Clinical trial results:
A Phase 2, Randomized Clinical Study of Intravenous or Intratumoral Administration of V937 in Combination with Pembrolizumab (MK-3475) Versus Pembrolizumab Alone in Participants with Advanced/Metastatic Melanoma

Summary

EudraCT number	2019-002034-36
Trial protocol	NO GB ES FR DE IT
Global end of trial date	12 July 2023

Results information

Result version number	v1
This version publication date	03 July 2024
First version publication date	03 July 2024

Trial information

Trial identification

Sponsor protocol code	V937-011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04152863
WHO universal trial number (UTN)	-

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@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.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	12 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2023
Global end of trial reached?	Yes
Global end of trial date	12 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the objective response rate (ORR) of participants treated with IV V937 administered in combination with pembrolizumab, ITu V937 administered in combination with pembrolizumab, or pembrolizumab alone per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) by blinded independent central review (BICR).

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 subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2020
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: 6
Country: Number of subjects enrolled	Chile: 10
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	South Africa: 43
Worldwide total number of subjects	85
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	52
From 65 to 84 years	30
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures completed within 28 days prior to treatment initiation, exceptions included were laboratory tests, evaluation of Eastern Cooperative Oncology Group, a urine or serum pregnancy test for women of childbearing potential within 72 hours; newly obtained tumor tissue was obtained within 90 days of treatment initiation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous (IV) Gebasaxturev + IV Pembrolizumab

Arm description:

Participants received gebasaxturev at a dose of 1 X 10^9 50% tissue culture infectious dose (TCID50) by IV infusion on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Arm type	Experimental
Investigational medicinal product name	Gebasaxturev IV
Investigational medicinal product code	
Other name	Coxsackievirus A21 (CVA21) Formerly known as CAVATAK® CAV21 V937
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an IV infusion of 1 X 10^9 TCID50

Arm title	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab

Arm description:

Participants received gebasaxturev at a dose of 3 X 10^8 TCID50 by ITu injection on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Arm type	Experimental
Investigational medicinal product name	Gebasaxturev ITu
Investigational medicinal product code	
Other name	Coxsackievirus A21 (CVA21) Formerly known as CAVATAK® CAV21 V937
Pharmaceutical forms	Infusion
Routes of administration	Intratumoral use

Dosage and administration details:

Administered as an ITu injection of 3 X 10^8 TCID50

Arm title	Pembrolizumab IV

Arm description:

Participants received pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day

1 of each subsequent 21-day cycle. Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475 Keytruda®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an IV infusion of 200 mg

Number of subjects in period 1	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV
Started	28	28	29
Completed	0	0	0
Not completed	28	28	29
Physician decision	1	1	1
Consent withdrawn by subject	2	1	3
Death	13	12	7
Participation in Study Terminated by Sponsor	12	14	18

Baseline characteristics

Reporting groups	
Reporting group title	Intravenous (IV) Gebasaxturev + IV Pembrolizumab
Reporting group description:	
Participants received gebasaxturev at a dose of 1 X 10^9 50% tissue culture infectious dose (TCID50) by IV infusion on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).	
Reporting group title	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab
Reporting group description:	
Participants received gebasaxturev at a dose of 3 X 10^8 TCID50 by ITu injection on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).	
Reporting group title	Pembrolizumab IV
Reporting group description:	
Participants received pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Pembrolizumab was administered for up to 35 cycles (up to 2 years).	

Reporting group values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV
Number of subjects	28	28	29
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)	13	19	20
From 65-84 years	14	8	8
85 years and over	1	1	1
Age Continuous Units: Years			
arithmetic mean	64.8	58.3	60.5
standard deviation	± 10.5	± 13.6	± 11.9
Sex: Female, Male Units: Participants			
Female	8	10	11
Male	20	18	18
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	1
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	3	3	2
White	23	24	26
More than one race	0	0	0
Unknown or Not Reported	0	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	6	3
Not Hispanic or Latino	25	21	26
Unknown or Not Reported	1	1	0
Cancer M Staging at Baseline			
A study specific characteristic, randomization was stratified based on 4 metastatic melanoma subsets: M1a (nonvisceral (distant cutaneous, subcutaneous, nodal); M1b (lung); M1c (noncentral nervous system (CNS) visceral); and M1d (involves the CNS),as defined by the AJCC (American Joint Committee on Cancer) Cancer Staging Manual, Eighth Edition. M1c and M1d have different prognoses compared to M1a and M1b, warranting stratification.			
Units: Subjects			
M1a	7	9	9
M1b	6	3	5
M1c	12	14	9
M1d	1	1	1
Missing	2	1	5

Reporting group values	Total		
Number of subjects	85		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	52		
From 65-84 years	30		
85 years and over	3		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	29		
Male	56		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	8		
White	73		

More than one race	0		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11		
Not Hispanic or Latino	72		
Unknown or Not Reported	2		
Cancer M Staging at Baseline			
A study specific characteristic, randomization was stratified based on 4 metastatic melanoma subsets: M1a (nonvisceral (distant cutaneous, subcutaneous, nodal); M1b (lung); M1c (noncentral nervous system (CNS) visceral); and M1d (involves the CNS),as defined by the AJCC (American Joint Committee on Cancer) Cancer Staging Manual, Eighth Edition. M1c and M1d have different prognoses compared to M1a and M1b, warranting stratification.			
Units: Subjects			
M1a	25		
M1b	14		
M1c	35		
M1d	3		
Missing	8		

End points

End points reporting groups

Reporting group title	Intravenous (IV) Gebasaxturev + IV Pembrolizumab

Reporting group description:

Participants received gebasaxturev at a dose of 1 X 10^9 50% tissue culture infectious dose (TCID50) by IV infusion on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Reporting group title	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab

Reporting group description:

Participants received gebasaxturev at a dose of 3 X 10^8 TCID50 by ITu injection on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Reporting group title	Pembrolizumab IV

Reporting group description:

Participants received pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Subject analysis set title	Intravenous (IV) Gebasaxturev + IV Pembrolizumab
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received gebasaxturev at a dose of 1 X 10^9 50% tissue culture infectious dose (TCID50) by IV infusion on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Subject analysis set title	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received gebasaxturev at a dose of 3 X 10^8 TCID50 by ITu injection on Days 1, 3, 5, and 8 of Cycle 1 (28-day cycle) and Day 1 of Cycles 2-8 (21-day cycles) plus pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Gebasaxturev was administered for up to 8 cycles (up to 6 months). Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Subject analysis set title	Pembrolizumab IV
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received pembrolizumab 200 mg by IV infusion on Day 8 of Cycle 1 (28-day cycle) and Day 1 of each subsequent 21-day cycle. Pembrolizumab was administered for up to 35 cycles (up to 2 years).

Primary: Objective Response Rate (ORR) per Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR)

End point title	Objective Response Rate (ORR) per Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR)

End point description:

ORR is defined as the percentage of participants who have a Complete Response (CR: disappearance of all lesions) or a Partial Response (PR: at least a 30% decrease in the sum of diameters of target lesions, without evidence of progression based on non-target or new lesions) as assessed by BICR per RECIST 1.1 which was modified for this study to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. The percentage of participants who experienced a CR or PR based on modified RECIST 1.1 is presented.

End point type	Primary
End point timeframe:	
Up to ~ 35 months	

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Percentage of Participants				
number (confidence interval 90%)	46.4 (30.1 to 63.4)	39.3 (23.8 to 56.5)	34.5 (20.0 to 51.4)	

Statistical analyses

Statistical analysis title	Percentage Difference in ORR
Statistical analysis description:	
Stratified Miettinen & Nurminen method. To ensure adequate number of participants, strata were combined according to sSAP when one treatment had 0 participants in a particular stratum.	
Comparison groups	Pembrolizumab IV v Intravenous (IV) Gebasaxturev + IV Pembrolizumab
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1812
Method	Stratified Miettinen and Nurminen method
Parameter estimate	Difference in percentage
Point estimate	11.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.5
upper limit	32.5

Statistical analysis title	Percentage Difference in ORR
Statistical analysis description:	
Difference in percentage based on Miettinen & Nurminen method.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	7.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.6
upper limit	28.2

Statistical analysis title	Percentage Difference in ORR

Statistical analysis description:

Stratified Miettinen & Nurminen method. To ensure adequate number of participants, strata were combined according to sSAP when one treatment had 0 participants in a particular stratum.

Comparison groups	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3548
Method	Stratified Miettinen and Nurminen method
Parameter estimate	Difference in percentage
Point estimate	4.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.2
upper limit	25.5

Secondary: Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR)

End point title	Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR)

End point description:

PFS is defined as the time from randomization to the first documented progressive disease (PD) or death due to any cause, whichever occurs 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 demonstrate an absolute increase of ≥5 mm. Note: The appearance of one or more new lesions is also considered PD. A value of 9999 indicates that upper limit 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 ~ 35 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Months				
median (confidence interval 95%)	12.7 (2.4 to 9999)	7.3 (2.7 to 9999)	8.6 (2.4 to 9999)	

Statistical analyses

Statistical analysis title	PFS Hazard Ratio
Statistical analysis description: Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.27

Statistical analysis title	PFS Hazard Ratio
Statistical analysis description: Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.04

Statistical analysis title	PFS Hazard Ratio

Statistical analysis description:	
Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	2.29

Secondary: Objective Response Rate (ORR) per RECIST 1.1, as Assessed by the Investigator

End point title	Objective Response Rate (ORR) per RECIST 1.1, as Assessed by the Investigator
End point description:	
ORR is defined as the percentage of participants who had 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, taking as reference the baseline sum diameters) per RECIST 1.1 modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. The percentage of participants who experienced a CR or PR based on modified RECIST 1.1 is presented.	
End point type	Secondary
End point timeframe:	
Up to ~ 35 months	

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Percentage of Participants				
number (confidence interval 90%)	39.3 (23.8 to 56.5)	39.3 (23.8 to 56.5)	41.4 (25.9 to 58.3)	

Statistical analyses

Statistical analysis title	Difference in percentage of ORR
Statistical analysis description:	
Based on Stratified Miettinen & Nurminen method.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Method	Stratified Miettinen & Nurminen method.
Parameter estimate	Difference in percentage
Point estimate	-2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.1
upper limit	19.2

Statistical analysis title	Difference in % of ORR
Statistical analysis description:	
Difference in percentage based on Miettinen & Nurminen method.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.2
upper limit	21.2

Statistical analysis title	Difference in percentage of ORR
Statistical analysis description:	
Difference in percentage based on Miettinen & Nurminen method.	
Comparison groups	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	-2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.1
upper limit	19.2

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR is defined as the time from first documented evidence of CR or PR until disease progression or death. A value of 9999 indicates that the median, upper and lower limit 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 ~ 35 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Months				
median (full range (min-max))	9999 (9999 to 9999)	9999 (4.1 to 9999)	9999 (9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) per RECIST 1.1, as assessed by the investigator

End point title	Duration of Response (DOR) per RECIST 1.1, as assessed by the investigator

End point description:

DOR is defined as the time from first documented evidence of CR or PR until disease progression or death. A value of 9999 indicates that the median, upper and lower limit 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 ~ 35 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Months				
median (full range (min-max))	9999 (7.1 to 9999)	9999 (9999 to 9999)	9999 (8.4 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) RECIST 1.1, as assessed by the investigator

End point title	Progression Free Survival (PFS) RECIST 1.1, as assessed by the investigator

End point description:

PFS is defined as the time from randomization to the first documented progressive disease (PD) or death due to any cause, whichever occurs 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 demonstrate an absolute increase of ≥5 mm. Note: The appearance of one or more new lesions is also considered PD. A value of 9999 indicates that upper limit 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 ~ 35 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Months				
median (confidence interval 95%)	4.6 (2.4 to 15.3)	6.5 (2.7 to 9999)	15.4 (2.4 to 9999)	

Statistical analyses

Statistical analysis title	PFS Hazard Ratio

Statistical analysis description:

Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.

Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	3.02

Statistical analysis title	PFS Hazard Ratio
Statistical analysis description:	
Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.22

Statistical analysis title	PFS Hazard Ratio
Statistical analysis description:	
Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.68

Secondary: Overall Survival (OS)	
End point title	Overall Survival (OS)
End point description:	
OS is the time from randomization to death due to any cause. A value of 9999 indicates that upper limit 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 ~ 35 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	29	
Units: Months				
median (confidence interval 95%)	17.5 (6.8 to 9999)	24.1 (11.4 to 9999)	9999 (14.0 to 9999)	

Statistical analyses

Statistical analysis title	OS Hazard Ratio
Statistical analysis description:	
Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	3.79

Statistical analysis title	OS Hazard Ratio
Statistical analysis description:	
Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.	
Comparison groups	Intravenous (IV) Gebasaxturev + IV Pembrolizumab v Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	3.02

Statistical analysis title	OS Hazard Ratio

Statistical analysis description:

Based on Cox regression model with Efron’s method of tie handling with treatment as a covariate.

Comparison groups	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab v Pembrolizumab IV
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	2.68

Secondary: Percentage of Participants Who Experienced an Adverse Event (AE)

End point title	Percentage of Participants Who Experienced an Adverse Event (AE)

End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study.

End point type	Secondary

End point timeframe:

Up to ~ 37 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	28	26	
Units: Percentage of Participants				
number (not applicable)	100	100	84.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Discontinued Study Drug Due to an AE

End point title	Percentage of Participants Who Discontinued Study Drug Due to an AE

End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study.

End point type	Secondary

End point timeframe:

Up to ~ 27 months

End point values	Intravenous (IV) Gebasaxturev + IV Pembrolizumab	Intratumoral (ITu) Gebasaxturev + IV Pembrolizumab	Pembrolizumab IV	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	28	26	
Units: Percentage of Participants				
number (not applicable)	14.3	7.1	3.8	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~ 37 months

Adverse event reporting additional description:

All-cause mortality (ACM) was analyzed in all randomized participants. Safety analyses were conducted in all randomized participants who received at least 1 dose of study intervention. Per protocol, MedDRA terms "Neoplasm progression (NP)", "Malignant NP" & "Disease progression" unrelated to study drug are excluded as AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Pembrolizumab IV + V937 IV
Reporting group description: -	
Reporting group title	Pembrolizumab IV
Reporting group description: -	
Reporting group title	Pembrolizumab IV + V937 IT
Reporting group description: -	

Serious adverse events	Pembrolizumab IV + V937 IV	Pembrolizumab IV	Pembrolizumab IV + V937 IT
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)	4 / 26 (15.38%)	5 / 28 (17.86%)
number of deaths (all causes)	14	9	12
number of deaths resulting from adverse events	3	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Axillary pain			

subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Overlap syndrome			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic rash			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	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	Pembrolizumab IV + V937 IV	Pembrolizumab IV	Pembrolizumab IV + V937 IT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)	22 / 26 (84.62%)	27 / 28 (96.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	3	0	3
Tumour haemorrhage			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Cancer pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	3 / 28 (10.71%)
occurrences (all)	3	0	5
Basal cell carcinoma			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	8	0	0
Vascular disorders			
Hot flush			

subjects affected / exposed	0 / 28 (0.00%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Hypertension			
subjects affected / exposed	2 / 28 (7.14%)	5 / 26 (19.23%)	5 / 28 (17.86%)
occurrences (all)	2	6	7
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	3	0	2
Asthenia			
subjects affected / exposed	2 / 28 (7.14%)	3 / 26 (11.54%)	3 / 28 (10.71%)
occurrences (all)	3	3	4
Axillary pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	2	0	2
Fatigue			
subjects affected / exposed	8 / 28 (28.57%)	6 / 26 (23.08%)	11 / 28 (39.29%)
occurrences (all)	8	7	11
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Oedema peripheral			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Xerosis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	1	1	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	2	0	2
Pneumonitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			

subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	4 / 28 (14.29%)
occurrences (all)	1	0	4
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 26 (7.69%)	4 / 28 (14.29%)
occurrences (all)	1	2	4
Depression			
subjects affected / exposed	0 / 28 (0.00%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	1 / 28 (3.57%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	1	3	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 28 (17.86%)	9 / 26 (34.62%)	5 / 28 (17.86%)
occurrences (all)	8	14	11
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	3 / 28 (10.71%)
occurrences (all)	8	6	5
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 28 (7.14%)	4 / 26 (15.38%)	3 / 28 (10.71%)
occurrences (all)	3	5	6
Blood bilirubin increased			
subjects affected / exposed	1 / 28 (3.57%)	2 / 26 (7.69%)	1 / 28 (3.57%)
occurrences (all)	4	4	2
Blood cholesterol increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	3
Blood creatinine increased			
subjects affected / exposed	3 / 28 (10.71%)	2 / 26 (7.69%)	1 / 28 (3.57%)
occurrences (all)	7	3	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	4 / 28 (14.29%)	4 / 26 (15.38%)	2 / 28 (7.14%)
occurrences (all)	6	4	2
Blood thyroid stimulating hormone increased			

subjects affected / exposed	2 / 28 (7.14%)	3 / 26 (11.54%)	3 / 28 (10.71%)
occurrences (all)	3	5	3
Weight decreased			
subjects affected / exposed	7 / 28 (25.00%)	2 / 26 (7.69%)	3 / 28 (10.71%)
occurrences (all)	7	2	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Fall			
subjects affected / exposed	0 / 28 (0.00%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	1 / 28 (3.57%)
occurrences (all)	6	5	1
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	4 / 26 (15.38%)	0 / 28 (0.00%)
occurrences (all)	3	4	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 28 (42.86%)	7 / 26 (26.92%)	5 / 28 (17.86%)
occurrences (all)	15	8	9
Lymphopenia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 26 (3.85%)	1 / 28 (3.57%)
occurrences (all)	2	3	3
Eosinophilia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	3 / 28 (10.71%)
occurrences (all)	1	1	7
Thrombocytosis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences (all)	3	0	2
Neutropenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	0	2	4
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 28 (0.00%)	4 / 26 (15.38%)	2 / 28 (7.14%)
occurrences (all)	0	4	2
Abdominal pain upper			
subjects affected / exposed	0 / 28 (0.00%)	3 / 26 (11.54%)	3 / 28 (10.71%)
occurrences (all)	0	4	3
Diarrhoea			
subjects affected / exposed	3 / 28 (10.71%)	3 / 26 (11.54%)	4 / 28 (14.29%)
occurrences (all)	3	4	5
Gastritis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	2
Nausea			
subjects affected / exposed	7 / 28 (25.00%)	2 / 26 (7.69%)	5 / 28 (17.86%)
occurrences (all)	10	3	6
Vomiting			
subjects affected / exposed	4 / 28 (14.29%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	6	2	0
Constipation			
subjects affected / exposed	6 / 28 (21.43%)	5 / 26 (19.23%)	3 / 28 (10.71%)
occurrences (all)	8	5	3
Skin and subcutaneous tissue disorders			
Vitiligo			
subjects affected / exposed	3 / 28 (10.71%)	3 / 26 (11.54%)	3 / 28 (10.71%)
occurrences (all)	3	3	3
Skin lesion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences (all)	3	0	1
Rash			
subjects affected / exposed	4 / 28 (14.29%)	2 / 26 (7.69%)	5 / 28 (17.86%)
occurrences (all)	5	2	5
Pruritus			
subjects affected / exposed	6 / 28 (21.43%)	5 / 26 (19.23%)	6 / 28 (21.43%)
occurrences (all)	9	8	9
Dermatitis			

subjects affected / exposed	0 / 28 (0.00%)	2 / 26 (7.69%)	1 / 28 (3.57%)
occurrences (all)	0	2	1
Rash maculo-papular			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Haematuria			
subjects affected / exposed	0 / 28 (0.00%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 28 (10.71%)	3 / 26 (11.54%)	3 / 28 (10.71%)
occurrences (all)	6	3	3
Hyperthyroidism			
subjects affected / exposed	3 / 28 (10.71%)	2 / 26 (7.69%)	0 / 28 (0.00%)
occurrences (all)	3	2	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	1	1	2
Arthralgia			
subjects affected / exposed	4 / 28 (14.29%)	5 / 26 (19.23%)	2 / 28 (7.14%)
occurrences (all)	5	5	2
Back pain			
subjects affected / exposed	2 / 28 (7.14%)	2 / 26 (7.69%)	1 / 28 (3.57%)
occurrences (all)	2	3	1
Muscle spasms			
subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	3 / 28 (10.71%)
occurrences (all)	1	1	4
Muscular weakness			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Myalgia			

subjects affected / exposed	2 / 28 (7.14%)	1 / 26 (3.85%)	1 / 28 (3.57%)
occurrences (all)	4	1	1
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 28 (7.14%)	2 / 26 (7.69%)	3 / 28 (10.71%)
occurrences (all)	2	2	5
Gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	3
Nasopharyngitis			
subjects affected / exposed	1 / 28 (3.57%)	3 / 26 (11.54%)	1 / 28 (3.57%)
occurrences (all)	1	4	1
Skin infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	4 / 28 (14.29%)
occurrences (all)	0	2	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 28 (10.71%)	1 / 26 (3.85%)	3 / 28 (10.71%)
occurrences (all)	4	1	3
Gout			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	0	2	3
Hypercalcaemia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	1	1	2
Hypercholesterolaemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Hyperglycaemia			
subjects affected / exposed	4 / 28 (14.29%)	1 / 26 (3.85%)	2 / 28 (7.14%)
occurrences (all)	5	5	2
Hyperphosphataemia			

subjects affected / exposed	3 / 28 (10.71%)	4 / 26 (15.38%)	0 / 28 (0.00%)
occurrences (all)	4	4	0
Hypoalbuminaemia			
subjects affected / exposed	3 / 28 (10.71%)	2 / 26 (7.69%)	2 / 28 (7.14%)
occurrences (all)	4	2	2
Hypocalcaemia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences (all)	2	1	0
Hypokalaemia			
subjects affected / exposed	2 / 28 (7.14%)	2 / 26 (7.69%)	1 / 28 (3.57%)
occurrences (all)	3	4	1
Hyponatraemia			
subjects affected / exposed	3 / 28 (10.71%)	2 / 26 (7.69%)	3 / 28 (10.71%)
occurrences (all)	4	2	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2020	The amendment purpose was to change the timing of peripheral blood mononuclear cells (PBMC) collection to Day 1 of Cycle 3, and to indicate it is to be performed only at selected study site(s).
27 September 2020	The purpose of the amendment was to eliminate the requirement of collecting throat swabs or sputum samples from close contacts or healthcare workers in relation to the viral transmission of V937 from participants. It aimed to address the requests made by the Health Authority and provide further clarifications.
10 February 2021	This amendment aims to remove C1D1 collection of blood/serum samples from Arm 3 and all biopsies from Arm 3.
24 August 2021	This amendment is for updating the dose modification and toxicity management guidelines for irAEs.
30 August 2022	Amendment 5 aimed for Merck Sharp & Dohme Corp. underwent an entity name and address change to Merck Sharp & Dohme LLC, Rahway, NJ, USA. This conversion resulted only in an entity name change and update to the address.
22 December 2022	Amendment 6 aimed for discontinuation of V937-011 due to the Sponsor's development decision. The overall rationale for this amendment is to allow eligible participants who are receiving pembrolizumab may be enrolled in a pembrolizumab extension study to continue receiving pembrolizumab monotherapy for up to 35 cycles.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was terminated due to the sponsor's development decision.

Notes: