Clinical trial results:
A Phase 2 Study of INCMGA00012 in Participants With Metastatic Merkel Cell Carcinoma

Summary

EudraCT number	2018-001627-39
Trial protocol	CZ DE FR ES GB PL HU IT
Global end of trial date	27 June 2024

Results information

Result version number	v1
This version publication date	26 June 2025
First version publication date	26 June 2025

Trial information

Trial identification

Sponsor protocol code	INCMGA 0012-201

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff, 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	27 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was conducted to determine the efficacy of retifanlimab in terms of the objective response rate in chemotherapy-naive participants with metastatic Merkel Cell carcinoma (MCC).

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and was conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was conducted.

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	Canada: 7
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 40
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	107
EEA total number of subjects	80

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)	35
From 65 to 84 years	63
85 years and over	9

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled and treated at 34 study centers in Italy, France, the United States, Poland, Canada, Switzerland, Hungary, the Czech Republic, Germany, Spain, and the United Kingdom.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemotherapy: Naïve

Arm description:

Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W).

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

Dosage and administration details:

unit dose strength/dosage level = 500 mg Q4W; administered over 60 minutes (+ 15 minutes)

Arm title	Chemotherapy: Refractory

Arm description:

Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.

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

Dosage and administration details:

unit dose strength/dosage level = 500 mg Q4W; administered over 60 minutes (+ 15 minutes)

Number of subjects in period 1	Chemotherapy: Naïve	Chemotherapy: Refractory
Started	101	6
Safety Evaluable Population	101	6
Enrolled Population	101	6
Full Analysis Set	65	6
Completed	0	0
Not completed	101	6
Consent withdrawn by subject	17	-
Death	38	3
Lost to follow-up	4	-
Discontinued Due to End of Study	42	3

Baseline characteristics

Reporting groups	
Reporting group title	Chemotherapy: Naïve
Reporting group description:	
Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W).	
Reporting group title	Chemotherapy: Refractory
Reporting group description:	
Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.	

Reporting group values	Chemotherapy: Naïve	Chemotherapy: Refractory	Total
Number of subjects	101	6	107
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)	32	3	35
From 65-84 years	60	3	63
85 years and over	9	0	9
Age Continuous Units: years			
arithmetic mean	71.1	63.8	
standard deviation	± 10.44	± 10.46	-
Gender Categorical Units: Subjects			
Female	33	1	34
Male	68	5	73
Race Units: Subjects			
Asian	1	0	1
White	78	6	84
Unknown or Not Reported	22	0	22
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	75	6	81
Unknown or Not Reported	25	0	25

End points

End points reporting groups

Reporting group title	Chemotherapy: Naïve

Reporting group description:

Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W).

Reporting group title	Chemotherapy: Refractory

Reporting group description:

Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.

Subject analysis set title	All Participants: PK Population
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.

Primary: Objective Response Rate (ORR)

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

End point description:

ORR=percentage of participants with a confirmed overall response of complete response (CR) or partial response (PR), per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (v1.1), as determined by Independent Central Radiographic Review (ICR), at any post-Baseline visit until the first progressive disease (PD) or new anti-cancer therapy. CR: disappearance of all target/non-target lesions and no appearance of new lesions. Any pathological lymph nodes (target or non-target) must have a reduction in the short axis to <10 millimeters (mm). PR: complete disappearance or ≥30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. Full Analysis Set (FAS): all enrolled participants who received ≥1 dose of study drug as of 15 October 2020 (selected to allow for ≥60 chemotherapy-naïve participants to be followed for at least 6 months after first response assessment).

End point type	Primary

End point timeframe:

up to 26.8 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: Statistical analysis was not conducted for this endpoint.

End point values	Chemotherapy: Naïve	Chemotherapy: Refractory		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[2]	0[3]		
Units: percentage of participants				
number (confidence interval 95%)	52.3 (39.5 to 64.9)	(to)		

Notes:

[2] - FAS. Analysis was based on the chemotherapy-naïve subset of the FAS.

[3] - FAS. Analysis was based on the chemotherapy-naïve subset of the FAS.

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=time from an initial objective response (CR or PR) per RECIST v1.1 until PD, or death due to any cause, as determined by ICR. CR: disappearance of all target/non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or a ≥30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. PD: progression of a target or non-target lesion or presence of a new lesion. A Kaplan-Meier estimate (estimated median) of the distribution function is reported. Safety Evaluable Population (SAP): all enrolled participants who received ≥1 dose of study drug. Analysis was based on the chemotherapy-naïve subset of the population. 9999=The median and the upper limit of the confidence interval were not estimable because too few participants had disease progression or died.

End point type	Secondary

End point timeframe:

up to 55.3 months

End point values	Chemotherapy: Naïve	Chemotherapy: Refractory		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55[4]	0[5]		
Units: months				
number (confidence interval 95%)	9999 (22.87 to 9999)	(to)		

Notes:

[4] - SAP. Participants with confirmed CR/PR prior to PD or start of new anticancer therapy were assessed.
[5] - SAP. Participants with confirmed CR/PR prior to PD or start of new anticancer therapy were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Number of participants with any treatment-emergent adverse event (TEAE)

End point description:

An adverse event (AE) is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. 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 study treatment. A TEAE was defined as either an AE reported for the first time or a worsening of a pre-existing event after the first dose of study drug until 90 days after the last dose of study drug. An AE with onset on/after starting a new anticancer therapy was not summarized as a TEAE.

End point type	Secondary

End point timeframe:

up to 846 days (up to approximately 2.3 years)

End point values	Chemotherapy: Naïve	Chemotherapy: Refractory		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101[6]	6[7]		
Units: participants				
number (not applicable)	92	5		

Notes:

[6] - Safety Evaluable Population

[7] - Safety Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time in months between the first dose date (Day 1) and the date of death due to any cause. Analysis was based on the chemotherapy-naïve subset of the population. Median overall survival time was estimated using the Kaplan-Meier method. CI for median overall survival time was calculated using the method of Brookmeyer and Crowley. 9999=The median and the upper limit of the confidence interval were not estimable because too few participants died.

End point type	Secondary

End point timeframe:

up to 60.4 months

End point values	Chemotherapy: Naïve	Chemotherapy: Refractory		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101[8]	0[9]		
Units: months				
median (confidence interval 95%)	9999 (45.24 to 9999)	(to)		

Notes:

[8] - Safety Evaluable Population

[9] - Safety Evaluable Population

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 was defined as the percentage of participants with a confirmed overall response (CR and PR) or stable disease (SD) (non-CR/non-PD) lasting at least 6 months from the start of treatment, until the first PD or new anti-cancer therapy, per RECIST v1.1 as determined by ICR. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. PD: progression of a target or non-target lesion or presence of a new lesion. SD: no change in target lesions to qualify for CR, PR, or PD. Analysis was based on the chemotherapy-naïve subset of the population. CIs were calculated based on the exact method for binomial distributions.

End point type	Secondary

End point timeframe:

up to 57.1 months

End point values	Chemotherapy: Naïve	Chemotherapy: Refractory		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101[10]	0[11]		
Units: percentage of participants				
number (confidence interval 95%)	60.4 (50.2 to 70.0)	(to)		

Notes:

[10] - Safety Evaluable Population

[11] - Safety Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)

End point description:

According to RESIST v1.1, PFS was defined the time from the start of therapy until disease progression, or death due to any cause, as determined by ICR. Evaluation of target lesions: PD: ≥20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. The sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered PD). Evaluation of non-target lesions: PD: Unequivocal progression of existing non-target lesions. (Note: the appearance of one or more new lesions is also considered PD). Analysis was based on the chemotherapy-naïve subset of the population. Median PFS time was estimated using the Kaplan-Meier method. The CI for median PFS time was calculated using the method of Brookmeyer and Crowley.

End point type	Secondary

End point timeframe:

up to 57.1 months

End point values	Chemotherapy: Naïve	Chemotherapy: Refractory		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101[12]	0[13]		
Units: months				
median (confidence interval 95%)	16.03 (9.03 to 32.23)	(to)		

Notes:

[12] - Safety Evaluable Population

[13] - Safety Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: First-dose Cmax of retifanlimab

End point title	First-dose Cmax of retifanlimab

End point description:

Cmax was defined as the maximum observed plasma concentration. The Pharmacokinetic (PK) Evaluable Population was comprised of all participants who received at least 1 dose of study drug and have provided a Baseline and at least 1 post-dose PK sample.

End point type	Secondary

End point timeframe:

preinfusion, 10 minutes postinfusion (± 10 minutes), and 4 hours postinfusion (± 10 minutes) on Day 1 of Cycle 1

End point values	All Participants: PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	102[14]			
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)	144 (± 32.6)			

Notes:

[14] - PK Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: First-dose Cmin of retifanlimab

End point title	First-dose Cmin of retifanlimab

End point description:

Cmin was defined as the minimum observed plasma concentration over the dose interval.

End point type	Secondary

End point timeframe:

preinfusion, 10 minutes postinfusion (± 10 minutes), and 4 hours postinfusion (± 10 minutes) on Day 1 of Cycle 1

End point values	All Participants: PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	102[15]			
Units: µg/mL				
arithmetic mean (standard deviation)	20.5 (± 7.23)			

Notes:

[15] - PK Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: First-dose AUC0-t of retifanlimab

End point title	First-dose AUC0-t of retifanlimab

End point description:

AUC0-t was defined as the area under the plasma concentration-time curve from time zero to time t.

End point type	Secondary

End point timeframe:

preinfusion, 10 minutes postinfusion (± 10 minutes), and 4 hours postinfusion (± 10 minutes) on Day 1 of Cycle 1

End point values	All Participants: PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	102[16]			
Units: day*mg/L				
arithmetic mean (standard deviation)	1770 (± 549)			

Notes:

[16] - PK Evaluable Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 846 days (up to approximately 2.3 years)

Adverse event reporting additional description:

TEAEs (AEs reported for the first time/worsening of pre-existing events after the first dose of study drug until 90 days after the last dose of study drug) are reported for the Safety Evaluable Population (enrolled participants who received ≥1 dose of study drug). AEs with onset on/after starting new anticancer therapy were not summarized as TEAEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Chemotherapy: Naïve

Reporting group description:

Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W).

Reporting group title	Total

Reporting group description:

Total

Reporting group title	Chemotherapy: Refractory

Reporting group description:

Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.

Serious adverse events	Chemotherapy: Naïve	Total	Chemotherapy: Refractory
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 101 (25.74%)	28 / 107 (26.17%)	2 / 6 (33.33%)
number of deaths (all causes)	39	42	3
number of deaths resulting from adverse events	4	4	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Ductal adenocarcinoma of pancreas			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 101 (2.97%)	3 / 107 (2.80%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Concomitant disease progression			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Influenza like illness			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Dyspnoea			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
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 disorder			

subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Pneumothorax			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Pneumonitis			
subjects affected / exposed	2 / 101 (1.98%)	2 / 107 (1.87%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Amylase increased			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal fracture			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 101 (1.98%)	2 / 107 (1.87%)	0 / 6 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Cardiac failure			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Atrioventricular block			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Pericardial effusion			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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			
Demyelinating polyneuropathy			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			

subjects affected / exposed	2 / 101 (1.98%)	2 / 107 (1.87%)	0 / 6 (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
Eosinophilic fasciitis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 101 (3.96%)	4 / 107 (3.74%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pneumonia			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 101 (1.98%)	2 / 107 (1.87%)	0 / 6 (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
Sepsis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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
Hypoglycaemia			

subjects affected / exposed	1 / 101 (0.99%)	1 / 107 (0.93%)	0 / 6 (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

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

Non-serious adverse events	Chemotherapy: Naïve	Total	Chemotherapy: Refractory
Total subjects affected by non-serious adverse events			
subjects affected / exposed	83 / 101 (82.18%)	88 / 107 (82.24%)	5 / 6 (83.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 101 (6.93%)	8 / 107 (7.48%)	1 / 6 (16.67%)
occurrences (all)	7	8	1
Hypotension			
subjects affected / exposed	2 / 101 (1.98%)	3 / 107 (2.80%)	1 / 6 (16.67%)
occurrences (all)	2	3	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	19 / 101 (18.81%)	21 / 107 (19.63%)	2 / 6 (33.33%)
occurrences (all)	24	27	3
Fatigue			
subjects affected / exposed	10 / 101 (9.90%)	13 / 107 (12.15%)	3 / 6 (50.00%)
occurrences (all)	12	15	3
Oedema peripheral			
subjects affected / exposed	7 / 101 (6.93%)	7 / 107 (6.54%)	0 / 6 (0.00%)
occurrences (all)	7	7	0
Pyrexia			
subjects affected / exposed	11 / 101 (10.89%)	13 / 107 (12.15%)	2 / 6 (33.33%)
occurrences (all)	14	19	5
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	10 / 101 (9.90%)	10 / 107 (9.35%)	0 / 6 (0.00%)
occurrences (all)	11	11	0
Nasal congestion			
subjects affected / exposed	1 / 101 (0.99%)	2 / 107 (1.87%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Pleural effusion			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 101 (5.94%)	6 / 107 (5.61%)	0 / 6 (0.00%)
occurrences (all)	6	6	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 101 (5.94%)	7 / 107 (6.54%)	1 / 6 (16.67%)
occurrences (all)	6	7	1
Alanine aminotransferase increased			
subjects affected / exposed	8 / 101 (7.92%)	8 / 107 (7.48%)	0 / 6 (0.00%)
occurrences (all)	8	8	0
Amylase increased			
subjects affected / exposed	8 / 101 (7.92%)	8 / 107 (7.48%)	0 / 6 (0.00%)
occurrences (all)	11	11	0
Blood creatinine increased			
subjects affected / exposed	7 / 101 (6.93%)	8 / 107 (7.48%)	1 / 6 (16.67%)
occurrences (all)	7	8	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 101 (1.98%)	3 / 107 (2.80%)	1 / 6 (16.67%)
occurrences (all)	2	3	1
Lipase increased			
subjects affected / exposed	9 / 101 (8.91%)	9 / 107 (8.41%)	0 / 6 (0.00%)
occurrences (all)	11	11	0
Low density lipoprotein increased			

subjects affected / exposed	1 / 101 (0.99%)	2 / 107 (1.87%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 101 (0.00%)	2 / 107 (1.87%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	2 / 101 (1.98%)	3 / 107 (2.80%)	1 / 6 (16.67%)
occurrences (all)	2	3	1
Tremor			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 101 (5.94%)	7 / 107 (6.54%)	1 / 6 (16.67%)
occurrences (all)	6	7	1
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	12 / 101 (11.88%)	12 / 107 (11.21%)	0 / 6 (0.00%)
occurrences (all)	13	13	0
Dyspepsia			
subjects affected / exposed	4 / 101 (3.96%)	5 / 107 (4.67%)	1 / 6 (16.67%)
occurrences (all)	6	7	1
Dry mouth			
subjects affected / exposed	6 / 101 (5.94%)	6 / 107 (5.61%)	0 / 6 (0.00%)
occurrences (all)	6	6	0
Diarrhoea			
subjects affected / exposed	19 / 101 (18.81%)	20 / 107 (18.69%)	1 / 6 (16.67%)
occurrences (all)	33	34	1
Nausea			

subjects affected / exposed	10 / 101 (9.90%)	13 / 107 (12.15%)	3 / 6 (50.00%)
occurrences (all)	11	14	3
Toothache			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Stomatitis			
subjects affected / exposed	4 / 101 (3.96%)	5 / 107 (4.67%)	1 / 6 (16.67%)
occurrences (all)	4	5	1
Vomiting			
subjects affected / exposed	5 / 101 (4.95%)	6 / 107 (5.61%)	1 / 6 (16.67%)
occurrences (all)	5	6	1
Skin and subcutaneous tissue disorders			
Hyperkeratosis			
subjects affected / exposed	1 / 101 (0.99%)	2 / 107 (1.87%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Erythema			
subjects affected / exposed	6 / 101 (5.94%)	6 / 107 (5.61%)	0 / 6 (0.00%)
occurrences (all)	6	6	0
Rash			
subjects affected / exposed	7 / 101 (6.93%)	7 / 107 (6.54%)	0 / 6 (0.00%)
occurrences (all)	8	8	0
Pruritus			
subjects affected / exposed	22 / 101 (21.78%)	23 / 107 (21.50%)	1 / 6 (16.67%)
occurrences (all)	26	27	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	8 / 101 (7.92%)	10 / 107 (9.35%)	2 / 6 (33.33%)
occurrences (all)	8	10	2
Hypophysitis			
subjects affected / exposed	1 / 101 (0.99%)	2 / 107 (1.87%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Hyperthyroidism			
subjects affected / exposed	6 / 101 (5.94%)	6 / 107 (5.61%)	0 / 6 (0.00%)
occurrences (all)	6	6	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	17 / 101 (16.83%)	19 / 107 (17.76%)	2 / 6 (33.33%)
occurrences (all)	23	28	5
Back pain			
subjects affected / exposed	5 / 101 (4.95%)	7 / 107 (6.54%)	2 / 6 (33.33%)
occurrences (all)	5	7	2
Groin pain			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	2 / 101 (1.98%)	3 / 107 (2.80%)	1 / 6 (16.67%)
occurrences (all)	2	3	1
Myalgia			
subjects affected / exposed	5 / 101 (4.95%)	7 / 107 (6.54%)	2 / 6 (33.33%)
occurrences (all)	5	8	3
Pain in extremity			
subjects affected / exposed	4 / 101 (3.96%)	5 / 107 (4.67%)	1 / 6 (16.67%)
occurrences (all)	4	5	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	5 / 101 (4.95%)	6 / 107 (5.61%)	1 / 6 (16.67%)
occurrences (all)	5	6	1
COVID-19			
subjects affected / exposed	10 / 101 (9.90%)	10 / 107 (9.35%)	0 / 6 (0.00%)
occurrences (all)	11	11	0
Oral candidiasis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 107 (0.93%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	5 / 101 (4.95%)	6 / 107 (5.61%)	1 / 6 (16.67%)
occurrences (all)	9	10	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 101 (5.94%)	6 / 107 (5.61%)	0 / 6 (0.00%)
occurrences (all)	6	6	0
Dehydration			

subjects affected / exposed	1 / 101 (0.99%)	2 / 107 (1.87%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Hyponatraemia			
subjects affected / exposed	1 / 101 (0.99%)	2 / 107 (1.87%)	1 / 6 (16.67%)
occurrences (all)	6	7	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2018	The primary purpose of this amendment was to address comments received from the United States Food and Drug Administration.
04 October 2018	The primary purpose of this amendment was to address comments received from the European Competent Authorities during the Voluntary Harmonization Procedure.
05 December 2018	The primary purpose of this amendment was to address comments received from Health Canada. Additional clarifications and administrative changes were also made.
16 August 2019	The primary purpose of this amendment was to expand the eligibility criteria to include participants with recurrent locoregional advanced disease in addition to participants with distant metastatic Merkel cell carcinoma.
09 April 2020	The primary purpose of this amendment was to clarify the definition of target lesions for participants who had progression in areas previously treated with locoregional therapy.
22 October 2020	The primary purpose of this amendment was to increase the sample size of the study to allow for more robust characterization of the primary and secondary endpoints.
16 December 2021	The primary purpose of this amendment was to update immune-related adverse event management guidelines to reflect updated published guidance and to provide guidance on the management of participants during the COVID-19 pandemic.
18 May 2023	The primary purpose of this amendment was to update the definition of the end of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported