	1/11 (9.09%)	1
Aspartate aminotransferase increased †1	37/475 (7.79%)	45	1/11 (9.09%)	1
Blood alkaline phosphatase increased †1	40/475 (8.42%)	41	0/11 (0.00%)	0
Weight decreased †1	35/475 (7.37%)	36	0/11 (0.00%)	0
Blood lactate dehydrogenase increased †1	4/475 (0.84%)	7	1/11 (9.09%)	1
Hepatic enzyme increased †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Metabolism and nutrition disorders				
Decreased appetite †1	102/475 (21.47%)	106	0/11 (0.00%)	0
Hypoalbuminaemia †1	35/475 (7.37%)	37	0/11 (0.00%)	0
Hypokalaemia †1	31/475 (6.53%)	33	0/11 (0.00%)	0

Hypomagnesaemia †1	37/475 (7.79%)	46	0/11 (0.00%)	0
Hyponatraemia †1	34/475 (7.16%)	36	1/11 (9.09%)	1
Hypocalcaemia †1	13/475 (2.74%)	13	1/11 (9.09%)	1
Hypoglycaemia †1	3/475 (0.63%)	3	1/11 (9.09%)	1
Musculoskeletal and connective tissue disorders				
Arthralgia †1	77/475 (16.21%)	101	2/11 (18.18%)	2
Back pain †1	56/475 (11.79%)	64	3/11 (27.27%)	4
Myalgia †1	38/475 (8.00%)	49	0/11 (0.00%)	0
Pain in extremity †1	30/475 (6.32%)	34	0/11 (0.00%)	0
Arthritis †1	5/475 (1.05%)	6	1/11 (9.09%)	1
Musculoskeletal chest pain †1	18/475 (3.79%)	18	1/11 (9.09%)	1
Nervous system disorders				
Dizziness †1	42/475 (8.84%)	54	0/11 (0.00%)	0
Headache †1	63/475 (13.26%)	73	1/11 (9.09%)	1
Memory impairment †1	3/475 (0.63%)	3	1/11 (9.09%)	1
Psychiatric disorders				
Depression †1	25/475 (5.26%)	26	0/11 (0.00%)	0
Insomnia †1	44/475 (9.26%)	45	0/11 (0.00%)	0
Renal and urinary disorders				

Hematuria †1	10/475 (2.11%)	19	1/11 (9.09%)	1
Reproductive system and breast disorders				
Vulvovaginal dryness †1	1/475 (0.21%)	1	1/11 (9.09%)	1
Respiratory, thoracic and mediastinal disorders				
Cough †1	69/475 (14.53%)	89	0/11 (0.00%)	0
Dyspnoea †1	60/475 (12.63%)	67	0/11 (0.00%)	0
Dysphonia †1	16/475 (3.37%)	17	1/11 (9.09%)	1
Pneumonitis †1	8/475 (1.68%)	8	1/11 (9.09%)	1
Skin and subcutaneous tissue disorders				
Dry skin †1	24/475 (5.05%)	25	2/11 (18.18%)	2
Pruritus †1	69/475 (14.53%)	88	2/11 (18.18%)	2
Rash †1	56/475 (11.79%)	71	1/11 (9.09%)	1
Rash maculo-papular †1	25/475 (5.26%)	28	0/11 (0.00%)	0
Dermatitis acneiform †1	3/475 (0.63%)	3	1/11 (9.09%)	1
Palmar-plantar erythrodysaesthesia syndrome †1	2/475 (0.42%)	2	1/11 (9.09%)	1
Rash pruritic †1	3/11 (27.27%)	5	1/11 (9.09%)	1
Intertrigo †1	0/475 (0.00%)	0	1/11 (9.09%)	1

Skin discolouration †1	0/475 (0.00%)	0	1/11 (9.09%)	1
Vascular disorders				
Hypotension †1	20/475 (4.21%)	21	1/11 (9.09%)	1
Jugular vein thrombosis †1	0/475 (0.00%)	0	1/11 (9.09%)	1

† Indicates events were collected by systematic assessment

1 Term from vocabulary, MedDRA 24.0

Limitations and Caveats

[Not Specified]

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Merck Sharp & Dohme LLC

Investigators

- Study Director: Medical Director, Merck Sharp & Dohme LLC

Publications

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- Alley EW, Lopez J, Santoro A, Morosky A, Saraf S, Piperdi B, van Brummelen E. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. Lancet Oncol. 2017 May;18(5):623-630. doi: 10.1016/S1470-2045(17)30169-9. Epub 2017 Mar 11. (https://pubmed.ncbi.nlm.nih.gov/28291584)
- Ott PA, Piha-Paul SA, Munster P, Pishvaian MJ, van Brummelen EMJ, Cohen RB, Gomez-Roca C, Ejadi S, Stein M, Chan E, Simonelli M, Morosky A, Saraf S, Emancipator K, Koshiji M, Bennouna J. Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal. Ann Oncol. 2017 May 1;28(5):1036-1041. doi: 10.1093/annonc/mdx029. (https://pubmed.ncbi.nlm.nih.gov/28453692)
- Hsu C, Lee SH, Ejadi S, Even C, Cohen RB, Le Tourneau C, Mehnert JM, Algazi A, van Brummelen EMJ, Saraf S, Thanigaimani P, Cheng JD, Hansen AR. Safety and Antitumor Activity of Pembrolizumab in Patients With Programmed Death-Ligand 1-Positive Nasopharyngeal Carcinoma: Results of the KEYNOTE-028 Study. J Clin Oncol. 2017 Dec 20;35(36):4050-4056. doi: 10.1200/JCO.2017.73.3675. Epub 2017 Aug 24. (https://pubmed.ncbi.nlm.nih.gov/28837405)
- Ott PA, Elez E, Hiret S, Kim DW, Morosky A, Saraf S, Piperdi B, Mehnert JM. Pembrolizumab in Patients With Extensive-Stage Small-Cell Lung Cancer: Results From the Phase Ib KEYNOTE-028 Study. J Clin Oncol. 2017 Dec 1;35(34):3823-3829. doi: 10.1200/JCO.2017.72.5069. Epub 2017 Aug 16. (https://pubmed.ncbi.nlm.nih.gov/28813164)
- Doi T, Piha-Paul SA, Jalal SI, Saraf S, Lunceford J, Koshiji M, Bennouna J. Safety and Antitumor Activity of the Anti-Programmed Death-1 Antibody Pembrolizumab in Patients With Advanced Esophageal Carcinoma. J Clin Oncol. 2018 Jan (https://pubmed.ncbi.nlm.nih.gov/2

From PubMed

These publications come from PubMed, a public database of scientific and medical articles. This list is automatically created by ClinicalTrials.gov Identifier (NCT Number), and these articles may or may not be about the study.

- Cristescu R, Aurora-Garg D, Albright A, Xu L, Liu XQ, Loboda A, Lang L, Jin F, Rubin EH, Snyder A, Lunceford J. Tumor mutational burden predicts the efficacy of pembrolizumab monotherapy: a pan-tumor retrospective analysis of participants with advanced solid tumors. J Immunother Cancer. 2022 Jan;10(1):e003091. doi: 10.1136/jitc-2021-003091. (https://pubmed.ncbi.nlm.nih.gov/35101941)
- Reardon DA, Kim TM, Frenel JS, Simonelli M, Lopez J, Subramaniam DS, Siu LL, Wang H, Krishnan S, Stein K, Massard C. Treatment with pembrolizumab in programmed death ligand 1-positive recurrent glioblastoma: Results from the multicohort phase 1 KEYNOTE-028 trial. Cancer. 2021 May 15;127(10):1620-1629. doi: 10.1002/cncr.33378. Epub 2021 Jan 26. (https://pubmed.ncbi.nlm.nih.gov/33496357)

- Piha-Paul SA, Oh DY, Ueno M, Malka D, Chung HC, Nagrial A, Kelley RK, Ros W, Italiano A, Nakagawa K, Rugo HS, de Braud F, Varga AI, Hansen A, Wang H, Krishnan S, Norwood KG, Doi T. Efficacy and safety of pembrolizumab for the treatment of advanced biliary cancer: Results from the KEYNOTE-158 and KEYNOTE-028 studies. Int J Cancer. 2020 Oct 15;147(8):2190-2198. doi: 10.1002/ijc.33013. Epub 2020 May 2. (https://pubmed.ncbi.nlm.nih.gov/32359091)
- Mehnert JM, Bergsland E, O'Neil BH, Santoro A, Schellens JHM, Cohen RB, Doi T, Ott PA, Pishvaian MJ, Puzanov I, Aung KL, Hsu C, Le Tourneau C, Hollebecque A, Elez E, Tamura K, Gould M, Yang P, Stein K, Piha-Paul SA. Pembrolizumab for the treatment of programmed death-ligand 1-positive advanced carcinoid or pancreatic neuroendocrine tumors: Results from the KEYNOTE-028 study. Cancer. 2020 Jul 1;126(13):3021-3030. doi: 10.1002/cncr.32883. Epub 2020 Apr 22. (https://pubmed.ncbi.nlm.nih.gov/32320048)
- Mehnert JM, Varga A, Brose MS, Aggarwal RR, Lin CC, Prawira A, de Braud F, Tamura (https://p

More Information

Record History

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed

The Sponsor must have the opportunity to review all proposed abstracts, manuscripts or presentations regarding this trial 45 days prior to submission for publication/presentation.

Any information identified by the Sponsor as confidential must be deleted prior to submission; this confidentiality does not include efficacy and safety results. Sponsor review can be expedited to meet publication timelines.