Clinical trial results:
A Phase 3 Open-label, Single Arm Study to Evaluate the Safety and Efficacy of Pembrolizumab (MK- 3475) as First-line Therapy in Participants With Advanced Merkel Cell Carcinoma (KEYNOTE-913)

Summary

EudraCT number	2018-002601-57
Trial protocol	SE FR ES IT
Global end of trial date	15 February 2024

Results information

Result version number	v1 (current)
This version publication date	31 January 2025
First version publication date	31 January 2025

Trial information

Trial identification

Sponsor protocol code	MK-3475-913

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03783078
WHO universal trial number (UTN)	-
Other trial identifiers	KEYNOTE-913: MSD

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	15 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2022
Global end of trial reached?	Yes
Global end of trial date	15 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a single-arm, open-label, multicenter, efficacy, and safety study of pembrolizumab in adult and pediatric participants with previously untreated advanced Merkel Cell Carcinoma (MCC). The primary objective of the trial was to assess the objective response rate, as assessed by blinded independent central review per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ, following administration of pembrolizumab.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human participants participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	55
EEA total number of subjects	44

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	12
From 65 to 84 years	36
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants of at least 12 years of age with advanced Merkel cell carcinoma (MCC) were recruited to evaluate the safety and efficacy of Pembrolizumab (MK-3475) as first-line therapy. A total of 55 participants from 8 countries were enrolled.

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	Pembrolizumab 200 mg

Arm description:

Adult participants received pembrolizumab (MK-3475) 200 mg or pediatric participants received 2 mg/kg (up to 200 mg) on Day 1 of each 3-week cycle (Q3W) intravenously (IV), for up to 35 administrations (approximately 2 years).

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab (MK-3475) 200 mg (adult participants) or 2 mg/kg (up to 200 mg; pediatric participants) on Day 1 of each 3-week cycle (Q3W) intravenous (IV), for up to 35 administrations (approximately 2 years)

Number of subjects in period 1	Pembrolizumab 200 mg
Started	55
Not Completed	55
Completed	0
Not completed	55
Death	31
Withdrawal by Parent/Guardian	1
Sponsor Decision	23

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab 200 mg
Reporting group description:	
Adult participants received pembrolizumab (MK-3475) 200 mg or pediatric participants received 2 mg/kg (up to 200 mg) on Day 1 of each 3-week cycle (Q3W) intravenously (IV), for up to 35 administrations (approximately 2 years).	

Reporting group values	Pembrolizumab 200 mg	Total	
Number of subjects	55	55	
Age categorical Units: Participants			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	36	36	
85 years and over	7	7	
Age Continuous Units: Years			
arithmetic mean	72.5		
standard deviation	± 11.7	-	
Sex: Female, Male Units: Participants			
Female	24	24	
Male	31	31	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	39	39	
More than one race	0	0	
Unknown or Not Reported	16	16	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	35	35	
Unknown or Not Reported	20	20	

End points

End points reporting groups

Reporting group title	Pembrolizumab 200 mg

Reporting group description:

Adult participants received pembrolizumab (MK-3475) 200 mg or pediatric participants received 2 mg/kg (up to 200 mg) on Day 1 of each 3-week cycle (Q3W) intravenously (IV), for up to 35 administrations (approximately 2 years).

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]

End point description:

ORR was defined as the percentage of participants with Complete Response (CR: disappearance of all target lesions) or Partial Response (PR: at least a 30% decrease in the sum of diameters of target lesions) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). The percentage of participants who experienced CR or PR as assessed by blinded independent central review (BICR) were presented. The analysis population consisted of all allocated participants who received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Up to ~34 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Percentage of participants				
number (confidence interval 95%)	49.1 (35.4 to 62.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Discontinued From Study Treatment Due to an AE

End point title	Number of Participants Who Discontinued From Study Treatment Due to an AE

End point description:

An AE was 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 from study treatment due to an AE was assessed. The analysis population consisted of all allocated participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to ~27 months

End point values	Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Participants	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from the first dose of study treatment until death from any cause. The analysis population consisted of all allocated participants who received at least 1 dose of study treatment. A value of 9999 means the upper limit was not reached at time of data cut-off due to insufficient number of participants with an event.

End point type	Secondary

End point timeframe:

Up to ~58 months

End point values	Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Months				
median (confidence interval 95%)	24.3 (12.4 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with One or More Adverse events (AEs)

End point title	Number of Participants with One or More Adverse events (AEs)

End point description:

An AE was 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. The analysis population consisted of all allocated

participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to ~58 months

End point values	Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Participants	52			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

For participants with a confirmed CR or PR per RECIST 1.1, DOR was the time from first documented evidence of 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 RECIST 1.1, PD was at least a 20% increase in the sum of diameters of target lesions & an absolute increase of at least a 5 mm in the sum of diameters. The appearance of one or more new lesions was also considered PD. DOR assessments were based on BICR with confirmation. The DOR using RECIST 1.1 for all participants who experienced a confirmed CR or PR was presented. The analysis population consisted of all allocated participants who received at least 1 dose of study treatment, and who experienced a confirmed CR or confirmed PR. A value of 9999 means the upper limit not reached at time of data cut-off due to insufficient number of responding participants with relapse.

End point type	Secondary

End point timeframe:

Up to ~58 months

End point values	Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Months				
median (confidence interval 95%)	39.8 (23.8 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)

End point description:

Progression-Free Survival was defined as the time from the first dose of study treatment to the first documented evidence of disease progression per RECIST 1.1 by BICR or death due to any cause, whichever occurred first. Per RECIST 1.1, PD was defined as ≥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 ≥5 mm. The appearance of one or more new lesions was also considered PD. PFS as assessed by BICR per RECIST 1.1 was presented. The analysis population consisted of all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to ~58 months

End point values	Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Months				
median (confidence interval 95%)	9.3 (3.0 to 25.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~58 months

Adverse event reporting additional description:

All-cause mortality includes all participants. AEs include participants who received ≥1 dose of study treatment. Disease progression was not considered an AE unless related to study treatment. MedDRA preferred terms "Neoplasm progression" "Malignant neoplasm progression" and "Disease progression" not related to study treatment were excluded as AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Pembrolizumab 200 mg

Reporting group description:

Adult participants received pembrolizumab (MK-3475) 200 mg or pediatric participants received 2 mg/kg (up to 200 mg) on Day 1 of each 3-week cycle (Q3W) intravenously (IV), for up to 35 administrations (approximately 2 years).

Serious adverse events	Pembrolizumab 200 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 55 (43.64%)		
number of deaths (all causes)	32		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			

subjects affected / exposed	2 / 55 (3.64%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Chronic inflammatory demyelinating polyradiculoneuropathy				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Parkinson's disease				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Obstructive pancreatitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspnoea exertional			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			

subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Muscular weakness				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Wound infection				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Erysipelas				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Cellulitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Empyema			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Encephalitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pembrolizumab 200 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 55 (89.09%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 55 (20.00%)		
occurrences (all)	20		
Oedema peripheral			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	14 / 55 (25.45%)		
occurrences (all)	18		
Pyrexia			

subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	6 / 55 (10.91%)		
occurrences (all)	6		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Investigations			
Amylase increased			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	6		
Alanine aminotransferase increased			
subjects affected / exposed	10 / 55 (18.18%)		
occurrences (all)	13		
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 55 (21.82%)		
occurrences (all)	14		
Weight decreased			
subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	7		
Lipase increased			
subjects affected / exposed	10 / 55 (18.18%)		
occurrences (all)	11		
Blood creatinine increased			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		

Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	 3 / 55 (5.45%) 4		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 4 / 55 (7.27%) 4 6 / 55 (10.91%) 7		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 9 / 55 (16.36%) 11		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 3 / 55 (5.45%) 4		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Diarrhoea	 9 / 55 (16.36%) 9 5 / 55 (9.09%) 6 5 / 55 (9.09%) 5 8 / 55 (14.55%) 10 5 / 55 (9.09%) 5		

subjects affected / exposed occurrences (all)	7 / 55 (12.73%) 11		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Actinic keratosis subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all)	 5 / 55 (9.09%) 6 13 / 55 (23.64%) 19 3 / 55 (5.45%) 3 5 / 55 (9.09%) 6 3 / 55 (5.45%) 3 4 / 55 (7.27%) 4		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Haematuria subjects affected / exposed occurrences (all)	 3 / 55 (5.45%) 3 4 / 55 (7.27%) 5		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	 3 / 55 (5.45%) 3 3 / 55 (5.45%) 3		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	10 / 55 (18.18%) 12		
Back pain subjects affected / exposed occurrences (all)	9 / 55 (16.36%) 11		
Myalgia subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 11		
Osteoarthritis subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 5		
Pain in extremity subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 5		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 6		
COVID-19 subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 7		
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2020	Amendment 1: The primary reasons for the amendment were to implement country-specific changes, make procedural updates, clarify objective response rate, and remove of substudy references for Future Biomedical Research.
28 July 2021	Amendment 2: The primary reasons for the amendment were to harmonize the presentation of safety information across all Food and Drug Administration-approved programmed cell death 1/programmed cell death ligand 1 antibody prescribing information and to update imaging frequency.
09 August 2022	Amendment 3: The primary reason for the amendment was to update the Sponsor's name.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported